Development of subject-specific tibiofemoral and patellofemoral joint kinematic models for children and adolescents with recurrent patellar dislocation

Martina Barzan
BSc, MSc

School of Allied Health Sciences
Menzies Health Institute Queensland
Griffith University

Submitted in fulfilment of the requirements of the degree of Doctor of Philosophy

October 2018
To my family
Abstract

Patellar dislocation is a complex pathoanatomical condition that affects approximately 1:1000 children and adolescents. Up to 71% of those affected are at risk of recurrent dislocations, that can lead to long-term complications, such as persistent knee pain, decreased activity levels and impairment of knee function. The cause of patellar dislocation is believed to be multifactorial, including lower limb misalignment, abnormal patellofemoral morphology and inadequate soft tissue restraints. While anatomical risk factors and thresholds for typical measures have been well established in adults, there is a paucity of normative and pathoanatomical data that contribute to patellar dislocation in paediatric populations, where the morphology of the patellofemoral joint (PFJ), as well as lower limb alignment, change with growth. Moreover, many surgical techniques common in adults (e.g., trochleoplasty) cannot be performed in a paediatric population due to the risk of growth disruption. Given the challenges in managing recurrent patellar dislocation in paediatric populations, treatment is often unsuccessful and commonly results in poor functional outcomes for the patient while incurring substantial costs.

Poor treatment outcomes may be due to limitations in current diagnosis and treatment methods. Nowadays, clinicians use static measures from medical imaging to inform diagnosis and treatment of recurrent patellar dislocation. These measures, despite providing valuable insights on the PFJ anatomy, are unable to provide understanding of the patellar dislocation mechanism during dynamic tasks. Conversely, subject-specific computational models of the musculoskeletal system, with individualised geometries and anatomical structures, have the potential to capture the complex functional relationship between multiple risk factors for patellar dislocation on an individual basis. Creating fully subject-specific models requires accurate personalisation of the joint kinematics, which will improve estimates of all the dependent quantities of interest for musculoskeletal modelling (e.g., muscle moment arms, articular contact points and ligament kinematics). Therefore, the general purpose of this thesis was to develop subject-specific rigid-body models of the tibiofemoral and patellofemoral joints in children and adolescents with recurrent patellar dislocation.

The first study systematically reviewed the current literature to characterise lower limb alignment, patellofemoral morphology and soft tissue restraints of the PFJ through medical imaging measurements in paediatric recurrent patellar dislocators (RPD) and age-matched typically developing (TD) participants. Moreover, the data were synthesised
to stratify the factors that influence PFJ stability and recommendations on the assessment and reporting of PFJ parameters in this patient population were provided. Results from a meta-analysis conducted on measures reported in two or more studies that included both a control and a patellar dislocator group showed that the tibial tuberosity to trochlear groove (TT-TG) distance and bony sulcus angle can be confidently used to predict the risk of recurrence in the paediatric population. These results can streamline the patient evaluation and best inform clinical decision-making. The paper describing these results was published as Barzan, M., Maine, S., Modenese, L., Lloyd, D.G., Carty, C.P., *Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation in children and adolescents: a systematic review*. JISAKOS 2018, 0:1-11. doi:10.1136/jisakos-2017-000189.

The aim of the second study was to analyse the differences in lower limb alignment, patellofemoral alignment and trochlea dysplasia between paediatric RPD patients and TD participants using magnetic resonance imaging (MRI). This was essential as results from the previous study revealed that there is a paucity of reported radiological parameters to define normal and pathoanatomical paediatric cohorts. A prospective cross-sectional study was conducted on 24 RPD children and adolescents and 25 age-matched TD participants. Significant differences between the two groups were found for acetabular inclination, tibial-femoral torsion, TT-TG distance, lateral patellar tilt, congruence angle and cartilaginous sulcus angle. TT-TG distance and cartilaginous sulcus angle were included in the final predictive model, which correctly classified 84.4% of cases of recurrent patellar dislocation. Therefore, these measures should be included in the evaluation of paediatric patients who present with recurrent patellar dislocation. The paper describing these results was submitted as Ngo-Nguyen, C., Maine, S., Barzan, M., Stockton, C.A., Modenese, L., Lloyd, D.G., Carty, C.P. *Radiological predictors of paediatric patellofemoral joint dislocation from medical imaging*. The Knee.

The purpose of study three was to develop three subject-specific tibiofemoral (TFJ) kinematic models, with either rigid or extensible ligament constraints, and a subject-specific PFJ model for eight healthy paediatric participants. The estimated joint and ligament kinematics from the three models were also validated against *in vivo* kinematics measured from MRIs at four different TFJ flexion angles. The three TFJ models were created from MRIs and used to solve the TFJ kinematics: (i) 5-rigid-link parallel mechanism with rigid surface contact and isometric anterior cruciate (ACL), posterior cruciate (PCL) and medial collateral (MCL) ligaments ($\Delta L_0$), (ii) 6-link parallel mechanism with minimised ACL, PCL, MCL and lateral collateral ligament (LCL) length.
changes ($\Delta L_{\text{min}}$) and (iii) 6-link parallel mechanism with prescribed ACL, PCL, MCL and LCL length variations ($\Delta L_{\text{match}}$). The $\Delta L_0$ and $\Delta L_{\text{match}}$ models compared best against MRI-measured data, with errors below $7^\circ$ and 7 mm for joint angles and displacements, respectively, and below 2 mm for ligament lengths. Therefore, these models can be used to estimate passive three-dimensional paediatric TFJ, PFJ and ligament kinematics and can be incorporated into lower-limb models to estimate joint kinematics and kinetics during dynamic tasks. The paper describing these results was submitted as Barzan, M., Modenese, L., Carty, C.P., Maine, S., Stockton, C.A., Sancisi, N., Lewis, A., Grant, J., Lloyd, D.G., Brito da Luz, S. Development and validation of subject-specific paediatric multibody knee kinematic models with ligamentous constraints. Journal of Biomechanics.

The fourth study assessed the TFJ and ligament kinematics during gait using a rigid-body lower limb model incorporating a fully subject-specific paediatric kinematic TFJ model with articular contacts and minimally deformable ligaments. This was essential to extend the findings of the previous study to dynamic tasks. To address this aim, eight healthy participants underwent MRI and three-dimensional gait analysis. For these participants, the TFJ was implemented in OpenSim, based on optimised MRI-measured geometrical parameters, as a 5-rigid-link parallel mechanism with spherical articular contacts and three knee ligaments (ACL, PCL and MCL). For each participant, TFJ angles and ligament lengths were calculated by tracking experimental markers while minimising ligament elongation using the least squares multibody optimisation (MBO) tool available in OpenSim. The kinematic results from MBO were compared against those obtained using the implicit 5-rigid-link mechanism $\Delta L_0$, with significant differences found for TFJ ab/adduction, ACL and PCL strains. The developed subject-specific TFJ kinematic models are promising tools to investigate the gait biomechanics of healthy children and future studies will extend their use to the analyses of pathological gait. The manuscript describing these results will be submitted as Barzan, M., Carty, C.P., Maine, S., Sancisi, N., Stockton, C.A., Edwards, J., Brito da Luz, S., Lloyd, D.G., Modenese, L. Implementation of a subject-specific paediatric kinematic model of the knee with minimally deformable ligaments in OpenSim. Journal of Biomechanics.

The purpose of study five was to develop subject-specific PFJ kinematic models to evaluate passive patellar tracking in paediatric RPD patients and TD controls. The resulting PFJ kinematics for RPD patients were also validated against in vivo kinematics measured from MRIs at four different TFJ flexion angles. Finally, the estimated PFJ
Abstract

kinematics between RPD patients and TD participants were compared. For RPD patients, we modelled the PFJ from MRIs using two different hinge mechanisms, which described (i) the lateral to medial translation of the patella into the trochlear groove from approximately 0° to 30° of TFJ flexion, and (ii) the motion of the patella after it reached a more congruent position in the trochlear groove. When compared to MRI data, the proposed PFJ models were able to characterise different patterns of patellar maltracking in RPD patients. Moreover, RPD patients exhibited a more externally rotated and lateralised patella than TD participants between 0° and 30° of TFJ flexion. These models provided accurate estimations of pathological PFJ kinematics and might be used to inform surgery planning and evaluation. The manuscript describing these results will be submitted as Barzan, M., Maine, S., Brito da Luz, S., Modenese, L., Stockton, C.A., Conconi, M., Sancisi, N., Lloyd, D.G., Carty, C.P. Development and validation of subject-specific patellofemoral joint kinematic models for children and adolescents with recurrent patellar dislocation. Journal of Orthopaedic Research.

In conclusion, this thesis examined the anatomical and functional differences at the knee between paediatric patients with recurrent patellar dislocation and age-matched controls. The unique TFJ and PFJ kinematic patterns observed in our paediatric cohort suggest that personalised musculoskeletal models are necessary to understand potential patellar instability mechanisms. Moreover, the developed and validated knee kinematic models provide a platform for muscle force integration, thereby enabling the calculation of PFJ contact forces. Importantly, informing surgical planning with personalised musculoskeletal models that can assist in elucidating the mechanisms of PFJ instability should result in better long-term surgical outcomes, such as reduced costs from surgical revision and improved patient quality of life.
I would like to express my sincere gratitude to all the people who assisted and supported me during the last three and a half years. Firstly, I would like to thank my five supervisors. I am profoundly grateful for being part of such a great and heterogeneous team, where everyone could share their different expertise and from which I have learnt a lot in different disciplines. To my principal supervisor, Dr Christopher Carty, thank you for always believing in me, for indulging my choices and, at the same time, guiding and assisting me. You always had encouraging words whenever I felt hopeless and you always found time to discuss problems when others were busy. To Professor David Lloyd, thank you for inspiring me with your immense knowledge and dedication to your work. Thank you for teaching me how to visualise the big picture aim and for guiding me towards the “good science” throughout your constructive critiques. To Dr Luca Modenese, thank you for your constant support, despite being on the other side of the world. I am truly thankful for your insightful advice and technical assistance over the years. I feel honoured to have had the chance to work with you once more. You are someone I admire and aspire to be. To Dr Sheanna Maine, thank you for teaching me how to approach a problem from a clinical point of view and for showing me how to translate science into clinical practice. Thank you for your guidance, patience and for always finding time for me in your busy schedule. Your enthusiasm and passion towards your job are admirable and always motivated me. To Dr Simao Brito da Luz, thank you for your technical support in the last phase of my PhD. Your precious assistance and encouragement made me feel hopeful when I felt completely lost.

To Julie Edwards and Christopher Stockton, as well as the other members of the Queensland Children’s Motion Analysis Service and the Department of Medical Imaging and Nuclear Medicine at the Lady Cilento Children’s Hospital, thank you for your valuable help with data collection. Thank you for always trying to accommodate my requests and for dedicating your weekends to this research project. You have been professional colleagues and also great companions to share some personal stories with. To all the children who participated in this study, and to their families, thank you for dedicating your time to make this research possible. Thank you also for constantly inspiring and motivating me.

To Dr Nicola Sancisi and Dr Michele Conconi, thank you for accepting to collaborate with me at a distance and for your availability. Your precious support strongly enhanced
the outcomes of this research. To Dr Hans Kainz, thank you for your warm welcome when I started my PhD, for your patience and your valuable help. To the academics at Griffith, and specifically to Dr David Saxby, Dr Claudio Pizzolato and Dr Laura Diamond, thank you for having your office doors always open for me whenever I needed your technical advice or simply a word of encouragement. To my PhD colleagues, Bas, Adrien, Conor, Amy, Jeff, Lexi, Melanie, Pre, Edin, Bryce, Eva, Jeremy, Daniel, Azi, Giorgio and Trevor, thank you for your continuous support, especially during the last months of this journey. You all made this unique experience more enjoyable.

To my close Italian friends, thank you for always being there for me when I thought it was all too hard. You always managed to show me your affection and support despite being physically distant. Special thanks to Marica, with whom I have shared my university studies and also this incredible PhD journey. Even if you were far away, I knew you would have understood the challenges I was facing, and I could always count on you.

To my family, and especially to my mum Assunta and my dad Lorenzo, thank you so much for allowing me to undertake this journey. I know it has been extremely hard for you to accept this choice and to cope with the distance, but you always managed to show me your limitless love and support. Your passion for what you do, your dedication and your hard work are an example for me and they helped me going through the toughest moments of this journey. To my brother Andrea and to my sister Michela, thank you for being close to mum and dad during these three and a half years, for your constant support and for physically being part of my Australian life. To my godmother Daniela, thank you for always being an impartial listener and for being close to me at the time I needed the most.

Lastly, to my soul mate Gavin, thank you for being an inspiring example of great organisation, dedication and hard work. Thank you for your endless support and patience, and for always pushing me out of my comfort zone. Thank you also for always making me smile and for teaching me how to have an optimistic attitude, even when everything seemed to go wrong. This PhD journey has been a great life experience and I am deeply grateful for having had you by my side. And special thanks go to your family, who made me feel like at home during these years.
Statement of originality

This work has not previously been submitted for a degree or diploma in any university. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made in the thesis itself.

(Signed) ___________________________________

Martina Barzan

17th October 2018
Publication list

The following publications were produced from this research:

Journal Articles


Referred Conference Papers and Abstracts

Podium presentations


with minimally deformable ligaments in OpenSim. 8\textsuperscript{th} World Congress of Biomechanics, Dublin, Ireland, 2018.


Poster presentations


Media

Media appearance in Our bodies and beyond, SCOPE, Network 10, October 2017.

# Table of contents

Abstract .................................................................................................................. i
Acknowledgements ................................................................................................. v
Statement of originality ........................................................................................... vii
Publication list .......................................................................................................... ix
List of figures .......................................................................................................... xvi
List of tables ........................................................................................................... xxix
List of equations ..................................................................................................... xxxi
List of abbreviations ............................................................................................... xxxii

## CHAPTER 1 ........................................................................................................... 1

1.1 Background ...................................................................................................... 1
1.2 Statement of the problem ............................................................................... 6
1.3 Thesis objective ............................................................................................... 6

## CHAPTER 2 ........................................................................................................... 11

2.1 Anatomy and function of the knee ................................................................. 11
  2.1.1 Tibiofemoral joint .................................................................................. 12
  2.1.2 Patellofemoral joint ............................................................................. 13
  2.1.3 Anatomical development of the lower limbs during childhood .......... 14
2.2 Patellar dislocation ......................................................................................... 14
  2.2.1 First-time lateral patellar dislocation ................................................. 14
  2.2.2 Recurrent patellar dislocation ............................................................. 16
  2.2.3 Aetiology ............................................................................................. 17
  2.2.4 Patient’s history and physical examination ........................................ 19
  2.2.5 Diagnostic imaging ............................................................................ 20
  2.2.6 Treatment ......................................................................................... 21
2.3 Using biomechanics to assess patellar instability .......................................... 22
  2.3.1 Gait analysis ...................................................................................... 22
  2.3.2 Musculoskeletal models ..................................................................... 24
  2.3.3 Knee joint kinematics models ............................................................ 28

## CHAPTER 3 ........................................................................................................... 35

3.1 Abstract .......................................................................................................... 36
3.2 Introduction ..................................................................................................... 37
3.3 Methods .......................................................................................................... 38
  3.3.1 Search strategy .................................................................................. 38
  3.3.2 Inclusion and exclusion criteria ......................................................... 38
  3.3.3 Study selection, methodological quality and measurement quality .... 39
### List of figures

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.3.4</td>
<td>Data extraction</td>
<td>39</td>
</tr>
<tr>
<td>3.4</td>
<td>Results</td>
<td>40</td>
</tr>
<tr>
<td>3.4.1</td>
<td>Search results</td>
<td>40</td>
</tr>
<tr>
<td>3.4.2</td>
<td>Study participants</td>
<td>41</td>
</tr>
<tr>
<td>3.4.3</td>
<td>Quality analysis</td>
<td>42</td>
</tr>
<tr>
<td>3.4.4</td>
<td>Lower limb alignment</td>
<td>44</td>
</tr>
<tr>
<td>3.4.5</td>
<td>PFJ alignment</td>
<td>48</td>
</tr>
<tr>
<td>3.4.6</td>
<td>Trochlea morphology</td>
<td>51</td>
</tr>
<tr>
<td>3.4.7</td>
<td>Soft tissue restraints</td>
<td>52</td>
</tr>
<tr>
<td>3.5</td>
<td>Discussion</td>
<td>52</td>
</tr>
<tr>
<td>3.6</td>
<td>Conclusion</td>
<td>57</td>
</tr>
<tr>
<td>3.7</td>
<td>Acknowledgements</td>
<td>57</td>
</tr>
<tr>
<td>4.1</td>
<td>Participants</td>
<td>59</td>
</tr>
<tr>
<td>4.2</td>
<td>Data collection</td>
<td>61</td>
</tr>
<tr>
<td>4.2.1</td>
<td>Questionnaire</td>
<td>61</td>
</tr>
<tr>
<td>4.2.2</td>
<td>Gait analysis</td>
<td>62</td>
</tr>
<tr>
<td>4.2.2.1</td>
<td>Laboratory set up</td>
<td>62</td>
</tr>
<tr>
<td>4.2.2.2</td>
<td>Participant preparation</td>
<td>63</td>
</tr>
<tr>
<td>4.2.2.3</td>
<td>Data acquisition</td>
<td>65</td>
</tr>
<tr>
<td>4.2.3</td>
<td>MRI</td>
<td>66</td>
</tr>
<tr>
<td>4.2.3.1</td>
<td>Participant preparation</td>
<td>67</td>
</tr>
<tr>
<td>4.2.3.2</td>
<td>Data acquisition</td>
<td>68</td>
</tr>
<tr>
<td>4.3</td>
<td>Data processing</td>
<td>70</td>
</tr>
<tr>
<td>4.3.1</td>
<td>Labelling and processing of motion capture data</td>
<td>70</td>
</tr>
<tr>
<td>4.3.2</td>
<td>Segmentation and registration of MRI data</td>
<td>70</td>
</tr>
<tr>
<td>4.4</td>
<td>Development of subject-specific knee kinematic models</td>
<td>72</td>
</tr>
<tr>
<td>4.4.1</td>
<td>TFJ passive kinematic models</td>
<td>72</td>
</tr>
<tr>
<td>4.4.1.1</td>
<td>Creation of subject-specific TFJ models</td>
<td>72</td>
</tr>
<tr>
<td>4.4.1.2</td>
<td>Optimisation of each TFJ model</td>
<td>75</td>
</tr>
<tr>
<td>4.4.2</td>
<td>PFJ passive kinematic models</td>
<td>77</td>
</tr>
<tr>
<td>4.4.2.1</td>
<td>Development of a subject-specific PFJ model for TD participants</td>
<td>77</td>
</tr>
<tr>
<td>4.4.2.2</td>
<td>Development of subject-specific PFJ models for RPD patients</td>
<td>81</td>
</tr>
<tr>
<td>4.5</td>
<td>Subject-specific full lower limb models</td>
<td>84</td>
</tr>
<tr>
<td>4.5.1</td>
<td>Development of subject-specific full lower limb models</td>
<td>84</td>
</tr>
<tr>
<td>4.5.2</td>
<td>Explicit implementation of the TFJ mechanism in OpenSim</td>
<td>87</td>
</tr>
<tr>
<td>4.5.3</td>
<td>TFJ, PFJ and ligament kinematics during gait</td>
<td>89</td>
</tr>
</tbody>
</table>
## List of figures

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.6</td>
<td>Statistical analysis</td>
<td>91</td>
</tr>
<tr>
<td>4.6.1</td>
<td>Validation of TFJ and PFJ passive mechanisms</td>
<td>92</td>
</tr>
<tr>
<td>4.6.2</td>
<td>Comparison of estimated TFJ and PFJ kinematics</td>
<td>92</td>
</tr>
<tr>
<td>CHAPTER 5</td>
<td>Validation of TFJ and PFJ passive mechanisms</td>
<td>95</td>
</tr>
<tr>
<td>5.1</td>
<td>Abstract</td>
<td>96</td>
</tr>
<tr>
<td>5.2</td>
<td>Introduction</td>
<td>97</td>
</tr>
<tr>
<td>5.3</td>
<td>Methods</td>
<td>98</td>
</tr>
<tr>
<td>5.3.1</td>
<td>Participant recruitment</td>
<td>98</td>
</tr>
<tr>
<td>5.3.2</td>
<td>Medical image acquisition and measurement</td>
<td>99</td>
</tr>
<tr>
<td>5.3.3</td>
<td>Statistical Analysis</td>
<td>104</td>
</tr>
<tr>
<td>5.4</td>
<td>Results</td>
<td>105</td>
</tr>
<tr>
<td>5.4.1</td>
<td>Stepwise logistic regression analysis</td>
<td>105</td>
</tr>
<tr>
<td>5.5</td>
<td>Discussion</td>
<td>106</td>
</tr>
<tr>
<td>5.6</td>
<td>Conclusion</td>
<td>108</td>
</tr>
<tr>
<td>5.7</td>
<td>Acknowledgements</td>
<td>108</td>
</tr>
<tr>
<td>CHAPTER 6</td>
<td>Validation of TFJ and PFJ passive mechanisms</td>
<td>109</td>
</tr>
<tr>
<td>6.1</td>
<td>Abstract</td>
<td>110</td>
</tr>
<tr>
<td>6.2</td>
<td>Introduction</td>
<td>110</td>
</tr>
<tr>
<td>6.3</td>
<td>Methods</td>
<td>112</td>
</tr>
<tr>
<td>6.3.1</td>
<td>Participants</td>
<td>112</td>
</tr>
<tr>
<td>6.3.2</td>
<td>Medical image acquisition and processing</td>
<td>112</td>
</tr>
<tr>
<td>6.3.3</td>
<td>Subject-specific TFJ and PFJ kinematic models</td>
<td>113</td>
</tr>
<tr>
<td>6.3.4</td>
<td>Tuning of each subject-specific TFJ model</td>
<td>114</td>
</tr>
<tr>
<td>6.3.5</td>
<td>Data analysis and statistics</td>
<td>116</td>
</tr>
<tr>
<td>6.4</td>
<td>Results</td>
<td>117</td>
</tr>
<tr>
<td>6.5</td>
<td>Discussion</td>
<td>125</td>
</tr>
<tr>
<td>6.6</td>
<td>Acknowledgments</td>
<td>128</td>
</tr>
<tr>
<td>6.7</td>
<td>Supplementary material</td>
<td>128</td>
</tr>
<tr>
<td>6.7.1</td>
<td>Statistical analysis results</td>
<td>128</td>
</tr>
<tr>
<td>6.7.2</td>
<td>Predicted and MRI-based knee and ligament kinematics</td>
<td>136</td>
</tr>
<tr>
<td>6.7.3</td>
<td>Multiple Objective Particle Swarm Optimisation</td>
<td>145</td>
</tr>
<tr>
<td>6.7.4</td>
<td>Error magnitudes</td>
<td>147</td>
</tr>
<tr>
<td>CHAPTER 7</td>
<td>Validation of TFJ and PFJ passive mechanisms</td>
<td>151</td>
</tr>
<tr>
<td>7.1</td>
<td>Introduction</td>
<td>151</td>
</tr>
<tr>
<td>7.2</td>
<td>Methods</td>
<td>153</td>
</tr>
<tr>
<td>7.2.1</td>
<td>Participants</td>
<td>153</td>
</tr>
<tr>
<td>7.2.2</td>
<td>Gait data collection and processing</td>
<td>154</td>
</tr>
</tbody>
</table>
List of figures

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.2.3</td>
<td>Medical image acquisition and processing</td>
<td>155</td>
</tr>
<tr>
<td>7.2.4</td>
<td>Subject-specific full lower limb models</td>
<td>156</td>
</tr>
<tr>
<td>7.2.5</td>
<td>Verification of the TFJ mechanism implemented in OpenSim</td>
<td>158</td>
</tr>
<tr>
<td>7.2.6</td>
<td>Inverse kinematics</td>
<td>158</td>
</tr>
<tr>
<td>7.2.7</td>
<td>Data analysis and statistics</td>
<td>160</td>
</tr>
<tr>
<td>7.3</td>
<td>Results</td>
<td>161</td>
</tr>
<tr>
<td>7.4</td>
<td>Discussion</td>
<td>165</td>
</tr>
<tr>
<td>7.4.1</td>
<td>Future work</td>
<td>168</td>
</tr>
<tr>
<td>7.5</td>
<td>Conclusion</td>
<td>170</td>
</tr>
<tr>
<td>8.1</td>
<td>Introduction</td>
<td>171</td>
</tr>
<tr>
<td>8.2</td>
<td>Methods</td>
<td>173</td>
</tr>
<tr>
<td>8.2.1</td>
<td>Participants</td>
<td>173</td>
</tr>
<tr>
<td>8.2.2</td>
<td>Medical image acquisition and processing</td>
<td>174</td>
</tr>
<tr>
<td>8.2.3</td>
<td>Subject-specific TFJ and PFJ kinematic models</td>
<td>174</td>
</tr>
<tr>
<td>8.2.3.1</td>
<td>TFJ kinematic model for TD and RPD participants</td>
<td>174</td>
</tr>
<tr>
<td>8.2.3.2</td>
<td>PFJ kinematic model for TD participants</td>
<td>175</td>
</tr>
<tr>
<td>8.2.3.3</td>
<td>PFJ kinematic models for RPD patients</td>
<td>176</td>
</tr>
<tr>
<td>8.2.4</td>
<td>Data analysis and statistics</td>
<td>179</td>
</tr>
<tr>
<td>8.3</td>
<td>Results</td>
<td>179</td>
</tr>
<tr>
<td>8.4</td>
<td>Discussion</td>
<td>184</td>
</tr>
<tr>
<td>8.4.1</td>
<td>Future work</td>
<td>185</td>
</tr>
<tr>
<td>8.5</td>
<td>Conclusion</td>
<td>188</td>
</tr>
<tr>
<td>9.1</td>
<td>Thesis summary</td>
<td>189</td>
</tr>
<tr>
<td>9.2</td>
<td>Modelling implications</td>
<td>192</td>
</tr>
<tr>
<td>9.3</td>
<td>Clinical implications</td>
<td>194</td>
</tr>
<tr>
<td>9.3.1</td>
<td>Understanding the patellar dislocation mechanism</td>
<td>194</td>
</tr>
<tr>
<td>9.3.2</td>
<td>Tailored surgeries to correct for patellar dislocation</td>
<td>196</td>
</tr>
<tr>
<td>9.4</td>
<td>Limitations</td>
<td>198</td>
</tr>
<tr>
<td>9.5</td>
<td>Future research directions</td>
<td>201</td>
</tr>
<tr>
<td>9.6</td>
<td>Conclusion</td>
<td>204</td>
</tr>
<tr>
<td>References</td>
<td></td>
<td>205</td>
</tr>
</tbody>
</table>
List of figures

**Figure 2.1** Lateral (a) and posterior (b) views of the knee. The main anatomical structures that represent the joint are shown (Pictures, 2003). .......................................................... 12

**Figure 2.2** Trochlea dysplasia classification (Dejour et al., 1994). ......................... 18

**Figure 2.3.** Five-rigid-link TFJ parallel mechanism (Parenti-Castelli et al., 2013). A₁-A₅ represent the ligament insertions on the tibia and the tibial sphere centres, while B₁-B₅ represent the ligament origins on the femur and the femoral sphere centres. .......... 30

**Figure 3.1** Systematic search strategy results. .................................................................. 40

**Figure 3.2** Description of most frequently reported measures of PFJ alignment and trochlea morphology. (a) Congruence angle: angle formed by bisecting the sulcus angle (α) and central patella ridge. (b) Lateral (left) and medial (right) stress ratios (%), defined as BC/AB x 100. Diagrams of the 2kg stress skyline view at 45° of knee flexion. (c) Insall-Salvati Index, defined as the ratio between patellar length (PL) and patellar tendon length (PT). (d) Lateral patellar tilt: angle between the posterior femoral condyles line and the line of maximum width of the patella. (e) Q angle: angle between a line drawn from the anterior superior iliac spine to central patella (solid red line) and a line drawn from central patella to tibial tubercle (dashed blue line). The Q-angle can be measured in laying or standing. (f) TT-TG distance: distance between a line bisecting the tibial tuberosity (TT) and a line bisecting the trochlear groove sulcus (TG), both perpendicular to the posterior femoral condyles line. (g) Bony sulcus angle: angle between lines joining the highest points of the bony medial and lateral condyles and the lowest bony point of the intercondylar sulcus. (h) Cartilaginous sulcus angle: angle between lines joining the highest points of the cartilaginous medial and lateral condyles and the lowest cartilaginous point of the intercondylar sulcus. ........................................................................ 50

**Figure 4.1.** MRI booking workflow developed in collaboration with LCCH. Each colour represents a person-specific task: yellow – orthopaedic surgeon, green – Medical Imaging, blue – researcher (MB). ................................................................. 61

**Figure 4.2.** Gait analysis laboratory at the QCMAS.......................... 62

**Figure 4.3.** Gait analysis marker set, frontal (a) and lateral (b) views. .................. 64

**Figure 4.4.** MRI scanning workflow developed in collaboration with LCCH. All the operations performed before, during and after scanning are described. Tasks in the green
boxes are under the responsibility of Medical Imaging, while tasks in the blue boxes are under the responsibility of the researcher (MB). .......................................................... 67

**Figure 4.5.** Full lower-limb MRI acquisition: participant’s setting up in the 1.5T scanner (a) and resulting scan (b). .......................................................... 68

**Figure 4.6.** Dedicated knee MRI acquisition: participant’s setting up in the 3T scanner (a) and resulting scan (b). .......................................................... 69

**Figure 4.7.** MRI knee scans collected for the same participant at three different TFJ flexion angles.......................................................... 69

**Figure 4.8.** Segmentation (left side and top right) and three-dimensional meshes (bottom right) of knee anatomical structures created using Mimics. Segmented tissues included: distal femur (orange), proximal tibia (red) and fibula (blue), patella (violet), articular cartilages (femoral – green, tibial – yellow, patellar – light blue), ligaments (ACL – light green, PCL – magenta, LCL – light purple, MCL – dark purple, patellar tendon – light pink) and markers (aqua). .......................................................... 71

**Figure 4.9.** Comprehensive representation of a participant’s pelvis and right leg following the registration process in 3-matic. This representation included markers (blue), full length bones (beige), knee cartilage (dark grey) and ligaments (pink)........................... 72

**Figure 4.10.** Representation of the geometrical parameters used to create the baseline 5-rigid-link TFJ parallel mechanism. Solid lines represent the ACL, PCL and MCL ligaments with attachments in the femur (B1, B2, B3) and in the tibia (A1, A2, A3), while dotted lines represent articular contacts between the medial and lateral condyles of the femur (blue spheres, with centres in B4 and B5) and tibia (red spheres, with centres in A4 and A5).......................................................... 74

**Figure 4.11.** Manual selection (pink areas) of the geometrical parameters used to create the baseline 5-rigid-link TFJ parallel mechanism. Femoral condyles (a), tibial plateaus (b) and ligament attachment regions (ACL, PCL and MCL) on the femur (c) and tibia (d) were delineated on the reconstructed bone and cartilage volumes.......................................................... 75

**Figure 4.12.** Representation of the PFJ hinge mechanism (Brito da Luz et al., 2017; Sancisi et al., 2011b). The solid black line represents the patellar tendon, with attachments on the tibia (C1) and on the patella (D1). Two spheres were best fitted to the medial and lateral patellofemoral articulating surfaces with hinge axis n1 represented as dashed line. Q1 and Q2 are the intersection points of the hinge axis, relative to Pcs and Fcs, with the x-y reference planes of Pcs and Fcs and λ is the fixed distance between these two points... 79
Figure 4.13. Manual delineation (pink areas) of patellofemoral articulating surfaces (a) and patellar tendon attachment regions (b) on the reconstructed bone and cartilage volumes. ........................................................................................................................................ 80

Figure 4.14. Patella position and orientation at different TFJ flexion angles in a RPD patient. The patella translates medially into the trochlear groove as the knee flexes (from a to d). ........................................................................................................................................ 82

Figure 4.15. Implementation of two PFJ mechanisms to estimate the passive PFJ kinematics of RPD patients. The poses of the patella at ~0° (purple) and ~30° (green) of TFJ flexion were registered on the same femur bone reconstruction (left). In the first PFJ mechanism (top), the articulating surface connecting the two poses of the patella was delineated and approximated by best fitting a cylinder (a). The patella was then constrained to rotate about the axis of this cylinder, starting from the position at ~30° and back to 0° of TFJ flexion (b). In the second mechanism, the articulating surfaces were defined as the medial and lateral patellofemoral articular surfaces, that were then approximated by best fitting two spheres (c). The patella was constrained to rotate about the vector connecting the centre of these two spheres, starting from the position at ~30° and up to 90° of TFJ flexion. In both PFJ mechanisms, the patellar tendon was considered isometric. ........................................................................................................................................ 83

Figure 4.16. Subject-specific right leg model created in NMSBuilder (a) and exported in OpenSim (b). ........................................................................................................................................ 86

Figure 4.17. Implementation of the explicit TFJ mechanism. Each ligament (i.e., ACL, PCL, MCL and LCL) was divided into a proximal and a distal part (a), for which a SCS was defined (b). The x-axis of each SCS (red arrow) coincided with the ligament longitudinal axis, defined as the vector connecting the optimised ligament attachment points. Each proximal ligament body was connected to the femur by means of a spherical joint and to the tibia by means of a point constraint (c). A prismatic joint was introduced between each proximal and distal ligament body to allow for minimal ligament elongation. ........................................................................................................................................ 88

Figure 4.18. Open tree structure of the right-leg OpenSim model, including the explicit TFJ mechanism. Each proximal ligament body (i.e., ACLprox_r, PCLprox_r, MCLprox_r and LCLprox_r) and each contact body (i.e., art_cont1_r and art_cont2_r) are connected to the femur via a spherical joint. Each distal ligament body (i.e., ACLdist_r, PCLdist_r, MCLdist_r and LCLdist_r) is connected to its corresponding proximal body by a prismatic pair. All distal ligament bodies (i.e., ACLdist_r, PCLdist_r,
MCLdist_r and LCLdist_r) and the two contact bodies (i.e., art_cont1_r and art_cont2_r) are connected to the tibia (i.e., tibia_r) via point constraints (not visible in the topological representation of the multibody system).

**Figure 4.19.** Ligament lengths (blue lines) and CSA (yellow area). A plane (magenta) perpendicular to the ligament’s longitudinal axis was created and used to cut each ligament at the mid-point between its attachment points.

**Figure 5.1** Acetabular inclination: measured on axial slices at the widest diameter of the femoral head. A line is drawn from the anterior and posterior most margins of the cartilaginous acetabulum (EF), and the angle between it and the reference plane (AC) calculated as acetabular inclination. AC: perpendicular to the line created horizontally from the left to right posterior ischial spines (BD).

**Figure 5.2** (A) Femoral neck angle: measured at the widest diameter of the femoral head using dedicated oblique transverse slices parallel to the femoral neck. A line was drawn through the centre of the femoral head and femoral neck (AB), and the angle between it and the horizontal reference plane (AC) used as the FNA (BAC). (B) Posterior femoral condylar axis: measured on axial slices at the widest point in the anteroposterior plane at the midline of the femoral condyles, and calculated as the angle (BAC) between the posterior-most aspect of the medial and lateral cartilaginous condyles (AB) and the horizontal reference plane (AC). (C) Posterior tibial condylar axis measured on axial slices at the widest point in the horizontal plane of the tibial condyles, and calculated as the angle (BAC) between the posterior-most aspect of the medial and lateral cartilaginous condyles (AB) and the horizontal reference plane (AC). (D) Intermalleolar axis: measured on axial slices at the greatest distance between the medial and lateral malleoli i.e. the intermalleolar distance from the most medial aspect of the medial malleolus to the most lateral aspect of the lateral malleolus (AB). The axis was calculated as the angle (BAC) between (AB) and the horizontal reference plane (AC).

**Figure 5.3** TT-TG Distance: is the horizontal distance from the tibial tuberosity to the trochlear groove. (A) Trochlear groove (two slices directly inferior to the point at which the trochlear cartilage is first visualised [cranial-to-caudal]). (B) Tibial tuberosity at its most anterior point. A mouse cursor is placed on the first slice (3A) at the deepest point on the trochlear groove (TG). Without moving the cursor and scrolling through the MRI slices (cranial-to-caudal), the horizontal distance between the pre-identified position of TG and the most anterior point of the tibial tuberosity (TT) is measured.
Figure 5.4 (A) Cartilage sulcus angle: measured on axial images, two slices inferior to the slice in which the trochlear cartilage is first visualised (cranial-to-caudal). The anterior-most cartilaginous points of the lateral (D) and medial (E) femoral condyles and the deepest point in the cartilaginous trochlear groove (A) create the CartSA (DAE). (B) Congruence angle: measured on axial slices at the widest point of the patella at its widest horizontal margin, using the CartSA as a reference point (BAC). A bisector line of the angle BAC was used as the reference plane (AD). Another line was drawn from the deepest point of the trochlear groove (A) to the inferior-most point of the patella articular ridge (AE). Congruence angle was determined by the angle created between these two lines (DAE). (C) Lateral patella tilt: measured on axial slices at the widest point of the patella from the most lateral point of the patella (B) to the most medial point (D) the reference plane (AC) is translated vertically until it meets point (B). The angle between the translated reference plane and the patella width (BD) gives you LPT. (D) Patella bisect offset ratio: measured using the same slice as LPT. a bisector line was created from the deepest point of the trochlear groove (F) until it met the reference plane (AC) at right angles. This line was then extended vertically until it bisected the patella width (BD) at point (E). Bisect offset is determined by the ratio at which the patella width was bisected from its lateral aspect (BE) to the total length of the patella width (BE:BD).

Figure 5.5 Patella trochlear ratio: The superior-most aspect (A) to the inferior-most aspect (B) of the articular surface produces the vertical length of the patellar cartilage (AB). The vertical distance between the superior-most point of the trochlear articular surface (C) and the inferior-most point of the patellar articular surface translated over horizontally (D) is calculated as a ratio to the patellar articular surface to produce the PTR (CD:AB).

Figure 6.1. Example of bone and TFJ ligament segmentation from the regional MRI scan (a). Baseline model of the TFJ ($\Delta L_0$) (b): the spherical surfaces (grey) approximate the geometry of the femoral condyles and tibia plateaus, while the rigid links (fuchsia) represent the isometric fibres of ACL, PCL and MCL.

Figure 6.2. Example of full-length bone segmentation from the full lower limb MRI scan (a). Example of bone segmentation from the regional MRI scans at approximately 0°(b), 7° (c), 15° (d) and 25° (e) of TFJ flexion and registration of these bones to the full-length bones (b, c, d, e).

Figure 6.3. Comparison between the average (a) TFJ and (b) PFJ kinematics as function of the TFJ flexion angle obtained from $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red).
models with those from published cadaveric data (grey) (TFJ: Ottoboni et al., 2010; Sancisi and Parenti-Castelli, 2011; PFJ: Anglin et al., 2008; Sancisi and Parenti-Castelli, 2011). Curves represent the average ± standard deviation across the eight participants.

Figure 6.4. Comparison between (a) TFJ and (b) PFJ kinematics from MRI-measured (black dots) and published cadaveric (grey) data (TFJ: Ottoboni et al., 2010; Sancisi and Parenti-Castelli, 2011; PFJ: Ottoboni et al., 2010; Sancisi and Parenti-Castelli, 2011) across the TFJ flexion ROM. The MRI-measured data include four poses for each participant.

Figure 6.5. Comparison of knee ligament strain (ACL, PCL, MCL and LCL) between published (Blankevoort et al., 1991; Belvedere et al., 2012) (grey) and MRI-measured data across the TFJ flexion ROM. The MRI-measured data (dots) include four poses for each participant and were calculated for ΔL0 (green), ΔLmin (blue) and ΔLmatch (red). To calculate the strain, the initial length at 0° TFJ flexion of each ligament was derived from the respective model estimates.

Figure 6.6. Average RMSEs and 95% CI for each degree of freedom of the TFJ kinematics (a), PFJ kinematics (b) and ligament length (c) for each model. The length of the LCL in ΔL0 (c) was computed as the distance between the centroid of the attachment areas throughout the TFJ flexion ROM.

Figure 6.7. Hotelling’s trajectories (SnPM(T^2)), depicting where the combined TFJ and PFJ degrees of freedom across the 8 participants differed between models. Results from the paired Hotelling’s T^2 tests between ΔL0 and ΔLmin (column a), ΔL0 and ΔLmatch (column b) and ΔLmin and ΔLmatch (column c) are reported. The horizontal dashed lines indicate the critical thresholds of T^2.

Figure 6.8. Average and standard deviation of TFJ ad/abduction (left) and TFJ internal/external rotation (right) obtained by ΔL0 (green), ΔLmin (blue) and ΔLmatch (red), as function of the TFJ flexion angle. T statistics calculated using the statistical non-parametric mapping (SnPM(t)) equivalent of a one-dimension two-tailed paired t-test, depicting where TFJ ad/abduction (left) and TFJ internal/external rotation (right) differed between models. The horizontal dashed lines indicate the critical thresholds (t) for significance.

Figure 6.9. Average and standard deviation of TFJ anterior/posterior (left) and TFJ proximal/distal (right) displacements obtained by ΔL0 (green), ΔLmin (blue) and ΔLmatch (red), as function of the TFJ flexion angle. T statistics calculated using the
statistical non-parametric mapping (SnPM(t)) equivalent of a one-dimension two-tailed paired t-test, depicting where TFJ anterior/posterior (left) and TFJ proximal/distal (right) displacements differed between models. The horizontal dashed lines indicate the critical thresholds (t) for significance. ................................................................. 131

**Figure 6.10.** Average and standard deviation of TFJ lateral/medial displacement obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red), as function of the TFJ flexion angle. T statistics calculated using the statistical non-parametric mapping (SnPM(t)) equivalent of a one-dimension two-tailed paired t-test, depicting where TFJ lateral/medial displacement differed between models. The horizontal dashed lines indicate the critical thresholds (t) for significance. ........................................................................................................ 132

**Figure 6.11.** Average and standard deviation of PFJ extension/flexion (left) and PFJ ad/abduction (right) obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red), as function of the TFJ flexion angle. T statistics calculated using the statistical non-parametric mapping (SnPM(t)) equivalent of a one-dimension two-tailed paired t-test, depicting where PFJ extension/flexion (left) and PFJ ad/abduction (right) differed between models. The horizontal dashed lines indicate the critical thresholds (t) for significance. ........................................................................................................ 133

**Figure 6.12.** Average and standard deviation of PFJ internal/external rotation (left) and PFJ anterior/posterior displacement (right) obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red), as function of the TFJ flexion angle. T statistics calculated using the statistical non-parametric mapping (SnPM(t)) equivalent of a one-dimension two-tailed paired t-test, depicting where PFJ internal/external rotation (left) and PFJ anterior/posterior displacement (right) differed between models. The horizontal dashed lines indicate the critical thresholds (t) for significance. ........................................................................................................ 134

**Figure 6.13.** Average and standard deviation of PFJ proximal/distal (left) and PFJ lateral/medial (right) displacements obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red), as function of the TFJ flexion angle. T statistics calculated using the statistical non-parametric mapping (SnPM(t)) equivalent of a one-dimension two-tailed paired t-test, depicting where PFJ proximal/distal (left) and PFJ lateral/medial (right) displacements differed between models. The horizontal dashed lines indicate the critical thresholds (t) for significance. ........................................................................................................ 135

**Figure 6.14.** Comparison between the average TFJ (a) and PFJ (b) kinematics obtained from $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red), as function of the TFJ flexion angle. The shaded areas represent the average ROM across the 8 participants and they are
compared against the ROM of published cadaveric kinematics (grey) and MRI-based kinematics (black dots).

**Figure 6.15.** TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by \( \Delta L_0 \) (green), \( \Delta L_{\text{min}} \) (blue) and \( \Delta L_{\text{match}} \) (red) for participant 1. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.

**Figure 6.16.** TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by \( \Delta L_0 \) (green), \( \Delta L_{\text{min}} \) (blue) and \( \Delta L_{\text{match}} \) (red) for participant 2. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.

**Figure 6.17.** TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by \( \Delta L_0 \) (green), \( \Delta L_{\text{min}} \) (blue) and \( \Delta L_{\text{match}} \) (red) for participant 3. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.

**Figure 6.18.** TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by \( \Delta L_0 \) (green), \( \Delta L_{\text{min}} \) (blue) and \( \Delta L_{\text{match}} \) (red) for participant 4. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.

**Figure 6.19.** TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by \( \Delta L_0 \) (green), \( \Delta L_{\text{min}} \) (blue) and \( \Delta L_{\text{match}} \) (red) for participant 5. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.

**Figure 6.20.** TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by \( \Delta L_0 \) (green), \( \Delta L_{\text{min}} \) (blue) and \( \Delta L_{\text{match}} \) (red) for participant 6. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.

**Figure 6.21.** TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by \( \Delta L_0 \) (green), \( \Delta L_{\text{min}} \) (blue) and \( \Delta L_{\text{match}} \) (red) for participant 7. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.

**Figure 6.22.** TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by \( \Delta L_0 \) (green), \( \Delta L_{\text{min}} \) (blue) and \( \Delta L_{\text{match}} \) (red) for participant 8. Model-based kinematics and
ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths. ................................................................. 144

**Figure 6.23.** Example of multiple TFJ solutions (n = 47 in this case) found with MOPSO for participant 8 using $\Delta L_{match}$. Each colour represents a different solution, with 30 optimised parameters (pink area) and three objective functions (green area). If the optimised ROMs were larger than the published ROMs, the solution with minimal difference between optimised and published TFJ ab/adduction and internal/external rotation ROMs was chosen to ensure that the kinematics was within reasonable ROMs for a paediatric population. Otherwise, the solution that provided the best match between the pattern of estimated and published experimental TFJ and PFJ kinematics was chosen. ........................................................................................................ 146

**Figure 6.24.** Comparison between the TFJ (a) and PFJ (b) kinematics obtained from $\Delta L_{0}$ (green) and $\Delta L_{match}$ (red), expressed as average ± SD across the 8 participants, and published cadaveric kinematics (grey) (Sancisi et al., 2011; Ottoboni et al., 2010, Anglin et al., 2008), expressed as average ± 2SD. ................................................................. 150

**Figure 7.1.** Illustration of marker placement on the participant’s skin (left) and anatomical description of each marker (right). The green markers were kept on the participant’s skin during MRI acquisition, while the pink markers (clusters and wands) were removed after motion data collection. ................................................................. 155

**Figure 7.2.** Joint definition in a right-leg skeletal OpenSim model.................................. 157

**Figure 7.3.** Explicit implementation of the 5-rigid-link TFJ mechanism. Each ligament (i.e., ACL, PCL and MCL) was divided into a proximal and distal part, for which a segment coordinate system (SCS) was defined. The x-axis of each SCS (red arrow) coincided with the ligament longitudinal axis, defined as the vector connecting the optimised ligament attachment points. Each proximal ligament body was connected to the femur by means of a spherical joint and to the tibia by means of a point constraint. A prismatic joint was introduced between each proximal and distal ligament body to allow for minimal ligament elongation during gait. ................................................................. 158

**Figure 7.4.** Comparison between the average TFJ kinematics during gait obtained from $\Delta L_{min}$, $MBO$ (blue) and $\Delta L_{0, implicit}$ (red). Curves represent the average ± standard deviation across the eight participants. Significant differences between the two methods were found at 51°-54° of TFJ flexion angle for TFJ adduction/abduction.................. 162
Figure 7.5. Comparison between the average TFJ kinematics during gait obtained from $\Delta L_{\text{min}}$, $MBO$ (blue) and $\Delta L_0$, implicit (red). Curves represent the average ± standard deviation across the eight participants and they are compared against MRI-measured passive kinematic data (black dots). ................................................................. 162

Figure 7.6. Comparison between the average ligament strain during gait obtained from $\Delta L_{\text{min}}$, $MBO$ (blue) and $\Delta L_0$, implicit (red). Curves represent the average ± standard deviation across the eight participants. Significant differences between the two methods were found for the ACL and PCL strains. It has to be noted that, even if the LCL was not included in the implementation of $\Delta L_0$, implicit, its length variation across the gait cycle was computed as the Euclidean distance between the centroids of the LCL attachment regions from the MRI reference pose at ~0° of TFJ flexion. ................................. 163

Figure 7.7. Comparison between the average ligament strain during gait obtained from $\Delta L_{\text{min}}$, $MBO$ (blue) and $\Delta L_0$, implicit (red). Curves represent the average ± standard deviation across the eight participants and they are compared against MRI-measured passive ligament strain (black dots). ................................................................. 164

Figure 7.8. Averaged ligament strain curves across the eight participants, as function of the TFJ flexion angle, obtained from $\Delta L_{\text{min}}$, $MBO$ (blue) and $\Delta L_0$, implicit (red). $\Delta L_{\text{min}}$, $MBO$ provided different strain values, depending on whether the limb is under stance (navy blue) or swing (light blue) phase at similar TFJ flexion angles. ............ 165

Figure 8.1. Axial left knee MRIs of a RPD patient at approximately 0° (a), 10° (b), 20° (c) and 30° (d) of TFJ flexion. The patella translates medially (M) into the trochlear groove as the knee flexes from a lateral (L) position at extended knee posture (from a to d). ................................................................. 176

Figure 8.2. Description of the four modelling approaches ($A_1$, $A_2$, $A_3$ and $A_4$) implemented to estimate the PFJ kinematics in RPD patients. $A_1$ used a single hinge mechanism, where the axis of rotation (black dotted line) was defined as the vector connecting the centre of the spheres (blue) fitted to the medial and lateral patellofemoral articulating surfaces in the trochlea (aqua). The initial pose of the patella was computed from the MRI reference pose (purple). Contrastingly, $A_2$, $A_3$ and $A_4$ used two hinge mechanisms: the first axis of rotation (black dotted line) was the axis of the cylinder fitted to the region (orange) where the patella was likely to articulate between 0° and 30° of TFJ flexion, while the second axis of rotation (black dotted line) was defined as for $A_1$. In $A_2$ the initial pose of the patella for the first mechanism was derived from the MRI reference pose at ~0° of TFJ flexion (purple), while the initial pose for the second
mechanism was the pose of the patella at ~30° of TFJ flexion (dark green). A3 and A4 used the same initial pose of the patella at ~30° of TFJ flexion (dark green) for both mechanisms. ........................................................... 178

Figure 8.3. Comparison of PFJ kinematics obtained from the four approaches (A1, A2, A3 and A4) as function of the TFJ flexion angle for one RPD patient (RPD1). Gradual improvements in the estimation of MRI-registered data and continuity of the PFJ kinematic curves were obtained from A1 (light green) to A4 (navy blue).................. 180

Figure 8.4. Comparison between A4-estimated (blue) and MRI-registered (black dots) PFJ kinematics, as function of the TFJ flexion angle, for one RPD patient (RPD1)..... 181

Figure 8.5. Comparison between A4-estimated (blue) and MRI-registered (black dots) PFJ kinematics, as function of the TFJ flexion angle, for one RPD patient (RPD2)..... 181

Figure 8.6. Comparison between A4-estimated (blue) and MRI-registered (black dots) PFJ kinematics, as function of the TFJ flexion angle, for one RPD patient (RPD3)..... 182

Figure 8.7. Comparison between A4-estimated (blue) and MRI-registered (black dots) PFJ kinematics, as function of the TFJ flexion angle, for one RPD patient (RPD4)..... 182

Figure 8.8. Average RMSEs and 95% CI for each motion component of the PFJ kinematics for RPD patients......................... 183

Figure 8.9. Comparison of the average PFJ kinematics, as function of the TFJ flexion angle, between RPD patients (blue) and TD participants (grey). Curves represent the average ± standard deviation across the eight TD participants and four RPD patients. Significant differences between the two groups were found for PFJ extension/flexion, external/internal rotation and medio/lateral translation................................. 183

Figure 8.10. Projection of initial patellar tendon length onto the reconstructed patellar tendon volume (pink). The adjusted patellar tendon length was obtained as the average of the lengths of the two projected curves. ................................................................. 186

Figure 8.11. PFJ kinematics obtained for the four RPD patients (RPD1, RPD2, RPD3, RPD4) using the congruence model. For each patient, the patella ab/adduction was locked at the value derived from the MRI reference pose. For all the four patients, the patella reached a stable position in the trochlea at ~60° of TFJ flexion (dotted vertical line). 187

Figure 9.1 Different levels of complexity and subject-specificity within the spectrum of TFJ musculoskeletal models. The red arrow lists the level of subject-specificity that can be achieved in the implementation of rigid-body models, while the green arrow lists the level of subject-specificity that can be achieved in the implementation of continuum
models. The figure highlights where the developed rigid-body knee kinematic models fit within the spectrum of TFJ musculoskeletal models. This figure focuses on the TFJ, but the same concept can be applied to other joints. ......................................................... 193

Figure 9.2. Workflow to create subject-specific lower limb kinematic models for TD participants (left) and RPD patients (right). Red watches correspond to patient and staff time, green watches to staff time only and blue watches to computational time. ........ 199

Figure 9.3. Different pathways (i.e., inverse and forward dynamic approaches) to estimate PFJ contact forces using the subject-specific models developed in this thesis. Dotted blue lines represent the main outputs.......................................................... 204
List of tables

Table 2.1. Attachment regions and primary functions of the four major TFJ ligaments. ................................................................................................................................. 13

Table 2.2. Reported incidence of first-time patellar dislocation in children and adolescents...................................................................................................................... 15

Table 3.1 Population characteristics ..................................................................................................................................................................................... 41

Table 3.2 Methodological quality assessment of included studies: Downs and Black checklist ........................................................................................................................................... 43

Table 3.3 Measures of lower limb and PFJ alignment, trochlea morphology and soft tissue restraints .................................................................................................................................................................................. 45

Table 3.4 Weighted average of most frequently reported measures ........................................................................................................................................................................ 51

Table 3.5 Weighted mean differences for measures reported in two or more studies that included a control cohort ........................................................................................................................................................................ 51

Table 4.1. Participants’ characteristics. Age, mass and height are expressed as average and standard deviation. ........................................................................................................................ 59

Table 4.2. Anthropometric measurement description and technique. ........................................................................................................................................................................ 63

Table 4.3. Marker locations and landmark identification. ................................................................................................................................................................................ 65

Table 4.4. Segment coordinate systems defined in NMSBuilder for each body. ................................................................................................................................................... 85

Table 5.1. Participants characteristics and medical imaging measurements for each group. ................................................................................................................................................................ 99

Table 5.2. Effectiveness of each medical imaging measurement in the determining patients with recurrent patella dislocation using ROC curve analysis. ................. 105

Table 6.1. Description of terms in equations 6.1-6.4 ................................................................................................................................................................................................. 115

Table 6.2. Pearson’s correlation coefficients across participants (average and standard deviation) between published and estimated TFJ and PFJ kinematics. .......................................................................................................... 120

Table 6.3. RMSE between model-based and MRI-registered TFJ kinematics for the four poses of comparison, ROM and percent error relative to the ROM. ........................................................................ 147

Table 6.4. RMSE between model-based and MRI-registered PFJ kinematics for the four poses of comparison, ROM and percent error relative to the ROM. ........................................................................ 148
List of tables

Table 6.5. RMSE between model-based and MRI-registered ligament length for the four poses of comparison, ligament length at ~0° TFJ flexion (L0) and percent error relative to the initial ligament length. ................................................................. 149

Table 7.1. Ligament stiffness factors for each participant........................................... 160

Table 7.2. Comparison of the marker errors obtained for each participant using the two methods.................................................................................................................. 161

Table 7.3. Ligament weights defined in previous studies (Gasparutto et al., 2012; Gasparutto et al., 2015; Sancisi et al., 2017) for the penalty-based method. ............... 166

Table 8.1. Participants’ characteristics. Age, mass and height are expressed as average and standard deviation. ................................................................................. 173
List of equations

Equation (4.1) ........................................................................................................ 73
Equation (4.2) ........................................................................................................ 73
Equation (4.3) ........................................................................................................ 78
Equation (4.4) ........................................................................................................ 78
Equation (4.5) ........................................................................................................ 78
Equation (4.6) ........................................................................................................ 78
Equation (4.7) ........................................................................................................ 78
Equation (4.8) ........................................................................................................ 80
Equation (4.9) ........................................................................................................ 81
Equation (4.10) ..................................................................................................... 84
Equation (4.11) ..................................................................................................... 84
Equation (4.12) ..................................................................................................... 90
Equation (4.13) ..................................................................................................... 90
Equation (6.1) ..................................................................................................... 115
Equation (6.2) ..................................................................................................... 115
Equation (6.3) ..................................................................................................... 115
Equation (6.4) ..................................................................................................... 115
Equation (6.5) ..................................................................................................... 116
Equation (6.6) ..................................................................................................... 116
Equation (8.1) ..................................................................................................... 176
Equation (8.2) ..................................................................................................... 176
Equation (8.3) ..................................................................................................... 178
Equation (8.4) ..................................................................................................... 178
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANOVA</td>
<td>Analysis of Variance</td>
</tr>
<tr>
<td>ACL</td>
<td>Anterior cruciate ligament</td>
</tr>
<tr>
<td>CartSA</td>
<td>Cartilage sulcus angle</td>
</tr>
<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CA</td>
<td>Congruence angle</td>
</tr>
<tr>
<td>CSA</td>
<td>Cross-sectional area</td>
</tr>
<tr>
<td>DoF</td>
<td>Degree of freedom</td>
</tr>
<tr>
<td>EMG</td>
<td>Electromyography</td>
</tr>
<tr>
<td>FNA</td>
<td>Femoral neck angle</td>
</tr>
<tr>
<td>ISB</td>
<td>International Society of Biomechanics</td>
</tr>
<tr>
<td>LLCH</td>
<td>Lady Cilento Children's Hospital</td>
</tr>
<tr>
<td>LCL</td>
<td>Lateral collateral ligament</td>
</tr>
<tr>
<td>LPT</td>
<td>Lateral patellar tilt</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>MCL</td>
<td>Medial collateral ligament</td>
</tr>
<tr>
<td>MPFL</td>
<td>Medial patellofemoral ligament</td>
</tr>
<tr>
<td>MBO</td>
<td>Multibody optimisation</td>
</tr>
<tr>
<td>MOPSO</td>
<td>Multiple objective particle swarm optimisation</td>
</tr>
<tr>
<td>MSK</td>
<td>Musculoskeletal</td>
</tr>
<tr>
<td>MAP</td>
<td>Musculoskeletal atlas project</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>PBOR</td>
<td>Patellar bisect offset ratio</td>
</tr>
</tbody>
</table>
List of abbreviations

PL - Patellar length
PT - Patellar tendon length
PTR - Patella trochlear ratio
PFJ - Patellofemoral joint
PCL - Posterior cruciate ligament
QCMAS - Queensland Children Motion Analysis Service
ROM - Range of motion
ROC - Receiver operator curve
RPD - Recurrent patellar dislocators
RMSE - Root-mean-square errors
SCS - Segment coordinate system
SPM - Statistical parametric mapping
TFJ - Tibiofemoral joint
TG - Trochlear groove
TT - Tibial tuberosity
TT-TG - Tibial tuberosity to trochlear groove
TD - Typically developing
VIF - Variance inflation factor
VL - Vastus medialis
VM - Vastus lateralis
Introduction

1.1 Background

Patellar dislocation is a common knee injury characterised by a complete, almost always lateral, displacement of the patella from the femoral trochlear groove. First-time patellar dislocation is particularly common in paediatric patients, accounting for approximately 25-36% of acute knee trauma in children and adolescents with knee hemarthrosis (Abbasi et al., 2012; Luhmann, 2003). First-time patellar dislocation annually affects from 13.5 to 147.7 per 100000 patients from nine to 19 years of age (Atkin et al., 2000; Fithian et al., 2004; Gravesen et al., 2017; Hsiao et al., 2010; Nietosvaara et al., 1994; Sanders et al., 2018b), while the annual prevalence drops to 1.5-11 per 100000 for patients over 20 years of age (Atkin et al., 2000). Moreover, up to 71% of children and adolescents who experience first-time dislocation are at risk of experiencing recurrent patellar dislocation (Gravesen et al., 2017; Jaquith et al., 2017; Kaewkongnok et al., 2018; Lewallen et al., 2013b; Palmu et al., 2008; Sanders et al., 2018a), which can result in substantial knee joint dysfunction (e.g., difficulties in performing activities of daily living) and reduced quality of life (Fithian et al., 2004; Moström et al., 2014; Vollnberg et al., 2012).

The aetiology of recurrent patellar dislocation is believed to relate to abnormal patellofemoral joint (PFJ) anatomy, lower limb misalignment and inadequate soft tissue restraints. Anatomical risk factors that predispose individuals to recurrent patellar dislocations have been well established and include trochlear dysplasia, patella alta, abnormal lateral patellar tilt and lateralisation of the tibial tuberosity (Dejour et al., 1994). Other predisposing risk factors include excessive femoral anteversion and/or excessive external rotation of the tibia (Diederichs et al., 2013; Parikh et al., 2011; Prakash et al., 2016), and inadequate soft tissue restraints (Elias et al., 2002). Most of these factors are measured from static medical images (e.g., X-ray, computed tomography (CT) or...
Introduction

magnetic resonance imaging (MRI)) which, together with the patient’s history and clinical examinations, define the current diagnostic methods for patellar dislocation (Arendt et al., 2017). However, while critical thresholds for these parameters have been identified to characterise adult patients with primary patellar dislocation (Arendt et al., 2017), there is a paucity of reported data that define normal and pathological values in paediatric populations, where the morphology of the patellofemoral joint (PFJ), as well as lower limb alignment, change with growth.

Standard treatment for recurrent patellar dislocation includes nonoperative and operative interventions. Nonoperative treatments, varying from brief immobilisation to physical therapy (Chotel et al., 2014), are strongly indicated for treatment of primary lateral patellar dislocation in young patients (Palmu et al., 2008). When symptoms do not improve with nonoperative treatments and/or the patient experiences subsequent dislocations, surgery is recommended. Typically, surgical procedures encompass a combination of techniques, varying from bony to soft tissue procedures. Of the common bony procedures, femoral derotational osteotomy is advocated to restore lower limb alignment in patients with excessive femoral anteversion (Weber et al., 2016a), while guided growth procedures are used to gradually correct bony deformity and/or misalignment (Kearney et al., 2015). In contrast, transfer of the tibial tubercle or trochleoplasty are not recommended in patients with open physes due to the high risk of violating bone growth. In fact, as the tibial tubercle is part of the proximal tibial growth plate and the trochlea sits at the distal femoral growth plate, any cuts or osteotomies in these areas would cause a fusion of the growth plate and subsequent growth would create deformity in the bones. Unlike some bony procedures, most soft tissue procedures are deemed safe in the paediatric population and, consequently, they are used more often. These treatments include vastus medialis obliquus advancement, medial patellofemoral ligament reconstruction, patellar tendon transfer and lateral retinacular release. An advancement of the vastus medialis obliquus is performed to rebalance the quadriceps force vector, while medial patellofemoral ligament reconstruction restores the restraining function of the ligament to lateral patellar displacement. Patellar tendon transfer is used to achieve distal alignment of the extensor mechanism, whereas lateral retinacular release can correct excessively lateral patellar tilt (e.g., >20º) (Weber et al., 2016a).

Despite the wide range of treatments available, the risk of experiencing subsequent episodes of dislocation after treatment remains high. Palmu et al. (2008) randomly assigned patients younger than 16 years of age to non-operative or operative (i.e., medial patellofemoral ligament repair or lateral retinacular release) treatment and
reported a redislocation rate of 71% and 67% at 14-year follow-up, respectively. Poor long-term functional outcomes of current treatments highlight the necessity for a better understanding of the patellar dislocation injury mechanism. While clinical examinations and medical imaging can provide valuable insights into the PFJ anatomy, these methods alone are not sufficient to establish cause-effect relationships in such a complex dynamic system.

Dynamic joint movements in recurrent patellar dislocators can be assessed during gait using clinical motion analysis. In clinical settings, the resulting kinematic and kinetic data of each patient are compared to the data of aged-matched healthy participants to identify each individual’s primary impairment. This comparison can highlight unique gait characteristics typical of patients with patellar dislocation, such as hyperextension of the knee during limb-support phase (Carnesecchi et al., 2016) or smaller knee extension moment compared to healthy subjects (Asaeda et al., 2016). Atypical gait patterns may be responsible for placing adverse forces on the patella (Smith et al., 2008a) or represent a compensatory mechanism to preserve patellar stability. However, simplified representations of the joints and the presence of soft tissue artefacts, make gait analysis unsuitable to accurately describe the joint motion in the coronal and axial planes (Andersen et al., 2010; Stagni et al., 2009; Stagni et al., 2005). Moreover, since gait analysis models do not include anatomical characteristics of the PFJ, they cannot provide patient-specific insights on the PFJ (dys)function.

Recently, user friendly musculoskeletal (MSK) modelling software (e.g., OpenSim (Delp et al., 2007) and AnyBody (Damsgaard et al., 2006)) has enabled accurate, non-invasive and personalised analyses (Gerus et al., 2013) of a participant’s joint kinematics, kinetics and internal loads (e.g., muscle and joint contact forces). MSK models are computational representations of a participant’s anatomy and consist of rigid bodies (bones), connected by joints and actuated by muscles. The lower limb MSK anatomy is generally obtained from dissections of healthy adult-male cadaveric specimens (Brand et al., 1982; Friederich et al., 1990; Horsman et al., 2007) and used to generate generic models (Arnold et al., 2010; Delp et al., 1990; Modenese et al., 2011), where the anatomy is linearly scaled to fit the anthropometry of individual participants. Despite linearly scaled-generic MSK models having been widely used and their outputs validated during different tasks (Lloyd et al., 2003; Winby et al., 2009), it is questionable, in the clinical setting, whether the results from these models can inform surgical planning on an individual basis (Blemker et al., 2007) or whether the kinematic, kinetic and muscle force results can accurately replicate pathological locomotion (Scheys et al., 2011b).
Introduction

In fact, even after scaling, a generic model may not accurately represent the MSK anatomy of the paediatric population, especially when pathology exists (Arnold et al., 2001; Correa et al., 2011).

As an alternative to linearly scaled-generic MSK models, subject-specific models can be created from medical images to potentially improve the accuracy of the MSK model’s outputs and expand their use in clinical practice. When compared to scaled-generic models, subject-specific models derived from medical imaging better predicted hip (Lenaerts et al., 2008) and tibiofemoral joint (TFJ) (Gerus et al., 2013; Marra et al., 2015) contact forces, hip (Scheys et al., 2011a) and TFJ (Tsai et al., 2012) joint moments, and musculotendon length and moment arms (Arnold et al., 2000). These studies implemented subject-specific models that were personalised in different ways, depending on their intended application and data availability.

Numerous studies have implemented subject-specific rigid-body models, with personalised MSK anatomy, for gait analysis in adults (Gerus et al., 2013; Lenhart et al., 2015; Marra et al., 2015; Martelli et al., 2015; Scheys et al., 2005; Taddei et al., 2012; Valente et al., 2014; Wesseling et al., 2016) and children with pathologies (Bosmans et al., 2014; Correa et al., 2011; Kainz et al., 2016; Modenese et al., 2018), while other models included personalised musculotendon geometry and properties (Blemker et al., 2006; Correa et al., 2011; Fernandez et al., 2005). However, for patients with irregular gait pattern (e.g., recurrent patellar dislocators) an additional level of personalisation is required to enable accurate estimation of the joint kinematics.

Scaled-generic MSK models and simplistic representation of the TFJ may poorly represent actual joint motion in both healthy and pathological populations. It has been demonstrated (Andersen et al., 2010; Gasparutto et al., 2015; Stagni et al., 2009) that representing the TFJ as a spherical or hinge joint, or using scaled-generic TFJ kinematics obtained from cadavers (Walker et al., 1988) cannot accurately estimate in vivo secondary TFJ kinematics (i.e., adduction/abduction, internal/external rotation and anterior/posterior, proximal/distal and medio/lateral displacements) in adults. Additionally, kinematic data from adult cadaveric participants might not be able to capture paediatric-specific anatomical characteristics (e.g., ligamentous hyperlaxity) or morphological abnormalities (e.g., dysplastic trochlea and/or patella) that can influence the TFJ (Amiri et al., 2006; Hashemi et al., 2008) and PFJ kinematics. Therefore, more complex and personalised TFJ and PFJ models are required to investigate pathological conditions, such as recurrent patellar dislocation, in children and adolescents.
Introduction

To overcome the limitations of simplistic joint representations, mechanism-based models have been proposed for the TFJ and PFJ. The TFJ consists of two rigid tibial and femoral contacts and isometric anterior cruciate (ACL), posterior cruciate (PCL) and medial collateral (MCL) ligaments (Feikes et al., 2003; Ottoboni et al., 2010; Parenti-Castelli et al., 2000; Sancisi et al., 2011a; Wilson et al., 1998), and the PFJ is represented as a hinge joint connecting the femur to the patella and an isometric patellar tendon (Sancisi et al., 2011a). These mechanisms well estimated each joints’ *in vitro* passive six motion components (three rotations, three translations) (Sancisi et al., 2011a) and they have been generated from MRI in healthy adults (Brito da Luz et al., 2017). Gasparutto et al. (2012) increased the complexity of the previously described 5-rigid-link TFJ mechanism by adding the lateral collateral ligament (LCL) and allowing for minimal ligament deformation during passive conditions.

Parallel TFJ mechanisms (Clément et al., 2015; Duprey et al., 2010; Gasparutto et al., 2015; Moissenet et al., 2014) and hinge PFJ mechanisms (Moissenet et al., 2014) have been recently integrated into full lower-limb scaled-generic MSK models to analyse dynamic tasks (i.e., gait, running, squatting) in adult populations. All of these authors employed cadaveric data both to generate the skeletal models (Delp et al., 1990) and to derive the TFJ mechanisms’ parameters (Ottoboni et al., 2010), apart from Clément et al. (2015), who used personalised bones to create the lower limb models and a mix of subject-specific and generic parameters for the TFJ mechanism. Compared to simple (e.g. hinge) and/or generic TFJ models, semi-personalised parallel TFJ mechanisms with minimally deformable ligaments better estimated TFJ abduction-adduction, internal-external rotation and antero-posterior displacement during squatting in healthy and osteoarthritic adult participants (Clément et al., 2015). Therefore, developing these models for children and adolescents who experience recurrent patellar dislocation could help characterise patellar dislocation injury mechanisms.

Concomitant with subject-specific rigid-body kinematic model development, validation against measured joint motion is a fundamental step towards the translation of this technology into clinical practice. Estimated subject-specific knee joint kinematics are commonly compared against *in vivo* knee kinematics measured using imaging techniques, such as biplanar radiography (Clément et al., 2015) or fluoroscopy (Lu et al., 2008; Marra et al., 2015), or intracortical pins (Benoit et al., 2006; Bonci et al., 2014; Reinschmidt et al., 1997). Nevertheless, radiation exposure or invasive procedures limit the use of these methods, especially in paediatric populations. Contrarily, MRI is a safe technology, with its non-invasive protocols and lack of ionizing radiation, and it could be used for
validation of knee mechanisms in children. To date, no studies have developed and validated subject-specific TFJ and PFJ mechanisms for children and adolescents using MRIs.

1.2 Statement of the problem

The available literature is insufficient to characterise anatomical and functional abnormalities in children and adolescents with recurrent patellar dislocation. This results in a lack of understanding of patellar dislocation injury mechanisms and, consequently, poor long-term treatment outcomes. Moreover, anatomical developmental changes of the lower limbs during growth highlights the importance of subject-specific evaluation methods and normative values when assessing patellar dislocation in children and adolescents.

1.3 Thesis objective

The purpose of this thesis was to develop and validate subject-specific rigid-body kinematic models of the TFJ and PFJ in children and adolescents with recurrent patellar dislocation. These kinematic models, which include individualised bone geometry and ligaments, have the potential to capture the complex functional relationship between multiple risk factors for patellar dislocation on an individual basis. To this end, this thesis was divided into five studies, each relating to a specific aim. The first two studies aimed at characterising anatomical differences between paediatric patients with recurrent patellar dislocation and age-matched controls, while the last three studies focussed on the development and validation of kinematic models of the TFJ and PFJ to elucidate any functional differences between pathological and healthy paediatric cohorts. Thus, the specific aims of this thesis were to:

1. Systematically and critically review the current literature to characterise the lower limb alignment, PFJ morphology and soft tissue restraints of the PFJ through medical imaging measurements in children with and without recurrent patellar dislocation. This review allowed us to stratify the factors that influence PFJ stability and provide recommendations on the assessment and reporting of PFJ parameters in this patient population.

2. Determine whether common imaging measures used to assess PFJ dislocation differ between children and adolescents with recurrent patellar dislocation and age-matched typically developing participants and elucidate the best independent and combined imaging predictors of recurrent patellar dislocation.
3. Develop three subject-specific TFJ models with varying complexity (i.e., have different ligamentous constraints), and a common subject-specific PFJ model from MRIs to estimate three-dimensional TFJ and PFJ kinematics in a healthy paediatric population. The resulting kinematics from the three different TFJ models were validated against knee kinematics and ligament lengths measured from MRIs collected at four knee flexion angles.

4. Develop rigid-body lower limb models incorporating a fully subject-specific paediatric kinematic knee model with articular contacts and minimally deformable ligaments to assess TFJ and ligament kinematics during gait in a healthy paediatric population. The resulting kinematics obtained using the deformable-ligament TFJ model were compared against those obtained employing the same TFJ kinematic model featuring three isometric ligaments.

5. Develop subject-specific PFJ models from MRIs with varying complexity (i.e., have different number of joints and constraints) to estimate three-dimensional passive PFJ kinematics in children and adolescents with recurrent patellar dislocation. The resulting PFJ kinematics were validated against PFJ kinematics measured from MRIs collected at four knee flexion angles and compared against results obtained for healthy paediatric participants.

The hypotheses associated with each specific aim were:

1. The complex relationship between lower limb alignment, PFJ morphology and soft tissue restraints of the PFJ would be lacking in the literature when assessing the risk of recurrent patellar dislocation in paediatric patients.

2. Radiological measurements of congruence angle, patella alta, lateral patellar tilt and the tibial tubercle to trochlear groove distance in children and adolescents with recurrent patellar dislocation would differ from age-matched typically developing participants and would be the best predictors of recurrent patellar dislocation.

3. Compared to the simplest model with three rigid knee ligaments, the two models with increased complexity, obtained by adding an extra knee ligament and by allowing for minimal or prescribed elongation of the ligaments, would provide better estimates of MRI-measured joint and ligament kinematics across the four knee flexion angles in a healthy paediatric population.
**Introduction**

4. The resulting TFJ and ligament kinematics during gait in a healthy paediatric population would differ between the isometric-ligament and the deformable-ligament TFJ models.

5. Compared to the simplest PFJ hinge model, the three PFJ models with increased complexity, obtained by adding a second hinge joint and different optimisation constraints, would provide better estimates of MRI-measured PFJ kinematics across the four knee flexion angles in paediatric patients with recurrent patellar dislocation. Moreover, it was hypothesised that, compared to healthy paediatric participants, patients with recurrent patellar dislocation would exhibit a more externally rotated and lateralised patella.

To address the specific aims and to test the corresponding hypotheses, five studies were designed and implemented, and they are presented as chapters in journal article format. In total, the thesis comprises nine chapters inclusive of this introduction. Specifically:

*Chapter 1* includes a general introduction to the thesis topic and describes the aim of the research.

*Chapter 2* provides an overview of the literature and identifies the current state of knowledge on patellar dislocation and musculoskeletal modelling approaches.

*Chapter 3* describes the findings from the first study that stratified the radiological parameters that influence PFJ stability in children and adolescents based on a systematic review of the literature. This chapter addresses the first specific aim of this thesis and has already been published in the Journal of the International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine (JISAKOS) (Barzan, Maine, Modenese, Lloyd, Cartly, 2018).

*Chapter 4* describes the overall methods and procedures used for data collection and processing within this thesis. This chapter includes a description of participant recruitment, data acquisition and processing methods, and statistical analyses undertaken. These data were used for experimental chapters 5, 6, 7 and 8.

*Chapter 5* addresses the second specific aim of this thesis and includes an assessment of lower limb alignment, patellofemoral alignment and trochlear dysplasia from MRI measures in children and adolescents with and without recurrent patellar dislocation. This work has been submitted to The Knee and it is currently under review.
Chapter 6 presents a methodology to create subject-specific TFJ and PFJ rigid body models with different ligamentous constraints from MRIs in healthy children and adolescents. The estimated TFJ and PFJ kinematics were similar to those measured \textit{in vivo} from MRIs acquired at four different TFJ flexion angles. This chapter addresses the third specific aim of this thesis and it is now under review in the Journal of Biomechanics.

Chapter 7 describes the implementation of a subject-specific kinematic model of the knee with minimally deformable ligaments to assess the TFJ and ligament kinematics during gait in healthy children and adolescents. This chapter addresses the fourth specific aim of this thesis, and the TFJ angles and ligament lengths were calculated using the least squares multibody optimisation tool in OpenSim. A manuscript will be prepared for submission to the Journal of Biomechanics.

Chapter 8 presents four different modelling approaches used to estimate passive PFJ kinematics from MRIs in children and adolescents with recurrent patellar dislocation. This chapter addresses the fifth specific aim of this thesis, and the kinematics results obtained from the best modelling approach will be presented in a manuscript that will be submitted to the Journal of Orthopaedic Research.

Chapter 9 discusses how all the thesis results can be used to better inform clinical decision-making in the treatment of recurrent patellar dislocation in children and adolescents.
CHAPTER 2

Literature review

This chapter provides an overview of the literature that identifies current state of knowledge on patellar dislocation and musculoskeletal modelling approaches. A brief anatomical section is firstly presented (Section 2.1), together with the major anatomical developmental changes of the lower limbs during childhood. This section is not intended to be a comprehensive dissertation on the human knee, but a brief reference to clarify the anatomy and function of specific structures that will be used in this thesis. Section 2.2 describes patellar dislocation in children and adolescents, with its causes, diagnostic methods and treatments. Finally, section 2.3 provides an overview of current biomechanical methods used to assess musculoskeletal pathological conditions.

2.1 Anatomy and function of the knee

The knee joint allows the relative motion between three lower limb bones, i.e. femur, tibia and patella. A fourth bone, i.e. the fibula, is strongly connected to the tibia by means of ligaments and, even if it is not considered part of the knee joint, it provides attachment for important muscles and ligaments. The knee joint consists of two sub-joints, namely the tibiofemoral (TFJ) and the patellofemoral (PFJ) joints, whose names derive from those of the bones that are in mutual contact during knee motion. These sub-joints include several anatomical passive and active structures. Passive structures, such as articular surfaces and ligaments, can generate forces only if externally stressed. Contrarily, active structures, such as muscles, can intrinsically generate forces. The following sections will briefly describe the main anatomical components of the TFJ and PFJ, together with their respective functions. Moreover, the last section will summarise the main anatomical changes of the lower limbs during childhood.
2.1.1 **Tibiofemoral joint**

The TFJ allows the relative motion between two articular surfaces of the distal femur (i.e. medial and lateral femoral condyles) and two articular surfaces of the proximal tibia (i.e. medial and lateral tibial plateaus). These surfaces are lined by low frictional cartilage and lubricating synovial fluid that facilitate movement and transmission of loads (Sophia Fox et al., 2009). The femoral condyles and the tibia plateaus are also separated by two fibrocartilaginous structures, i.e. *menisci*, that play an important role in load transmission, shock absorption, as well as nutrition and lubrication of articular cartilage (LaPrade et al., 2017). The femur and the tibia-fibula complex are interconnected by four major ligaments: the *anterior cruciate* (ACL), the *posterior cruciate* (PCL), the *medial collateral* (MCL) and the *lateral collateral* (LCL) ligaments (Figure 2.1). These ligaments provide a bone-to-bone connection between the femur and tibia-fibula complex. The attachment regions of each ligament in the femur and in the tibia-fibula complex will be called *origin* and *insertion*, respectively. These four ligaments provide passive stability in all directions to the TFJ. Their attachment regions in the respective bones and their primary functions (Moore et al., 2010) are reported in Table 2.1.

![Figure 2.1 Lateral (a) and posterior (b) views of the knee. The main anatomical structures that represent the joint are shown (Pictures, 2003).](Image)
Table 2.1. Attachment regions and primary functions of the four major TFJ ligaments.

<table>
<thead>
<tr>
<th>Ligament</th>
<th>Origin</th>
<th>Insertion</th>
<th>Primary functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACL</td>
<td>Posterior part of the medial side of the lateral condyle of the femur</td>
<td>Anterior intercondylar area of the tibia</td>
<td>Limit posterior rolling of the femoral condyles on the tibia plateaus during TFJ flexion, prevent posterior displacement of the femur on the tibia and TFJ hyperextension</td>
</tr>
<tr>
<td>PCL</td>
<td>Anterior part of the lateral surface of the medial condyle of the femur</td>
<td>Posterior intercondylar area of the tibia</td>
<td>Limit anterior rolling of the femur on the tibia plateaus during TFJ extension, prevent anterior displacement of the femur on the tibia and posterior displacement of the tibia on the femur, prevent TFJ hyperextension</td>
</tr>
<tr>
<td>MCL</td>
<td>Medial epicondyle of the femur</td>
<td>Medial condyle of the tibia</td>
<td>Permit and limit rotation of the knee during TFJ flexion and resist angulation of the TFJ in the coronal plane</td>
</tr>
<tr>
<td>LCL</td>
<td>Lateral epicondyle of the femur</td>
<td>Lateral surface of the fibula head</td>
<td></td>
</tr>
</tbody>
</table>

The TFJ is a gliding hinge joint, or *trochoginglymos*, whose kinematics consists of spinning, rolling and sliding (Hirschmann et al., 2015). Mechanically, the TFJ motion can be described by six motion components, three rotations and three translations. Rotational movements include flexion-extension, internal-external, and varus-valgus, while translational movements occur in anterior-posterior and medial-lateral directions, but also by compression and distraction of the joint.

### 2.1.2 Patellofemoral joint

The patella is a large sesamoid bone that is anchored to the TFJ, both in the longitudinal and transverse directions, by a complex soft tissue system, composed by both active and passive structures. Inferiorly, the patellar tendon limits the proximal displacement of the patella from the tibia. This tendon originates at the distal apex of the patella and it inserts into the tibial tubercle, a pronounced tuberosity on the proximal-anterior aspect of the tibia. Superiorly, the patella is connected to the quadriceps muscles, a group of four muscles located in front of the thigh, via the quadriceps tendon. The rectus femoris muscle produces a force that acts along the femoral axis, while the oblique muscles, vastus medialis (VM) and vastus lateralis (VL), generate a transverse force vector (Amis et al., 2003; Farahmand et al., 2004). In the transverse direction, the patella is connected to the TFJ by ligaments, including the medial patellofemoral ligament (MPFL), the medial patellomeniscal and the medial patellotibial ligaments, and the retinaculum. All these structures, together with the PFJ articular geometry, contribute to
patellar stability. The posterior surface of the patella is covered by a thick layer (1-6 mm) of low frictional cartilage.

In a congruent PFJ, the patella moves slightly medially during early TFJ flexion. The patella then articulates to the *trochlea*, i.e. the articular portion of the anterior surface of the distal femur, at approximately 20-30° of TFJ flexion (Fulkerson, 2004).

The primary function of the patella is to facilitate the TFJ extension by increasing the moment arm of the quadriceps, especially in early degrees of TFJ flexion, from 30% near extension to 15% at 30° of TFJ flexion (Kaufer, 1971). Moreover, the patella centralises the divergent forces from the four quadriceps muscles, transmitting these forces to the patellar tendon.

### 2.1.3 Anatomical development of the lower limbs during childhood

The physis (or epiphyseal cartilage, or growth plate) is a hyaline cartilage plate at the end of a long bone. It mediates the longitudinal growth of the axial skeleton and, in addition to other bony extremities, it is responsible for shaping the trochlear groove. When the physis is ossified, the longitudinal growth is completed. Ossification of the physis occurs at approximately 14 years in girls and at about 16 years in boys (Hägg et al., 1991, 1992).

The alignment of the lower limbs has been shown to be age dependent. For example, there is a progressive change from bowlegs (TFJ varus) in the new-born to knock knees (TFJ valgus) at about 1-4 years of age (Popkov et al., 2015). Two to eight year-old children also exhibit a normal slight hyperextension of the TFJ, that diminishes over time (Soucie et al., 2011). Furthermore, femoral anteversion has been shown to decrease from around 25° at 8 years of age to 16° between 14 and 16 years of age, and it has been associated with a subsequent decrease in internal rotation of the femur (Mudge et al., 2014). These lower limb alignment characteristics are similar between boys and girls. However, contrarily from boys, girls have a higher generalised joint hyperlaxity at the beginning of puberty.

### 2.2 Patellar dislocation

#### 2.2.1 First-time lateral patellar dislocation

Patellar dislocation is a form of patellar instability that consists of a lateral movement of the patella outside the trochlear groove, resulting in a complete loss of contact between the articular surfaces of the femur and the patella. First-time patellar dislocation represents the cause of 3.3% of all sports related knee injuries in adults and children (Majewski et al., 2006). It is a relatively common injury in the paediatric and
adolescent population (Deie et al., 2003; Sillanpää et al., 2010; Stein et al., 2007), accounting for approximately 25-31.3% of acute knee trauma in skeletally immature patients with hemarthrosis (Abbasi et al., 2012; Luhmann, 2003). It is also the second most common cause of traumatic hemarthrosis in adolescents, after ruptures of the ACL (Abbasi et al., 2012). The annual incidence rate of first-time patellar dislocation varies between 13.5 and 147.7 per 100000 in individuals aged nine to 19 years (Atkin et al., 2000; Fithian et al., 2004; Gravesen et al., 2017; Hsiao et al., 2010; Nietosvaara et al., 1994; Sanders et al., 2018b). Given the relatively large span of reported incidence in the literature, probably due to different criteria and age groups included in the studies, a detailed description of the incidence of primary patellar dislocation found in the different studies is provided in Table 2.2. The risk of acute dislocation is particularly high in females aged ten to 17 years (Fithian et al., 2004; Nikku et al., 2005; Sillanpää et al., 2008), with a reported annual incidence of 108 per 100000 (Gravesen et al., 2017). However, despite reporting higher rates of primary patellar dislocation associated with female adolescents, some studies did not find significant differences between genders when comparing the risk of dislocation (Atkin et al., 2000; Gravesen et al., 2017; Waterman et al., 2012).

Table 2.2. Reported incidence of first-time patellar dislocation in children and adolescents.

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Age group</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nietosvaara (1994)</td>
<td>&lt; 16 years</td>
<td>43 per 100000</td>
</tr>
<tr>
<td>Atkin (2000)</td>
<td>10-19 years</td>
<td>31 per 100000</td>
</tr>
<tr>
<td>Fithian (2004)</td>
<td>10-17 years</td>
<td>30 per 100000</td>
</tr>
<tr>
<td>Hsiao (2010)</td>
<td>&lt; 20 years</td>
<td>112 per 100000</td>
</tr>
<tr>
<td>Gravesen (2017)</td>
<td>10-17 years</td>
<td>108 per 100000</td>
</tr>
<tr>
<td>Sanders (2018)</td>
<td>&lt;14</td>
<td>13.5 per 100000</td>
</tr>
<tr>
<td></td>
<td>14-18 years</td>
<td>147.7 per 100000</td>
</tr>
</tbody>
</table>

Primary (first-time) lateral patellar dislocation may be triggered by a traumatic event in patients with normal patellofemoral alignment or it may occur in patients with pre-existing misalignments, especially in the presence of patellar subluxation (Diederichs et al., 2013). Patellar dislocation often occurs during sports activities, where the TFJ is slightly flexed (between 20˚ and 30˚ of flexion), internally rotated and in valgus with the foot fixed to the ground, and the quadriceps activated (Cash et al., 1988; Gross, 1986; Lewallen et al., 2013b; Nikku et al., 2009; Sarimo et al., 2003). This mechanism of injury has been shown to be responsible of up to 93% of primary patellar dislocations (Sillanpää et al., 2008). Two other possible, but quite rare, injury mechanisms include TFJ acceleration or deceleration from a deep flexed position. In fact, Nikku et al. (2009) found that the 8% of 126 patients involved in their study experienced primary patellar
dislocation while extending the knee, during an accelerating movement from a bent start (e.g., standing up from a seat, taking off to a jump, lifting from a bent position). Few patients (3%) experienced patellar dislocation due to a decelerating mechanism at high degrees of TFJ flexion (70-90˚) (Nikku et al., 2009). The primary acute dislocation frequently occurs as a sudden event and it may lead to a fall and severe discomfort at the knee. However, following the first occurrence of dislocation the knee is still visibly unstable and the apprehension of a recurrent episode is the most outstanding symptom (Chotel et al., 2014), often together with pain and swelling. Ongoing pain, patellar instability and limitations in highly demanding physical activities have been shown to affect up to 58% of patients who experienced first time dislocation (Atkin et al., 2000; Hawkins et al., 1986). Often, after the dislocation, the patella spontaneously relocates in the trochlear groove as the patient extends the knee. If this is not the case, the patella must be relocated in the trochlear groove by a health professional.

2.2.2 Recurrent patellar dislocation

Some patients will only experience a single episode of patellar dislocation, while others could experience a second or subsequent episode of dislocation. Patients in the latter category are defined as recurrent patellar dislocators, not be confused with habitual patellar dislocators, who experience involuntary patellar dislocation and relocation with every cycle of knee flexion and extension, or with congenital patellar dislocators, whose dislocation is caused by intrauterine lower limb deformities (Parikh et al., 2016).

Recurrent patellar dislocation is the mildest, but also the most common form of patellar instability (Chotel et al., 2014). After an acute patellar dislocation, the risk of recurrent dislocation in children and adolescents has been reported to be up to 67% following MPFL reconstruction (Palmu et al., 2008), between 24.7% and 71% following non-operative treatment (Jaquith et al., 2017; Kaewkongnok et al., 2018; Lewallen et al., 2013b; Palmu et al., 2008) and between 35.5% and 44.8% irrespective of treatment (Gravesen et al., 2017; Sanders et al., 2018a). The rate of recurrent dislocation after an acute first time patellar dislocation is higher in children and adolescents compared to adults (Buchner et al., 2005; Cash et al., 1988; Gravesen et al., 2017; Kaewkongnok et al., 2018; Larsen et al., 1982) and in patients aged less than 15 compared to patients aged 15-18 (Jaquith et al., 2017) or 15-19 (Kaewkongnok et al., 2018). The coincidence of the peak age with puberty may reflect both changes in axial alignment of the lower limbs and in level of activity of the subject. Moreover, patients under the age of 17 have been shown
to be at highest risk (11.1%, against 5% in patients aged 18 or older) of suffering a patellar dislocation in the other knee after a primary patellar dislocation (Gravesen et al., 2017).

2.2.3 Aetiology

It has been shown that patellar instability is associated with family history of instability in 28% of the cases (Crosby et al., 1976), however, the pattern of inheritance has not been identified yet. Some anatomical risk factors might be evident already in utero. The quadriceps muscle can be discerned at approximately four weeks of gestation, soon after the limb bud appears. During the 7th week of gestation, a first evidence of a cartilaginous patella can be identified between the quadriceps and the femoral condyles (Walmsley, 1940). At 13 weeks of gestation the femoral condyles have a similar morphology to the adult knee, and by 23 weeks of gestation the lateral patellar facet is pronounced (Glard et al., 2005a; Glard et al., 2005b; Walmsley, 1940). Two recent studies (Øye et al., 2016; Øye et al., 2015) examined the shape of the femoral trochlea in newborns using ultrasounds, finding that trochlear dysplasia can be found at birth.

Several risk factors that predispose an individual to recurrent patellar dislocation have been proposed, including young age, female sex, prior dislocation, family history and sports participation (Fithian et al., 2004). Moreover, numerous morphological risk factors have been identified. Dejour et al. (1994) described major and minor anatomical factors that characterise patients with patellar instability. According to their classification, major risk factors included a dysplastic trochlea, patella alta, a laterally located tibia tubercle and patellar tilt.

A dysplastic trochlea is characterised by abnormal trochlear morphology and a shallow trochlear groove. Dejour et al. (1994) classified trochlea dysplasia into four groups (Figure 2.2), where:

- Type A defines a normal shape of the trochlea, but a shallow trochlear groove;
- Type B defines a markedly flattened/convex trochlea;
- Type C defines trochlear facet asymmetry, with too high lateral facet;
- Type D defines Type C features and a vertical link between facets.
In the presence of a dysplastic trochlea, the trochlear groove is unable to provide adequate anatomical restraints to the patella, which is likely to dislocate. Nowadays, many studies use this classification to assess the risk of recurrent dislocation in children and adolescents. In fact, it has been shown that trochlea dysplasia is present in up to 67% of young patients who suffer from recurrent patellar dislocation (Jaquith et al., 2017; Nelitz et al., 2013; Schoettle et al., 2005; Seeley et al., 2012). However, the Dejour’s classification should be interpreted with caution in paediatric populations as an incomplete ossification of the trochlea might lead to incorrect classifications.

Patella alta describes a scenario where the position of the patella is considered high. This parameter has been commonly reported to assess the risk of recurrent dislocation in young individuals (Deie et al., 2003; Edmonds et al., 2016; Jaquith et al., 2017; Nelitz et al., 2013; Palmu et al., 2008; Regalado et al., 2014). Patella alta decreases contact between the patella and the trochlea, because the degree of TFJ flexion at which the patella engages in the trochlea is higher than in a normal knee. This contributes to decreasing resistance to lateral translation of the patella (Singerman et al., 1994; Ward et al., 2007a).

A lateralisated position of the tibia tubercle reflects torsional abnormalities of the lower limbs and it increases lateral force displacement on the patella during motion (Balcarek et al., 2011). This amount of lateralisation is generally measured as the distance between the tibia tuberosity and the trochlear groove (TT-TG distance). Higher values of TT-TG distance have been measured in young recurrent patellar dislocators with respect to age-matched healthy controls (Dickens et al., 2014; Pennock et al., 2014).
Other minor factors that have been associated with patellar instability are excessive femoral anteversion, excessive external rotation of the tibia, genu recurvatum and genu valgum (Dejour et al., 1994) and inadequate soft tissue restraints. The MPFL is the major passive soft-tissue restraint to lateral patellar displacement, providing 50% to 60% of lateral restraint from 0º to 30º of TFJ flexion (Desio et al., 1998). In patients who experienced lateral patellar dislocation the MPFL is generally ruptured due to the large excursion of the dislocated patella. Furthermore, active muscle contributions from the VM and the VL can pull the patella medially or laterally and, therefore, an imbalance of strength or orientation between these two muscles can lead to patellar instability (Senavongse et al., 2005).

2.2.4 Patient’s history and physical examination

A detailed history of the paediatric patellar dislocator should be gathered, including previous trauma, age at primary dislocation, the number of dislocation events and family history of patellar instability. During the examination, anatomical abnormalities, together with the size and the position of the patella should be observed. Joint laxity and hypermobility are also quantified, commonly by using the Beighton score, a simple nine-point system, where the higher the score the higher the laxity (Beighton et al., 1973; Smits-Engelsman et al., 2011). Patellar tracking during normal TFJ flexion and extension is also evaluated, as it can reveal deviation from the normal trajectory. The J-sign is a common diagnostic test used to identify abnormal patellar tracking. A positive J-sign describes an exaggerated lateral to medial translation of the patella into the trochlear groove in early TFJ passive flexion. Standing examinations are also performed, as they can clinically reveal genu valgum and increased quadriceps angle, or Q-angle. The Q-angle is the angle between the line that runs from the anterior superior iliac spine to the centre of the patella and the line that runs from the centre of the patella to the tibial tubercle (Brattström, 1964). An increased Q-angle causes a lateral patellar shift in early TFJ flexion. Assessment of lower limb miserable malalignment, such as excessive femoral anteversion and external tibial torsion, is commonly performed. The apprehension test can also be conducted to identify patients with excessive patellar mobility. This test is considered positive when the knee is relaxed at 30º of TFJ flexion and, when the examiner tries to push the patella laterally, this causes anxiety or involuntary quadriceps muscle contraction in the patient. Finally, lateral mobility of the patella is assessed, by applying lateral pressure to the patella and observing the amount of lateral translation (Tanner et al., 2003).
2.2.5 Diagnostic imaging

Several imaging techniques and measurements can be used to assess the various causes of patellar dislocation. This section will highlight those used in paediatric cohorts to assess the anatomical risk factors previously described. A more detailed description of all the measurements will be provided in Chapters 3 and 4.

Standard workup for patients with patellar instability includes lateral, anteroposterior, and one of the several patellofemoral radiographic views (sunrise/skyline view or Merchant view) (Merchant et al., 1974; Popkin et al., 2018).

The sulcus angle, defined as the angle between the highest points of the medial and lateral femoral condyles and the lowest point of the intercondylar sulcus, is used to assess trochlear dysplasia. These measurement has been performed by using different medical imaging techniques, varying from computed tomography (CT) (Aulisa et al., 2012), radiographs (Deie et al., 2003), Ultrasound (Nietosvaara et al., 1997) and MRI (Seeley et al., 2012). Compared to healthy participant, young patellar dislocators exhibited shallower sulcus angle (157°±7° compared to 145°±6° in controls) (Nietosvaara et al., 1997).

Patellar height is generally assessed on lateral radiographs with the knee flexed at 30°. A common index used for the assessment of patella alta is the Insall-Salvati index, which is defined as the ratio between the patellar tendon length and the length of the patella. However, challenges exist when measuring patellar height in a more cartilaginous knee of a child from radiographs. This might explain the finding that patella alta measured from radiographs was not a risk factor for patellar dislocation in young patients (Lewallen et al., 2013b).

The TT-TG distance is measured by superimposing the MRI (or CT) slide that best represents the trochlea and the slide that passes through the tibial tuberosity. Two lines, one passing through the bottom of the trochlear groove and one at the centre of the tibial tuberosity, are drawn perpendicularly to the posterior condylar line. This parameter has been shown to increase logarithmically with age (Dickens et al., 2014).

Lower limb alignment and rotational profile abnormalities (i.e., femoral anteversion and tibial torsion) can be assessed by using CT or MRI (Muhamad et al., 2012). Moreover, MRI can help evaluating the integrity of soft-tissue stabilisers of the patella (e.g., MPFL, VM) and identifying associated chondral injuries.
2.2.6 Treatment

Nonoperative treatment is highly recommended for primary lateral patellar dislocation in young patients (Palmu et al., 2008). Nonoperative management varies from brief immobilisation (two to four weeks) to immediate motion and physical therapy (Chotel et al., 2014). Physical therapy that focuses on strengthening the vastus medialis obliquus and gluteus muscles can improve patellar stability (McConnell, 2007). Lateral stabilisation braces can also enhance the sense of stability of the patient (Khormaei et al., 2015). Surgery is indicated when symptoms do not improve with nonoperative treatment and/or subsequent dislocation events are experienced. Atkin et al. (2000) showed that, at six months after nonoperative treatment for primary patellar dislocation, 58% of patients still had limitations with demanding sports activities and 55% had not returned to sports.

More than 100 surgical procedures have been introduced for the treatment or prevention of recurrent patellar dislocation after a fist-time episode (Fithian et al., 2001), suggesting a lack of understanding or agreement of the contributing factors to patellar stability. Surgical procedures typically involve a combination of methods, varying from bony to soft tissue procedures. Bony procedures include femoral derotational osteotomy, guided growth procedures, trochleoplasty and tibial tubercle transfer. Femoral derotational osteotomy is indicated for patients with excessive femoral anteversion (>20º) (Weber et al., 2016b). In this procedure the femur is cut at its proximal end and then rotated laterally. Guided growth procedures are possible in skeletally immature patients and involve manipulating growth of the physis to gradually correct bony deformity. These type of procedures are used, in presence of genu valgum, to restore the anatomical relationship between the knee joint and the extensor mechanism by aligning the patient’s mechanical axis to the centre of the knee (Kearney et al., 2015). A trochleoplasty procedure may be indicated in patients with abnormal trochlea morphology and involves creation of a deeper trochlear sulcus removing cancellous bone in the groove and repositioning the cortical bone to provide more anatomical patellar stability (Dejour et al., 2018). On the other hand, realignment of the tibial tubercle is indicated in case of patellar maltracking secondary to an increased TT-TG distance. Patella alta may also be corrected in this manner, if it is present. Anteromedialisation of the tibial tubercle (Fulkerson procedure) (Fulkerson, 1983) and medial tubercle transfer (Elmslie-Trillat procedure) (Trillat et al., 1964) are two of the most common forms of tibial tubercle transfer. However, trochleoplasty and tibial tubercle transfer are contraindicated in patients with open physes, as they can violate bone growth (Weber et al., 2016b). Contrarily, soft tissue procedures are deemed safe in the paediatric population and,
therefore, they are more common. These procedures include VM obliquus advancement, MPFL reconstruction, patellar tendon transfer and lateral retinacular release. When the VM obliquus has a proximal insertion onto the patella, a VM obliquus advancement is performed to rebalance the quadriceps force vector. This procedure consists of a detachment of the insertion of the muscle and a subsequent attachment onto the middle and distal aspects of the patella. MPFL reconstruction involves creating a new ligament to compensate for the damaged one. One technique involves removal of a hamstring tendon which is then fashioned into a new ligament. It has been shown (Ostermeier et al., 2006) that reconstruction of the MPFL better stabilised patellar movement under a laterally directed force than medial transfer of the tibial tuberosity. The medial transfer of the lateral part of the patellar tendon is defined as Roux-Goldthwait procedure and it is used to achieve distal alignment of the extensor mechanism. Medialisation of the patellar tendon attachment can be combined with lateral retinacular release. The latter procedure might be indicated when patellar tilt is higher than 20º and the patella cannot be adducted to neutral during physical examination (Weber et al., 2016b).

2.3 Using biomechanics to assess patellar instability

Clinical examinations, patient’s history and diagnostic imaging methods can provide valuable information regarding PFJ anatomy and mechanics. However, these methods alone cannot fully describe the PFJ injury mechanism and they are not sufficient to establish cause-effect relationships in such a complex dynamic system. In fact, most of the aforementioned metrics are static measurements of PFJ alignment and they are unable to characterise the patellar dislocation mechanism during dynamic tasks. Clinical gait analysis and more advanced computational models can complement clinical examination and medical imaging findings in treatment planning for recurrent patellar dislocation.

2.3.1 Gait analysis

Clinical motion analysis has been extensively used to assess dynamic joint movements during everyday activities, such as gait. Gait analysis uses three-dimensional motion capture system to track the position of markers attached to the participant’s skin and force plates to measure the loads applied to the ground through the participant’s feet (i.e. ground reaction forces). The collected data are then processed by using simple biomechanical models that are mostly based on the Newington Children’s Hospital (Davis et al., 1991) and the Helen Hayes models (Kadaba et al., 1990). These models, which use the minimal number of markers to compute three-dimensional joint kinematics, can be computed in motion capture software such as Vicon Nexus (Vicon Motion...
Systems, Oxford, UK) using the Plug-in-Gait model. This model uses a direct kinematics approach (Kadaba et al., 1990), which assumes that the experimental markers are rigidly attached to the bony segments, to estimate joint kinematics. Joint kinematics are then computed as Cardan angles between adjacent segments defined from the three-dimensional marker position (Cappozzo et al., 2005) and inertial properties of the body segments are estimated by using regression equations (Davis et al., 1991). In clinical settings, the resulting kinematic and kinetic data of each patient are compared to the data of aged-matched healthy participants to identify each individual’s primary impairment. The findings from this comparison are then used to inform the clinical decision making process (Baker, 2013).

Nowadays, gait analysis is commonly used to identify the causes of abnormal gait characteristics in children with cerebral palsy (Chang et al., 2006). However, it can also be used to evaluate if patients with patellar instability exhibit peculiar gait patterns that may functionally place adverse forces on the patella (Smith et al., 2008a). It has been shown (Carnesecchi et al., 2016; Fulkerson, 2004; Sowiński et al., 2010) that, when compared to normal gait, the gait of patients affected by patellar dislocation is characterised by reduced gait speed, reduced step frequency and hyperextension of the knee during limb-support phase. Furthermore, patients suffering from patellar dislocation exhibit a significantly smaller knee extension moment than healthy subjects during the whole gait cycle (Asaeda et al., 2016). Also, gait analysis can help understand the interplay of the segments and joints of the lower extremity, which may have an effect on PFJ mechanics (Powers, 2003).

Therefore, gait analysis can help investigate unique gait characteristics typical of patients with patellar dislocation. However, this approach has some limitations. First, while this approach can detect altered lower-extremity kinematics and kinetics, it is unable to accurately track the patella motion. In fact, even if a marker is applied on the skin above the patella, this marker will not follow potential underlying movements of the patella. For this reason, studies that measured in vivo patellar tracking during gait used intracortical pins (Lafortune, 1984). Nevertheless, this method is invasive and cannot be used in paediatric populations. Second, gait analysis uses link-based models and simplified representations of the joints, which cannot provide accurate measure of joint kinematics. For example, it has been shown that spherical or hinge knee joints, that are commonly employed in gait analysis models, cannot accurately estimate in vivo secondary knee kinematics, especially joint translations (Andersen et al., 2010; Stagni et al., 2009). Finally, since gait analysis models do not include anatomical characteristics of
the PFJ, they cannot provide patient-specific insights on the PFJ (dys)function. Recently, user friendly musculoskeletal (MSK) modelling software (e.g., Opensim (Delp et al., 2007) and AnyBody (Damsgaard et al., 2006)) has enabled accurate, non-invasive and personalised analyses (Gerus et al., 2013) of the participant’s joint kinematics, kinetics and internal loads (e.g., muscle and joint contact forces).

2.3.2 Musculoskeletal models

MSK models are computational representations of a participant’s MSK anatomy. These models are multibody systems consisting of rigid bodies (bones) connected by joints and actuated by muscle actuators that are represented as linear or curvilinear pathways. The lower limb MSK anatomy is generally obtained from dissections of healthy adult-male cadaveric specimens (Brand et al., 1982; Friederich et al., 1990; Horsman et al., 2007) and used to generate generic models (Arnold et al., 2010; Delp et al., 1990; Modenese et al., 2011). Furthermore, the inertial properties of the lower limb body segments (i.e., mass, centre of mass and moments of inertia) are estimated from predictive equations reported in literature (De Leva, 1996; McConville et al., 1980).

Prior to any application of these models, the bone dimensions and the inertial properties of the body segments are linearly scaled to fit the anthropometry of individual participants. Thus, the dimension of the bones in MSK models is adjusted, for each individual, using bone measurements obtained from three-dimensional motion capture skin markers placed over bony prominences (e.g., anterior superior iliac spine). Consequently, the muscle attachments are adjusted according to the scaled bone dimensions, which will then adjust musculotendon lengths and physiological muscle properties (Winby et al., 2009). Moreover, the mass of each body segment is estimated based on the redistribution of the total body mass according to the scaled dimension of the bodies (De Leva, 1996). Once the MSK model is scaled to match the participant’s anthropometry, it can be used to perform further analyses.

Conversely to traditional gait analysis, MSK modelling software generally uses inverse kinematics approaches to compute joint angles (Andersen et al., 2009; Duprey et al., 2010). The inverse kinematics approach consists of adjusting the joint angles of the model to obtain the best match between modelled and experimental marker positions. When compared to Plug-in-Gait models, generic MSK models together with an inverse kinematics approach showed less variability in joint kinematics results and they were deemed appropriate for clinical gait analysis (Kainz et al., 2017). The benefit of MSK models, together with an inverse kinematic approach, is the ability to perform additional MSK analyses. For example, the joint angles obtained from the inverse kinematics,
combined with the measured ground reaction forces, can be used in the inverse dynamics analysis to estimate joint kinetics (Zajac et al., 2002). The resulting joint moments can then be used to estimate muscle forces using optimisation approaches that best match the joint moments resulting from inverse dynamics and the joint moments generated by the muscle forces (Delp et al., 2007). Optimisation approaches include static optimisation (Zajac, 1989), computed muscle control (Thelen et al., 2003) and dynamic optimisation (Anderson et al., 2001). However, all the listed optimisation approaches cannot account for variation in muscle activations between individuals (Lloyd et al., 2001) and tasks (Buchanan et al., 1995). An alternative approach to overcome this limitation consists of using electromyography (EMG) informed models, where EMG signals and joint angles are used to estimate individual muscle forces (Buchanan et al., 2004; Lloyd et al., 2003) and joint contact forces (Saxby et al., 2016).

Scaled-generic MSK models have been widely used and their performance have been validated against different tasks. For example, it has been shown that scaled-generic models well predicted knee moments during running and cutting manoeuvres (Lloyd et al., 2003) and medial and lateral knee contact forces during gait in healthy participants (Winby et al., 2009). However, in the clinical setting, it is questionable whether the results from these scaled-generic MSK models can inform surgical planning on an individual basis (Blemker et al., 2007) or whether the kinematic, kinetic and muscle force results can accurately replicate pathological locomotion (Scheys et al., 2011b). Problems might arise due to the fact that, as mentioned before, the anatomical parameters included in generic MSK models were derived from a limited set of adult cadavers with no musculoskeletal deformities. Therefore, even after scaling, a generic model may not accurately represent the MSK anatomy of the paediatric population, especially when pathology exists (Arnold et al., 2001; Correa et al., 2011). Moreover, it has been shown that, in addition to skeletal geometry, the outputs of dynamic simulations are sensitive to muscle attachment location and joint definition (Lenaerts et al., 2008). As an alternative to generic MSK models, subject-specific models can be created using medical imaging techniques. Therefore, personalised MSK anatomy and joint parameters can be incorporated into the models to increase the accuracy of MSK model’s predictions and, potentially, expand their use in clinical practice.

Subject-specific models can encompass both MSK and neuromuscular properties of an individual. Hence, different levels of personalisation can be incorporated in a model, depending on the intended application and data availability. The process of generating subject-specific models starts with medical imaging acquisition, such as MRI or CT,
which can be used to measure different modelling parameters. These data include tissue volumes and densities to calculate inertial properties of the lower limb bodies (e.g., thigh, shank), body landmarks locations to determine body and joint reference systems, muscle attachment positions to define the geometry of the muscles and musculotendon properties to compute the capacity of a muscle to generate force. This information is then assembled to create personalised models into MSK software (i.e., OpenSim or AnyBody). The final model, driven by motion capture and ground reaction force data, will then allow estimation of joint kinematics, kinetics and internal loads.

Numerous subject-specific rigid-body models, that include personalised MSK anatomy, have been created for gait analysis in adults (Gerus et al., 2013; Lenhart et al., 2015; Marra et al., 2015; Martelli et al., 2015; Scheys et al., 2005; Taddei et al., 2012; Valente et al., 2014; Wesseling et al., 2016) and children with pathologies (Bosmans et al., 2014; Correa et al., 2011; Kainz et al., 2016; Modenese et al., 2018). However, some of these studies, rather than using the fully reconstructed three-dimensional anatomy, merged generic bone volumes with image-based bony volumes (Marra et al., 2015) or with the bone volumes adjacent to the joints (Lenhart et al., 2015). Moreover, two of these studies (Modenese et al., 2018; Valente et al., 2014) have also incorporated personalised inertial properties (i.e., mass, centre of mass and moments of inertia) of the body segments. These properties were estimated using NMSBuilder software (Valente et al., 2017), which was specifically designed to create subject-specific models for OpenSim. This software computes the inertial properties based on the tissue density and the measured tissue’s volume. Other subject-specific models, including personalised musculotendon geometry and properties (Blemker et al., 2006; Correa et al., 2011; Fernandez et al., 2005), have been proposed and used for gait analysis. Furthermore, an additional level of subject specificity can be achieved by personalising the definition of the joint kinematic models. Given that this aspect is one of the primary aims of this thesis, it will be discussed separately in the next section of this chapter.

As previously mentioned, the capability of incorporating personalised and/or abnormal MSK characteristics makes subject-specific models particularly attractive, especially if the goal is to translate the outputs of these models into clinical practice to inform operative management. Moreover, when compared to scaled-generic models, subject-specific models derived from medical imaging better predicted joint contact forces (Gerus et al., 2013) and knee joint moments (Tsai et al., 2012). Gerus et al. (2013) also showed that, when incorporating personalised anatomy and TFJ kinematics into an EMG-driven model, the estimation of medial and lateral knee contact forces improved by
Literature review

47% and 7%, respectively, compared to scaled-generic models. Furthermore, subject-specific models provided better estimates of TFJ (Marra et al., 2015) and hip (Lenaerts et al., 2008) contact forces, hip and joint moments (Scheys et al., 2011a), musculotendon length and moment arms (Arnold et al., 2000) during gait, compared to scaled-generic models.

Despite the attractiveness of these subject-specific models, their development and applications are limited by the demanding process of model creation that requires specialised skills across multiple applications and can be costly and highly time-consuming. In fact, three-dimensional reconstruction of MSK anatomy is based on image segmentation, which requires the delineation of the tissue of interest on the two-dimensional medical imaging slides to create a three-dimensional anatomical mesh. This process can be manual or semi-automatic and can be very time consuming. For example, Brito da Luz et al. (2017) reported that the time required to reconstruct single leg bones, articular cartilage and ligaments for one participant was approximately 11 hours. Finally, the creation of subject-specific models for paediatric populations is even more challenging, given the limited choice of medical imaging techniques that do not expose the participant to ionizing radiation. MRI is a safe technology for children, however, the acquisition time can be considerably long (approximately 60 minutes in a clinical service) and not tolerable for some participants. Additionally, the restraining size and shape of the MRI scanner can be intimidating for some children.

Statistical models of bone shape are emerging techniques that have the potential to reduce MRI acquisition times and avoid the full segmentation of individual tissues. In fact, statistical shape modelling methods can be used to rapidly create personalised anatomical models from sparse medical imaging data and three-dimensional motion capture data (Zhang et al., 2016a). For example, high resolution MRIs of the proximal femur have been used to reconstruct a full-length femur (Zhang et al., 2014a). These methods consist of a preliminary registration of the generic bone volume based on the position of anatomical landmarks from three-dimensional motion capture, and a subsequent registration of the point clouds generated from the sparse manual segmentation of medical images to the generic bone volume. The latter registration is performed by using two algorithms of principal components fitting and parametric mesh fitting, both implemented in the open source Musculoskeletal Atlas Project (MAP) client software (Zhang et al., 2014b). However, the use of statistical shape modelling methods, despite providing clinically feasible runtimes, cannot be used to generate personalised paediatric models at this stage. In fact, these models are trained on a medical imaging
dataset sampled from a population of interest. At the moment, the population included in the dataset has an average age of 53.3±19.9 years (Zhang et al., 2016b) and, therefore, may not be representative of the paediatric anatomy, even after registration and morphing. The lack of a comprehensive paediatric imaging database limits the use of these methods in children. Moreover, these models might not be able to capture abnormal bony morphology in patients suffering from recurrent patellar dislocation (e.g., trochlea dysplasia), limiting their use for individualised surgical planning.

2.3.3 Knee joint kinematics models

The relative motion of rigid-body segments in MSK models is described by joint kinematic models. For the lower limbs, these joint models include the hip, TFJ, PFJ, the ankle (often defined as talocrural joint and subtalar joint) and the foot (often simplified to the metatarsophalangeal joint) (Delp et al., 1990). The definition of these joints varies from simple mechanical connections (e.g., spherical joint, hinge joint) to more complex relationships, according to the research question being addressed (Hicks et al., 2015). Given that the aim of this thesis was to model the TFJ and PFJ in a paediatric population, this section will describe the several approaches used to model those two specific joints.

Generic rigid-body MSK models employed for gait analysis use different implementations of the TFJ and PFJ, with different number of degrees of freedom (DoF). For example, Delp et al. (1990) defined both the TFJ and PFJ as 1-DoF planar mechanisms, which describe the sagittal motion of the tibia relative to the femur (TFJ) and the sagittal motion of the patella relative to the tibia (PFJ) as function of the TFJ flexion angle. These mechanisms are a three-dimensional modification of a planar model of the knee (Yamaguchi et al., 1989). The geometry of the femoral condyles and the tibia plateaus was obtained from a cadaver and represented as an ellipse and a line segment, respectively. The tibiofemoral contact throughout the TFJ flexion ROM was maintained according to data reported by Nisell et al. (1986). The TFJ hinge axis was defined as the segment connecting the medial and lateral femoral epicondyles. The flexion/extension rotation for the PFJ was derived from experimental measurements (Van Eijden et al., 1985) and the patellar tendon was considered rigid, i.e. no change in length was allowed. This TFJ model has been slightly modified in some studies to allow TFJ internal/external rotation (Winby et al., 2009) and also TFJ ab/adduction (Gerus et al., 2013). The ROM of these rotations was constrained, using either cadaveric data (Kanamori et al., 2000) or in vivo bone-pin measurements (Benoit et al., 2007), to ensure physiological kinematics.

Alternatively, other authors (Arnold et al., 2010; Rajagopal et al., 2016) used the joint kinematic equations defined by Walker et al. (1988) to describe the TFJ kinematics.
in their MSK models. Walker et al. (1988) used 22 cadaver subjects to define two TFJ rotations (internal/external and ab/adduction) and three TFJ translations (anterior/posterior, proximal/distal and medio/lateral) as function of the TFJ flexion angle. Rajagopal et al. (2016) additionally modified the PFJ such that the patella articulated with the femur, rather than with the tibia.

Prior to any use of a generic MSK model, the joint kinematics are linearly scaled, using the same scale-factors defined for the anatomy and inertial properties of the body segments. Despite the convenience and ease of this approach, some limitations have been described. First, it has been demonstrated (Andersen et al., 2010; Stagni et al., 2009) that simplistic representations of the TFJ (i.e., spherical or hinge joints) cannot accurately estimate in vivo secondary knee kinematics, especially joint translations. Second, Gasparutto et al. (2015) showed that scaled-generic TFJ kinematics obtained from Walker et al. (1988) do not accurately estimate TFJ ab/adduction and internal/external rotations measured from in vivo bone-pin data. Third, the TFJ and PFJ kinematics reported in literature derive from adult cadaveric participants and they might not be able to capture paediatric-specific anatomical characteristics (e.g., ligamentous hyperlaxity), especially when pathology exists (e.g., trochlea dysplasia). In fact, as the morphology of the TFJ articulating surfaces directly affects the TFJ kinematics (Amiri et al., 2006; Hashemi et al., 2008), a dysplastic trochlea and/or patella are likely to influence the PFJ kinematics in patients with recurrent patellar dislocation. Therefore, more complex and personalised TFJ and PFJ models are required to investigate pathological conditions, such as recurrent patellar dislocation, in children and adolescents.

Subject-specific TFJ kinematic models used in rigid-body MSK models vary in terms of level of personalisation and also number of DoFs. For example, some authors (Martelli et al., 2015; Valente et al., 2014) incorporated a simple 1-DoF hinge TFJ, with only TFJ flexion/extension, in their subject-specific MSK models to perform gait analysis. Scheys et al. (2011b) linearly adjusted the TFJ anterior/posterior and proximal/distal translations, which were based on a generic model (Yamaguchi et al., 1989), according to the size of the participant’s femur and tibia measured from CT. A similar approach was used by Arnold et al. (2000), who used a cadaveric-based model (Walker et al., 1988) and linearly scaled TFJ translations based on the bone dimensions measured from MRI. Conversely, Gerus et al. (2013) adjusted the generic spline functions (Donnelly et al., 2012), which describe the generic TFJ kinematics, to represent experimental TFJ translations measured using fluoroscopy.
Alternatively, more complex TFJ models based on parallel mechanisms have been developed. These mechanisms are suitable to model the joint passive motion, in other words the motion of the joint under virtually unloaded conditions, which is believed to have fundamental relevance for a thorough insight of the joint kinematics (Goodfellow et al., 1978). Passive motion involves only the passive structures that guide the motion of the joint, i.e. bones and ligaments. Experimental analyses showed that a bundle of fibres of the ACL, PCL and MCL remains almost isometric during passive TFJ flexion (Fuss, 1989; Rovick et al., 1991). Therefore, if the isometric ligamentous fibres are assumed as truly isometric (i.e., no change in length is allowed) and the contact between femur and tibia is assumed to occur on two points, a three-dimensional rigid-link parallel mechanism can be defined for the TFJ (Figure 2.3). The five rigid links in this mechanism are the vectors connecting the tibiofemoral articulating surfaces and the origins and insertions of the ACL, PCL and MCL. This mechanism describes the TFJ as a 1-DoF mechanism, guided by TFJ flexion and with coupled rotations (ab/adduction, internal/external) and translations (anterior/posterior, proximal/distal, medio/lateral).

![Figure 2.3. Five-rigid-link TFJ parallel mechanism (Parenti-Castelli et al., 2013). $A_1$-$A_5$ represent the ligament insertions on the tibia and the tibial sphere centres, while $B_1$-$B_5$ represent the ligament origins on the femur and the femoral sphere centres.](image)

Several 5-rigid-link parallel mechanism have been introduced over the last years to describe the passive TFJ kinematics, from Wilson et al. (1997) to other similar models with several similarities but with increased complexity (Di Gregorio et al., 2003; Feikes et al., 2003; Ottoboni et al., 2010; Parenti-Castelli et al., 2000; Parenti-Castelli et al., 2004; Sancisi et al., 2011a). These authors approximated the articular contacts of the femoral condyles and tibia plateaus with different geometric objects: i) spheres-on-planes (Di Gregorio et al., 2003; Parenti-Castelli et al., 2000; Wilson et al., 1997), ii) ellipsoid-on-spheres (Di Gregorio et al., 2003; Ottoboni et al., 2010) and iii) spheres-on-spheres (Di Gregorio et al., 2003; Parenti-Castelli et al., 2000; Sancisi et al., 2011a). When
compared to experimental TFJ kinematics measured from cadavers, the sphere-on-spheres approximation produced the most accurate results and low computational time (Ottoboni et al., 2010). It has to be noted that all the aforementioned TFJ mechanisms have been implemented by deriving the geometrical parameters (e.g., sphere centres, location and orientation of the planes, as well as ligaments’ attachment points) from cadavers. Moreover, the experimental TFJ passive kinematics were measured on cadavers and used both to optimise the geometrical parameters of the model and to validate the estimated TFJ kinematics (Ottoboni et al., 2010; Sancisi et al., 2011b). Only Brito da Luz et al. (2017) developed a new optimisation method to estimate subject-specific passive TFJ kinematics of 14 healthy adults. In this study, each participant’s geometrical parameters were estimated from MRIs and used to solve a 5-rigid-link parallel mechanism. Moreover, this study used previously published kinematic data to constrain the pattern of the estimated TFJ kinematics. This study represents an important step towards personalisation of complex knee models, however, it has not been directly validated yet.

Gasparutto et al. (2012) further increased the complexity of the previously described 5-rigid-link parallel mechanism by introducing the LCL (6-links) and allowing for minimal deformation of the four ligaments (i.e., ACL, PCL, MCL, LCL). This model was able to estimate ligament length variations during passive knee flexion and loaded conditions (i.e., during gait). It has been shown (Gasparutto et al., 2015) that, when compared to null ligament length variations, minimised or prescribed ligament length variations (Bergamini et al., 2011; Gasparutto et al., 2012) better predicted TFJ internal-external rotation during gait. However, despite providing encouraging results, the latter TFJ model is not fully personalised, given that it includes a mix of subject-specific and generic parameters. Moreover, except for Sancisi et al. (2011a) and Brito da Luz et al. (2017), all the previously described TFJ parallel mechanisms do not include the PFJ.

The stabilizing role of the patella on the loaded knee makes it crucial to incorporate a PFJ mechanism in MSK models to perform dynamic analyses during tasks such as walking. Often, knee models do not incorporate a representation of the PFJ mainly because this joint has no influence on the relative motion of the femur and tibia in passive conditions (Sancisi et al., 2011a). However, when the knee is loaded, the TFJ and PFJ are closely coupled, given that the pose of the patella depends on the direction of the quadriceps and patellar tendon. Sancisi et al. (2011a) proposed a passive PFJ mechanism, characterised by a hinge joint between the femur and the patella and an isometric ligament (i.e., patellar tendon). This mechanism enabled estimation of all the PFJ rotations and
Literature review

translations as function of the TFJ flexion angle. Like in the aforementioned TFJ 5-rigid-link mechanism, the geometrical parameters for this mechanism were also derived from cadaveric individuals and the experimental cadaveric kinematics were used both to optimise the geometrical parameters and to validate the estimated kinematics. Again, Brito da Luz et al. (2017) personalised the above mentioned PFJ mechanism by using MRIs to obtain the geometrical parameters of 14 healthy participants. Nevertheless, this subject-specific mechanism has not been validated in the literature, nor has it been applied to pathological populations, such as children and adolescents with recurrent patellar dislocation.

Recently, parallel TFJ mechanisms (Clément et al., 2015; Duprey et al., 2010; Gasparutto et al., 2015; Moissenet et al., 2014) and hinge PFJ mechanisms (Moissenet et al., 2014) have been incorporated into full lower-limb scaled-generic MSK models. In these mechanisms, the geometrical parameters were not measured from the participant but they were derived from cadaveric data. However, these mechanisms provided promising results. In fact, when compared to simple and/or generic TFJ models, semi-personalised parallel TFJ mechanisms with minimally deformable ligaments better estimated TFJ abduction-adduction, internal-external rotation and antero-posterior displacement during squatting in healthy and osteoarthritic adult participants (Clément et al., 2015).

The use of personalised TFJ and PFJ mechanisms in MSK models has important advantages. First, employing semi subject-specific (Clément et al., 2015) and more complex (compared to hinge) TFJ models has been shown to provide better estimates of secondary joint kinematics when using multibody kinematic optimisation (Begon et al., 2018). Second, the proposed rigid-body models, despite requiring initial tuning, are a good compromise between simplistic non-physiological joint kinematic models and complex and computationally expensive deformable models (e.g., finite element or elastic foundation models). Finally, these models enable to incorporate morphological developmental changes typical of the paediatric populations.

However, before being translated into clinical practice, these models need to be validated. Indeed, a justified confidence that the joint kinematic models are adequate representation of the systems they simulate is necessary. Generally, estimated subject-specific knee joint kinematics are compared against in vivo knee kinematics measured using imaging techniques, such as fluoroscopy (Lu et al., 2008; Marra et al., 2015) or biplanar radiography (Clément et al., 2015), or intracortical pins (Benoit et al., 2006; Bonci et al., 2014; Reinschmidt et al., 1997). However, radiation exposure or invasive
procedures limit the use of these methods, especially in paediatric populations. On the other hand, MRI is a safe technology, with its non-invasive protocols and lack of ionizing radiation, and it could be used for validation of knee mechanisms in children. Moreover, the use of dynamic MRI could track the movement of soft tissues and bones under loading conditions across the TFJ flexion ROM (Macri et al., 2018). To date, no studies have validated subject-specific knee mechanisms for children by using MRIs.
CHAPTER 3

Patellofemoral joint alignment is a major risk factors for recurrent patellar dislocation in children and adolescents: a systematic review

Acknowledgement of co-authorship

This chapter includes a co-authored paper that has been re-formatted for this thesis. The bibliographic details/status of the co-authored paper, including all authors, are:


I made a substantial contribution in the conception and design of this study, literature search, paper selection and scoring, analysis and interpretation of the data, and drafting and revising of the final manuscript.

Student/ Corresponding author: Martina Barzan

Principal supervisor: Christopher P Carty
3.1 Abstract

**Importance:** The complex interplay of risk factors that predispose individuals to recurrent patellar dislocation is poorly understood, especially in paediatric patients who exhibit the most severe forms.

**Aim:** The primary aim of this study was to systematically review the current literature to characterise the lower limb alignment, patellofemoral morphology and soft tissue restraints of the patellofemoral joint (PFJ) through medical imaging measurements in paediatric recurrent patellar dislocators and age-matched control participants. The secondary aims were to synthesise the data to stratify the factors that influence PFJ stability and provide recommendations on the assessment and reporting of PFJ parameters in this patient population.

**Evidence Review:** A systematic search was performed using CINAHL, the Cochrane Library, EMBASE, PubMed and Web of Science databases until June 2017. Two authors independently searched for studies that included typical children and adolescents who experienced patellar dislocation and also had direct measures of structural and dynamic risk factors. The methodological quality of the included studies was assessed through a customised version of the Downs and Black checklist. Weighted averages and standard deviations of measures that have been reported in more than one study were computed. A fixed-effects model was used to estimate the mean differences with 95% CIs regarding the association of recurrent patellar dislocation with patella alta, tibia tuberosity to trochlear groove (TT-TG) distance and bony sulcus angle.

**Findings:** Twenty of 718 articles met the inclusion criteria. Thirty-one risk factors were found, however only ten of these measurements had been assessed in multiple articles and only 4 had both dislocator and control population results. With respect to controls, patients with recurrent patellar dislocations had higher TT-TG distance (p<0.01) and higher bony sulcus angle (p<0.01).

**Conclusions and Relevance:** Based on the current scientific literature, increased TT-TG distances and bony sulcus angles predispose children and adolescents to recurrent patellar dislocation. Besides these measurements, studies reporting on recurrent patellar dislocation in children and adolescents should also include characterisation of lower limb alignment in coronal and axial planes and assessment of generalised ligamentous laxity.

**Level of Evidence:** Systematic review of Prognostic, Levels II-IV
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation

What is already known:

- Recurrent patellar dislocation is found most commonly in children and adolescents.
- Several structural and functional factors have been identified as possible risk factors for recurrent patellar dislocation in children and adolescents.

What are the new findings:

- There is a paucity of reported radiological parameters for healthy children and adolescents.
- Numerous studies report measurements of patellofemoral joint malalignment, making it a primary risk factor for recurrent patellar dislocation in this patient population.
- High TT-TG distance and high bony sulcus angle can confidently predict the risk of recurrent patellar dislocation in children and adolescents.

3.2 Introduction

Patellar dislocation is relatively common in the paediatric and adolescent populations, with an estimated annual incidence of 43 per 100,000 individuals in children (Nietosvaara et al., 1994) and a prevalence of six to 77 per 100,000 (Atkin et al., 2000; Fithian et al., 2004; Hawkins et al., 1986; Sillanpää et al., 2008) in adolescents. Furthermore, there is a significantly higher re-dislocation rate following an acute first-time dislocation in children and adolescents compared to adults (Buchner et al., 2005; Larsen et al., 1982), and in patients aged less than 15 compared to patients aged 15-18 (Cash et al., 1988). Consequently, children and adolescents are likely to experience recurrent instability, at a rate ranging from 38.4% to 91% (Lewallen et al., 2013b; Palmu et al., 2008).

Patellar dislocation is believed to be the result of an abnormal interplay between lower limb alignment, bony geometry of the trochlea and patella, passive restraints of ligaments and retinaculum and the action of the quadriceps. Medical imaging studies have identified anatomical parameters that may predispose adult individuals to patellofemoral joint (PFJ) instability (Dejour et al., 1994; Stefancin et al., 2007). Other studies have attempted to describe the complex interaction between bony and soft tissue (active and passive) restraints of the PFJ (Andrish, 2005; Balcarek et al., 2010; Balcarek et al., 2014;
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation

Fithian et al., 2004) and their relative effect on PFJ stability throughout the tibiofemoral joint range of motion (Fitzpatrick et al., 2016). Nevertheless, the interplay of risk factors that predispose individuals to recurrent patellar dislocation remains poorly understood, because the parameters have been reported either in isolation or in sparse combination and in varying magnitudes.

Challenges associated with managing recurrent patella dislocations in the skeletally immature population include a paucity of normative and pathoanatomical data that contribute to PFJ instability. Surgical techniques that do not violate the physis have not been adequately assessed in terms of their specific indications, given the variability of factors that contribute to dislocation in this patient population.

The primary aim of this study was to summarise the current literature to characterise the lower limb alignment, patellofemoral morphology and soft tissue restraints of the PFJ through medical imaging measurements in children and adolescents with and without recurrent patellar dislocation. Our secondary aims were to synthesise the data to stratify the factors that influence PFJ stability and provide recommendations on the assessment and reporting of PFJ parameters in this patient population.

3.3 Methods

3.3.1 Search strategy

To identify relevant papers on this topic, a systematic search was performed of the following computerised databases: CINAHL (2010-June 2017), the Cochrane Library (1979-June 2017), EMBASE (1955-June 2017), PubMed (1963-June 2017) and Web of Science (1955-June 2017). The adopted search strategy included MeSH terms for ‘knee joint’ AND ‘dislocation’ AND ‘(‘child’ OR ‘adolescent’)’. It was ensured that patellar dislocation was captured by use of the search terms ‘knee joint’ and ‘dislocation’. References from relevant papers were also screened to guarantee the inclusion of all key studies.

3.3.2 Inclusion and exclusion criteria

Studies which included typically developing children (1-12 years old) and adolescents (13-18 years old) who experienced recurrent patellar dislocation and also had direct measures of structural and functional factors were investigated (Population: children and adolescents; Intervention/Cause: structural and functional factors; Comparison: pre/post dislocation; Outcome: patellar dislocation). Studies which
examined patients suffering from congenital or first-time acute traumatic patellar dislocation were excluded.

3.3.3 Study selection, methodological quality and measurement quality

After removing duplicates, the titles and abstracts of the papers obtained from the initial search were independently assessed by two authors (MB and SM). When the title and abstract were not sufficient the full text was screened. Any disagreement between the two reviewers was discussed until a consensus was reached. Full text papers were then retrieved and independently read again by the two authors (MB and SM). Conference abstracts were excluded. The methodological quality of the included studies was independently evaluated by two reviewers (MB and CC) based on a customised version of the Downs and Black checklist (Downs et al., 1998). The 27-item checklist evaluates the quality of reporting, external validity, bias, confounding and power. Items 4, 8, 9, 13, 14, 19, 23, 24 and 26 were excluded due to inapplicability to the studies investigated. Each item is scored 0 or 1 (‘no’ or ‘yes’) except for item 5 which is scored from 0 to 2 (‘no’, ‘partially’ or ‘yes’). The scoring for item 27, dealing with statistical power, was simplified from a 0 to 5 scale to a ‘yes’ or ‘no’ choice depending on whether the study had sufficient power to detect a clinically important effect (Chudyk et al., 2009; Samoocha et al., 2010).

3.3.4 Data extraction

Data extracted included population demographics and measures of evaluated risk factors. Risk factors were grouped into four categories:

- Lower limb alignment, which included any mention of coronal or axial plane alignment;
- PFJ alignment, which included any measure of the relationship between the patella, femur or tibia;
- Trochlea morphology, which included any measure or angle contained within the trochlea itself;
- Soft tissue restraints, which included any mention of soft tissue influence or integrity.

The specific method of measurement for quantitative risk factors was documented, along with mean and standard deviation being derived, if not provided, as recommended by the Cochrane guidelines (Higgins et al., 2011). For measures that have been reported in more than one study, weighted averages and standard deviations were
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation computed for patients and, when possible, for control participants. Meta-analysis was conducted in Review Manager (RevMan), version 5.2 for Windows, (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) on measures reported in two or more studies that included both a control and a patellar dislocator group. Weighted mean differences and 95% confidence intervals (CI) were calculated for each measure with a fixed effects model.

3.4 Results

3.4.1 Search results

The initial search yielded 712 potentially relevant articles, with an additional six articles included that were references from key papers. After removing duplicates and screening of titles and abstract, 69 full-text articles were fully screened for eligibility. Of these, 49 were excluded predominantly due to the lack of direct measures and to the exclusion of recurrent patella dislocators from the patient population (Figure 3.1).

*Figure 3.1 Systematic search strategy results.*
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation

3.4.2 Study participants

Of the 20 included studies, six included a control population, while three split the patients’ group into subcategories based on undergoing treatment (Edmonds et al., 2016; Palmu et al., 2008) (Table 3.1). Eight studies (Aulisa et al., 2012; Edmonds et al., 2016; Horikawa et al., 2011; Ji et al., 2012; Kan et al., 2009; Nelitz et al., 2013; Schoettle et al., 2005; Zhao et al., 2012) only included patients suffering from recurrent patellar dislocation, while the other studies included a combination of single acute and recurrent dislocation (Jaquith et al., 2017; Palmu et al., 2008; Yeoh et al., 2016) or habitual and recurrent dislocation (Deie et al., 2003; Kumahashi et al., 2012). Two (Horikawa et al., 2011; Ji et al., 2012; Kan et al., 2009; Nelitz et al., 2013; Schoettle et al., 2005) of the 20 studies were case studies. Mean age of the participants ranged from 11.1 to 17.3 years.

Table 3.1 Population characteristics

<table>
<thead>
<tr>
<th>First author (date)</th>
<th>Participants</th>
<th>Category</th>
<th>Number (n)</th>
<th>Sex (m/f)</th>
<th>Dislocation (A/H/R)</th>
<th>Age (years)</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aulisa (2012)</td>
<td>P</td>
<td></td>
<td>14</td>
<td>4/10</td>
<td>0/0/14</td>
<td>11.1</td>
<td>-</td>
<td></td>
<td>9.2-</td>
</tr>
<tr>
<td>Deie (2003)</td>
<td>P</td>
<td></td>
<td>4</td>
<td>2/2</td>
<td>0/3/1</td>
<td>15.5</td>
<td>-</td>
<td></td>
<td>15-16</td>
</tr>
<tr>
<td>Dickens (2014)</td>
<td>P</td>
<td></td>
<td>76</td>
<td>28/48</td>
<td>-</td>
<td>12.6</td>
<td>-</td>
<td>0-15</td>
<td></td>
</tr>
<tr>
<td>Edmonds (2015)</td>
<td>C</td>
<td></td>
<td>495</td>
<td>220/275</td>
<td>0/0/20</td>
<td>12.6</td>
<td>-</td>
<td>0-15</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C</td>
<td></td>
<td>20 (10 IR, 10 MPFLR)</td>
<td></td>
<td>0/0/20</td>
<td>15.6</td>
<td>2.2</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Horikawa (2011)</td>
<td>P</td>
<td></td>
<td>1</td>
<td>0/1</td>
<td>0/0/1</td>
<td>15</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Jaquith (2015)</td>
<td>P</td>
<td></td>
<td>250</td>
<td>119/147a</td>
<td>266/0/77b</td>
<td>13.7</td>
<td>2.3</td>
<td>8-18</td>
<td></td>
</tr>
<tr>
<td>Ji (2012)</td>
<td>P</td>
<td></td>
<td>17c</td>
<td>0/0/17d</td>
<td>15</td>
<td>12-18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kan (2009)</td>
<td>P</td>
<td></td>
<td>4</td>
<td>0/4</td>
<td>0/0/4</td>
<td>17.3</td>
<td>1.2</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>4</td>
<td>0/4</td>
<td>14.5</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kumahashi (2012)</td>
<td>P</td>
<td></td>
<td>5</td>
<td>2/3</td>
<td>0/1/4</td>
<td>13.6</td>
<td>-</td>
<td>11-15</td>
<td></td>
</tr>
<tr>
<td>Nelitz (2013)</td>
<td>P</td>
<td></td>
<td>21</td>
<td>15/6</td>
<td>0/0/21</td>
<td>12.2</td>
<td>-</td>
<td>10.3</td>
<td></td>
</tr>
<tr>
<td>Nietosvaara (1997)</td>
<td>P</td>
<td></td>
<td>33</td>
<td>11/22</td>
<td>-</td>
<td>15.6</td>
<td>-</td>
<td>12-17</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>25</td>
<td>11/14</td>
<td>14.8</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palmu (2009)</td>
<td>P</td>
<td></td>
<td>62</td>
<td>16/46</td>
<td>64/0/44b</td>
<td>13</td>
<td>2</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>(27 CG, 35 SG)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pennock (2014)</td>
<td>P</td>
<td></td>
<td>45</td>
<td>23/22</td>
<td>-</td>
<td>15.4</td>
<td>2</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>180</td>
<td>104/76</td>
<td>16</td>
<td>2</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Putney (2012)</td>
<td>P</td>
<td></td>
<td>63</td>
<td>33/30</td>
<td>-</td>
<td>13.6</td>
<td>-</td>
<td>15-17</td>
<td></td>
</tr>
<tr>
<td>Regalado (2014)</td>
<td>P</td>
<td></td>
<td>29</td>
<td>-</td>
<td>-</td>
<td>13</td>
<td>-</td>
<td>11-16</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>10</td>
<td>-</td>
<td>13</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schoettle (2005)</td>
<td>P</td>
<td></td>
<td>1</td>
<td>0/1</td>
<td>0/0/1</td>
<td>15</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Vahasarja (1995)</td>
<td>P</td>
<td></td>
<td>48</td>
<td>5/43</td>
<td>-</td>
<td>13.4</td>
<td>-</td>
<td>7.5-16</td>
<td></td>
</tr>
<tr>
<td>Yeoh (2016)</td>
<td>P</td>
<td></td>
<td>43</td>
<td>20/23</td>
<td>43/0/13c</td>
<td>-</td>
<td>-</td>
<td>10-17</td>
<td></td>
</tr>
<tr>
<td>Zhao (2012)</td>
<td>P</td>
<td></td>
<td>54</td>
<td>9/45</td>
<td>0/0/54</td>
<td>14.7</td>
<td>1.3</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>(28 MRP, 26 VMP)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRP</td>
<td>15.2</td>
<td>1.6</td>
<td>-</td>
<td>VMP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- = not reported; P = patients; C = controls; A = acute; H = habitual (i.e. involuntary patellar dislocation and relocation with every cycle of knee flexion and extension (Parikh et al., 2016)); R = recurrent; IR = patients undergoing Insall realignment (Insall et al., 1976); MPFLR = patients undergoing MPFL reconstruction (Insall et al., 1976); MRP = patients undergoing MPFL reconstruction (Parikh et al., 2016); VMP = patients undergoing VMP reconstruction (Parikh et al., 2016).
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation; a knees; b knees with evidence of acute dislocation which experienced also recurrent dislocation; c one patient lost to follow-up; d in the paper, the term “recurrent” have been interchanged with “habitual”, however, “recurrent” have been chosen according to Batra (2014); e patients with acute dislocation who developed recurrent dislocation; CG = conservative group; SG = surgical group; MRP = patients undergoing medial retinaculum plasty; VMP = patients undergoing vastus medialis plasty.

3.4.3 Quality analysis

Methodologic quality had modified Downs and Black checklist scores ranging from 4 to 18, where the maximum score is 19 (Table 3.2). An overall score below 50% was assigned to five studies (Deie et al., 2003; Horikawa et al., 2011; Nietosvaara et al., 1997; Putney et al., 2012; Schoettle et al., 2005), two of which (Horikawa et al., 2011; Schoettle et al., 2005) were case reports. Only 33% of the included studies (Aulisa et al., 2012; Dickens et al., 2014; Jaquith et al., 2017; Palmu et al., 2008; Pennock et al., 2014; Seeley et al., 2012) scored above 70%. Generally, lower scores were in reference to distribution of principal confounders, sample representativeness, length of follow-up of patients, adjustment for confounding and power (20% of the included studies obtained the highest score). On the other hand, the characteristics of the patients involved in the studies were always clearly described and the main outcomes to be measured were accurately defined in 95% of the studies.
The customised Downs and Black checklist items refer to hypothesis/aim/objective (1), main outcomes (2), characteristics of the patients (3), principal confounders (5), main findings (6), randomisation (7), sample representativeness (11), source population (12), statistical tests (18), accuracy of the main outcomes (20), case-control population source (21), recruiting period (22), adjustment for confounding (25) and power (27).

<table>
<thead>
<tr>
<th>Study</th>
<th>Item</th>
<th>Maximum Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhao et al.</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Yeoh et al.</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Vahasarja et al.</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td>Seeley et al.</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Schoettle et al.</td>
<td>12.5</td>
<td>0</td>
</tr>
<tr>
<td>Regalado et al.</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Putney et al.</td>
<td>15.5</td>
<td>0</td>
</tr>
<tr>
<td>Palmu et al.</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Nietosvaara et al.</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Nelitz et al.</td>
<td>11.5</td>
<td>0</td>
</tr>
<tr>
<td>Kumahashi et al.</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Kan et al.</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Edmonds et al.</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>Dickens et al.</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Deie et al.</td>
<td>14.5</td>
<td>0</td>
</tr>
<tr>
<td>Aulisa et al.</td>
<td>19</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 3.2** Methodological quality assessment of included studies: Downs and Black checklist.
3.4.4 Lower limb alignment

There were only two studies (Nelitz et al., 2013; Schoettle et al., 2005) (one being a case report) (Schoettle et al., 2005) that had made an attempt to document overall alignment of the lower limb (Table 3.3). The other had specifically aimed to exclude patients with abnormal alignment parameters from their patient population. Schoettle et al. (2005) reported measures of femoral anteversion and tibial torsion, measured on computed tomography (CT) scans, for a patellar dislocator diagnosed with lower limb rotational malalignment associated with trochlea dysplasia. However, neither of the two pathological conditions was addressed during surgery, and medial patellofemoral ligament (MPFL) reconstruction, together with lateral release, were chosen instead.

Measurements of femoral anteversion, mechanical axis, and tibial torsion were reported only in one study, therefore it was not possible to derive an average value for any of these measurements.
<table>
<thead>
<tr>
<th>Measure (unit)</th>
<th>Category</th>
<th>Lower limb deformity</th>
<th>Pelvis deformity</th>
<th>Femoral elevation</th>
<th>Patellar tilt</th>
<th>Femoral version</th>
<th>Knee angle</th>
<th>Mechanical axis</th>
<th>Femoral mechanical axis</th>
<th>Patellar mobility and soft issue tension</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lateral stress ratio (%): angle (˚)</td>
<td>Mechanical axis</td>
<td>[20.3°]</td>
<td>[0.73°]</td>
<td>[0.01°]</td>
<td>[23.8°]</td>
<td>[1.06°]</td>
<td>[0.06°]</td>
<td>[26.8°]</td>
<td>[1.30°]</td>
<td>[1.29°]</td>
</tr>
<tr>
<td>Lateral patellofemoral congruence angle (˚)</td>
<td>Mechanical axis</td>
<td>[2.0°]</td>
<td>[0.10°]</td>
<td>[0.01°]</td>
<td>[0.7°]</td>
<td>[0.06°]</td>
<td>[0.01°]</td>
<td>[0.7°]</td>
<td>[0.06°]</td>
<td>[0.06°]</td>
</tr>
<tr>
<td>Knee effusion</td>
<td>Femoral mechanical axis</td>
<td>[0.2mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Patellar thickness, body coil</td>
<td>Femoral mechanical axis</td>
<td>[2.3mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Patella alta</td>
<td>Femoral mechanical axis</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Knee effusion, body coil</td>
<td>Femoral mechanical axis</td>
<td>[0.3mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Patellar thickness, body coil</td>
<td>Femoral mechanical axis</td>
<td>[2.3mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Patella alta</td>
<td>Femoral mechanical axis</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Knee effusion</td>
<td>Femoral mechanical axis</td>
<td>[0.3mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Patellar thickness, body coil</td>
<td>Femoral mechanical axis</td>
<td>[2.3mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Patella alta</td>
<td>Femoral mechanical axis</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Knee effusion</td>
<td>Femoral mechanical axis</td>
<td>[0.3mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Patellar thickness, body coil</td>
<td>Femoral mechanical axis</td>
<td>[2.3mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Patella alta</td>
<td>Femoral mechanical axis</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Knee effusion</td>
<td>Femoral mechanical axis</td>
<td>[0.3mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Patellar thickness, body coil</td>
<td>Femoral mechanical axis</td>
<td>[2.3mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Patella alta</td>
<td>Femoral mechanical axis</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Knee effusion</td>
<td>Femoral mechanical axis</td>
<td>[0.3mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Patellar thickness, body coil</td>
<td>Femoral mechanical axis</td>
<td>[2.3mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
<td>[0.1mm]</td>
<td>[0.0mm]</td>
<td>[0.0mm]</td>
</tr>
<tr>
<td>Study</td>
<td>Method</td>
<td>Measurements</td>
<td>Values</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------</td>
<td>-------------------------</td>
<td>-------------------------------------</td>
<td>--------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Radius of trochlea</td>
<td>25.3 ± 15.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q angle (°)</td>
<td>19.4 ± 1.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TT-TG distance (mm)</td>
<td>21.5 ± 1.75</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhao (2012)</td>
<td>MR, VMP, 2mm slice thickness</td>
<td>Trochlea index</td>
<td>1.4 ± 0.2, 1.2 ± 0.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TT-TG index</td>
<td>157 ± 1.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aulisa (2012)</td>
<td>AP X-ray, axial view</td>
<td>Q angle (°)</td>
<td>19.4 ± 1.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TT-TG distance (mm)</td>
<td>21.5 ± 1.75</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Horikawa (2011)</td>
<td>AP X-ray</td>
<td>Q angle (°)</td>
<td>20.0 ±</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TT-TG distance (mm)</td>
<td>12.2 ± 2.4, 8.6 ± 1.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vahasarja (1995)</td>
<td>AP X-ray</td>
<td>Q angle (°)</td>
<td>9.0 ± 2.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TT-TG distance (mm)</td>
<td>16.0 ± 2.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhao (2012)</td>
<td>MR, VMP, 2mm slice thickness</td>
<td>Trochlea index</td>
<td>1.6 ± 0.5, 1.5 ± 0.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TT-TG index</td>
<td>164 ± 9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aulisa (2012)</td>
<td>AP X-ray, axial view</td>
<td>Q angle (°)</td>
<td>16.3 ± 5.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TT-TG distance (mm)</td>
<td>16.3 ± 5.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Horikawa (2011)</td>
<td>AP X-ray, axial view</td>
<td>Q angle (°)</td>
<td>15.9 ± 4.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TT-TG distance (mm)</td>
<td>15.9 ± 4.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Yeoh (2016)         | RD MRI                  | Trochlea morphology Dejour classification (%) | 27% type A, 16% types BCD,
|                    |                         |                                       | 47% type D, 23% type A, 28% type B, 11% type C, 5% type D,
| Jaquith (2015)      | RD MRI                  | Trochlea morphology Dejour classification (%) | 27% type A, 16% types BCD,
|                    |                         |                                       | 47% type D, 23% type A, 28% type B, 11% type C, 5% type D,
| Nelitz (2013)       | RD MRI                  | Trochlea morphology Dejour classification (%) | 27% type A, 16% types BCD,
|                    |                         |                                       | 47% type D, 23% type A, 28% type B, 11% type C, 5% type D,
| Seeley (2012)       | RD MRI                  | Trochlea morphology Dejour classification (%) | 27% type A, 16% types BCD,
|                    |                         |                                       | 47% type D, 23% type A, 28% type B, 11% type C, 5% type D,
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation.  

<table>
<thead>
<tr>
<th>Measure</th>
<th>Recurrent Dislocation Group</th>
<th>Non-Recurrent</th>
<th>AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trochlear depth (mm)</td>
<td>RD</td>
<td>1.6 [0.6]</td>
<td>1.8 [0.6]</td>
</tr>
<tr>
<td>Trochlear facet asymmetry (%)</td>
<td>RD</td>
<td>52.1 [14.9]</td>
<td>53% tear, 47% stretching</td>
</tr>
<tr>
<td>Generalised ligamentous laxity (%)</td>
<td></td>
<td>62.5%</td>
<td>53% tear, 47% stretching</td>
</tr>
<tr>
<td>VLO Pennation angle (˚)</td>
<td></td>
<td>14.8 [1.0]</td>
<td>14.5 [2.6]</td>
</tr>
<tr>
<td>VLO/VMO ACSA</td>
<td></td>
<td>5.6 [3.4]</td>
<td>5.2 [2.8]</td>
</tr>
<tr>
<td>VLO/VMO PCSA</td>
<td></td>
<td>5.8 [3.4]</td>
<td>5.3 [2.6]</td>
</tr>
<tr>
<td>MPFLR reaction force/quadriceps force (%)</td>
<td></td>
<td>0.94 [0.92]</td>
<td>0.76 [0.92]</td>
</tr>
<tr>
<td>MPFLR Patella ligament/quadriceps tendon force</td>
<td></td>
<td>1.21 [1.22]</td>
<td>1.18 [1.22]</td>
</tr>
<tr>
<td>PFJ reaction force/quadriceps force (%)</td>
<td></td>
<td>0.94 [0.92]</td>
<td>0.76 [0.92]</td>
</tr>
<tr>
<td>VLO/VMO ACSA</td>
<td></td>
<td>1.9 [0.4]</td>
<td>1.6 [0.2]</td>
</tr>
<tr>
<td>VLO/VMO PCSA</td>
<td></td>
<td>1.6 [0.4]</td>
<td>1.4 [0.2]</td>
</tr>
<tr>
<td>VLO elevation (%)</td>
<td></td>
<td>2.78 [3.35]</td>
<td>2.5 [2.8]</td>
</tr>
<tr>
<td>VLO Pennation angle (˚)</td>
<td></td>
<td>14.8 [1.6]</td>
<td>11.4 [2.0]</td>
</tr>
<tr>
<td>VLO/VMO ACSA</td>
<td></td>
<td>1.9 [0.4]</td>
<td>1.6 [0.2]</td>
</tr>
<tr>
<td>VLO/VMO PCSA</td>
<td></td>
<td>1.6 [0.4]</td>
<td>1.4 [0.2]</td>
</tr>
<tr>
<td>VLO Pennation angle (˚)</td>
<td></td>
<td>14.8 [1.6]</td>
<td>11.4 [2.0]</td>
</tr>
<tr>
<td>VLO/VMO ACSA</td>
<td></td>
<td>1.9 [0.4]</td>
<td>1.6 [0.2]</td>
</tr>
</tbody>
</table>
3.4.5 PFJ alignment

Studies frequently reported abnormal measurements of PFJ alignment including congruence angle, patella alta, lateral patellar tilt, Q angle and lateral position of the tibial tubercle relative to the trochlear groove (TT-TG distance) (Table 3.3).

Measurements of congruence angle in recurrent dislocators were performed in three studies (Kan et al., 2009; Kumahashi et al., 2012; Zhao et al., 2012) by using three different imaging procedures. Kan et al. (2009) found that control participants had slightly medially deviated congruence angles (-9°±12).

Eight studies (Deie et al., 2003; Edmonds et al., 2016; Jaquith et al., 2017; Kumahashi et al., 2012; Nelitz et al., 2013; Palmu et al., 2008; Regalado et al., 2014; Vähäsarja et al., 1995) quantified patella alta in their assessment of recurrent patellar dislocators, while Aulisa et al. (2012) only commented that 43% of the patients were affected. All the articles used the Insall-Salvati Index (Insall et al., 1971) as their measurement tool, except for Jaquith et al. (2017) who used the Caton-Deschamps Index (Caton et al., 1982). Most of the measures were performed using lateral X-ray. The studies that compared the Insall-Salvati Index in patellar dislocators and healthy controls did not find significant difference between the two groups (Edmonds et al., 2016; Regalado et al., 2014).

Lateral patellar tilt angle was measured in five studies (Ji et al., 2012; Kumahashi et al., 2012; Regalado et al., 2014; Vähäsarja et al., 1995; Zhao et al., 2012), mostly using X-ray. In contrast with the other studies, Regalado et al. (2014) computed lateral patellar tilt as the angle between the lines joining the posterior femoral condyles and the maximum width of the patella, therefore obtaining lower values for patients with respect to controls.

Three studies (Aulisa et al., 2012; Horikawa et al., 2011; Vähäsarja et al., 1995) measured Q angle in their assessment of patients with recurrent patellar dislocation. However, there were no comparative measurements made in control subjects and the measurement method was not defined.

Seven studies (Aulisa et al., 2012; Dickens et al., 2014; Nelitz et al., 2013; Pennock et al., 2014; Schoettle et al., 2005; Yeoh et al., 2016; Zhao et al., 2012) documented the TT-TG distance in recurrent patellar dislocators. The measurement was performed on MRI in five studies and on CT in two studies. Only Dickens et al. (2014) tested the intra and inter observer reliability of the MRI measurement, finding excellent results. Significantly higher TT-TG distance was found in patients with dislocation than
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation

controls (Dickens et al., 2014; Pennock et al., 2014). Contrary to Pennock et al. (2014),
Dickens et al. (2014) showed that older children tended to have higher TT-TG distances
and suggested an adjustment of the measure for age.

Patients with recurrent dislocation exhibited a laterally deviated congruence angle
(Figure 3.2), with an average value of 23.6° (Table 3.4). Overall, alta was universally
found in all dislocators, with an average Insall-Salvati Index of 1.28±0.05 between
studies. On the other hand, only 20 control participants were assessed, with an average
Insall-Salvati Index of 1.20±0.01. The average lateral patellar tilt between the studies that
performed the measurement in patellar dislocators using X-ray and CT scans was
20.8°±4.8. A mean Q angle of 11.2°±4.2 was calculated for the patellar dislocators across
the studies (weighted mean patients’ age: 12.9±1 years, age range: 9.2-16 years). The
mean TT-TG distance in patellar dislocators was 15.5±2.5 mm (patients’ age range: 0-17
years), while the average value for 675 controls was 9.4±1.4 mm (weighted mean
participants’ age: 13.5±1.5 years, age range: 0-15 years).
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation.

**Figure 3.2** Description of most frequently reported measures of PFJ alignment and trochlea morphology. (a) Congruence angle: angle formed by bisecting the sulcus angle (α) and central patella ridge. (b) Lateral (left) and medial (right) stress ratios (%), defined as BC/AB x 100. Diagrams of the 2kg stress skyline view at 45° of knee flexion. (c) Insall-Salvati Index, defined as the ratio between patellar length (PL) and patellar tendon length (PT). (d) Lateral patellar tilt: angle between the posterior femoral condyles line and the line of maximum width of the patella. (e) Q angle: angle between a line drawn from the anterior superior iliac spine to central patella (solid red line) and a line drawn from central patella to tibial tubercle (dashed blue line). The Q-angle can be measured in laying or standing. (f) TT-TG distance: distance between a line bisecting the tibial tuberosity (TT) and a line bisecting the trochlear groove sulcus (TG), both perpendicular to the posterior femoral condyles line. (g) Bony sulcus angle: angle between lines joining the highest points of the bony medial and lateral condyles and the lowest bony point of the intercondylar sulcus. (h) Cartilaginous sulcus angle: angle between lines joining the highest points of the cartilaginous medial and lateral condyles and the lowest cartilaginous point of the intercondylar sulcus.
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation

Table 3.4 Weighted average of most frequently reported measures

<table>
<thead>
<tr>
<th>Category</th>
<th>Measure (unit)</th>
<th>Weighted average [SD]</th>
<th>Knees assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Patients</td>
<td>Controls</td>
</tr>
<tr>
<td>PFJ alignment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Congruence angle (°)</td>
<td>23.6 [4.4]</td>
<td>-9.0 [12.0]</td>
</tr>
<tr>
<td></td>
<td>Lateral stress ratio (%)</td>
<td>36.3 [5.2]</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Medial stress ratio (%)</td>
<td>-12.5 [8.7]</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Patella alta</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Insall-Salvati Index</em></td>
<td>1.28 [0.05]</td>
<td>1.20 [0.01]</td>
</tr>
<tr>
<td></td>
<td>Lateral patellar tilt (°)</td>
<td>20.8 [4.8]</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Q-angle (°)</td>
<td>11.2 [4.2]</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>TT-TG distance (mm)</td>
<td>15.5 [2.5]</td>
<td>9.4 [1.4]</td>
</tr>
<tr>
<td>Trochlea morphology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dejour classification (%)</td>
<td>50.2 [11.1]</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Sulcus angle (°)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>bony</em></td>
<td>150.2 [6.4]</td>
<td>140.4 [6.1]</td>
</tr>
<tr>
<td>Soft tissue restraints</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MPFL injury (%)</td>
<td>88.6 [0.2]</td>
<td>-</td>
</tr>
</tbody>
</table>

Results from the fixed effects model (Table 3.5) showed that that the weighted mean for TT-TG distance was significantly different (p < 0.01) between recurrent patellar dislocators and controls.

Table 3.5 Weighted mean differences for measures reported in two or more studies that included a control cohort.

<table>
<thead>
<tr>
<th>Category</th>
<th>Measure (unit)</th>
<th>Weighted Mean Difference [95% CI]</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFJ alignment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patella alta</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Insall-Salvati Index</em></td>
<td>0.05 [-0.02-0.12]</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>TT-TG distance (mm)</td>
<td>3.71 [3.18-4.23]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Trochlea morphology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sulcus angle (°)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>bony</em></td>
<td>11.72 [8.54-14.9]</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

3.4.6 Trochlea morphology

Characterisation of trochlea morphology included predominantly measures of the sulcus angle and trochlea dysplasia, according to the Dejour’s classification (Dejour et al., 1994). Ten studies (Aulisa et al., 2012; Deie et al., 2003; Horikawa et al., 2011; Kan et al., 2009; Kumahashi et al., 2012; Nietosvaara et al., 1997; Palmu et al., 2008; Regalado et al., 2014; Seeley et al., 2012; Vähäsarja et al., 1995) measured the sulcus angle in recurrent patellar dislocators. Four studies performed the measurement using X-ray, three using MRI, two using CT scans and one using ultrasound. The knee flexion angle at which the measurement was taken also varied across the studies, ranging from 15° to 90°.
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation

Trochlea dysplasia in recurrent dislocators was considered in five studies (Jaquith et al., 2017; Nelitz et al., 2013; Putney et al., 2012; Schoettle et al., 2005; Seeley et al., 2012). Putney et al. (2012) reported that the incidence of trochlear dysplasia in their cohort was 19%, but they did not specify which criteria they used.

The weighted average across the studies for the bony sulcus angle was 150.2°±6.4 for dislocators and 140.4°±6.1 for controls. Nietosvaara et al. (1997) and Seeley et al. (2012) provided an additional measure of cartilaginous sulcus angle, which resulted being 159.1°±4.9 on average in patellar dislocators. Furthermore, it resulted that 50.2±11.1% of patients with recurrent dislocation had a form (types A, B, C, D) of dysplastic trochlea, according to Dejour’s classification.

The weighted mean for bony sulcus angle was significantly different (p < 0.01) between recurrent patellar dislocators and controls (Table 3.5).

3.4.7 Soft tissue restraints

Few studies (Aulisa et al., 2012; Edmonds et al., 2016; Kan et al., 2009; Putney et al., 2012; Seeley et al., 2012; Zhao et al., 2012) reported measurements of passive (ligaments) and active (muscle) soft tissue restraints of the PFJ, and these measurements were often performed only in one study. Indeed, only one study (Aulisa et al., 2012) reported measures of generalised ligamentous laxity found by the Carter-Wilkinson test (Carter et al., 1964). Zhao et al. (2012) also reported that most of recurrent dislocators had hyperlaxity, but they did not specify how this was determined. Three studies evaluated the integrity of the MPFL by visual inspection. Putney et al. (2012) considered only patients with MPFL injury and he reported that, of those, 53% involved tears and 47% involved stretching. From two studies, it resulted that, on average, 88.6±0.2% of recurrent dislocators exhibited either a MPFL strain or tear.

3.5 Discussion

The paediatric cohort of PFJ dislocators reflects a highly variable group of patients who often have a constellation of predisposing biomechanical factors towards PFJ instability. The primary aim of this article was to quantify from the current literature which measurable radiological parameters were most likely to cause PFJ instability by comparing control and dislocator populations. The secondary aim was to stratify the individual parameters to determine which factor would be the most likely to contribute to instability in children.
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation

Overall, we were able to find thirty-one reported parameters, however only ten of these measurements had been assessed in multiple articles. Only 4 of these parameters (congruence angle, patella alta, TT-TG distance, sulcus angle) had both dislocator and control population results. Due to the paucity of data, it was difficult to draw conclusions based on this information, however it is possible to make recommendations that future studies in this population should quantify factors that cover all the main categories that can contribute to pathology, particularly the parameters that are considered relevant in the general literature.

In terms of extrinsic lower limb alignment, genu valgum is very commonly seen in paediatric patients as part of normal limb development. Cases of excessive valgus can be corrected by guided growth procedures with minimal morbidity (Ballal et al., 2010) in older children with an intermalleolar distance of more than 8cm. In a recurrent patellar dislocator with excessive genu valgum, correction of valgus alignment contributes to improved patella tracking and provide an extrinsic method of improving stability by effectively decreasing the TT-TG distance.

Likewise, in children with persistent femoral anteversion or miserable malalignment contributing to patella instability, derotational osteotomy provides realignment of the extensor mechanism relative to the trochlea without violation of the knee itself (Gordon et al., 2005). This procedure, while more invasive, is also well tolerated in children compared to adults. There is no literature that supports how much anteversion is considered significantly abnormal, how much derotation is required or consequently at what level the procedures should be performed. Without consistent documentation of both coronal and axial plane alignment, it will be difficult to generate the body of information required to answer these clinical questions.

The most frequently reported radiological factors involving intrinsic PFJ alignment included congruence angle, patella alta, patella tilt and the TT-TG distance. It is well accepted that all of these factors play a role in the adult population however it was evident that patella alta was not as reliable a measure in the paediatric cohort of patients.

The average values of the Insall-Salvati Index were equal to or greater than 1.2 in both groups, suggesting that this factor was not able to discriminate between controls and dislocators in the paediatric population. This might derive from the lack of ossification in the tibial plateau which generates a falsely high measurement in the control group of children. The poor reproducibility of the measure may also have been due to difficulty in
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation. Conversely, the Caton-Deschamps Index has been shown to be a simple, accurate and reproducible measure to derive patellar height in children, but age-based values should be considered, given that the index increases as the age decreases (Thévenin-Lemoine et al., 2011). An alternative measure of patellar height is the patellotrochlear index, which is believed to reflect the functional patellar height more accurately (Biedert et al., 2006) and could be computed from MRI. These results might also be affected by the low number of control participants for which the measurement was computed.

The TT-TG distance appears to discriminate between patients and controls, with dislocators demonstrating higher TT-TG distances than controls. Previous studies (Rhee et al., 2012; Weber et al., 2016a) used a 20mm threshold (Dejour et al., 1994) as the rationale for medialising tibial tubercle osteotomy in skeletally mature patients. There have not been any studies to our knowledge that define the role of TT-TG distance prior to a Roux-Goldthwait style procedure for the skeletally immature patient (Marsh et al., 2006). The average TT-TG distance for patients reported in this review (15.55±2.53mm) is lower than expected, possibly because this parameter has been shown to increase logarithmically with age (Dickens et al., 2014). MRI values for the TT-TG distance have been shown to be smaller than those measured on CT. It is the authors feeling that CT in the paediatric population should be avoided and that MRI should be adopted as the standard tool for assessment, therefore values should be standardised for MRI. Differences in TT-TG distance measurements on MRI have been reported however, with significantly lower values when measured on higher resolution MRI (Aarvold et al., 2014; Dickens et al., 2014) due to flexion of the knee when positioned in a dedicated knee coil. The tibial tubercle is subsequently lateralised due to the screw-home mechanism. The TT-TG distance is also sensitive to small changes (5°) in knee adduction and abduction relative to neutral axis alignment, with an alteration of the measurement by as much as 40% (Yao et al., 2014). Consequently, this measure should be taken with the knee in full extension with images reconstructed in neutral axis alignment while using a body coil.

The results from this review suggest that a TT-TG distance threshold measured on MRI >15mm might be a good indication for medial tibial tubercle transfer in skeletally mature patients with recurrent patellar instability, as proposed by Schoettle et al. (2006). Nonetheless, an adjustment for age is recommended.

It was surprising to find that Q angle was not well reported in the literature. There is considerable controversy about how to measure the Q angle as well as the implications.
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation of an elevated result (Smith et al., 2008b). Variability exists in the number of degrees of flexion the knee should be positioned in, as well as the state of contraction of the quadriceps muscle (Guerra et al., 1994). A significant negative relationship between Q angle and TT-TG distance was reported by Cooney et al. (2012) in symptomatic patients with relaxed knees, implying that one cannot substitute the clinical for the radiological measure.

Morphologic features of the trochlea were primarily assessed by measuring the sulcus angle (Brattström, 1964; Powers, 2000). With respect to patellar dislocators and controls, the dislocators exhibited shallower bony (150.2°±6.4) and cartilaginous (159.1°±4.9) sulcus angles. A shallow sulcus angle may be the consequence of abnormal biomechanics of the PFJ in the first instance, as cartilage shape occurs partly as a result of the applied forces. It has been shown (Düppe et al., 2016) that bony and cartilaginous sulcus angles are age dependent, with general higher values for older participants with patellar instability. Therefore, this should be taken into account when establishing the predictive value of the measurement. Different imaging techniques and methods have been used to measure the sulcus angle. It has been shown that there is a reasonable level of inter-observer and intra-observer reliability and validity for this measurement when using CT and MRI (Davies et al., 2000; Toms et al., 2009). Van Huyssteen et al. (2006) demonstrated that there is a highly significant difference between bony and cartilaginous sulcus angle measured in patients with a dysplastic trochlea. Although the bony trochlea is dysplastic in these patients, the cartilage morphology can worsen this abnormal shape. MRI is therefore preferable to CT in facilitating surgical planning in a paediatric population.

Meta-analysis was only possible for three measures, the Insall-Salvati Index, TT-TG distance and bony sulcus angle, as these were the only parameters documented in comparisons of PFJ dislocators and controls in two or more studies. A statistically significant difference in weighted mean averages between controls and dislocators was found for the TT-TG distance and bony sulcus angle, indicating that, in paediatric patients, it is likely that these are the only two parameters we can confidently use to predict risk of recurrence.

The evidence base exhibited a number of substantial methodological limitations. Firstly, the majority of risk factors for patellar instability were measured from two-dimensional medical images collected in static postures. Construct validity is questionable, as patellar instability is a consequence of dynamic factors that change with
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation

many variables including joint kinematics and force vector contributions from the quadriceps. Secondly, normative values for potential predictors of patellar dislocation were difficult to derive, mainly because of the lack of matching controls in most studies. The heterogeneity of factors predisposing to patellar dislocation could also influence the categorisation of values into normal and abnormal ranges. For example, increased severity of trochlea dysplasia has been shown to affect measurements of TT-TG distance, with an underestimation of the value up to 3mm (Tscholl et al., 2016) and a decreased inter and intra observer agreement (Dornacher et al., 2014). Overall, none of the included studies conducted a comprehensive predictive analysis to estimate the relationship between lower limb and PFJ alignment, trochlea morphology and soft tissue restraints of the PFJ. Finally, the quality of the studies should be taken into account when evaluating the external validity and generalizability of the results. According to the quality assessment, only 35% of the included studies scored above 70% on the Downs and Black checklist (Downs et al., 1998) and could therefore be deemed to be of sufficient quality to be considered for meta-analysis. However, there was not enough consistency between studies to attempt a meta-analysis.

Based on the current evidence, the authors believe that studies reporting on recurrent patellar dislocation in children and adolescents should include at the very minimum, assessment of (i) lower limb alignment in the coronal and axial planes; (ii) PFJ alignment to include TT-TG distance and congruence angle; (iii) trochlea morphology measurements to include sulcus angle and (iv) assessment of generalised ligamentous laxity. Laxity has been unanimously shown to predispose to recurrent patella dislocation (Carter et al., 1964; De Palma, 1954). In this review it has only been reported in one study (Aulisa et al., 2012) and was found in 62.5% of patients. A standardised clinical Q angle protocol needs to be established and validated before including this measurement in the assessment of recurrent patellar dislocation. These recommendations could change in the future, when a more comprehensive dataset of factors predisposing to patellar dislocation in a paediatric cohort will be available.

The cause of recurrent patellar dislocation cannot currently be predicted from traditional statistical methods given the complex interplay between lower limb bone morphology, bony alignment and soft tissue restraints of the PFJ. Algorithms based on predictive analyses can only provide general information at a population level. Often, results are presented from mixed populations of children, adolescents and adults which may lead to inaccurate conclusions, since the lower extremity characteristics change
according to age and skeletal maturity. Most of contemporary metrics are static measures of the PFJ alignment and are inappropriate to investigate the patellar dislocation mechanism during dynamic tasks. Clinical gait analysis (Kirtley, 2006) cannot provide patient-specific insights on PFJ (dys)function, because this joint is not included in currently employed models. Conversely, computational models of the musculoskeletal system (Damsgaard et al., 2006; Delp et al., 2007) can incorporate patient-specific lower limb bone models, and may allow us to evaluate the PFJ dynamic function by combining gait analysis typical measurements with estimation of internal loads (Lenhart et al., 2015). Such biomechanical methods may therefore provide insight into the complex aetiology of patellar dislocation, help identify individualised risk factors for recurrent patellar dislocation, and quantitatively describe patellar stability throughout the knee range of motion in static and dynamic activities.

3.6 Conclusion

The findings of this review suggest that PFJ alignment is a major risk factor for recurrent patellar dislocation. Our meta-analysis showed that children and adolescents with recurrent patellar dislocation exhibited significantly higher TT-TG distance and bony sulcus angle with respect to age-matched control participants. These findings indicate that TT-TG distance and bony sulcus angle are the only two parameters we can confidently use to predict the risk of recurrence in paediatric patients. These results can streamline the patient evaluation and best inform clinical decision making.

3.7 Acknowledgements

L. Modenese and C.P. Carty were supported by an Imperial College Research Fellowship and an Advance Queensland Research Fellowship, respectively.
Patellofemoral joint alignment is a major risk factor for recurrent patellar dislocation
CHAPTER 4

General methods

This chapter describes the overall methods and procedures used for data collection and processing within this thesis. To summarise, participants recruited for this study (section 4.1) underwent MRI examination at the Lady Cilento Children’s Hospital and gait analysis at the Queensland Children Motion Analysis Service (section 4.2). These data were processed (section 4.3) and used to create subject-specific kinematic knee models (section 4.4) and subject-specific full lower limb models (section 4.5). Finally, statistical analysis was performed to investigate the differences between the different models and to validate the outputs of the models (section 4.6).

4.1 Participants

Forty-nine participants were recruited for this study, of which 25 were patients with recurrent patellar dislocation (RPD) and 24 were age-matched typically developing (TD) control participants (Table 4.1).

Table 4.1. Participants’ characteristics. Age, mass and height are expressed as average and standard deviation.

<table>
<thead>
<tr>
<th></th>
<th>TD (n=24)</th>
<th>RPD (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/female)</td>
<td>13/11</td>
<td>6/19</td>
</tr>
<tr>
<td>Age (years)</td>
<td>13.9 [3.1]</td>
<td>14.3 [2.6]</td>
</tr>
<tr>
<td>Mass [kg]</td>
<td>49.7 [11.6]</td>
<td>60.9 [19.9]</td>
</tr>
<tr>
<td>Height [m]</td>
<td>1.62 [0.13]</td>
<td>1.62 [0.12]</td>
</tr>
</tbody>
</table>

All the participants had MRIs taken at the Lady Cilento Children’s Hospital (LCCH) (Brisbane, Australia) and underwent gait analysis at the Queensland Children Motion Analysis Service (QCMAS) (Brisbane, Australia). A clinical pathway for patients’ recruitment was developed in collaboration with the LCCH and the QCMAS.
General methods

(Figure 4.1), which included completing an MRI request form, MRI booking and confirmation of the appointment.

RPD patients were offered enrolment following outpatient orthopaedic consultations at LCCH. Patients were considered eligible for the study if they were between six and 18 years old, experienced multiple (two or more) dislocations of minimal energy and they could walk independently on level surfaces for 50 m (rating five or above on the Functional Mobility Scale (Graham et al., 2004)). Patients were excluded if they experienced congenital patellar dislocations. TD participants, free from musculoskeletal or neurological impairment or lower limb injury within the prior six months, were recruited from the local community. Additional exclusion criteria for both groups included congenital limb abnormalities, previous surgical intervention affecting the anatomy of the knee or extensor mechanism, any past medical history of bony or soft tissue trauma or infection that may have affected bony or soft tissue anatomy, and inability to tolerate or deemed unsafe for MRI, identified using a safety questionnaire. Ethics approval was obtained from the Children’s Health Queensland Hospital and Health Services human research ethics committee (HREC/13/QRCH/197) and the Griffith University human research ethics committee (AHS/42/14/HREC), and participants’ guardians provided their written informed consent prior to data collection.
4.2 Data collection

4.2.1 Questionnaire

The Paediatric International Knee Documentation Committee subjective knee form (Pedi-IKDC) (Kocher et al., 2011) was used to assess patients’ perspectives on knee injuries. The 15-item questionnaire evaluates the patient’s symptoms, sports activities and
General methods

knee function. Patients completed the questionnaire either by themselves or with the help of their guardian.

4.2.2 Gait analysis

4.2.2.1 Laboratory set up

A ten-camera motion analysis system (Vicon Motion Systems Ltd, UK) was used to detect the position of skin-mounted retroreflective markers in a three-dimensional capture volume. The position of the motion capture cameras was fixed and designed to minimise marker occlusion in the capture volume (Figure 4.2). Prior to motion data collection in each testing session, reflections of objects other than markers (e.g., reflections from opposing camera strobe rings) were masked. Subsequently, the cameras were calibrated using an active wand provided by the system manufacturers. This wand included light-emitting diodes that can be detected by the cameras. The calibration process consisted of waving the active wand throughout the capture volume until 2000 frames of wand data were captured by each camera. After each attempt, the quality of the calibration was checked by ensuring that the image error for all the cameras was below 2 mm. If this was not achieved, then the calibration was repeated. The largest image error obtained in the calibration, together with the number of the camera that produced that error, were reported in the “Data collection and processing” form provided by the QCMAS.

Figure 4.2. Gait analysis laboratory at the QCMAS.

Additionally, four force platforms (510 mm x 465 mm, AMTI, Watertown, MA, USA) were used to record ground reaction forces (GRFs) during gait. Prior to data collection in each testing session, a T-shaped wand was placed on the third platform (from the laboratory entrance door) and used to set the origin of the force platforms capture volume. Afterwards, eight reflective markers were placed along the path where the
participant was supposed to walk (blue path, Figure 4.2) and the z-coordinate of each marker, corresponding to its vertical position, was derived. The vertical position of all the markers was considered acceptable if it ranged between 3 and 6 mm, as this meant that the walking path was at the same vertical level. If this was not achieved, the T-shaped wand was repositioned. After zeroing the force platforms, a walking trial was collected to ensure that the point of application, trend and magnitude of the forces were reasonable.

Finally, two video cameras (Panasonic) were positioned at the end and to the side of the walking path to simultaneously record the participant’s gait from a frontal and lateral view, respectively.

4.2.2.2 Participant preparation

Each participant was asked to wear elastic shorts without any metallic or retroreflective parts. At the beginning of each testing session, an experienced gait analyst collected anthropometric data for each participant. These data included the participant’s height, mass, leg length, frontal plane knee alignment (i.e., knee varus/valgus), knee width and ankle width (see Table 4.2 for full description of measurement methods). These participant’s details (except for knee varus/valgus measurements) were entered into the subject’s details in Vicon Nexus 2.5 (Vicon, Oxford, UK) prior to motion data collection.

Table 4.2. Anthropometric measurement description and technique.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Description</th>
<th>Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>Participant height</td>
<td>Standard stadiometer. Participant removes shoes and stands facing forward with head looking up.</td>
</tr>
<tr>
<td>Body mass</td>
<td>Participant mass</td>
<td>Participant remove shoes and stands on force platform with head looking forward.</td>
</tr>
<tr>
<td>Leg length</td>
<td>Distance between anterior superior iliac spine and medial malleolus, via the knee joint</td>
<td>A standard measuring tape is used while participants lie supine on physiotherapy bed.</td>
</tr>
<tr>
<td>Knee varus/valgus</td>
<td>Angle between the centre of the mid-thigh and centre of the ankle</td>
<td>The goniometer is placed on the frontal aspect of the knee, in correspondence to the midpoint between medial and lateral femoral epicondyles while participants are standing.</td>
</tr>
<tr>
<td>Knee width</td>
<td>Distance between medial and lateral femoral epicondyles</td>
<td>A calliper is placed at the back of the knee while participants are standing.</td>
</tr>
<tr>
<td>Ankle width</td>
<td>Distance between medial and lateral malleoli</td>
<td>A calliper is placed at the back of the ankle while participants are standing.</td>
</tr>
</tbody>
</table>

Two sets of MRI-compatible marker sets were constructed to allow concurrent assessment of two participants. Individual reflective markers were built using paintballs (diameter = 11.18 mm), which were covered in retroreflective tape and glued to a flexible
General methods

piece of fabric, which was the base of the marker. The retroreflective tape and liquid contained in the paintball allowed these markers to be visible both during gait analysis and MRI acquisition (Campbell et al., 2009). Moreover, these markers were deemed safe for MRI as they did not contain any metallic part. Four clusters of three markers were also built on a rubber rigid base, and four additional wand markers were used from the QCMAS marker set. In total, each marker set comprised 51 MRI-compatible reflective markers and four wand markers, which were attached to the participant’s body (Figure 4.3) by an experienced gait analyst with more than 10 years of experience in marker placement. Markers were placed in accordance with Kainz et al. (2017) and included few additional markers on the centre of the patella, medial/lateral tibial epicondyles, tibial tuberosity and first metatarsal (Table 4.3).

Figure 4.3. Gait analysis marker set, frontal (a) and lateral (b) views.
General methods

Table 4.3. Marker locations and landmark identification.

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Anatomical description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C7</td>
<td>Spinous process of the 7th cervical vertebra</td>
</tr>
<tr>
<td>T10</td>
<td>Spinous process of the 10th thoracic vertebra</td>
</tr>
<tr>
<td>CLAV</td>
<td>Clavicle</td>
</tr>
<tr>
<td>RBAK</td>
<td>Right Back</td>
</tr>
<tr>
<td>STRN</td>
<td>Sternum</td>
</tr>
<tr>
<td>R/L ASI</td>
<td>Most prominent point of the anterior superior iliac spine</td>
</tr>
<tr>
<td>R/L PSI</td>
<td>Most prominent point of the posterior superior iliac spine</td>
</tr>
<tr>
<td>R/L IC</td>
<td>Iliac crest</td>
</tr>
<tr>
<td>R/L THI</td>
<td>Thigh wand marker</td>
</tr>
<tr>
<td>R/L TH1-3</td>
<td>Rigid cluster of 3 markers on the thigh</td>
</tr>
<tr>
<td>R/L MKNE</td>
<td>Medial femoral epicondyle</td>
</tr>
<tr>
<td>R/L PAT</td>
<td>Centre of the patella</td>
</tr>
<tr>
<td>R/L KNE</td>
<td>Lateral femoral epicondyle</td>
</tr>
<tr>
<td>R/L TB5</td>
<td>Medial tibial epicondyle</td>
</tr>
<tr>
<td>R/L TUB</td>
<td>Tibial tuberosity</td>
</tr>
<tr>
<td>R/L TB4</td>
<td>Lateral tibial epicondyle</td>
</tr>
<tr>
<td>R/L TIB</td>
<td>Tibia wand marker</td>
</tr>
<tr>
<td>R/L TB1-3</td>
<td>Rigid cluster of 3 markers on the tibia</td>
</tr>
<tr>
<td>R/L MMA</td>
<td>Medial malleolus</td>
</tr>
<tr>
<td>R/L ANK</td>
<td>Lateral malleolus</td>
</tr>
<tr>
<td>R/L HEE</td>
<td>Calcaneus</td>
</tr>
<tr>
<td>R/L TOE</td>
<td>2nd metatarsal</td>
</tr>
<tr>
<td>R/L MT5</td>
<td>5th metatarsal</td>
</tr>
<tr>
<td>R/L MT1</td>
<td>1st metatarsal</td>
</tr>
</tbody>
</table>

4.2.2.3 Data acquisition

Three-dimensional marker trajectories were collected at 100 Hz using the ten-camera motion analysis system and Vicon Nexus, version 2.5. The ground-embedded force platforms were used to simultaneously acquire GRFs at 1000 Hz. After marker placement, participants completed a standing calibration trial and a series of walking trials. In the standing calibration trial, participants stood still on a single force platform with open arms and then performed three squats. Frontal and lateral videos of the participant performing these squats were also collected. In accordance with standard clinical practices at QCMAS, the Vicon Plug-in-Gait model was used for quality assurance to calculate pelvis and foot segment kinematics, and hip, knee and ankle joint kinematics for this trial to evaluate the knee ab/adduction kinematic profile. If the knee varus/valgus kinematic profile exceeded a range of motion of 10° and exhibited cross-talk with knee flexion/extension kinematic profile, the thigh wand marker was adjusted, and a new static trial was collected. Following the static trial (and possible wand adjustment), participants were instructed to complete a series of walking trials at their self-selected speed. Immediately after each trial, GRFs were inspected to ensure clean right/left foot force platform strikes and participants completed walking trials until at least six clean trials were obtained. Finally, two videos of the participant’s gait were acquired. At the end of each testing session, the last walking trial was analysed to make sure that
**General methods**

all the marker trajectories and GRFs were properly captured. If this was the case, the torso markers, the clusters of markers and the wand markers were removed, while the other markers were left on the participant’s skin for MRI acquisition. Otherwise, additional walking trials were re-collected.

4.2.3 MRI

After completing the gait analysis session at QCMAS, participants and their guardians were accompanied to medical imaging at LCCH through an underground tunnel that connects the two buildings. Participants walked barefoot to preserve the location of the feet markers. A workflow describing all the steps required on the day of scanning was developed in collaboration with Medical Imaging at LCCH and is presented in Figure 4.4.
4.2.3.1 Participant preparation

Prior to MRI acquisition, participants were asked to remove any metallic part (e.g., earrings) and their guardians were asked to complete a MRI safety questionnaire to ensure that participants had no metallic implants. Guardians could accompany the participants in the MRI scanning room if the participants were not comfortable by themselves. In this case, guardians were asked to complete another MRI safety questionnaire for themselves. Moreover, participants could select a movie to watch during MRI acquisition.
4.2.3.2 **Data acquisition**

The radiographer guided participants into the first MRI scanning room and positioned them on the MRI flat bed. Participants laid supine on the bed with two flexible array coils wrapped around their lower limbs (i.e., from iliac crests to malleoli) and with a rigid coil around their feet. Pillows, a blanket, headphones and a safety button were provided for safety reasons and to make the image acquisition as comfortable as possible (Figure 4.5a). The first MRI scan was performed on a 1.5 T scanner (SIEMENS MAGNETOM Avanto_fit syngo MR VE11B, Germany) and captured full-length lower limb bones (i.e., femur, patella, tibia, fibula, foot) and pelvis (3D PD SPACE sequence, slice thickness: 1.0 mm, voxel size: 0.83x0.83x1.0 mm³) according to (Kainz et al., 2016) (Figure 4.5b). Depending on the length of the lower limbs, the time required to complete this image acquisition ranged between 25 and 35 minutes.

![Figure 4.5. Full lower-limb MRI acquisition: participant's setting up in the 1.5T scanner (a) and resulting scan (b).](image)

After the first scan, participants were guided into another MRI scanner room and laid supine on the flat bed. A dedicated rigid knee coil was positioned around the most affected knee for RPD patients and the right knee for controls and used to acquire a second, regional MRI scan (3T scanner, SIEMENS MAGNETOM Skyra, Germany, 3D SPC T2, slice thickness: 0.53 mm, voxel size: 0.53x0.53x0.53 mm³) (Figure 4.6). Due to the bulky shape of the rigid knee coil, the participant’s knee was not exactly at 0° of TFJ flexion but slightly flexed. During pilot testing, this T2-weighted sequence was chosen over other sequences (e.g., T1-weighted) as it provided good image definition of all the tissues of interest, such as bones, articular cartilage and ligaments. Scanning time for this specific sequence ranged between 20 and 25 minutes.
General methods

Figure 4.6. Dedicated knee MRI acquisition: participant’s setting up in the 3T scanner (a) and resulting scan (b).

For validation purposes, three additional knee scans were acquired, using the same 3T scanner and sequence adopted for the high definition knee scan, on a subset of participants (n = 13, 5 RPD, 8 TD). At each scan, participants were asked to flex the knee with an increased TFJ flexion angle (approximately 10°, 20° and 30° of TFJ flexion) (Figure 4.7), the limits of which were determined by the restraining size of the space within the MRI scanner. The amount of TFJ flexion at each scan was measured by using a standard goniometer, the centre of which was placed on the lateral femoral epicondyle of the knee of interest. The TFJ flexion angle was defined as the angle between the ipsilateral femoral head and lateral malleolus. Once an appropriate position was defined, a set of foam positioning aids were placed underneath the knee to provide leg support and maintain the leg position during MRI acquisition. A flexible body coil was wrapped around the knee and each scan required approximately 15 minutes to complete. Results from pilot testing revealed that, compared to a coronal sequence, a sagittal sequence better reduced image artefact caused by the presence of the other leg in the same scanning volume, therefore, the sagittal sequence was chosen for the additional knee scans.

Figure 4.7. MRI knee scans collected for the same participant at three different TFJ flexion angles.
4.3 Data processing

4.3.1 Labelling and processing of motion capture data

Each session of raw marker and GRF data was reconstructed and cleaned in Vicon Nexus 2.5 using a custom pipeline that included labelling and processing operations. First, missing three-dimensional marker trajectories were interpolated using a Woltring algorithm (quintic spline) if the gap length was equal to or lower than 10 frames. Spline, pattern or rigid body fills were chosen otherwise. Markers trajectories and GRFs were then filtered using a fourth order (zero lag) Butterworth filter with a cut-off frequency of 6 Hz. Gait events, such as heel strike and toe-off, were automatically identified using the vertical GRF component of the foot in contact with the force platform at a detection threshold of 20 N. Only gait trials containing a single and complete foot strike on a force platform were considered and processed.

All marker trajectories and GRFs were then prepared for OpenSim using the open-source MOtoNMS pipeline (Mantoan et al., 2015) in Matlab (R2014b, The MathsWorks, USA). This pipeline facilitates the conversion of acquired motion data (c3d files) to a format supported by OpenSim (trc and mot files). Files in the MOtoNMS acquisition interface were modified to match the QCMAS laboratory setup (e.g., number of force platforms, coordinate system orientation) and the adopted marker set. Ground reaction forces were processed but will not be used in the rest of the thesis.

4.3.2 Segmentation and registration of MRI data

Medical images from MRI scans were saved into a Digital Imaging and Communications in Medicine (DICOM) format. These images were then imported into Mimics Research 20.0 (Materialise, Leuven) and anonymised. Two-dimensional images were then segmented by manually delineating the contour of the part of interest (i.e., bones, articular cartilages or ligaments) and using an in-built interpolating function that allowed the user to skip manual delineation in some slides. Specifically, segmentation included (i) full-length bones (i.e., pelvis, femur, patella, tibia, fibula, foot) of the most affected limb for RPD patients and right leg for TD participants from the full-lower limb scan and (ii) knee bone regions (i.e., distal femur, patella, proximal tibia and fibula), articulating knee cartilage (i.e., femoral, patellar and tibial cartilages) and major knee ligaments (i.e. ACL, PCL, MCL, LCL and patellar tendon) from the high resolution knee scan (Figure 4.8). Segmentation of the knee anatomical structures for the first participants were performed with the guide of an orthopaedic surgeon, to ensure that the correct tissues and regions were selected. Moreover, all the markers were segmented and, for those participants who had additional knee MRIs taken at different TFJ flexion angle,
distal femur, patella, proximal tibia and fibula were reconstructed at each position. From the segmented two-dimensional images, three-dimensional meshes were automatically created in Mimics and subsequently wrapped (smallest detail = smallest pixel size, closing distance = 2 x smallest pixel size) and smoothed with a first order Laplacian method (smoothing factor = 0.5, number of iterations = 10). Each participant’s lower limb and knee were segmented in approximately eight hours, and the segmentation of additional knee scans required two additional hours.

**Figure 4.8.** Segmentation (left side and top right) and three-dimensional meshes (bottom right) of knee anatomical structures created using Mimics. Segmented tissues included: distal femur (orange), proximal tibia (red) and fibula (blue), patella (violet), articular cartilages (femoral – green, tibial – yellow, patellar – light blue), ligaments (ACL – light green, PCL – magenta, LCL – light purple, MCL – dark purple, patellar tendon – light pink) and markers (aquamarine).

The reconstructed structures were then exported into 3-matic (Materialise, Leuven) as stereolithography (stl) format and the global reference system was rotated in order to have the x-axis defining the anterior (+)/posterior (-) direction, the y-axis defining the proximal (+)/distal (-) direction and the z-axis defining the lateral (+)/medial (-) direction of the stl files, according to the International Society of Biomechanics (ISB) convention (Wu et al., 2002). Furthermore, as the full lower-limb and the detailed knee scans were acquired in different image coordinate systems, their corresponding three-dimensional reconstructed meshes had to be aligned. Therefore, full length femur, tibia and fibula were registered into the distal femur, proximal tibia and fibula using an iterative closest point algorithm (Besl et al., 1992) in 3-matic. Pelvis, foot and markers were moved along with the full-length bones during the registration process. In this way, a comprehensive representation of the participant’s leg, inclusive of markers, bones, knee cartilage and ligaments was obtained (Figure 4.9). For validation purposes, full length
femur, tibia and fibula were also registered into the distal femur, proximal tibia and fibula reconstructed from the MRIs at different knee flexion angles. For each registration step, the registration error was computed in 3-matic and the final error was saved (< 0.1 mm for each bone).

![Figure 4.9](image)

**Figure 4.9.** Comprehensive representation of a participant’s pelvis and right leg following the registration process in 3-matic. This representation included markers (blue), full length bones (beige), knee cartilage (dark grey) and ligaments (pink).

### 4.4 Development of subject-specific knee kinematic models

#### 4.4.1 TFJ passive kinematic models

Three different passive kinematic models of the TFJ with different ligamentous constraints were developed from MRI. These models were applied to a subgroup of eight healthy children and adolescents and the resulting kinematics were validated against MRI-measured kinematics at different TFJ flexion angles. The TFJ model that had the best agreement with *in vivo* TFJ and ligament kinematics was then used to estimate passive TFJ kinematics both in TD participants and RPD patients.

#### 4.4.1.1 Creation of subject-specific TFJ models

Two segment coordinate systems (SCSs) were defined using anatomical landmarks manually located onto the bone segmented meshes to obtain the pose of the femur relative to the tibia. The femur SCS ($F_{cs}$) was defined with origin coincident with the midpoint between the lateral and medial femoral epicondyles, $x$-axis (anterior/posterior) orthogonal to the plane defined by the two epicondyles and the head of the femur (i.e., hip joint centre), $y$-axis (proximal/distal) directed from the SCS origin to the head of the femur and $z$-axis (medio/lateral) according to the right hand rule.
General methods

(Belvedere et al., 2007; Cappozzo et al., 1995b). The tibia SCS \( T_{cs} \) was defined with origin coincident with the deepest point in the sulcus between the medial and lateral tibial intercondylar tubercles, \( x \)-axis orthogonal to the plane defined by the medial and lateral malleoli and the tibia centre, \( y \)-axis directed from the mid-point between the malleoli to the tibia centre and \( z \)-axis according to the right-hand rule (Belvedere et al., 2007; Cappozzo et al., 1995b)

A baseline passive kinematic model of the TFJ was implemented as a 5-rigid-link parallel mechanism including two sphere-on-sphere contacts (representing the medial and lateral contacts between the femoral condyles and the tibia plateaus) and three ligaments (ACL, PCL and MCL) (Brito da Luz et al., 2017; Sancisi et al., 2011b). The geometrical parameters of the TFJ model included the coordinates of the sphere centres and ligament attachment points in the femur \( B_i \) and in the tibia \( A_i \) \((i = 1, \ldots, 5)\), expressed in \( F_{cs} \) and \( T_{cs} \), respectively, and the lengths \( L_i \) \((i = 1, \ldots, 5)\) of the links \( A_iB_i \) (Figure 4.10). The relative pose of the tibia with respect to the femur was derived by solving the following closure equations of the TFJ model:

\[
\|B_i - R_{ft}A_i - P_{ft}\| = L_i \quad i = 1, \ldots, 5
\]  

(4.1)

where \( R_{ft} \) is a 3x3 rotation matrix for the transformation of vector components from \( T_{cs} \) to \( F_{cs} \) and \( P_{ft} \) is the translation vector pointing from the origin of \( F_{cs} \) to the origin of \( T_{cs} \), expressed in \( F_{cs} \). The matrix \( R_{ft} \) was defined, with \( zyx \) order of rotation (Craig, 2005; Grood et al., 1983), as a function of three angles \( \alpha, \beta, \gamma \):

\[
R_{ft} = \begin{bmatrix}
\cos \alpha \cos \gamma + \sin \alpha \sin \beta \sin \gamma & \sin \alpha \cos \beta & \cos \alpha \sin \gamma - \sin \alpha \sin \beta \cos \gamma \\
-\sin \alpha \cos \gamma + \cos \alpha \sin \beta \sin \gamma & \cos \alpha \cos \beta & -\sin \alpha \sin \gamma - \cos \alpha \sin \beta \cos \gamma \\
-\cos \beta \sin \gamma & \sin \beta & \cos \beta \cos \gamma
\end{bmatrix}
\]  

(4.2)

where \( \alpha, \beta, \gamma \) correspond to the flexion, ab/adduction and internal/external rotation angles of the tibia with respect to the femur. Once the flexion angle \( \alpha \) was assigned, ab/adduction (\( \beta \)), internal/external rotation (\( \gamma \)) and three translations (i.e., anterior/posterior, proximal/distal and medio/lateral) of the tibia with respect to the femur could be estimated. However, it should be noted that, compared to the closure equations used to solve cadaveric-based TFJ mechanisms (Sancisi et al., 2011b), two modifications were implemented in the above equations (Equations (4.1)(4.2)) according to Brito da Luz et al. (2017). The first modification allowed to estimate the motion of the tibia relative to the femur (rather than the motion of the femur relative to the tibia) and the second one altered the order of rotation from \( yxz \) to \( zxy \). These modifications were made to facilitate
the comparison of the TFJ kinematics between different studies and to use ISB standard order of rotation (Grood et al., 1983; Wu et al., 2002), respectively.

**Figure 4.10.** Representation of the geometrical parameters used to create the baseline 5-rigid-link TFJ parallel mechanism. Solid lines represent the ACL, PCL and MCL ligaments with attachments in the femur (B₁, B₂, B₃) and in the tibia (A₁, A₂, A₃), while dotted lines represent articular contacts between the medial and lateral condyles of the femur (blue spheres, with centres in B₄ and B₅) and tibia (red spheres, with centres in A₄ and A₅).

For each participant, the geometry of the TFJ contact surfaces (i.e., articulating femoral condyles and tibial plateaus) and ligaments (i.e., attachment regions) was derived from the comprehensive three-dimensional representation of the participant’s leg previously obtained in 3-matic (Figure 4.11). Subsequently, the femoral condyles and tibial plateaus were approximated by best fitting spheres in Matlab (R2014b, MathWorks). The attachment points of the ligaments were computed as centroids of the segmented ligament attachment regions and ligament lengths were defined as Euclidean distance between the attachment points of each ligament. The TFJ baseline model was then extended by adding the LCL, the geometry of which was defined with the same procedure used for the other ligaments, so obtaining a 6-link mechanism.
General methods

Three different subject-specific TFJ models were created with different ligamentous constraints. The first (or baseline) was a 5-rigid-link TFJ model where the ACL, PCL and MCL were considered isometric ($\Delta L_0$) over the TFJ flexion range of motion (ROM). The second was a 6-link TFJ model which had minimal changes in length of the ACL, PCL, MCL and LCL ($\Delta L_{min}$) over the TFJ flexion ROM. The third was also a 6-link TFJ model, but with ACL, PCL, MCL and LCL length changes that tracked the pattern of published experimental ligament length changes (Belvedere et al., 2012; Bergamini et al., 2011; Blankevoort et al., 1991) over the TFJ flexion ROM ($\Delta L_{match}$). In all the three TFJ models, the two articular contacts were considered rigid, therefore no penetration or separation was allowed.

4.4.1.2 Optimisation of each TFJ model

After each subject-specific TFJ model was created, the model’s geometrical parameters, that were initially measured off the MRI, were optimised to ensure that the TFJ mechanism could be solved (Brito da Luz et al., 2017). Different optimisation approaches were used for the three TFJ models ($\Delta L_0$, $\Delta L_{min}$, and $\Delta L_{match}$). Each optimisation approach consisted of a nested optimisation problem, including an outer and

Figure 4.11. Manual selection (pink areas) of the geometrical parameters used to create the baseline 5-rigid-link TFJ parallel mechanism. Femoral condyles (a), tibial plateaus (b) and ligament attachment regions (ACL, PCL and MCL) on the femur (c) and tibia (d) were delineated on the reconstructed bone and cartilage volumes.
General methods

an inner loop. The outer loop optimised each participant’s MRI-measured geometrical parameters (i.e., sphere centres and ligament attachment points), while the inner loop solved the closure equations of the TFJ mechanism. In the outer loop, the three-dimensional coordinates of the centre of the spheres fitted to the TFJ articulating surfaces were allowed to deviate up to 20mm from their initial MRI-measured position. The radii of these spheres were also updated by minimising the summed least square residuals between fitted spheres and MRI-segmented cartilages, while ensuring that the residuals were <5% of the optimised radii. Furthermore, the optimised attachment points of the ligaments were maintained within their respective bone attachment regions. However, differently from cadaveric-based model, the centre of the spheres fitted to the femoral condyles were not optimised because these segmented cartilage surfaces were well fitted with small residual values (Brito da Luz, 2016). Therefore, this allowed to reduce the number of geometrical parameters that required optimisation.

Depending on the TFJ model (i.e., \( \Delta L_0, \Delta L_{\text{min}}, \) and \( \Delta L_{\text{match}} \)), different objective functions were optimised in the outer loop. All the four objective functions will be described in detail in Section 6.3.4. However, to summarise, the first objective function achieved the best match between the patterns of the estimated and published experimental TFJ kinematics (Ottoboni et al., 2010; Sancisi et al., 2011b), while the second minimised the difference between MRI-measured and optimised geometrical parameters. The third minimised the difference between optimised and published paediatric TFJ ab/adduction and internal/external rotation ROMs (Leardini et al., 2007), if the optimised ROMs were larger than the published ROMs, and the fourth sought the best match between the patterns of the estimated and published experimental changes in ligament length (Belvedere et al., 2012; Bergamini et al., 2011; Blankevoort et al., 1991). The first three objective functions were used for all TFJ models, while the fourth one was used only for \( \Delta L_{\text{min}} \).

Using a Multiple Objective Particle Swarm Optimisation (MOPSO) algorithm implemented in Matlab, the outer loop optimised the MRI-measured geometrical parameters to minimise the corresponding objective functions. With this algorithm it was possible to find multiple solutions from which the best solution had to be selected (see Section 6.7.3 for further details). The optimisation ran using 50 particles and 200 iterations.

Subsequently, the inner loop used the optimised geometrical parameters to solve the closure equations of the TFJ mechanisms for 1° increments of the TFJ flexion angle.
For all three methods, the inner loop solved the mechanisms equations to avoid discontinuities, which ensured that the estimated kinematic curves were continuous. Moreover, the inner loop minimised the estimated ligament length changes for $\Delta L_0$ and $\Delta L_{\text{min}}$, while it minimised the difference between estimated and published experimental ligament length change for $\Delta L_{\text{match}}$. The closure equations of the TFJ mechanisms were solved by using the $fsolve$ function in Matlab, with a trust-region algorithm for $\Delta L_0$, and a Levenberg-Marquardt method for $\Delta L_{\text{min}}$ and $\Delta L_{\text{match}}$, given that, in the latter models, the number of closure equations was higher than the number of kinematic variables. The resulting TFJ kinematics, that described the position of the tibia relative to the femur, included five motion components (i.e., ab/adduction, internal/external rotation, anterior/posterior, proximal/distal and medio/lateral translations) expressed as function of the TFJ flexion angle.

### 4.4.2 PFJ passive kinematic models

The PFJ was modelled as a hinge joint in control participants (Brito da Luz et al., 2017; Sancisi et al., 2011a). However, as the MRIs at different TFJ flexion angles revealed abnormal patellar kinematics in RPD patients, a hinge joint model was not appropriate to describe the patellar kinematics in this patient group. Therefore, a different PFJ model had to be implemented to better describe the patellar kinematics in RPD patients.

#### 4.4.2.1 Development of a subject-specific PFJ model for TD participants

The patella SCS ($P_{cs}$) was also defined using anatomical landmarks manually located onto the patella segmented mesh to obtain the pose of the patella relative to the femur. Precisely, the origin was coincident with the mid-point between the lateral and medial patellar apices, the $x$-axis was orthogonal to the plane defined by the lateral, medial and distal patellar apices, the $y$-axis was directed from the distal patellar apex to the origin and the $z$-axis was defined according to the right-hand rule (Belvedere et al., 2007).

A hinge joint was used to characterise the motion of the patella with respect to the femur in control participants. Specifically, in these participants the patella was constrained to rotate about and at a constant distance from an axis, defined by the centre of two spheres fitted to the medial and lateral patellofemoral articular surfaces, while maintaining constant patellar tendon length (Brito da Luz et al., 2017; Sancisi et al., 2011b) (Figure 4.12). The geometrical parameters used in the PFJ hinge model included: i) the components of the unit vectors $\mathbf{n}_1$ (expressed in $F_{cs}$) and $\mathbf{n}_2$ (expressed in $P_{cs}$) of the
rotation axis, ii) the coordinates of the vectors $Q_1$ (expressed in $\mathcal{P}_{cs}$) and $Q_2$ (expressed in $\mathcal{P}_{cs}$) of the intersections of the hinge axis with the x-y reference planes, iii) the coordinates of the patellar tendon attachments points $C_1$ (expressed in $\mathcal{T}_{cs}$) and $D_1$ (expressed in $\mathcal{P}_{cs}$), iv) the constant distance $L$ between $C_1$ and $D_1$ and v) the constant distance $\lambda$ between $Q_1$ and $Q_2$. The pose of the patella relative to the femur was derived by solving the following closure equations of the PFJ model (Sancisi et al., 2011b):

$$R_{fp} n_2 = n_1$$

$$R_{fp} Q_2 + P_{fp} = \lambda n_1 + Q_1$$

$$\|R_{tf}(R_{fp} D_1 + P_{fp}) + P_{tf} - C_1\| = L$$

where the 3x3 rotation matrix $R_{fp}$ and the translation vector $P_{fp}$ were expressed similarly to Eq. (4.2). Finally, due to the modifications made to solve the TFJ mechanism (section 4.4.1.1), the rotation matrix $R_{tf}$ and the translation vector $P_{tf}$ used in Eq. (4.5) were determined as follows:

$$R_{tf} = R_{ft}'$$

$$P_{tf} = -R_{ft}' * P_{ft}$$
**Figure 4.12.** Representation of the PFJ hinge mechanism (Brito da Luz et al., 2017; Sancisi et al., 2011b). The solid black line represents the patellar tendon, with attachments on the tibia ($C_i$) and on the patella ($D_i$). Two spheres were best fitted to the medial and lateral patellofemoral articulating surfaces with hinge axis $n_1$ represented as dashed line. $Q_1$ and $Q_2$ are the intersection points of the hinge axis, relative to $P_{cs}$ and $F_{cs}$, with the x-y reference planes of $P_{cs}$ and $F_{cs}$ and $\lambda$ is the fixed distance between these two points.

For each participant, the geometry of the PFJ contact surfaces and the attachment regions of the patellar tendon were manually identified on the comprehensive three-dimensional representation of the participant’s leg previously obtained in 3-matic (Figure 4.13). Subsequently, the PFJ articulating surfaces were approximated by best fitting spheres in Matlab and the geometry of the patellar tendon (i.e. attachment points and length) was defined with the same procedure used for the other TFJ ligaments.
General methods

Figure 4.13. Manual delineation (pink areas) of patellofemoral articulating surfaces (a) and patellar tendon attachment regions (b) on the reconstructed bone and cartilage volumes.

The same optimisation approach described for the TFJ model, consisting of an outer and inner loop, was used for the PFJ model. Thus, the outer loop optimised each participant’s MRI-measured geometrical parameters (i.e., sphere centres and patellar tendon attachment points), while the inner loop solved the closure equations (Eq. (4.3)-(4.5) of the PFJ mechanism. In the outer loop, the three-dimensional coordinates of the sphere centres could deviate up to 5 mm from their initial MRI-measured position. The radii of these spheres were also updated by minimising the summed least square residuals between fitted spheres and MRI-segmented cartilages, while ensuring that the residuals were <5% of the optimised radii. Finally, the optimised attachment points of the patellar tendon were maintained within their respective bone attachment regions. However, contrarily to cadaveric-based PFJ models (Sancisi et al., 2011b), the geometrical parameters \( n_1, n_2, Q_1, Q_2 \) and \( \lambda \) were not optimised to avoid redundancy, since these parameters were determined from the optimised sphere centres and ligament attachment points.

The outer loop minimised for two objective functions (Eq. 4.8 - 4.9), where the first (Eq. 4.6) best matched the pattern, i.e. correlation \( (\rho_i) \), between estimated and published experimental \( i \)-th motion component of PFJ kinematics (Anglin et al., 2008; Sancisi et al., 2011b), while the second minimised the difference between MRI-measured \( (g_{m,k}) \) and optimised \( (g_{o,k}) \) geometrical parameters (i.e., sphere centres and patellar tendon attachment points).

\[
J_1 = (1 - \rho_i)^2 \\
i = 1, ..., 6
\]  

\[
(4.8)
\]
As for the TFJ model, the MOPSO algorithm optimised the geometrical parameters to minimise the two objective functions in the outer loop. The optimisation for the PFJ ran using 50 particles and 50 iterations. The number of iterations for the PFJ was lower than that required for the TFJ because the PFJ mechanism found solutions quicker than the TFJ mechanism in pilot testing. In fact, during pilot testing, MOPSO provided very few discontinuous solutions for the PFJ mechanism, even when setting a low number of iterations. Within the multiple MOPSO solutions, the solution that achieved the best match between the patterns of the estimated and published experimental PFJ kinematics (i.e., solution with minimum $J_1$) was chosen, given that the geometrical parameters were always within the limits of reasonable anatomical variability.

Subsequently, the inner loop used the optimised geometrical parameters to solve the closure equations of the PFJ mechanisms for 1° increments of the TFJ flexion angle while ensuring that the estimated kinematic curves were continuous. The resulting PFJ kinematics, that described the position of the patella relative to the femur, included 6 motion components: flexion/extension, ab/adduction, internal/external rotation, anterior/posterior, proximal/distal and medio/lateral translations.

4.4.2.2 Development of subject-specific PFJ models for RPD patients

As previously mentioned, the analysis of the MRIs acquired at four different TFJ flexion angles for five RPD patients suggested that the PFJ does not behave like a single hinge in this pathological population. Indeed, in RPD patients the patella exhibited an exaggerated lateral to medial translation into the trochlear groove during early stages of passive TFJ flexion (approximately between 0°-30°), confirming patellar J tracking, as described in section 2.2.4 (Figure 4.14). Therefore, for this patients’ group we modelled the PFJ with two different mechanisms: the first mechanism described the lateral to medial translation of the patella into the trochlear groove during early stages of TFJ flexion, while the second described the motion of the patella after it reached a more congruent position into the trochlear groove. Both PFJ mechanisms were hinge joint models, where the patella was constrained to rotate about and at a constant distance from an axis, which was different for the two mechanisms, while maintaining constant patellar tendon length. To create these models, femur and patella SCSs were defined using the same anatomical landmarks chosen for the previously described TFJ and PFJ mechanisms (Belvedere et al., 2007; Cappozzo et al., 1995b)

\[ J_2 = \left( g_{m,k} - g_{o,k} \right)^2 \quad k = 1, ..., 12 \]
General methods

Figure 4.14. Patella position and orientation at different TFJ flexion angles in a RPD patient. The patella translates medially into the trochlear groove as the knee flexes (from a to d).

The geometrical parameters for both PFJ mechanisms (i.e., articulating patellofemoral surfaces and patellar tendon attachments) were derived from the three-dimensional reconstruction of the participant’s most affected knee obtained from the dedicated knee scan at approximately 0° of TFJ flexion (Figure 4.14a). The reconstructed volume of the patella from the knee scan at the highest TFJ flexion angle (Figure 4.14d) was registered onto the three-dimensional anatomical reconstruction obtained from the dedicated knee scan at approximately 0° of TFJ flexion using an iterative closest point algorithm (Figure 4.15). This way, the amount of lateral to medial translation of the patella during the first ~30° of TFJ flexion could be visualised. For the first PFJ mechanism, a surface connecting the two poses of the patella (i.e., at 0° and 30° of TFJ flexion) was manually delineated on the reconstructed femoral cartilage (Figure 4.15a), as an approximation of the region where the patella was likely to articulate between 0° and 30° of TFJ flexion. A cylinder was best fitted in 3-matic to this articulating surface and its axis was then used to define the hinge axis of rotation of the first PFJ mechanism. Contrarily, for the second PFJ mechanism, the articulating surfaces were defined as the medial and lateral patellofemoral articular surfaces (Figure 4.15c), as for the PFJ mechanism implemented for healthy participants. The PFJ articulating surfaces were approximated by two best fitting spheres in Matlab, with the hinge axis of rotation for the second PFJ mechanism defined as the vector connecting the centre of these two spheres.
Figure 4.15. Implementation of two PFJ mechanisms to estimate the passive PFJ kinematics of RPD patients. The poses of the patella at ~0° (purple) and ~30° (green) of TFJ flexion were registered on the same femur bone reconstruction (left). In the first PFJ mechanism (top), the articulating surface connecting the two poses of the patella was delineated and approximated by best fitting a cylinder (a). The patella was then constrained to rotate about the axis of this cylinder, starting from the position at ~30° and back to 0° of TFJ flexion (b). In the second mechanism, the articulating surfaces were defined as the medial and lateral patellofemoral articulating surfaces, that were then approximated by best fitting two spheres (c). The patella was constrained to rotate about the vector connecting the centre of these two spheres, starting from the position at ~30° and up to 90° of TFJ flexion. In both PFJ mechanisms, the patellar tendon was considered isometric.

To facilitate continuity between the two PFJ mechanisms, the pose of the patella at ~30° of TFJ flexion was used as initial guess for both mechanisms to solve their corresponding closure equations (Figure 4.15b,d). Thus, the first mechanism estimated the patellar kinematics from ~30° to 0° of TFJ flexion, while the second one estimated the patellar kinematics from ~30° to 90° of TFJ flexion. The final solution, i.e. the patellar kinematics described between 0° to 90° of TFJ flexion, was obtained by merging the resulting kinematics of the two PFJ mechanisms.

A similar optimisation approach described for the PFJ mechanism implemented for healthy participants was used for both PFJ mechanisms. However, the objective functions defined in the outer loop were different (Equations 4.8-4.9). First, to approximate the lateral to medial translation of the patella between 0° and 30° of TFJ
General methods

flexion, the mean difference between mechanism-estimated \( T_{i,o} \) and MRI-measured medio/lateral translation \( T_{i,m} \) at approximately 0° and 30° of TFJ flexion was minimised (Eq. 4.8). Second, to ensure continuous and smooth kinematics, the mean range of the second order derivative \( (D^2) \) of the kinematic curves \( f_j \) was minimised (Eq. 4.9). Moreover, given the abnormal patellar tracking in this patients’ group, the correlation between estimated and published experimental PFJ kinematics (from healthy participants) (Anglin et al., 2008; Sancisi et al., 2011b) was not considered.

\[
J_1 = \text{mean}(\sqrt{(T_{i,o} - T_{i,m})^2}) \quad i = -0^\circ \text{ and } 30^\circ \text{ of TFJ flexion} \quad (4.10)
\]

\[
J_2 = \text{mean}[\text{max}(D^2(f_j)) - \text{min}(D^2(f_j))] \quad j = 1, \ldots, 6 \quad (4.11)
\]

Within the multiple MOPSO solutions, the solution that achieved the best match between the estimated and MRI-measured medio/lateral PFJ translation at approximately 0° and 30° of TFJ flexion (i.e., solution with minimum \( J_1 \)) was chosen, as it better tracked MRI-registered data while ensuring continuous PFJ kinematics.

4.5 Subject-specific full lower limb models

4.5.1 Development of subject-specific full lower limb models

Full lower limb subject-specific models were created for the eight TD participants from whom we collected additional knee scans at different TFJ flexion angles. Each model was a single-leg model (right leg) that included each participant’s three-dimensional lower limb bone meshes (i.e., pelvis, right femur, patella, tibia, fibula and foot) and knee cartilage (i.e., femoral, patellar and tibial). These meshes were imported as stl objects into NMSBuilder software (Valente et al., 2017) and were grouped into five bodies: pelvis, femur (i.e., right femur and femoral cartilage), patella (i.e., right patella and patellar cartilage), tibia (i.e., right tibia, fibula and tibial cartilage) and foot (Figure 4.16a). SCSs were defined for each body from anatomical landmarks virtually palpated onto the bone meshes (Table 4.4). Moreover, the markers captured during the MRI acquisition, the position of which was computed in Matlab, were imported into the software and attached to the corresponding body (Figure 4.16b).
### General methods

**Table 4.4.** Segment coordinate systems defined in NMSBuilder for each body.

<table>
<thead>
<tr>
<th>Segment</th>
<th>Definition</th>
</tr>
</thead>
</table>
| **Pelvis** (Cappozzo et al., 1995b) | o: Mid-point between LASI and RASI landmarks  
   z: From the origin to RASI  
   x: Perpendicular to the medio-lateral axis in plane with the mid-point between RPSI and LPSI landmarks  
   y: According to the right-hand rule |
| **Femur** (Belvedere et al., 2007) | o: Mid-point between the lateral and medial femoral epicondyles  
   y: From origin to the head of the femur (i.e., centre of the sphere fitted to the femoral head)  
   x: Orthogonal to the plane defined by the two femoral epicondyles and the head of femur  
   z: According to the right-hand rule |
| **Patella** (Belvedere et al., 2007) | o: Mid-point between the lateral and medial patellar apices  
   y: From the distal patellar apex to the origin  
   x: Orthogonal to the plane defined by the lateral, medial and distal patellar apices  
   z: According to the right-hand rule |
| **Tibia** (Belvedere et al., 2007) | o: Deepest point in the sulcus between the medial and lateral tibial intercondylar tubercles  
   y: From the mid-point of the malleoli to the tibia origin  
   x: Orthogonal to the plane defined by the two malleoli and the tibia origin  
   z: According to the right-hand rule |
| **Foot** (Kainz et al., 2016) | o: Most inferior point of the calcaneus  
   x: From origin to mid-point between the most inferior point of the 1st and 5th metatarsal heads  
   z: Perpendicular to anterior-posterior axis in plane with most inferior point of the 5th metatarsal head pointing laterally  
   y: According to the right-hand rule |
Figure 4.16. Subject-specific right leg model created in NMSBuilder (a) and exported in OpenSim (b).

While the hip and ankle joints were defined as spherical joints (i.e., three rotations were allowed), the TFJ and PFJ were defined as custom joints (i.e. six motion components were allowed: three rotations and three translations). Results from the TFJ and PFJ mechanisms implemented for healthy participants were incorporated into the full-lower limb model by means of cubic splines, which guided the TFJ and PFJ relative orientation and position as function of the TFJ flexion angle. The names of the joints and of the coordinates of the resulting OpenSim model, as well as the rotation orders, were updated (Modenese et al., 2018) in order to match those of standard OpenSim models (Delp et al., 1990). Finally, two clusters of three markers were manually placed on the model according to their position on the participant’s thigh and shank, which was verified by checking the participant’s video. Using the scaling tool available in OpenSim, the cluster of markers in the OpenSim model were moved to match the experimental marker location in the static pose, until the maximum marker and RMSE errors were below 2 cm and 1 cm, respectively, according to the OpenSim best practices (Hicks et al., 2015).
4.5.2 Explicit implementation of the TFJ mechanism in OpenSim

To allow for minimal ligament elongation during walking, the previously described TFJ mechanisms were explicitly implemented into the full lower limb OpenSim models. Firstly, we decided to explicitly implement $\Delta L_0$ (5-rigid-link mechanism) so that we could compare the resulting TFJ kinematics with those obtained from the implicit mechanism (i.e., mechanism that was implemented in Matlab) and ensure that the implementation was correct. To this end, we imported the three-dimensional ligament meshes in NMSBuilder as stl files. Each ligament (i.e., ACL, PCL, MCL and LCL) consisted of two parts (i.e. proximal and distal) that were obtained using the “cut” tool in 3-matic (Figure 4.17a). Even if the LCL was not modelled in the implicit 5-rigid-link mechanism, it was included in the explicit mechanism implementation to obtain a more realistic representation of the TFJ during walking. SCSs were defined for each body using the optimised ligament attachment points obtained from the implicit TFJ mechanism. Specifically, each SCS of the proximal ligament bodies had origin coincident with the optimised ligament attachment point on the femur and $x$-axis directed towards the optimised ligament attachment point on the tibia. Similarly, each SCS of the distal ligament bodies had origin coincident with the mid-point of the two optimised attachment points and $x$-axis directed towards the optimised ligament attachment point on the tibia (Figure 4.17b). For the LCL, the attachment points were defined as the centroids of the LCL attachment regions onto the femur and the fibula. A spherical joint was created between each proximal ligament body and the femur and a point constraint was introduced between each distal body and the tibia. The point constraint is the OpenSim equivalent of a spherical joint, given that it fixes a point defined with respect to two bodies, impeding any relative translations between the two bodies. The choice of introducing a point constraint, rather than a spherical joint, was dictated by the fact that, in OpenSim, each body can be connected only by one joint to a parent body, so creating a chain or open tree structure (i.e., each child body needs to have only one parent body) that can be closed using constraints (Figure 4.18). Moreover, a prismatic joint was defined between each proximal and distal ligament body to allow for ligament elongation in the longitudinal axis of the ligament (Figure 4.17c). In the implementation of $\Delta L_0$, the prismatic joints for the ACL, PCL and MCL were locked to keep the ligament isometric. Finally, two bodies with negligible inertia were introduced to represent the medial and lateral TFJ articular contacts, respectively. These two bodies were connected to the femur by means of spherical joints and to the tibia by means of point constraints, for the same reason explained before. As the contact between the two articulating surfaces was
considered rigid in the parallel mechanisms, no prismatic pairs were introduced for these bodies.

**Figure 4.17.** Implementation of the explicit TFJ mechanism. Each ligament (i.e., ACL, PCL, MCL and LCL) was divided into a proximal and a distal part (a), for which a SCS was defined (b). The $x$-axis of each SCS (red arrow) coincided with the ligament longitudinal axis, defined as the vector connecting the optimised ligament attachment points. Each proximal ligament body was connected to the femur by means of a spherical joint and to the tibia by means of a point constraint (c). A prismatic joint was introduced between each proximal and distal ligament body to allow for minimal ligament elongation.
Figure 4.18. Open tree structure of the right-leg OpenSim model, including the explicit TFJ mechanism. Each proximal ligament body (i.e., ACLprox_r, PCLprox_r, MCLprox_r and LCLprox_r) and each contact body (i.e., art_cont1_r and art_cont2_r) are connected to the femur via a spherical joint. Each distal ligament body (i.e., ACLdist_r, PCLdist_r, MCLdist_r and LCLdist_r) is connected to its corresponding proximal body by a prismatic pair. All distal ligament bodies (i.e., ACLdist_r, PCLdist_r, MCLdist_r and LCLdist_r) and the two contact bodies (i.e., art_cont1_r and art_cont2_r) are connected to the tibia (i.e., tibia_r) via point constraints (not visible in the topological representation of the multibody system).

After verifying that the explicit 5-rigid-link mechanism (i.e., ΔL₀) provided the same results as the equivalent implicit mechanism, we decided to employ the explicit mechanism also in simulations with deformable ligaments. In fact, based on the comparison between estimated and in vivo joint and ligament kinematics (see Section 6.4), ΔL₀ was deemed appropriate to estimate both passive joint and ligament kinematics. Therefore, the prismatic pairs between the proximal and distal bodies of the ACL, PCL and MCL were unlocked to allow for ligament elongation.

4.5.3 TFJ, PFJ and ligament kinematics during gait

Joint and ligament kinematics during gait for the eight TD participants were computed in two ways: i) using the implicit 5-rigid-link TFJ mechanism and ii) using the explicit mechanism and allowing for active elongation of the four ligaments (i.e., ACL, PCL, MCL and LCL). In both methods, each participant’s joint and ligament kinematics of five walking trials were obtained using the inverse kinematic tool in OpenSim.
General methods

The first method ($\Delta L_{0,\text{spl}}$) used the full-lower limb OpenSim model where the TFJ and PFJ kinematics were obtained from the implicit $\Delta L_0$ mechanism and incorporated into the OpenSim model as cubic splines (see Section 4.5.1). In this approach, the length of the ACL, PCL and MCL was maintained constant. In the inverse kinematic analysis, a weight for each of the $i$th marker ($w_i$) was defined and used to solve the weighted least squares problem (Eq. 4.8), where the error between measured ($x_i^{\text{exp}}$) and model-determined ($x_i(q)$) marker positions was minimised. The same solution could have been achieved by using the explicit implementation of $\Delta L_0$ but, due to the more complex implementation of the explicit model, this would have increased the inverse kinematics analysis time (~15 seconds versus ~3 seconds when using the implicit mechanism).

$$\min_q \left[ \sum_i w_i \left( x_i^{\text{exp}} - x_i(q) \right)^2 \right]$$

Contrarily, the second method ($\Delta L_{0,MBO}$) used the full-lower limb OpenSim model where $\Delta L_0$ was explicitly implemented and the prismatic pairs between each proximal and distal ligament bodies were unlocked to allow for ligament elongation (see Section 4.5.2). In the inverse kinematic analysis, a weight for each of the $i$th marker ($w_i$), as well as for each of the $j$th coordinate ($p_j$), was defined and used to solve the weighted least squares problem (Eq. 4.9), where both the error between measured ($x_i^{\text{exp}}$) and model-determined ($x_i(q)$) marker positions and between experimental ($q_j^{\text{exp}}$) and model-determined ($q_j$) coordinate values were minimised.

The coordinates included in Eq. 4.9 corresponded to the elongation of the ACL, PCL, MCL and LCL (i.e., the translation between the proximal and distal part of each ligament, along the $x$-axis, allowed by the prismatic pair). This approach consists on a multibody optimisation approach, where the position and orientation of the multi-body lower-limb model are optimised to minimise both the distance between measured and model-determined marker trajectories and the ligament elongation.

$$\min_q \left[ \sum_i w_i \left( x_i^{\text{exp}} - x_i(q) \right)^2 + \sum_j k_j \left( q_j^{\text{exp}} - q_j \right)^2 \right]$$

While all the markers were tracked with $w_i = 1$, the weight $k_j$ used for each ligament elongation was derived from MRI as an estimation of the stiffness of each ligament. Assuming that all the four ligaments had the same Young’s modulus, the axial stiffness was defined as the ratio between each ligament’s cross-sectional area (CSA) and its length from the MRI at $\sim 0^\circ$ TFJ flexion. For each ligament, the cross-sectional area
was obtained by cutting the ligament in the middle (i.e., mid-point between the optimised attachment points), perpendicular to its longitudinal axis (Muneta et al., 1997), while the length was defined as the length of the centroid of the ligaments, between the optimised attachment points (Figure 4.19).

**Figure 4.19.** Ligament lengths (blue lines) and CSA (yellow area). A plane (magenta) perpendicular to the ligament’s longitudinal axis was created and used to cut each ligament at the mid-point between its attachment points.

### 4.6 Statistical analysis

Statistical analyses were performed to (i) compare the resulting knee and ligament kinematics obtained from the passive mechanisms against MRI-measured kinematics at different TFJ flexion angles and (ii) to compare the kinematics obtained from different TFJ and PFJ mechanisms. To this end, traditional statistical tests were used to compared model-estimated and MRI-measured kinematics, while tests from statistical parametric mapping (Pataky et al., 2013), which consider the two-dimensional nature of the kinematic data, were used to compared estimated kinematics from different mechanisms. Analyses were performed using IBM SPSS Statistics for Windows (IBM Corp, Armonk, NY) v22.0 and the open-source SPM1D code (version M.0.4.2, [www.spm1d.org](http://www.spm1d.org)) in Matlab (Pataky, 2012).
4.6.1 Validation of TFJ and PFJ passive mechanisms

The reconstructed bone volumes from the MRIs at different TFJ flexion angles acquired for eight TD participants and five RPD patients were used for validation (data from only four RPD patients will be used in this thesis). For each participant, we determined the experimental poses of the tibia and the patella with respect to their femur. The anatomical landmarks identified in the MRI-reference 0° position, and used to create the initial \( f_{cs}, t_{cs} \) and \( p_{cs} \) were identified on the corresponding registered bones at approximately 10°, 20° and 30° positions. These landmarks were used to create the bones’ SCSs and six DoF kinematics at the four TFJ joint angles. The transformation matrices aligning the SCSs in the MRI-reference pose to the SCSs in 10°, 20° and 30° flexion angles were computed and used to derive the ligaments’ attachment points in all poses. Moreover, only for the eight TD participants, ligaments’ lengths were computed as Euclidean distance between the optimised attachment points at all four different poses for all the three TFJ models (i.e., \( \Delta L_0 \), \( \Delta L_{\text{min}} \) and \( \Delta L_{\text{match}} \)). Given that the optimised ligament attachment points differed for each model, the MRI-measured length of each ligament at each pose was slightly different depending on the TFJ model.

For the eight TD participants, the Root-Mean-Square Errors (RMSEs) between each participant’s predicted and MRI-measured TFJ and PFJ kinematics and ligament lengths were computed for each TFJ model and averaged across the four TFJ flexion angles. Ninety-five percent confidence intervals (CI) were also computed. A one-way repeated measures Analysis of Variance (ANOVA) with a priori contrasts was performed to determine differences in the average RMSE between each kinematic model at each TFJ and PFJ degree of freedom and ligament length (\( \alpha=0.05 \)). For the four RPD patients, the same approach was used to compare each patient’s predicted and MRI-measured PFJ kinematics.

4.6.2 Comparison of estimated TFJ and PFJ kinematics

Prior to any comparisons, the normality of kinematic data was assessed with the Shapiro-Wilk test using the SPM1D code. If kinematic data were normally distributed, Statistical Parametric Mapping (SPM) was used to determine if there were significant differences between the kinematic curves at any TFJ flexion angle (Pataky et al., 2013), otherwise Statistical non-Parametric Mapping (SnPM) was used (Pataky et al., 2015). Statistical comparisons were made between three different sets of kinematic data: first, the resulting TFJ and PFJ kinematic curves for the eight TD participants obtained from the three passive TFJ models (i.e., \( \Delta L_0 \), \( \Delta L_{\text{min}} \) and \( \Delta L_{\text{match}} \)) were compared; second, the resulting TFJ kinematic curves for the eight TD participants obtained from inverse
kinematics using $\Delta L_{0,spline}$ and $\Delta L_{0,MBO}$ were compared; third, the resulting passive PFJ kinematic curves of eight TD participants and four RPD patients were compared.

In the first and second comparisons, one-dimension two-tailed paired $t$-tests were conducted on the TFJ and PFJ kinematics of the eight TD participants, taking into consideration the dependency of all points of each TFJ flexion ROM ($\alpha=0.05$) to calculate the critical threshold ($t^*$) (Penny et al., 2011). Similarly, on the third comparison, a one-dimension two-tailed unpaired $t$-test was conducted on the resulting PFJ kinematics of the eight TD participants and four RPD patients.
General methods
CHAPTER 5

Radiological predictors of paediatric patellofemoral joint dislocation from medical imaging

Acknowledgement of co-authorship

This chapter includes a co-authored paper that has been re-formatted for this thesis. The bibliographic details/status of the co-authored paper, including all authors, are:


I made a substantial contribution in the conception and design of this study, data collection, and drafting and revising of the final manuscript.

Student/Corresponding author: Martina Barzan

Principal supervisor: Christopher P Carty
5.1 Abstract

**Background:** Recurrent patellar dislocation (RPD) is found most commonly in the paediatric population. While risk factors have been well-established in adults, there remains a paucity in radiographical data to define normal and pathoanatomical paediatric cohorts. The purpose of this paper was to elucidate the differences between RPD and typically developed (TD) populations, using Magnetic Resonance Imaging (MRI) measurements to assess the paediatric patellofemoral joint (PFJ), to determine the best independent and combined predictors of RPD.

**Methods:** A prospective cross-sectional study was conducted with 24 RPD and 25 TD participants aged between 8 and 19 years. MR images were obtained to assess common measures of lower limb alignment, patellofemoral alignment, and trochlear dysplasia.

**Results:** Significant differences were evident for acetabular inclination, tibial-femoral torsion, tibial-tuberosity-trochlear groove (TT-TG) distance, lateral patella tilt (LPT), congruence angle (CA), and cartilage sulcus angle (CartSA). TT-TG and CartSA were included in the final predictive model, which correctly classified 84.4% of RPD cases.

**Conclusions:** Radiographical parameters that stratify risk of RPD in adults are also able to predict RPD in the paediatric population (TT-TG, LPT, CA, and CartSA). Together, TT-TG and CartSA, accurately identified 84.4% of RPD. These measures should be included in the evaluation of paediatric patients who present with PFJ dislocation.

**Level of Evidence:** Level II – prospective cross-sectional study.
5.2 Introduction

Acute patellar dislocation commonly arises during childhood and adolescence (Atkin et al., 2000), with a reported overall incidence of 42 per 100,000 in the paediatric population (0 to 16 years) (Nietosvaara et al., 1994) and six to 77 per 100,000 in adolescence (Atkin et al., 2000; Fithian et al., 2004; Hawkins et al., 1986; Sillanpää et al., 2008). Up to 58% of patients suffer ongoing pain, instability and significant limitations to physical activity (Atkin et al., 2000; Clark et al., 2017; Colvin et al., 2008; Fithian et al., 2004; Moström et al., 2014). Paediatric populations also experience the highest risk of recurrence (Popkin et al., 2018; Seeley et al., 2012). Risk factors for recurrence include gender (female), age, prior dislocation, sports participation and family history (Clark et al., 2017; Lewallen et al., 2013a). Numerous morphological risk factors also exist; lower limb alignment (femoral anteversion, tibial torsion), patellofemoral alignment (congruence angle - CA), patella alta, lateral patella tilt (LPT), tibial tuberosity to trochlear groove (TT-TG) distance, patellar and trochlear dysplasia, i.e. bony and cartilage sulcus angle (CartSA), trochlear depth and facet morphology, and soft tissue restraints, such as medial patellofemoral ligament (MPFL) and medial/lateral retinaculum (Andrish, 2017; Askenberger et al., 2017; Meyers et al., 2016). However, the interplay between these factors is poorly understood.

While recurrent patellar dislocation has been extensively studied, there remains a paucity of adequate radiographic studies to define normal and pathoanatomical data, specifically in the paediatric population. In a recently published systematic review evaluating recurrent patella dislocation (RPD) risk in children, only four of 31 included studies reported measures for both dislocator and control cohorts and these measures were limited to CA, patella alta, TT-TG distance and sulcus angle (Barzan et al., 2018). Patella alta, in particular, is a commonly used radiographic measure of pathology in adults; however, it can produce unreliable results depending on the index used (Grelsamer et al., 1992; Thévenin-Lemoine et al., 2011). The Caton-Deschamps Index has been shown to be a relatively simple and reliable, although its applicability in paediatric populations needs to take into account the inverse relationship between its index values and age (Thévenin-Lemoine et al., 2011). The patella trochlear index and its variations have been suggested as alternatives for patella height (Biedert et al., 2006; Dejour et al., 2013).

Magnetic resonance imaging (MRI) has been shown to be a useful tool in both diagnosing acute soft and bony tissue injuries following patella dislocation. MRI can be also used to detect the presence of any pathoanatomical morphology, which may predispose individuals to dislocation recurrence (Askenberger et al., 2017; Seeley et al.,
Subject-specific paediatric knee kinematic models with ligamentous constraints

Importantly, the use of MRI allows young patients to avoid ionizing radiation risks associated with other imaging modalities such as computed tomography (CT), while MRI offers superior multiplanar evaluation of soft tissues (Li et al., 2016; Pai et al., 2011). MRI’s diagnostic utility and potential to direct morphology-based management has quickly cemented it as the preferred imaging modality for evaluating patellofemoral instability (Askenberger et al., 2017; Charles et al., 2013; Diederichs et al., 2013; Leschied et al., 2017; Seeley et al., 2012). However, the question remains: what are the predictors of paediatric patellofemoral joint dislocation that can be detected via MRI?

The aims of this study were twofold: (1) determine whether common imaging measures used to assess PFJ dislocation differ between paediatric patients with a history of RPD and a typically developed (TD) cohort, and (2) elucidate the best independent and combined imaging predictors of RPD. It was hypothesised that that CA, patella alta, LPT and the TT-TG distance would differ from controls and be the best predictors of PFJ dislocation.

5.3 Methods

5.3.1 Participant recruitment

Forty-nine participants (25 RPD participants, 24 TD controls) were recruited for this prospective cross-sectional study (Table 5.1). RPD participants were offered enrolment following outpatient orthopaedic consultations at the Lady Cilento Children’s Hospital (LCCH) in Brisbane, Australia. TD participants, free from musculoskeletal or neurological impairment or lower limb injury within the prior six months, were recruited from the local community. Additional exclusion criteria for both groups included congenital limb abnormalities, history of bony or soft tissue pathology affecting anatomy (trauma or infection), prior lower limb surgery affecting the PFJ and/or lower limb alignment, inability to tolerate or deemed unsafe for MRI, identified using a safety questionnaire. Ethics approval was gained from the institutional ethics committee with participants and parents giving their informed, written consent prior to commencement.
Table 5.1. Participants characteristics and medical imaging measurements for each group.

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=24)</th>
<th>PFJ dislocators (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong> (male/female)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong> years</td>
<td>13.9 [3.1]</td>
<td>14.3 [2.6]</td>
</tr>
<tr>
<td><strong>Mass [kg]</strong></td>
<td>49.7 [11.6]</td>
<td>60.9 [19.9]*</td>
</tr>
<tr>
<td><strong>Height [m]</strong></td>
<td>1.62 [0.13]</td>
<td>1.62 [0.12]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Affected side</th>
<th>Unaffected Side</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetabular inclination (°)</td>
<td>14.1 [4.8]</td>
<td>17.3 [5.6]</td>
</tr>
<tr>
<td>Femoral antversion (°)</td>
<td>14.3 [6.6]</td>
<td>17.1 [10.6]</td>
</tr>
<tr>
<td>Tibial torsion (°)</td>
<td>-34.6 [7.4]</td>
<td>-34.6 [9.2]</td>
</tr>
<tr>
<td>Tibial-femoral torsion (°)</td>
<td>-2.1 [4.0]</td>
<td>-8.0 [8.3]</td>
</tr>
<tr>
<td>Patella trochlear ratio PTR</td>
<td>0.37 [0.14]</td>
<td>0.35 [0.12]</td>
</tr>
<tr>
<td>TT-TG distance (mm)</td>
<td>8.1 [3.2]</td>
<td>14.2 [4.2]</td>
</tr>
<tr>
<td>Congruence angle (°)</td>
<td>-5.7 [15.1]</td>
<td>25.3 [26.9]</td>
</tr>
<tr>
<td>Patella bisect offset ratio PBOR</td>
<td>0.56 [0.07]</td>
<td>0.84 [0.16]</td>
</tr>
</tbody>
</table>

*significant difference between control and PFJ dislocator group; †significant difference between control and affected leg of PFJ dislocator group, ‡significant difference between control and unaffected leg of PFJ dislocator group.

5.3.2 Medical image acquisition and measurement

MRIs were collected in the Department of Medical Imaging and Nuclear Medicine, LCCH, Brisbane, Australia. An MRI scan (1.5T scanner, SIEMENS MAGNETOM Avanto_fit syngo MR VE11B, Germany) of the entire pelvis and lower limbs (3D PD SPACE sequence, slice thickness: 1.0 mm, voxel size: 0.83x0.83x1.0 mm³) was performed with the participant supine to capture full-length lower limb bones. A second, regional MRI scan (3T scanner, SIEMENS MAGNETOM Skyra, Germany) of the affected knee for PFJ dislocators and the right knee for controls (3D SPC T2, slice thickness: 0.53 mm, voxel size: 0.53x0.53x0.53 mm³) was performed with approximately 10° of knee flexion using a dedicated knee coil to capture knee articular cartilage and ligaments. Measurements from the full-length pelvis and lower limb MRI included acetabular inclination, femoral neck angle (FNA), posterior femoral condylar axis, posterior tibial condylar axis, intermalleolar axis and TT-TG distance. Measurements using dedicated unilateral knee MRI consisted of CartSA, LPT, patella bisect offset ratio (PBOR) CA and PTR.

*Acetabular inclination* was the divergence of the acetabular tangential line from the sagittal plane of the pelvis (Figure 5.1). *FNA, posterior femoral condylar axis, posterior tibial condylar axis and intermalleolar axis* were measured using the horizontal plane as reference (Figure 5.2) and the following were derived: *femoral anteversion* - the relative angle between FNA and the posterior femoral condylar index in the axial plane;
Subject-specific paediatric knee kinematic models with ligamentous constraints

tibial femoral torsion - the relative angle the posterior femoral condylar index and the posterior tibial condylar axis in the axial plane; and tibial torsion - the relative angle between the posterior tibial condylar axis and the intermalleolar axis in the axial plane.

Figure 5.1 Acetabular inclination: measured on axial slices at the widest diameter of the femoral head. A line is drawn from the anterior and posterior most margins of the cartilaginous acetabulum (EF), and the angle between it and the reference plane (AC) calculated as acetabular inclination. AC: perpendicular to the line created horizontally from the left to right posterior ischial spines (BD).
Figure 5.2 (A) Femoral neck angle: measured at the widest diameter of the femoral head using dedicated oblique transverse slices parallel to the femoral neck. A line was drawn through the centre of the femoral head and femoral neck (AB), and the angle between it and the horizontal reference plane (AC) used as the FNA (BAC). (B) Posterior femoral condylar axis: measured on axial slices at the widest point in the anteroposterior plane at the midline of the femoral condyles, and calculated as the angle (BAC) between the posterior-most aspect of the medial and lateral cartilaginous condyles (AB) and the horizontal reference plane (AC). (C) Posterior tibial condylar axis measured on axial slices at the widest point in the horizontal plane of the tibial condyles, and calculated as the angle (BAC) between the posterior-most aspect of the medial and lateral cartilaginous condyles (AB) and the horizontal reference plane (AC). (D) Intermalleolar axis: measured on axial slices at the greatest distance between the medial and lateral malleoli i.e. the intermalleolar distance from the most medial aspect of the medial malleolus to the most lateral aspect of the lateral malleolus (AB). The axis was calculated as the angle (BAC) between (AB) and the horizontal reference plane (AC).

TT-TG distance represents the anatomical lateralisation of the patella tendon (Figure 5.3). CartSA, CA, PBOR and LPT were measured using the posterior femoral
condylar axis as the reference plane (Figure 5.4). PTR was measured using sagittal slices depicting the patella at its maximal vertical length (Figure 5.5).

**Figure 5.3 TT-TG Distance: is the horizontal distance from the tibial tuberosity to the trochlear groove. (A) Trochlear groove (two slices directly inferior to the point at which the trochlear cartilage is first visualised [cranial-to-caudal]). (B) Tibial tuberosity at its most anterior point. A mouse cursor is placed on the first slice (3A) at the deepest point on the trochlear groove (TG). Without moving the cursor and scrolling through the MRI slices (cranial-to-caudal), the horizontal distance between the pre-identified position of TG and the most anterior point of the tibial tuberosity (TT) is measured.**
**Figure 5.4** (A) Cartilage sulcus angle: measured on axial images, two slices inferior to the slice in which the trochlear cartilage is first visualised (cranial-to-caudal). The anterior-most cartilaginous points of the lateral (D) and medial (E) femoral condyles and the deepest point in the cartilaginous trochlear groove (A) create the CartSA (DAE). (B) Congruence angle: measured on axial slices at the widest point of the patella at its widest horizontal margin, using the CartSA as a reference point (BAC). A bisector line of the angle BAC was used as the reference plane (AD). Another line was drawn from the deepest point of the trochlear groove (A) to the inferior-most point of the patella articular ridge (AE). Congruence angle was determined by the angle created between these two lines (DAE). (C) Lateral patella tilt: measured on axial slices at the widest point of the patella from the most lateral point of the patella (B) to the most medial point (D) the reference plane (AC) is translated vertically until it meets point (B). The angle between the translated reference plane and the patella width (BD) gives you LPT. (D) Patella bisect offset ratio: measured using the same slice as LPT, a bisector line was created from the deepest point of the trochlear groove (F) until it met the reference plane (AC) at right angles. This line was then extended vertically until it bisected the patella width (BD) at point (E). Bisect offset is determined by the ratio at which the patella width was bisected from its lateral aspect (BE) to the total length of the patella width (BE:BD).
5.3.3 Statistical Analysis

Analysis of Variance (ANOVA) was used to assess the effect of group (2 levels: controls and PFJ dislocators) on the age, body mass and height. Analysis of Covariance (ANCOVA) was used to assess the effect of group (3 levels: controls, affected and unaffected lower limb of PFJ dislocators) on imaging measurements, using covariates of age, height and body mass. A priori contrasts were performed to assess differences between controls and the affected lower limb of PFJ dislocators and between controls and the unaffected lower limb of PFJ dislocators. Forward stepwise binary logistic regression analysis was undertaken to determine the variable(s) that best predicted odds of PFJ dislocator group membership, with only measures from the affected lower limb of PFJ dislocators and from the right leg of controls included. Predictor variables assessed were; acetabular inclination, femoral anteversion, tibial torsion, tibial-femoral torsion, patella trochlear ratio (PTR), TT-TG distance, LPT, CA, CartSA and PBOR. Multicollinearity was assessed through an inspection of tolerance and VIF values with cut off levels of <0.2 and >5 respectively. Prior to entry into the model predictor variables were transformed into tertiles. The significance of the odds ratios was assessed using the Wald test, while the goodness of fit of the multivariate model was assessed using the likelihood ratio test statistic (Chi-square). Receiver operating characteristic (ROC) curves were used to evaluate the effectiveness of each medical imaging measurement with optimal cut-points being calculated with the Youden Index (Ruopp et al., 2008) and interpreted with caution.
when >0.5. All statistical analyses were performed using SPSS (Version 22, SPSS, USA) and significance was accepted for p < 0.05.

5.4 Results

The PFJ dislocators were on average heavier and contained a higher percentage of females compared to their TD counterparts (Table 5.1). There was no difference in height or age between groups. The affected lower limb of the RPD group showed significantly higher mean acetabular inclination, tibial femoral torsion, TT-TG distance, LPT, CA, CartSA and PBOR compared to the control group. The best independent predictors of RPD group membership were PBOR, PT, CartSA. TT-TG distance and CA, with all of these measures exhibiting AUC > 0.80 (Table 5.2).

Table 5.2. Effectiveness of each medical imaging measurement in the determining patients with recurrent patella dislocation using ROC curve analysis.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>AUC [95%CI]</th>
<th>J</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>c*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetabular inclination (°)</td>
<td>0.66 [0.50-0.82]</td>
<td>0.37</td>
<td>0.63</td>
<td>0.75</td>
<td>16</td>
</tr>
<tr>
<td>Femoral anteversion (°)</td>
<td>0.59 [0.42-0.76]</td>
<td>0.292</td>
<td>0.29</td>
<td>1.00</td>
<td>26</td>
</tr>
<tr>
<td>Tibial torsion (°)</td>
<td>0.60 [0.43-0.77]</td>
<td>0.348</td>
<td>0.70</td>
<td>0.65</td>
<td>-34</td>
</tr>
<tr>
<td>Tibial-femoral torsion (°)</td>
<td>0.77 [0.63-0.91]</td>
<td>0.519</td>
<td>0.73</td>
<td>0.79</td>
<td>-5</td>
</tr>
<tr>
<td>Patella trochlear ratio</td>
<td>0.53 [0.37-0.70]</td>
<td>0.13</td>
<td>0.63</td>
<td>0.50</td>
<td>0.33</td>
</tr>
<tr>
<td>TT-TG distance (mm)</td>
<td>0.87 [0.76-0.97]</td>
<td>0.60</td>
<td>0.60</td>
<td>1.00</td>
<td>14</td>
</tr>
<tr>
<td>Patella tilt (°)</td>
<td>0.91 [0.83-0.99]</td>
<td>0.75</td>
<td>0.92</td>
<td>0.83</td>
<td>9</td>
</tr>
<tr>
<td>Congruence angle (°)</td>
<td>0.85 [0.74-0.96]</td>
<td>0.63</td>
<td>0.67</td>
<td>0.96</td>
<td>16</td>
</tr>
<tr>
<td>Cartilage sulcus angle (°)</td>
<td>0.88 [0.78-0.97]</td>
<td>0.59</td>
<td>0.80</td>
<td>0.79</td>
<td>145</td>
</tr>
<tr>
<td>Patella bisect offset ratio</td>
<td>0.95 [0.88-1.00]</td>
<td>0.79</td>
<td>0.96</td>
<td>0.83</td>
<td>0.60</td>
</tr>
</tbody>
</table>

AUC = area under the ROC curve, J = Youden Index, c* = optimal cut-point

5.4.1 Stepwise logistic regression analysis

Of the predictors entered into the forward stepwise logistic regression analysis, PBOR was excluded from the analysis based on detection of multicollinearity with other independent variables (tolerance = 0.15, VIF = 6.63). The final logistic regression model was statistically significant, χ²(2) = 30.39, p < .0005, explained 66.6% (Nagelkerke R²) of the variance in patella dislocation and correctly classified 84.4% of cases. Independent variables retained in the final model were TT-TG distance and CartSA. An increase in TT-TG distance by one tertile increased the odds of being a patella dislocator by a factor
of 6.98 (OR: 0.13, 95% CI: 0.03-0.59), and an increase in CSA by one tertile increased the odds of being a patella dislocator by a factor of 3.32 (OR: 0.33, 95% CI: 0.1-1.1).

5.5 Discussion

We conducted a comprehensive, cross sectional, prospective evaluation of radiographical measures in paediatric patients who presented with RPD and controls of similar age with no history of lower limb musculoskeletal impairment. Significant group differences were evident for acetabular inclination, tibial-femoral torsion, TT-TG distance, LPT, CA, CartSA and PBOR. The multivariate model combined TT-TG distance and CartSA, predicting RPD group membership with 84.4% accuracy, suggesting that at minimum these measurements should be included in the evaluation of paediatric patients who present with PFJ dislocation.

In partial agreement with our first hypothesis, CA, LPT and TT-TG distance were significantly different in the affected leg of dislocators compared to controls. We also found differences for acetabular inclination, tibial femoral torsion, CartSA and PBOR. Interestingly, significant differences to the TD group remained when considering the unaffected limbs of dislocators. Previous studies with adults using CT (Demehri et al., 2014) and adolescents during dynamic MRI (Regalado et al., 2014) have demonstrated the same in relation to TT-TG, PBOR, and LPT. This might suggest that the anatomical differences inherent in unaffected knees will predispose RPD participants for contralateral dislocation should they be exposed patella lateralizing forces.

TT-TG distance is a reliable measure for intervention of extensor mechanism defects in patellar instability (Dickens et al., 2014). Consistent with the literature, our data demonstrated a mean TT-TG distance of 8mm in controls and 14mm in affected limbs of dislocators (Askenberger et al., 2017; Dickens et al., 2014). While a significant difference was found in unaffected limbs of dislocators (12.6 ± 5.1mm), it did not reach the pathological cut-off point, suggesting that intervention may not be necessary up to 14mm. Düppe et al. (2016) found similar cut-offs when comparing paediatric and adult populations. Balcarek et al. and Koëter et al. have recommended a cut-off distance of 15mm before intervention (Balcarek et al., 2011; Koeter et al., 2007).

Using the same pathological cut-off values for CartSA as employed by others (Askenberger et al., 2017; Seeley et al., 2012) we found significant differences in CartSA between dislocators and controls. A CartSA >145° is a part of the Dejour classification of trochlear dysplasia, often used when considering trochleoplasty (Dejour et al., 2018; Nelitz et al., 2014). Other trochlear dysplasia measures have been suggested, although
Nelitz et al. (2014) could not classify these into the four Dejour classifications. Nonetheless, CartSA in combination with TT-TG was shown to offer superior predictability for RPD than when either is used alone.

Our study demonstrated similar significant differences between normal and pathological cohorts for LPT as adults (Escala et al., 2006). This could be due to insufficient soft tissue restraints at the PFJ, such as medial ligamentous laxity, or reflect a torn MPFL. Given the difference in our study remained true when considering the unaffected limbs of dislocators, the former appears more likely. While generalised ligamentous laxity is a well-known risk factor, Nomura et al. (2006) found that a hypermobile patella was more significantly associated with RPD.

The PTR in theory should be a very good predictor of RPD since it considers variations in the cartilaginous articular surfaces (Biedert et al., 2006; Clark et al., 2017). However, we found patella alta (using PTR) was not significantly different and was a poor predictor of RPD. This is echoed by Askenberger et al. (2017) who studied first-time PFJ dislocators. This should be interpreted with caution as Askenberger et al. (2017) did find differences when using other measures of patella alta (Caton-Deschamps and Insall-Savati Indices), which were not measured in our study due to positioning of the PFJ in the MRI. Indeed, use of MRI as an imaging modality to calculate patella alta as opposed to lateral radiographs is suggested to represent an inaccurate depiction of true articular congruence (Biedert et al., 2006; Staeubli et al., 2002).

The PBOR was excluded from the multiple logistic regression analysis due to detection of multicollinearity with other measures. This was likely because the PBOR is a consequence of anatomical abnormalities, rather than a precipitating factor. We suggest that PBOR be interpreted as a severity rating for dislocation rather than a direct risk factor.

Acetabular inclination was significantly higher for dislocators (17°) compared to TD controls (14°), although this was not likely to be clinically significant. ROC analysis revealed low confidence in its use as a predictor. Femoral anteversion, tibial torsion and tibial-femoral alignment did not produce significant differences between cohorts, nor were they predictive of RPD. A medially rotated proximal tibia relative to femoral condyles (tibial-femoral torsion) was a predictor of RPD possibly due to its influence on the line of pull of the patellar tendon. This suggests that lower limb alignment, bar tibial-femoral torsion, while linked to increased risk of patellar instability (Andrish, 2017; Camathias, 2015; Meyers et al., 2016), is not as valuable as other radiographic measures when used as a predictor for RPD. It is possible that normal bony and cartilaginous
constraints may be enough to counter any laterally-directed forces as a result of malalignment. Nonetheless, femoral anteversion had 100% specificity in identifying RPD (7/25) when the cut-point was >26°, indicating femoral antversion might be a contributing factor for RPD for a subset of patients and should not be completely ignored.

A limitation of this study was grouping the paediatric population into a single cohort instead of stratifying measurements according to age. Unlike adults, pathological cut-off points in the paediatric population must take into account normal changes in development. Previous studies have suggested that some (e.g. CartSA), but not all (e.g. TT-TG, patella alta), pathological cut-off points for risk factors vary with age (Düppe et al., 2016). Furthermore, we classified participants using chronological and not bone age. As children enter their growth spurts at varying ages, age is not necessarily a direct indicator of skeletal maturity. Furthermore, while plain radiographs would have been desirable to mirror the investigations routinely obtained in the treatment of dislocators, it was felt inappropriate to subject the TD children to an unnecessary dose of radiation. A knee series was therefore not included in the protocol.

In the radiological assessment of first-time dislocators and RPD, patients with a TT-TG >14mm or a CartSA >145° have a moderate risk of redislocation. If surgery is considered, the intervention chosen should take into account co-existing morphology. Patients with both risk factors should be considered high risk; surgical intervention should be considered. Patients with femoral antversion >26° should also be considered high risk. Again, decisions for surgery need to consider co-existing morphology. The authors acknowledge that this algorithm is not absolute. It is to be interpreted in the context of history and examination, guiding individual surgical prescription and decision-making.

5.6 Conclusion

Many adult radiographical risk factors have also been demonstrated, in this paper, to predict dislocation in the paediatric population (TT-TG, LPT, CA, and CartSA). Our predictive model included TT-TG and CartSA, which was able to accurately identify 84.4% of RPD. These measures should be included in the evaluation of paediatric patients who present with PFJ dislocation.

5.7 Acknowledgements

Martina Barzan was supported by a Griffith University Research Higher Degree Scholarship. Christopher P Carty was supported by an Advance Queensland Innovation Fellowship.
CHAPTER 6

Development and validation of subject-specific paediatric multibody knee kinematic models with ligamentous constraints

Acknowledgement of co-authorship

This chapter includes a co-authored paper that has been re-formatted for this thesis. The bibliographic details/status of the co-authored paper, including all authors, are:


I made a substantial contribution in the conception and design of this study, data collection, analysis and interpretation of data, drafting and revising of the final manuscript.

Student/Corresponding author: Martina Barzan

Principal supervisor: Christopher P Carty
6.1 Abstract

Computational knee models that replicate the joint motion are important tools to discern difficult-to-measure functional joint biomechanics. Numerous knee kinematic models of different complexity, with either generic or subject-specific anatomy, have been presented and used to predict three-dimensional tibiofemoral (TFJ) and patellofemoral (PFJ) joint kinematics of cadavers or healthy adults, but not paediatric populations.

The aims of this study were: (i) to develop three subject-specific TFJ kinematic models, with either rigid or extensible ligament constraints, and a subject-specific PFJ model for eight healthy paediatric participants and (ii) to validate the estimated joint and ligament kinematics against in vivo kinematics measured from magnetic resonance imaging (MRI) at four TFJ flexion angles.

Three different TFJ models were created from MRIs and used to solve the TFJ kinematics: (i) 5-rigid-link parallel mechanism with rigid surface contact and isometric anterior cruciate (ACL), posterior cruciate (PCL) and medial collateral (MCL) ligaments ($\Delta L_0$), (ii) 6-link parallel mechanism with minimised ACL, PCL, MCL and lateral collateral ligament (LCL) length changes ($\Delta L_{min}$) and (iii) 6-link parallel mechanism with prescribed ACL, PCL, MCL and LCL length variations ($\Delta L_{match}$). Optimisations were performed using Multiple Objective Particle Swarm algorithm.

When compared to MRI-measured data, $\Delta L_0$ and $\Delta L_{match}$ performed the best, with errors below 6.93° and 4.23 mm for TFJ and PFJ angles and displacements, respectively, and below 2.01 mm for ligament lengths. Therefore, these models can be used to estimate three-dimensional paediatric TFJ, PFJ and ligament kinematics and can be incorporated into lower-limb models to estimate joint kinematics and kinetics during dynamic tasks.

6.2 Introduction

Numerous kinematic models have been developed for the main lower limb joints (i.e. hip, knee and ankle) and vary from simple mechanisms (i.e. hinge, spherical, universal joints) to more complex relationships that describe the coupled motions with anatomical constraints (e.g. ligaments) (Moissenet et al., 2017). Previous studies (Andersen et al., 2010; Stagni et al., 2009) demonstrated that knees represented as
spherical or hinge joints cannot accurately estimate \textit{in vivo} secondary knee kinematics, especially joint translations. However, more realistic 5-rigid-link parallel mechanisms have been proposed for the tibiofemoral joint (TFJ), consisting of two rigid tibial and femoral contacts and isometric anterior cruciate (ACL), posterior cruciate (PCL) and medial collateral (MCL) ligaments (Feikes et al., 2003; Ottoboni et al., 2010; Parenti-Castelli et al., 2000; Sancisi et al., 2011a; Wilson et al., 1998), and patellofemoral joint (PFJ), represented as a hinge joint between the femur and the patella and an isometric patellar tendon (Sancisi et al., 2011a). These mechanisms well estimated each joints’ \textit{in vitro} passive 6 motion components (3 rotations, 3 translations) (Sancisi et al., 2011a). Furthermore, they have been generated from Magnetic Resonance Imaging (MRI) in healthy adults (Brito da Luz et al., 2017), and extended to perform dynamic analyses (Moissenet et al., 2014).

More complex TFJ models have also been proposed. Gasparutto et al. (2012) added the lateral collateral ligament (LCL) to the previously described 5-rigid link model and then allowed for minimal ligament deformation during passive and loaded gait conditions. It was shown (Gasparutto et al., 2015) that these models better predicted TFJ internal-external rotation during gait when compared to isometric ligament models (Bergamini et al., 2011; Gasparutto et al., 2012). Moreover, when compared to simple and/or generic TFJ models, personalised parallel TFJ mechanisms with minimally deformable ligaments can better estimate TFJ abduction-adduction, internal-external rotation and antero-posterior translation during squatting in healthy and osteoarthritic adults (Clément et al., 2015). In addition, Moissenet et al. (2014) included a passive PFJ mechanism in their musculoskeletal model to perform gait analysis. However, these TFJ and PFJ models have only been implemented in adult populations, and seldom validated (Clément et al., 2015; Gasparutto et al., 2015). Therefore, it is unclear if they can accurately describe the TFJ and PFJ motion in children and adolescents, who exhibit high inter-subject anatomical variability and increased TFJ laxity that diminishes with increasing age (Flynn et al., 2000; Hinton et al., 2008).

For validation purposes, estimated subject-specific knee joint kinematics are generally compared against \textit{in vivo} knee kinematics measured using imaging techniques, such as fluoroscopy (Lu et al., 2008; Marra et al., 2015) or biplanar radiography (Clément et al., 2015), or intracortical pins (Benoit et al., 2006; Bonci et al., 2014; Reinschmidt et al., 1997). However, radiation exposure or invasive procedures limit the use of these methods, especially in paediatric populations. Alternatively, MRI is a safe technology for
validation of knee mechanisms in children. To date, no studies have developed and validated subject-specific TFJ and PFJ mechanisms for children using MRIs.

Therefore, this study first aimed to use MRIs to generate three subject-specific TFJ models, with varying complexity (i.e. have different ligamentous constraints), each combined with a subject-specific PFJ model to estimate three-dimensional TFJ and PFJ kinematics in a healthy paediatric population. The second aim was to validate the kinematics results from the three different TFJ models against knee kinematics and ligament lengths measured from MRIs collected at four knee flexion angles. It was hypothesised that, compared to the simplest model with three rigid knee ligaments, the two models with increased complexity, obtained by adding an extra knee ligament and by allowing for minimal or prescribed elongation of the ligaments, would provide better estimates of MRI-measured joint and ligament kinematics across the four knee flexion angles.

6.3 Methods

6.3.1 Participants

Eight healthy children and adolescents (4 males and 4 females, mean±SD: age 14.0±2.6 years, mass 51.1±10.5kg, height 1.64±0.11m) were recruited. Study approval was obtained from the Children’s Health Queensland Hospital and Health Services human research ethics committee (HREC/13/QRCH/197) and participants’ guardians provided written informed consent.

6.3.2 Medical image acquisition and processing

Three sets of MRIs were collected at the Lady Cilento Children’s Hospital (Brisbane, Australia) from each participant. First, an MRI scan (1.5T, SIEMENS MAGNETOM Avanto fit syngo MR VE11B, Germany) of both lower limbs (3D PD SPACE, slice thickness: 1.0mm, voxel size: 0.83x0.83x1.0mm³) was performed with the participant in a supine position. Second, a regional MRI scan (3T, SIEMENS MAGNETOM Skyra, Germany) of the participant’s right knee (3D SPC T2, slice thickness: 0.53mm, voxel size: 0.53x0.53x0.53mm³) was performed with the knee close to 0° TFJ flexion using a dedicated knee coil. Third, for each participant, three additional dedicated right knee scans were acquired at approximately 7°, 15° and 25° of TFJ flexion by using a flexible array coil wrapped around the knee.
Three-dimensional lower limb bones, knee ligamentous and cartilaginous structures were segmented in Mimics Research 20.0 (Materialise, Belgium). Segmented bones included the femur, patella, tibia and fibula, while ligaments included the ACL, PCL, MCL and LCL (Fig. 6.1) and patellar tendon. Three-dimensional full-length bones were registered with the three-dimensional knee reconstructions through an iterative closest point algorithm (Besl et al., 1992) in 3-matic (Materialise, Belgium) to obtain a comprehensive three-dimensional reconstruction of the participant’s anatomy at each considered knee angle.

6.3.3 Subject-specific TFJ and PFJ kinematic models

A baseline TFJ model was implemented as a 5-link parallel mechanism including two sphere-on-sphere contacts (representing the medial and lateral contacts between the femoral condyles and the tibial plateaus) and three ligaments (ACL, PCL and MCL) (Brito da Luz et al., 2017; Sancisi et al., 2011a) (Fig. 6.1b). The two articular contacts were considered rigid, with no penetration or separation permitted. The geometry of the contact surfaces (i.e. sphere centres and radii) was obtained from MRI by approximating the femoral condyles and tibial plateaus by best-fitting spheres (Matlab R2014b, MathWorks). The geometry of the ligaments (i.e. ligament lengths, attachment points) was derived from the MRI close to 0° TFJ flexion by computing the centroids of the segmented ligament attachment regions on the corresponding bones. The TFJ baseline model was then extended by adding the LCL (i.e. 6-link), whose geometry was defined with the same procedure used for the other ligaments.

Figure 6.1. Example of bone and TFJ ligament segmentation from the regional MRI scan (a). Baseline model of the TFJ (ΔL0) (b): the spherical surfaces (grey) approximate the geometry of the femoral condyles and tibial plateaus, while the rigid links (fuchsia) represent the isometric fibres of ACL, PCL and MCL.
Different TFJ models were created with three different ligament models. The first was a 5-rigid-link TFJ model where the ACL, PCL and MCL were considered isometric ($\Delta L_0$) over the TFJ flexion range of motion (ROM). The second was a 6-link TFJ model with minimal ACL, PCL, MCL and LCL ($\Delta L_{\text{min}}$) length variations over the TFJ flexion ROM. The third was a 6-link TFJ model where the ACL, PCL, MCL and LCL length variations tracked the pattern of published experimental ligament length variations ($\Delta L_{\text{match}}$) (Bergamini et al., 2011; Blankevoort et al., 1991) over the TFJ flexion ROM.

The PFJ was modelled as a hinge joint, where the patella was constrained to rotate about and at a constant distance from an axis while maintaining constant patellar tendon length. The axis was defined by the centre of two spheres fitted to the medial and lateral patellofemoral articular surfaces (Brito da Luz et al., 2017; Sancisi et al., 2011a). Finally, femur, tibia and patella segment coordinate systems (SCSs) were defined (Cappozzo et al., 1995a) using anatomical landmarks manually located onto the bone segmented surfaces to derive the relative poses of the bones as a result of the model.

6.3.4 Tuning of each subject-specific TFJ model

After each subject-specific TFJ and PFJ model was created, tuning (i.e., optimisation) of the model’s geometrical parameters (initially measured off the MRIs) was undertaken to ensure physiologically feasible mechanisms (Brito da Luz et al., 2017). For the three different TFJ ligament models, we employed different optimisation approaches, each consisting of an outer and inner loop. The outer loop optimised each participant’s MRI-measured geometrical parameters (i.e. sphere centres and ligament attachment points), while the inner loop solved the TFJ and PFJ mechanisms. In the outer loop, the three-dimensional coordinates of the sphere centres were adjusted within a range that was proportional to the size of the spheres (20mm for the TFJ models, 5mm for the PFJ model). The radii of these spheres were also updated by minimising the summed least square residuals between fitted spheres and MRI segmented cartilages and ensuring that the residuals were <5% of the optimised radii. Finally, the optimised attachment points of the ligaments were maintained within their respective bone attachment regions.

Depending on the TFJ ligament model, the outer loop optimised for four different objective functions; see Equations (1)-(4) and Table 6.1 for full definition of terms. Equations (1)-(3) were used for all ligament models, while Equation (4) only for $\Delta L_{\text{min}}$. Equation (1) best matched the pattern between estimated and published experimental TFJ and PFJ kinematics, while Equation (2) minimised the difference between MRI-measured and optimised geometrical parameters. Equation (3) minimised the difference between
Subject-specific paediatric knee kinematic models with ligamentous constraints

optimised and published TFJ ab/adduction and internal/external rotation ROMs, if the optimised ROMs were larger than the published ROMs, and Equation (4) best matched the pattern between estimated and published experimental ligament length variations.

\[ J_1 = (1 - \rho_{\text{joint},i})^2 \quad i = 1, \ldots, N_{\text{DoF}} \]  
\[ J_2 = (g_{m,k} - g_{o,k})^2 \quad k = 1, \ldots, N_{\text{geom}} \]  
\[ J_3 = \begin{cases} 
  0 & \text{if } ROM_{o,n} \leq ROM_{m,n} \\
  \text{mean}\{(ROM_{o,n} - ROM_{m,n})^2\} & \text{if } ROM_{o,n} > ROM_{m,n} 
\end{cases} \quad n = 1, \ldots, N_{\text{DoF} \text{ bound}} \]  
\[ J_4 = (1 - \rho_{\text{ligament},l})^2 \quad l = 1, \ldots, N_{\text{lig}} \]  

\[ \text{(6.1)} \]  
\[ \text{(6.2)} \]  
\[ \text{(6.3)} \]  
\[ \text{(6.4)} \]

**Table 6.1. Description of terms in equations 6.1-6.4.**

<table>
<thead>
<tr>
<th>Equation</th>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$\rho_{\text{joint},i}$</td>
<td>Pearson’s correlation between $i^{th}$ estimated and published TFJ (Ottoboni et al., 2010; Sancisi and Parenti-Castelli, 2011) and PFJ (Anglin et al., 2008; Sancisi and Parenti-Castelli, 2011) $N_{\text{DoF}}$ kinematics total number of TFJ ($N_{\text{DoF}} = 5$) and PFJ ($N_{\text{DoF}} = 6$) dependent degrees of freedom</td>
</tr>
<tr>
<td>2</td>
<td>$g_{m,k}$</td>
<td>$k^{th}$ measured geometrical parameter</td>
</tr>
<tr>
<td></td>
<td>$g_{o,k}$</td>
<td>$k^{th}$ optimised geometrical parameter</td>
</tr>
<tr>
<td></td>
<td>$N_{\text{geom}}$</td>
<td>total number of TFJ geometrical parameters (i.e. centre of the two spheres fitted to the tibial plateaus and ligament attachment points) used in $\Delta L_0$ ($N_{\text{geom}} = 24$), $\Delta L_{\min}$ and $\Delta L_{\text{match}}$ ($N_{\text{geom}} = 30$)</td>
</tr>
<tr>
<td>3</td>
<td>$ROM_{o,n}$</td>
<td>$n^{th}$ optimised ROM</td>
</tr>
<tr>
<td></td>
<td>$ROM_{m,n}$</td>
<td>$n^{th}$ measured ROM during gait in children (Leardini et al., 2007)</td>
</tr>
<tr>
<td></td>
<td>$N_{\text{DoF bound}}$</td>
<td>total number of bounded TFJ ROM degrees of freedom ($N_{\text{DoF bound}} = 2$ in this case, i.e. TFJ ab/adduction and internal/external rotation)</td>
</tr>
<tr>
<td>4</td>
<td>$\rho_{\text{ligament},l}$</td>
<td>Pearson’s correlation between the $l^{th}$ estimated and published (Belvedere et al., 2012; Bergamini et al., 2011; Blankevoort et al., 1991) ligament kinematics total number of ligaments used in $\Delta L_{\min}$ ($N_{\text{lig}} = 4$)</td>
</tr>
</tbody>
</table>

Multiple Objective Particle Swarm Optimisation (MOPSO) (Coello et al., 2004) (Matlab) optimised the geometrical parameters to minimise the corresponding objective functions in the outer loop. MOPSO generated multiple solutions (Figure 6.23 in section 6.7.3) from which the following criteria were used to choose a unique solution ($S$):
Importantly, $J_2$ was never included in the choice of optimal solutions because the geometrical parameters were always within the limits of reasonable anatomical variability.

The inner loops for the TFJ and PFJ mechanisms used the set of geometrical parameters to solve the closure equations of the joint mechanisms for 1° increments of the TFJ flexion angle from 0° to 90°. The solved equations estimated the remaining TFJ rotations and translations while ensuring these were continuous, i.e. without singularities. Depending on the type of ligament model, the inner loop minimised the estimated ligament length changes for $\Delta L_0$ and $\Delta L_{\text{min}}$, or the difference between estimated and published experimental ligament length change for $\Delta L_{\text{match}}$. The joint mechanisms’ closure equations were solved by using the $\text{fsolve}$ function in Matlab, with a trust-region algorithm for $\Delta L_0$, and a Levenberg-Marquardt method for $\Delta L_{\text{min}}$ and $\Delta L_{\text{match}}$, since in these two models the number of closure equations was higher than the number of dependent degrees of freedom.

### 6.3.5 Data analysis and statistics

Kinematic data were not normally distributed according to Shapiro-Wilk test results. Therefore, Statistical non-Parametric Mapping (SnPM) was used to assess the models’ outputs (Pataky et al., 2015). Subsequently, the resulting average kinematic curves from the three models were compared to determine if significant differences existed between the curves at any TFJ flexion angle (Pataky et al., 2013). To this-end, a nonparametric one-dimension two-tailed paired $t$-test was conducted on the TFJ and PFJ kinematics, taking into consideration the dependency of all points of each TFJ flexion ROM ($\alpha=0.05$) to calculate the critical threshold ($t^*$) (Penny et al., 2011). All SnPM analyses were performed in Matlab using the open-source SPM1D code (version M.0.4.2, [www.spm1d.org](http://www.spm1d.org)). Additionally, the similarity of the pattern of the TFJ and PFJ kinematic curves from the three models with those from published kinematics was examined using Pearson’s correlation ($\rho$).

For validation, we determined the experimental poses of each participant’s tibia and patella with respect to their femur from the MRIs at approximately 0°, 7°, 15° and 25° of TFJ flexion angle (Fig. 6.2). The anatomical landmarks identified in the MRI-reference 0° position, and used to create the initial SCSs, were identified on the corresponding

\[
S_{\Delta L_0,\Delta L_{\text{match}}} = \begin{cases} 
\min J_1 & \text{if } J_3 = 0 \\
\min J_3 & \text{if } J_3 > 0
\end{cases}
\]

\[
S_{\Delta L_{\text{min}}} = \begin{cases} 
\min[\text{mean}(J_1,J_3)] & \text{if } J_3 = 0 \\
\min J_3 & \text{if } J_3 > 0
\end{cases}
\]

\[\text{(6.5)}\]

\[\text{(6.6)}\]
registered bones at 7°, 15° and 25° positions (Fig. 6.2b-e). These landmarks were used to create the bones’ SCSs and 6 DoF kinematics at the four TFJ joint angles. The transformation matrices aligning the SCSs in the MRI-reference pose to the SCSs in 7°, 15° and 25° flexion angles were computed and used to derive the ligaments’ attachment points in all poses. For each model, ligaments’ lengths were then computed as Euclidean distance between the attachment points at all four different poses. The Root-Mean-Square Errors (RMSEs) between each participant’s predicted and MRI-measured TFJ, PFJ and ligament kinematics were computed for each kinematic model and averaged across the four TFJ flexion angles. Ninety-five percent confidence intervals (CI) were also computed. A one-way repeated measures Analysis of Variance (ANOVA) with a priori contrasts was performed to determine differences in the average RMSE between each kinematic model at each TFJ and PFJ degree of freedom and ligament length (α=0.05).

**Figure 6.2.** Example of full-length bone segmentation from the full lower limb MRI scan (a). Example of bone segmentation from the regional MRI scans at approximately 0°(b), 7° (c), 15° (d) and 25° (e) of TFJ flexion and registration of these bones to the full-length bones (b, c, d, e).

### 6.4 Results

Three different ligament models were produced and optimised for each participant and estimated their TFJ, PFJ and ligament kinematics (Fig. 6.3 and Figures 6.15-6.22 in section 6.7.2). The optimisation of the models’ geometric parameters required ~5 hours using a standard PC (Intel i5-4590S, 8GB-RAM). Paired t-tests showed differences in the modelled TFJ kinematics between the three models, while no differences were found in the PFJ kinematics between the three models (Figures 6.7-6.13 in section 6.7.1). The
mean TFJ ab/adduction for $\Delta L_{\text{match}}$ exhibited a more adducted pattern with respect to the other two models (Fig. 6.3), with significant differences at 14-69° of TFJ flexion with respect to $\Delta L_0$ and at 0-34° of TFJ flexion with respect to $\Delta L_{\text{min}}$. Differences in TFJ ab/adduction were also found between $\Delta L_0$ and $\Delta L_{\text{min}}$ at 0-26° of TFJ flexion. The mean TFJ proximal/distal translation for $\Delta L_{\text{match}}$ exhibited a less distal pattern with respect to the other two models, with significant differences at 24-63° of TFJ flexion with respect to $\Delta L_0$ and at 56-69° of TFJ flexion with respect to $\Delta L_{\text{min}}$.

**Figure 6.3.** Comparison between the average (a) TFJ and (b) PFJ kinematics as function of the TFJ flexion angle obtained from $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red) models with those from published cadaveric data (grey) (TFJ: Ottoboni et al., 2010; Sancisi and Parenti-Castelli,
Curves represent the average ± standard deviation across the eight participants.

The correlations between published and estimated TFJ and PFJ kinematics were very similar for the three models (Table 6.2). Specifically, for all three models, the resulting anterior/posterior and proximal/distal TFJ translations exhibited strong positive correlation with published kinematics ($\rho>0.9$, $p<0.01$), while model-estimated TFJ rotations showed very weak correlation with published kinematics ($-0.23<\rho<0.11$) and large variability. Conversely, PFJ kinematics had generally strong positive correlation with published kinematics, except for PFJ internal/external rotation ($\rho\geq0.69$, $p<0.01$).
Subject-specific paediatric knee kinematic models with ligamentous constraints

<table>
<thead>
<tr>
<th>Joint</th>
<th>Model</th>
<th>Flexion/Extension</th>
<th>Anteroposterior</th>
<th>Lateral/Medial</th>
<th>Proximal/Distal</th>
</tr>
</thead>
<tbody>
<tr>
<td>TFJ</td>
<td>Δψ</td>
<td>0.93 (0.04)</td>
<td>0.69 (0.28)</td>
<td>&gt;0.99 (&lt;0.01)</td>
<td>&gt;0.99 (&lt;0.01)</td>
</tr>
<tr>
<td></td>
<td>Δθ</td>
<td>0.93 (0.03)</td>
<td>0.69 (0.28)</td>
<td>&gt;0.99 (&lt;0.01)</td>
<td>&gt;0.99 (&lt;0.01)</td>
</tr>
<tr>
<td></td>
<td>ΔΓ</td>
<td>0.92 (0.03)</td>
<td>0.70 (0.29)</td>
<td>&gt;0.99 (&lt;0.01)</td>
<td>&gt;0.99 (&lt;0.01)</td>
</tr>
</tbody>
</table>

**Table 6.2** Pearson’s correlation coefficients across participants (average and standard deviation) between published and estimated TFJ and PFL
Compared to published cadaveric data, the MRI-measured kinematic data generally overlapped with the published TFJ and PFJ kinematics ROMs, except for TFJ internal/external rotation (Figure 6.4a) and PFJ extension/flexion (Figure 6.4b). In fact, participants in this study exhibited a more externally rotated tibia and a more extended patella with respect to cadaveric kinematics. Moreover, compared to cadaveric ligament strain (Blankevoort et al., 1991), the MRI-measured data generally exhibited a slightly larger length variation with respect to the initial ligament length at 0° TFJ flexion (Figure 6.5).
Figure 6.4. Comparison between (a) TFJ and (b) PFJ kinematics from MRI-measured (black dots) and published cadaveric (grey) data (TFJ: Ottoboni et al., 2010; Sancisi and Parenti-Castelli, 2011; PFJ: Ottoboni et al., 2010; Sancisi and Parenti-Castelli, 2011) across the TFJ flexion ROM. The MRI-measured data include four poses for each participant.
Subject-specific paediatric knee kinematic models with ligamentous constraints

Figure 6.5. Comparison of knee ligament strain (ACL, PCL, MCL and LCL) between published (Blankevoort et al., 1991; Belvedere et al., 2012) (grey) and MRI-measured data across the TFJ flexion ROM. The MRI-measured data (dots) include four poses for each participant and were calculated for \( \Delta L_0 \) (green), \( \Delta L_{\text{min}} \) (blue) and \( \Delta L_{\text{match}} \) (red). To calculate the strain, the initial length at 0° TFJ flexion of each ligament was derived from the respective model estimates.

The RMSEs showed good agreement between estimated and MRI-measured knee and ligament kinematics (Fig. 6.6). Generally, \( \Delta L_0 \) and \( \Delta L_{\text{match}} \) exhibited lower average RMSEs for TFJ (rotations <6.93°, translations <1.91 mm) and PFJ (rotations <3.90°, translations <4.23 mm) kinematics than \( \Delta L_{\text{min}} \) (TFJ rotations <13.42°, TFJ translations <3.15 mm, PFJ rotations <5.76°, PFJ translations <5.42 mm), suggesting that they better match the MRI-registered static poses (Figs. 6.6a,b). The average RMSEs for TFJ kinematics between \( \Delta L_0 \) and \( \Delta L_{\text{match}} \) were not significantly different. Contrarily, average RMSEs in \( \Delta L_{\text{min}} \) were significantly different to \( \Delta L_{\text{match}} \) for TFJ ab/adduction (\( \Delta L_{\text{min}} \): 3.49° [2.73; 4.25 CI], \( \Delta L_{\text{match}} \): 1.81° [1.30; 2.32 CI]) and to \( \Delta L_0 \) for TFJ internal/external rotation (\( \Delta L_{\text{min}} \): 13.41° [9.42; 17.40 CI], \( \Delta L_0 \): 5.41° [3.99; 6.83 CI]) (Fig. 6.6a). The magnitude of the RMSE in each TFJ and PFJ motion component was generally acceptable when assessed against the corresponding total ROM for each
Subject-specific paediatric knee kinematic models with ligamentous constraints participant (Table 6.3, Table 6.4, section 6.7.4). The average RMSEs for ligament kinematics were comparable between the three models (between 0.60 mm and 2.01 mm) (Fig. 6.6c) and remained close (<4.2%) to the MRI-registered ligament length at ~0° of TFJ flexion (Table 6.5 section 6.7.4).

**Figure 6.6.** Average RMSEs and 95% CI for each degree of freedom of the TFJ kinematics (a), PFJ kinematics (b) and ligament length (c) for each model. The length of the LCL in $\Delta L_0$ (c) was computed as the distance between the centroid of the attachment areas throughout the TFJ flexion ROM.
6.5 Discussion

For the first time we developed subject-specific paediatric TFJ and PFJ mechanisms from MRIs using three different ligament models, i.e. isometric ($\Delta L_0$) and extensible ligaments ($\Delta L_{\text{min}}, \Delta L_{\text{match}}$). Each model was used to compute passive three-dimensional knee and ligament kinematics. We also validated the resulting kinematics from the three models against in vivo knee and ligament kinematics obtained from MRIs at four different TFJ flexion angles. The estimated TFJ and PFJ kinematics were similar to those measured from MRIs, with generally low RMSEs for all the three models. Furthermore, the three models well estimated MRI-measured ligament lengths.

Three different subject-specific TFJ models, each combined with a PFJ model, were developed in this study. To this end, we assumed that the ligaments and articular surfaces of the TFJ guide the passive TFJ motion (O’Connor et al., 1989; Rovick et al., 1991; Wilson et al., 1997), and previously published knee models (Feikes et al., 2003; Ottoboni et al., 2010; Sancisi et al., 2011a; Wilson et al., 1997) indirectly confirmed this, since cadaveric motion was replicated by excluding the potential influence of the muscles. A first TFJ model with null ligament elongation was implemented to verify to which extent the assumption of isometric ligaments, though less realistic than in adult populations, is still able to capture the kinematics of paediatric populations. The implementation of two additional TFJ models with minimal ($\Delta L_{\text{min}}$) or prescribed ($\Delta L_{\text{match}}$) ligament elongation was introduced to assess whether adding minimally deformable ligaments to these models can help capture anatomical characteristics typical of the paediatric population, such as high inter-subject anatomical variability and increased TFJ laxity that diminishes with increasing age (Flynn et al., 2000; Hinton et al., 2008). The agreement with in vivo passive joint and ligament kinematics shows that secondary TFJ and PFJ kinematics have a strong dependence on joint three-dimensional anatomical geometry and may not necessarily rely on soft tissue restraints.

Since it was an exploratory study, the developed models were used to estimate three-dimensional TFJ and PFJ kinematics in a relatively small population (i.e., eight participants). Due to the lack of studies with a similar approach and/or focus in the literature for paediatric participants, we could not perform a power analysis to statistically justify the number of participants and models that were tested to identify the best model. Moreover, it must be noted that studies with subject-specific models (Brito da Luz et al., 2017; Dzialo et al., 2018; Marra et al., 2015; Martelli et al., 2015; Modenese et al., 2018;
Subject-specific paediatric knee kinematic models with ligamentous constraints

Smale et al., 2019) tend to have a small number of participants because of the effort required to create each model.

Contrary to our hypothesis, $\Delta l_{\text{min}}$ provided the highest RMSEs for joint and ligament kinematics. In comparison, small average RMSEs were found for $\Delta l_0$ and $\Delta l_{\text{match}}$, indicating that $\Delta l_{\text{min}}$ had the worst agreement with in vivo joint and ligament kinematics. The poor results for $\Delta l_{\text{min}}$ could be due to an inaccurate estimation of the initial ligament lengths, which were adjusted using previously published in vitro adult ligament length measures (Blankevoort et al., 1991), and may differ to those in children and adolescents (Figure 6.5). In comparison, $\Delta l_0$ and $\Delta l_{\text{match}}$ provided smaller average RMSEs (mean RMSEs <6.9° and 4.2 mm), which were consistent with those obtained by Clément et al. (2015) (mean RMSEs <5.2° and 4.3 mm) and Gasparutto et al. (2015) (mean RMSEs <11.5° and 2.9 mm) using parallel TFJ mechanisms. Nevertheless, $\Delta l_0$ best predicted the MRI-measured length of ACL, PCL and MCL in the 0-25° TFJ flexion ROM, with RMSE magnitudes consistent with Sancisi et al. (2017), suggesting that these ligaments exhibit low length variation in the 0-25° TFJ flexion ROM (absolute average strain <8%, Fig. 6.5), as previously observed (Blankevoort et al., 1991). Therefore, $\Delta l_{\text{match}}$ may be the best model choice over a full range of knee flexion ROM. It must be noted, however, that ligament lengths were minimised through parameter optimisation at the stage of model creation, and not through multibody optimisation as in previous works (Gasparutto et al., 2015; Sancisi et al., 2017).

The resulting TFJ and PFJ kinematics obtained by using $\Delta l_0$ and $\Delta l_{\text{match}}$ were generally within two standard deviations of published experimental adult kinematics (Anglin et al., 2008; Ottoboni et al., 2010; Sancisi et al., 2011a) (Figure 6.24 section 6.7.4), satisfying the validation best practices recommended by Hicks et al. (2015). Therefore, the comparison of our results with previously validated studies and published experimental kinematics evidences that $\Delta l_0$ and $\Delta l_{\text{match}}$ can describe joint and ligament kinematics in healthy paediatric individuals with satisfying accuracy.

Between the joint motion components, TFJ internal/external rotation exhibited the highest error ($\Delta l_0$: 5.41°, $\Delta l_{\text{min}}$: 13.41°, $\Delta l_{\text{match}}$: 6.92°), in agreement with Clément et al. (2015), who showed that the largest average RMSE (5.2 ± 3.8°) occurred for TFJ internal/external rotation, when comparing active TFJ kinematics estimated by a TFJ parallel mechanism to those measured by biplanar radiography. However, when compared to published adult cadaveric data, paediatric participants exhibited a more externally rotated tibia, together with a more extended patella. This might be a
consequence of knee laxity in children (Baxter, 1988; Flynn et al., 2000; Hinton et al., 2008) in passive supine position, as confirmed by the larger MRI-measured ligament length variation, especially for the ligaments’ fibres used for $\Delta L_{match}$ (Figure 6.5).

Why is predicting personalised paediatric knee and ligament kinematics using rigid-body models relevant for research? First, employing subject-specific (Clément et al., 2015) and more complex (compared to hinge) TFJ models has been shown to provide better estimates of secondary joint kinematics when using multibody kinematic optimisation (Begon et al., 2018). Moreover, more accurate moment arm and muscle force estimates were achieved when using personalised TFJ kinematic models (Arnold et al., 2000; Navacchia et al., 2017). Second, the proposed rigid-body models, despite requiring initial tuning, provided quick estimates of secondary knee kinematics compared to more complex and computationally expensive simulations (e.g., finite element) (Dhaher et al., 2010). Finally, morphological developmental changes at growth stresses the importance of child-specific knee kinematic models.

The proposed knee kinematic models and validation process have some limitations. Firstly, due to MRI scanner size restraints, validation data were acquired only at TFJ flexion angles $<25^\circ$, which hindered validation at larger ROMs. Secondly, due to the lack of published paediatric knee and ligament kinematic data, the developed models were tuned using adult cadaveric data, presupposing comparable knee and ligament kinematics. This assumption seems reasonable for most degrees of freedom and ligaments, based on the agreement between MRI-measured and cadaveric data (Figures 6.4-6.5). Future research could investigate the use of dynamic MRI to track the movement of soft tissues and bones under loading conditions across TFJ flexion ROM (Macri et al., 2018), which would expand the model validation to larger TFJ flexion ROM and extend the applications of the model to task such as running and jumping.

In conclusion, this paper presented a methodology to create subject-specific TFJ and PFJ rigid body models with different ligamentous constraints from MRIs and applied it to a group of healthy children and adolescents. When compared to MRI-measured data, $\Delta L_0$ and $\Delta L_{match}$ performed the best (i.e. lowest RMSEs on average) and yielded similar results. Therefore, future model users could opt for $\Delta L_0$ to accurately estimate passive paediatric knee kinematics, or for $\Delta L_{match}$ to additionally well estimate ligament elongations. This work represents a step towards the creation of a fully subject-specific rigid-body model of the knee joint in paediatric populations, based on personalised geometries and anatomical structures. The importance of this development relies on the
possibility of personalizing the joint kinematics and, therefore, improving all the dependent quantities of interest for musculoskeletal modelling such as muscle moment arms, articular contact points and ligament kinematics.

6.6 Acknowledgments

L. Modenese was funded by an Imperial College Research Fellowship granted by Imperial College London, while C.P. Carty was funded by an Advance Queensland Research Fellowship granted by the Queensland Government.

6.7 Supplementary material

This material is provided with the article: Barzan, M., Modenese, L., Carty, C.P., Maine, S., Stockton, C.A., Sancisi, N., Lewis, A., Grant, J., Lloyd, D.G., Brito da Luz, S. Development and validation of subject-specific paediatric multibody knee kinematic models with ligamentous constraints. Journal of Biomechanics (Submitted).

6.7.1 Statistical analysis results

This section illustrates the results of the statistical tests conducted on the TFJ and PFJ kinematics obtained by using the three models $\Delta L_0$, $\Delta L_{\text{min}}$ and $\Delta L_{\text{match}}$. Firstly, given that the TFJ and PFJ degrees of freedom are not independent, kinematic differences between the three models were firstly evaluated by performing a paired Hotelling’s $T^2$ test (Fig. 6.7). Secondly, a one-dimension two-tailed paired $t$-test was conducted on the TFJ and PFJ kinematics. The results of each paired comparison are shown in Figures 6.8-6.13).
Figure 6.7. Hotelling’s trajectories (SnPM(T^2)), depicting where the combined TFJ and PFJ degrees of freedom across the 8 participants differed between models. Results from the paired Hotelling’s T^2 tests between ΔL_0 and ΔL_min (column a), ΔL_0 and ΔL_match (column b) and ΔL_min and ΔL_match (column c) are reported. The horizontal dashed lines indicate the critical thresholds of T^2.
Subject-specific paediatric knee kinematic models with ligamentous constraints.
Subject-specific paediatric knee kinematic models with homogeneous constraints

Figure 6.9. Average and standard deviation of TFJ angular position (left) and TFJ proximal/distal (right) displacements obtained by \( \Delta X \) (green), \( \Delta Y \) (blue) and \( \Delta Z \) (red) as a function of the TFJ flexion angle. T statistics calculated using the statistical non-parametric mapping (SnPM(t)) equivalent of a one-dimensional two-tailed paired t-test, depicting where TFJ angular position (left) and TFJ proximal/distal (right) displacements differed between models. The horizontal dashed lines indicate the critical thresholds (t) for significance.
**Figure 6.10.** Average and standard deviation of TFJ lateral/medial displacement obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red), as function of the TFJ flexion angle. $T$ statistics calculated using the statistical non-parametric mapping (SnPM($t$)) equivalent of a one-dimension two-tailed paired $t$-test, depicting where TFJ lateral/medial displacement differed between models. The horizontal dashed lines indicate the critical thresholds ($t$) for significance.
Subject-specific paediatric knee kinematic models with ligamentous constraints.

Figure 6.11. Average and standard deviation of PFJ extension/flexion (left) and PFJ adduction/abduction (right) as function of the TFJ flexion angle. 

*Figure 6.11*: Average and standard deviation of PFJ flexion/extension (left) and PFJ adduction/abduction (right) obtained by Δ$^{a}$ (green), Δ$^{b}$ (blue) and Δ$^{c}$ (red), as function of the TFJ flexion angle. T statistics calculated using the statistical non-parametric mapping (SnPM(t)) equivalent of a one-dimensional two-tailed paired t-test, depicting where PFJ extension/flexion (left) and PFJ adduction/abduction (right) differed between models. The horizontal dashed lines indicate the critical thresholds (t) for significance.
Figure 6.12. Average and standard deviation of PFJ internal/external rotation (left) and PFJ anterior/posterior displacement (right) obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red), as function of the TFJ flexion angle. $T$ statistics calculated using the statistical non-parametric mapping (SnPM(t)) equivalent of a one-dimension two-tailed paired t-test, depicting where PFJ internal/external rotation (left) and PFJ anterior/posterior displacement (right) differed between models. The horizontal dashed lines indicate the critical thresholds (t) for significance.
Subject-specific paediatric knee kinematic models with ligamentous constraints
6.7.2 Predicted and MRI-based knee and ligament kinematics

This section includes a comparison between the average TFJ and PFJ kinematics predicted by the three models, cadaveric and MRI-based kinematics (Figure 6.14). Moreover, comparisons between each individual’s predicted and MRI-based TFJ, PFJ and ligament kinematics are reported (Figures 6.15-6.22).

Figure 6.14. Comparison between the average TFJ (a) and PFJ (b) kinematics obtained from $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red), as function of the TFJ flexion angle. The shaded areas represent the average ROM across the 8 participants and they are compared against the ROM of published cadaveric kinematics (grey) and MRI-based kinematics (black dots).
Figure 6.15. TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red) for participant 1. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.
Figure 6.16. TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red) for participant 2. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.
Figure 6.17. TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red) for participant 3. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.
Figure 6.18. TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red) for participant 4. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.
Figure 6.19. TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red) for participant 5. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.
Figure 6.20. TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red) for participant 6. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.
Figure 6.21. TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red) for participant 7. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.
Figure 6.22. TFJ (a) and PFJ (b) kinematics and ligament lengths (c) obtained by $\Delta L_0$ (green), $\Delta L_{\text{min}}$ (blue) and $\Delta L_{\text{match}}$ (red) for participant 8. Model-based kinematics and ligament lengths are compared against MRI-based (dots) and cadaveric (grey) kinematic and ligaments lengths.
6.7.3 Multiple Objective Particle Swarm Optimisation

The MOPSO is a global optimisation algorithm that has recently gained prominence. The use of this algorithm in this study led to many advantages. First, it allowed us to simultaneously minimise multiple objective functions. In fact, this algorithm consisted of a parallel coordinate method that included 24 (for $\Delta L_0$) or 30 (for $\Delta L_{\text{min}}$ and $\Delta L_{\text{match}}$) design variables (i.e. tibial sphere centres and ligament attachment points) and three (for $\Delta L_0$ and $\Delta L_{\text{match}}$) or four (for $\Delta L_{\text{min}}$) cost functions that were simultaneously minimised (Figure 6.23). Second, it provided multiple solutions rather than just a unique solution. This allowed us to determine a criterion to choose the best solution within different ones. Third, when compared to previously used global search algorithms (e.g. simulated annealing (Brito da Luz et al., 2017) and genetic algorithm
(Ottoboni et al., 2010)), the introduction of the MOPSO algorithm allowed to halve the computation time required to tune the model to avoid singularities.

In this study, the optimisation ran using 50 particles and 200 iterations for the TFJ and 50 particles and only 50 iterations for the PFJ, given that the PFJ mechanism found solutions quicker in pilot testing.

**Figure 6.23.** Example of multiple TFJ solutions (n = 47 in this case) found with MOPSO for participant 8 using $\Delta L_{\text{match}}$. Each colour represents a different solution, with 30 optimised parameters (pink area) and three objective functions (green area). If the optimised ROMs were larger than the published ROMs, the solution with minimal difference between optimised and published TFJ ab/adduction and internal/external rotation ROMs was chosen to ensure that the kinematics was within reasonable ROMs for a paediatric population. Otherwise, the solution that provided the best match between the pattern of estimated and published experimental TFJ and PFJ kinematics was chosen.
### 6.7.4 Error magnitudes

**Table 6.3.** RMSE between model-based and MRI-registered TFJ kinematics for the four poses of comparison, ROM and percent error relative to the ROM.

<table>
<thead>
<tr>
<th>Subject</th>
<th>( \Delta L_0 )</th>
<th>( \Delta L_{\text{min}} )</th>
<th>( \Delta L_{\text{match}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RMSE (%)</td>
<td>Error (%)</td>
<td>RMSE (%)</td>
</tr>
<tr>
<td>S1</td>
<td>2.3</td>
<td>5</td>
<td>3.0</td>
</tr>
<tr>
<td>S2</td>
<td>1.9</td>
<td>17.2</td>
<td>3.3</td>
</tr>
<tr>
<td>S3</td>
<td>4.3</td>
<td>38</td>
<td>2.3</td>
</tr>
<tr>
<td>S4</td>
<td>1.0</td>
<td>7.7</td>
<td>3.9</td>
</tr>
<tr>
<td>S5</td>
<td>2.1</td>
<td>4.6</td>
<td>5.3</td>
</tr>
<tr>
<td>S6</td>
<td>1.0</td>
<td>1.3</td>
<td>3.6</td>
</tr>
<tr>
<td>S7</td>
<td>2.8</td>
<td>23.1</td>
<td>2.7</td>
</tr>
<tr>
<td>S8</td>
<td>1.6</td>
<td>5.6</td>
<td>3.8</td>
</tr>
<tr>
<td>Mean</td>
<td>2.1</td>
<td>12.8</td>
<td>3.5</td>
</tr>
<tr>
<td>(SD)</td>
<td>(1.1)</td>
<td>(12.5)</td>
<td>(0.9)</td>
</tr>
<tr>
<td>S1</td>
<td>6.2</td>
<td>14.7</td>
<td>15.6</td>
</tr>
<tr>
<td>S2</td>
<td>7.5</td>
<td>35.2</td>
<td>17.1</td>
</tr>
<tr>
<td>S3</td>
<td>7.5</td>
<td>53.3</td>
<td>8.4</td>
</tr>
<tr>
<td>S4</td>
<td>4.0</td>
<td>32.7</td>
<td>12.3</td>
</tr>
<tr>
<td>S5</td>
<td>3.5</td>
<td>45.3</td>
<td>10.8</td>
</tr>
<tr>
<td>S6</td>
<td>3.3</td>
<td>51.9</td>
<td>18.4</td>
</tr>
<tr>
<td>S7</td>
<td>6.2</td>
<td>52.3</td>
<td>6.0</td>
</tr>
<tr>
<td>S8</td>
<td>5.0</td>
<td>34.9</td>
<td>18.7</td>
</tr>
<tr>
<td>Mean</td>
<td>5.4</td>
<td>40.9</td>
<td>13.4</td>
</tr>
<tr>
<td>(SD)</td>
<td>(1.7)</td>
<td>(13.3)</td>
<td>(0.9)</td>
</tr>
<tr>
<td>S1</td>
<td>1.1</td>
<td>14.5</td>
<td>3.6</td>
</tr>
<tr>
<td>S2</td>
<td>1.0</td>
<td>23.2</td>
<td>5.3</td>
</tr>
<tr>
<td>S3</td>
<td>0.6</td>
<td>26.2</td>
<td>1.0</td>
</tr>
<tr>
<td>S4</td>
<td>0.9</td>
<td>15.6</td>
<td>1.2</td>
</tr>
<tr>
<td>S5</td>
<td>4.0</td>
<td>26.5</td>
<td>0.8</td>
</tr>
<tr>
<td>S6</td>
<td>1.7</td>
<td>18.7</td>
<td>3.7</td>
</tr>
<tr>
<td>S7</td>
<td>2.1</td>
<td>15.4</td>
<td>1.8</td>
</tr>
<tr>
<td>S8</td>
<td>0.6</td>
<td>18.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Mean</td>
<td>1.1</td>
<td>19.8</td>
<td>2.2</td>
</tr>
<tr>
<td>(SD)</td>
<td>(0.5)</td>
<td>(4.8)</td>
<td>(3.7)</td>
</tr>
<tr>
<td>S1</td>
<td>1.9</td>
<td>2.6</td>
<td>1.5</td>
</tr>
<tr>
<td>S2</td>
<td>1.4</td>
<td>5.3</td>
<td>0.5</td>
</tr>
<tr>
<td>S3</td>
<td>1.0</td>
<td>14.1</td>
<td>1.2</td>
</tr>
<tr>
<td>S4</td>
<td>0.3</td>
<td>14.1</td>
<td>0.5</td>
</tr>
<tr>
<td>S5</td>
<td>1.1</td>
<td>12.4</td>
<td>1.0</td>
</tr>
<tr>
<td>S6</td>
<td>0.9</td>
<td>19.1</td>
<td>1.8</td>
</tr>
<tr>
<td>S7</td>
<td>1.9</td>
<td>23.1</td>
<td>1.9</td>
</tr>
<tr>
<td>S8</td>
<td>0.9</td>
<td>5.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Mean</td>
<td>1.2</td>
<td>12.0</td>
<td>1.2</td>
</tr>
<tr>
<td>(SD)</td>
<td>(0.5)</td>
<td>(7.2)</td>
<td>(0.6)</td>
</tr>
<tr>
<td>S1</td>
<td>1.4</td>
<td>9.6</td>
<td>3.5</td>
</tr>
<tr>
<td>S2</td>
<td>1.8</td>
<td>2.3</td>
<td>6.5</td>
</tr>
<tr>
<td>S3</td>
<td>1.2</td>
<td>11.7</td>
<td>3.1</td>
</tr>
<tr>
<td>S4</td>
<td>0.6</td>
<td>5.6</td>
<td>7.4</td>
</tr>
<tr>
<td>S5</td>
<td>0.6</td>
<td>14.8</td>
<td>1.1</td>
</tr>
<tr>
<td>S6</td>
<td>0.9</td>
<td>12.2</td>
<td>1.4</td>
</tr>
<tr>
<td>S7</td>
<td>2.0</td>
<td>13.7</td>
<td>0.7</td>
</tr>
<tr>
<td>S8</td>
<td>0.7</td>
<td>3.8</td>
<td>1.5</td>
</tr>
<tr>
<td>Mean</td>
<td>1.1</td>
<td>9.2</td>
<td>3.1</td>
</tr>
<tr>
<td>(SD)</td>
<td>(0.5)</td>
<td>(4.7)</td>
<td>(2.5)</td>
</tr>
</tbody>
</table>
Table 6.4. RMSE between model-based and MRI-registered PFJ kinematics for the four poses of comparison, ROM and percent error relative to the ROM.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Mean</th>
<th>S1</th>
<th>S2</th>
<th>S3</th>
<th>S4</th>
<th>S5</th>
<th>S6</th>
<th>S7</th>
<th>S8</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anterior/posterior</strong></td>
<td><strong>deg</strong></td>
<td>(SD)</td>
<td>(10.4)</td>
<td>(11.8)</td>
<td>(12.7)</td>
<td>(14.8)</td>
<td>(16.5)</td>
<td>(18.6)</td>
<td>(20.7)</td>
</tr>
<tr>
<td>Flexion/extension</td>
<td>3.9</td>
<td>83.9</td>
<td>15.4</td>
<td>14.7</td>
<td>13.8</td>
<td>15.6</td>
<td>18.0</td>
<td>19.7</td>
<td>20.4</td>
</tr>
<tr>
<td>Ad/abduction</td>
<td>(4.6)</td>
<td>(12.3)</td>
<td>(7.5)</td>
<td>(7.6)</td>
<td>(7.7)</td>
<td>(7.6)</td>
<td>(7.6)</td>
<td>(7.6)</td>
<td>(7.6)</td>
</tr>
<tr>
<td>In/external rotation</td>
<td>(4.7)</td>
<td>(19.6)</td>
<td>(13.1)</td>
<td>(11.7)</td>
<td>(12.3)</td>
<td>(13.1)</td>
<td>(12.3)</td>
<td>(12.3)</td>
<td>(12.3)</td>
</tr>
<tr>
<td>Anterior/posterior</td>
<td>(3.2)</td>
<td>(10.7)</td>
<td>(11.2)</td>
<td>(10.8)</td>
<td>(10.7)</td>
<td>(10.7)</td>
<td>(10.7)</td>
<td>(10.7)</td>
<td>(10.7)</td>
</tr>
<tr>
<td>Proximal/distal</td>
<td>(3.1)</td>
<td>(2.0)</td>
<td>(2.2)</td>
<td>(2.5)</td>
<td>(2.4)</td>
<td>(2.7)</td>
<td>(2.8)</td>
<td>(2.9)</td>
<td>(2.8)</td>
</tr>
<tr>
<td>Lateral/medial</td>
<td>(3.2)</td>
<td>(0.8)</td>
<td>(0.8)</td>
<td>(0.8)</td>
<td>(0.8)</td>
<td>(0.8)</td>
<td>(0.8)</td>
<td>(0.8)</td>
<td>(0.8)</td>
</tr>
</tbody>
</table>

**ROM**: Rotation of comparison, RM and percent error relative to the ROM.
Table 6.5. RMSE of model-based and MRI-registered ligament length for the four poses of comparison, ligament length at ~0° TFJ flexion ($L_0$) and percent error relative to the initial ligament length.

<table>
<thead>
<tr>
<th>Subject</th>
<th>$\Delta L_{0}$</th>
<th>$\Delta L_{\text{min}}$</th>
<th>$\Delta L_{\text{match}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RMSE</td>
<td>$L_0$</td>
<td>error (%)</td>
</tr>
<tr>
<td>S1</td>
<td>0.7</td>
<td>31.4</td>
<td>2.3</td>
</tr>
<tr>
<td>S2</td>
<td>1.0</td>
<td>26.7</td>
<td>3.7</td>
</tr>
<tr>
<td>S3</td>
<td>0.4</td>
<td>27.3</td>
<td>1.5</td>
</tr>
<tr>
<td>S4</td>
<td>0.3</td>
<td>27.6</td>
<td>1.0</td>
</tr>
<tr>
<td>S5</td>
<td>1.1</td>
<td>37.0</td>
<td>2.9</td>
</tr>
<tr>
<td>S6</td>
<td>1.4</td>
<td>34.3</td>
<td>4.1</td>
</tr>
<tr>
<td>S7</td>
<td>2.2</td>
<td>33.0</td>
<td>6.6</td>
</tr>
<tr>
<td>S8</td>
<td>0.7</td>
<td>26.0</td>
<td>2.6</td>
</tr>
<tr>
<td>Mean</td>
<td>1.0</td>
<td>30.4</td>
<td>3.1</td>
</tr>
<tr>
<td></td>
<td>(SD)</td>
<td>(4.6)</td>
<td>(1.8)</td>
</tr>
<tr>
<td>ACL [mm]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1</td>
<td>0.8</td>
<td>33.8</td>
<td>2.2</td>
</tr>
<tr>
<td>S2</td>
<td>1.0</td>
<td>26.0</td>
<td>3.9</td>
</tr>
<tr>
<td>S3</td>
<td>0.3</td>
<td>30.5</td>
<td>1.1</td>
</tr>
<tr>
<td>S4</td>
<td>0.5</td>
<td>29.2</td>
<td>1.6</td>
</tr>
<tr>
<td>S5</td>
<td>0.5</td>
<td>34.7</td>
<td>1.6</td>
</tr>
<tr>
<td>S6</td>
<td>0.7</td>
<td>39.2</td>
<td>1.7</td>
</tr>
<tr>
<td>S7</td>
<td>0.6</td>
<td>28.6</td>
<td>2.2</td>
</tr>
<tr>
<td>S8</td>
<td>0.4</td>
<td>34.4</td>
<td>1.1</td>
</tr>
<tr>
<td>Mean</td>
<td>0.6</td>
<td>32.1</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>(SD)</td>
<td>(0.2)</td>
<td>(0.9)</td>
</tr>
<tr>
<td>PCL [mm]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1</td>
<td>1.1</td>
<td>63.2</td>
<td>1.7</td>
</tr>
<tr>
<td>S2</td>
<td>0.9</td>
<td>66.4</td>
<td>1.4</td>
</tr>
<tr>
<td>S3</td>
<td>0.6</td>
<td>71.9</td>
<td>0.9</td>
</tr>
<tr>
<td>S4</td>
<td>0.5</td>
<td>60.3</td>
<td>0.9</td>
</tr>
<tr>
<td>S5</td>
<td>0.8</td>
<td>79.8</td>
<td>0.9</td>
</tr>
<tr>
<td>S6</td>
<td>0.6</td>
<td>85.2</td>
<td>0.7</td>
</tr>
<tr>
<td>S7</td>
<td>0.5</td>
<td>64.2</td>
<td>0.7</td>
</tr>
<tr>
<td>S8</td>
<td>1.4</td>
<td>74.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Mean</td>
<td>0.8</td>
<td>70.7</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td>(SD)</td>
<td>(0.3)</td>
<td>(0.8)</td>
</tr>
<tr>
<td>MCL [mm]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1</td>
<td>1.8</td>
<td>55.5</td>
<td>3.2</td>
</tr>
<tr>
<td>S2</td>
<td>2.3</td>
<td>69.3</td>
<td>3.3</td>
</tr>
<tr>
<td>S3</td>
<td>2.7</td>
<td>57.0</td>
<td>4.7</td>
</tr>
<tr>
<td>S4</td>
<td>1.4</td>
<td>56.8</td>
<td>2.5</td>
</tr>
<tr>
<td>S5</td>
<td>2.1</td>
<td>67.9</td>
<td>3.1</td>
</tr>
<tr>
<td>S6</td>
<td>1.6</td>
<td>65.8</td>
<td>2.4</td>
</tr>
<tr>
<td>S7</td>
<td>3.0</td>
<td>55.8</td>
<td>5.4</td>
</tr>
<tr>
<td>S8</td>
<td>1.1</td>
<td>57.5</td>
<td>1.9</td>
</tr>
<tr>
<td>Mean</td>
<td>2.0</td>
<td>60.7</td>
<td>3.3</td>
</tr>
<tr>
<td></td>
<td>(SD)</td>
<td>(0.7)</td>
<td>(5.9)</td>
</tr>
<tr>
<td>LCL [mm]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a the initial ligament length ($L_0$) was computed, for each TFJ model, as Euclidean distance between the optimised ligament attachment points.
Figure 6.24. Comparison between the TFJ (a) and PFJ (b) kinematics obtained from $\Delta L_0$ (green) and $\Delta L_{\text{match}}$ (red), expressed as average ± SD across the 8 participants, and published cadaveric kinematics (grey) (Sancisi et al., 2011; Ottoboni et al., 2010, Anglin et al., 2008), expressed as average ± 2SD.
CHAPTER 7

Implementation of a subject-specific paediatric kinematic model of the knee with minimally deformable ligaments in OpenSim

This chapter presents a methodology to create subject-specific lower limb models that incorporate fully subject-specific paediatric knee models with articular contacts and minimally deformable ligaments. These models are used to assess knee and ligament kinematics during gait in eight healthy participants. The manuscript describing these results will be submitted as Barzan, M., Carty, C.P., Maine, S., Sancisi, N., Stockton, C.A., Edwards, J., Brito da Luz, S., Lloyd, D.G., Modenese, L. Implementation of a subject-specific paediatric kinematic model of the knee with minimally deformable ligaments in OpenSim. Journal of Biomechanics.

7.1 Introduction

Three-dimensional gait analysis is extensively used for treatment planning and outcome assessment in children with neuromusculoskeletal disorders, e.g. cerebral palsy (Chang et al., 2006). In fact, based on the calculated gait kinematics, clinicians can quantify normal and pathological patterns of locomotion, which will then inform the clinical decision making process (Baker, 2013). Gait kinematics can be obtained by tracking the three-dimensional positions of reflective skin markers placed on anatomical prominences of the participant's lower limbs (Kadaba et al., 1990; Perry et al., 1992). This procedure requires an underlying kinematic model of the lower extremities, which defines bony segments and joints.
Conventional kinematic models employed in gait analysis consist of link-based models with simplified representations of the joints (Davis et al., 1991; Kadaba et al., 1990). These simplistic rigid-body models are poorly representative of the participant’s anatomy and joint motion, especially of more complex joints, such as the tibiofemoral joint (TFJ). These simplifications, together with the presence of soft tissue artefacts, make gait analysis unsuitable to accurately describe the joint motion in the coronal and axial planes (Andersen et al., 2010; Stagni et al., 2009; Stagni et al., 2005) and could compromise the clinical decision making. Alternatively, subject-specific computational models of the musculoskeletal (MSK) system, that include each individual’s anatomy, can provide accurate, non-invasive and personalised analyses (Gerus et al., 2013; Marra et al., 2015) of the participant’s joint kinematics, kinetics and internal loads (e.g., muscle and joint contact forces).

Numerous subject-specific rigid-body models have been created from medical images for gait analysis in adults (Gerus et al., 2013; Lenhart et al., 2015; Marra et al., 2015; Martelli et al., 2015; Scheys et al., 2005; Taddei et al., 2012; Valente et al., 2014; Wesseling et al., 2016) and children with pathologies (Bosmans et al., 2014; Correa et al., 2011; Kainz et al., 2016; Modenese et al., 2018; Scheys et al., 2011b). Subject-specific TFJ kinematic models used in these rigid-body MSK models vary in terms of level of personalisation and also number of degrees of freedom (DoF). For example, the abovementioned paediatric subject-specific models include a 1-DoF hinge TFJ (Modenese et al., 2018), a 3-DoF spherical TFJ (Kainz et al., 2016) or a modified (Bosmans et al., 2014; Correa et al., 2011; Scheys et al., 2011b) 1-DoF planar joint (Yamaguchi et al., 1989). However, it has been shown (Andersen et al., 2010; Stagni et al., 2009) that simplistic representations of the TFJ (i.e., spherical or hinge joints) cannot accurately estimate in vivo secondary knee kinematics, especially joint translations.

More complex TFJ models based on parallel mechanisms, which introduce more anatomical and physiological DoF couplings, have been developed. Some of the TFJ parallel mechanisms developed so far (Di Gregorio et al., 2003; Feikes et al., 2003; Ottoboni et al., 2010; Parenti-Castelli et al., 2000; Parenti-Castelli et al., 2004; Sancisi et al., 2011a) included two rigid tibio-femoral contacts and three isometric ligaments, namely the anterior cruciate ligament (ACL), posterior cruciate ligament (PCL) and medial collateral ligament (MCL). This 5-rigid-link mechanism has been recently incorporated into a full-lower limb scaled-generic MSK models (Moissenet et al., 2014) and used for gait analysis. Other authors have added a fourth ligament to the previously described 5-rigid-link mechanism and allowed for ligament elongation, using a multibody
optimisation approach, to analyse dynamic tasks such as gait (Sancisi et al., 2017), running (Gasparutto et al., 2015) and squatting (Clément et al., 2015). The multibody optimisation method consists in the optimisation of the position and orientation of a multibody model of the limb to minimise the distances between the model-determined and the experimental marker trajectories. It is implemented as a quadratic optimisation problem and additional terms can be added to the marker-tracking objective function, for example ligament elongation. While most of these TFJ mechanisms used geometrical parameters from cadaveric data (Gasparutto et al., 2015; Moissenet et al., 2014; Sancisi et al., 2017), Clément et al. (2015) employed semi-personalised parallel TFJ mechanisms with minimally deformable ligaments, which allowed to achieve better estimates of TFJ abduction-adduction, internal-external rotation and antero-posterior displacement compared to simple and/or generic TFJ models. Despite providing promising results, fully personalised TFJ parallel mechanisms have never been incorporated into subject-specific lower limb MSK models to assess gait kinematics in children.

Therefore, this study first aimed to implement rigid-body lower limb models incorporating fully subject-specific paediatric kinematic TFJ models with articular contacts and four deformable ligaments (i.e., ACL, PCL, MCL and lateral collateral ligament (LCL)). These models were used to compute the TFJ and ligament kinematics during gait using a multibody optimisation approach that tracks the experimental kinematics while minimising the ligaments’ elongation from their resting pose. The second aim was to compare the kinematics results from the deformable-ligament TFJ model against those obtained employing the same TFJ kinematic model featuring three isometric ligaments (i.e., ACL, PCL and MCL), as previously proposed (Duprey et al., 2010; Gasparutto et al., 2015). It was hypothesised that the TFJ and ligament kinematics during gait would differ between the isometric-ligament and the deformable-ligament TFJ models.

7.2 Methods

7.2.1 Participants

Eight typically developing (TD) children and adolescents (4 males and 4 females, age: 14.0±2.6 years, mass: 51.1±10.5 kg, height: 1.64±0.11 m) were recruited and presented for motion capture and magnetic resonance imaging (MRI) data collection sessions. The Children’s Health Queensland Hospital and Health Services (CHQ HHS) human research ethics committee (HREC/13/QRCH/197), CHQ HHS site specific approval (SSA/14/QRCH/46) and Griffith University Research Ethics committee
Subject-specific knee kinematic models with deformable ligaments in OpenSim

(AHS/42/14/HREC) approved the study protocol. All the participants’ guardians provided written informed consent prior to participation.

7.2.2 Gait data collection and processing

Three-dimensional motion capture data were collected at the Queensland Children’s Motion Analysis Service (QCMAS), Centre for Children’s Health Research (Brisbane, Australia). Forty-six MRI compatible reflective markers (diameter = 11.18 mm) and four wand markers were attached to each participant’s body by a physiotherapist with >10 years of experience in marker placement. Markers were placed in accordance with Kainz et al. (2017), with few additional markers on the pelvis, patella, tibia and foot (Figure 7.1). In accordance with standard clinical practices at QCMAS, one static trial was collected and processed to evaluate the knee ab/adduction kinematic profile. If the knee ab/adduction kinematic profile exceeded a range of motion of 10° and exhibited cross-talk with knee flexion/extension kinematic profile, the thigh wand marker was adjusted, and a new static trial was collected. Following the static trial, marker trajectories of at least six walking trials at a self-selected speed were collected at 100 Hz using a ten-camera, three-dimensional motion capture system (Vicon Motion Systems, Oxford, UK). Marker trajectories were labelled and filtered in Vicon Nexus 2.5 (Vicon Motion Systems, Oxford, UK) using a Butterworth fourth order zero-lag low pass filter with a cut-off frequency of 6 Hz, and prepared for OpenSim using the open-source MOtoNMS pipeline (Mantoan et al., 2015) in Matlab (Matlab R2014b, MathWorks). Following motion data collection, the clusters of markers and the wand markers were removed, while the other markers were left on the participant’s skin for MRI acquisition.
Figure 7.1. Illustration of marker placement on the participant’s skin (left) and anatomical description of each marker (right). The green markers were kept on the participant’s skin during MRI acquisition, while the pink markers (clusters and wands) were removed after motion data collection.

7.2.3 Medical image acquisition and processing

Three sets of MRIs were collected at the Department of Medical Imaging and Nuclear Medicine, Lady Cilento Children’s Hospital (Brisbane, Australia), following motion capture. First, an MRI scan (1.5T scanner, SIEMENS MAGNETOM Avanto_fit syngo MR VE11B, Germany) of the entire lower limbs (3D PD SPACE sequence, slice thickness: 1.0 mm, voxel size: 0.83x0.83x1.0 mm³) was performed with the participant in a supine position to capture full length lower limb bones. A second, regional MRI scan (3T scanner, SIEMENS MAGNETOM Skyra, Germany) of the participant’s right knee (T2 SPC RST SAG P2 ISO, slice thickness: 0.53 mm, voxel size: 0.5x0.5x0.5 mm³) was performed with the knee close to 0° tibiofemoral joint (TFJ) flexion using a dedicated knee coil to capture knee articular cartilage and ligaments. Third, for each participant, three additional dedicated right knee scans were acquired at approximately 7°, 15° and 25° of TFJ flexion by using a flexible array coil wrapped around the knee.

Three-dimensional lower limb bones, markers, knee ligamentous and cartilaginous structures were reconstructed in Mimics Research 20.0 (Materialise, Belgium). Segmented bones included the pelvis, right femur, patella, tibia, fibula and foot, while ligaments included the anterior cruciate (ACL), posterior cruciate (PCL), medial collateral (MCL) and lateral collateral (LCL) ligaments and patellar tendon.
Three-dimensional pelvis, full-length femur, tibia, fibula and foot were registered into the femur and tibia volumes obtained from the knee scans through an iterative closest point algorithm (Besl et al., 1992) in 3-matic (Materialise, Belgium) (Figure 4.9) to obtain a single and comprehensive three-dimensional reconstruction of the participant’s anatomy at each considered knee angle.

7.2.4 Subject-specific full lower limb models

Right-leg skeletal models were created for the eight participants using NMSBuilder (Valente et al., 2017). To this end, full-length bone and knee cartilage meshes were imported into NMSBuilder and grouped into five bodies (i.e., pelvis, femur, patella, tibia and foot). For each body, segment coordinate systems (SCSs) were defined from anatomical landmarks virtually palpated onto the bone meshes (Table 4.4). Moreover, the markers captured during the MRI acquisition, the position of which was computed in Matlab, were imported into the software and attached to the corresponding body.

While the hip and ankle joints were defined as spherical joints (i.e., three rotations were allowed), the PFJ and TFJ were defined as custom joints (i.e., six motion components were allowed: three rotations and three translations) (Seth et al., 2010). The PFJ was modelled as a hinge mechanism (Section 4.4.2.1) and the resulting kinematics (Section 6.4) were incorporated into the full-lower limb model by means of cubic spline functions coupling the relative orientation and position of the PFJ and the TFJ flexion angle, considered as free coordinate. This coupling was defined using the ‘CoordinateCoupler’ class in OpenSim.

Differently, the TFJ was modelled as a 5-rigid-link parallel mechanism (Section 4.4.1.1) (Brito da Luz et al., 2017; Sancisi et al., 2011a) with rigid spherical articular contacts and three isometric ligaments (ACL, PCL and MCL) (Figure 7.2). This mechanism was explicitly replicated in OpenSim, based on optimised MRI-measured geometrical parameters, in order to take advantage of the Inverse Kinematic tool available in the software. To this end, the proximal and distal parts of each knee ligament (i.e., ACL, PCL and MCL) were imported into NMSBuilder and their respective SCSs were defined using the optimised ligament attachment points obtained from the implicit TFJ mechanism (Section 4.5.2). A spherical joint was created between each proximal ligament body and the femur, and a point constraint, constraining the same DoF of a spherical joint while maintaining the model open tree structure, was introduced between each distal body and the tibia. The ligament length in the MRI reference pose was considered as the rest (i.e., non-elongated) length. Moreover, a prismatic joint was defined
between each proximal and distal ligament body to allow for ligament elongation in the longitudinal axis of the ligament during gait (Figure 7.3). However, these prismatic joints were initially locked to replicate the 5-rigid-link mechanism. Subsequently, a fourth ligament (i.e., LCL) was added to the explicit implementation of the 5-rigid-link mechanism, using the same process described for the other ligaments, to obtain a more realistic representation of the TFJ during gait. The attachment points for the LCL were defined as the centroids of the LCL attachment regions onto the femur and the fibula and the prismatic pair between the LCL proximal and distal parts was unlocked to preserve the same number of degrees of freedom of the mechanism. The names of the joints and of the coordinates of the resulting OpenSim model, as well as the rotation orders, were updated (Modenese et al., 2018) in order to match those of standard OpenSim models (Delp et al., 1990).

**Figure 7.2.** Joint definition in a right-leg skeletal OpenSim model.
7.2.5 Verification of the TFJ mechanism implemented in OpenSim

Given the complexity of the explicit implementation of the mechanism, a verification procedure was established. The same TFJ mechanism was created and solved in Matlab, by optimising each participant’s MRI-measured geometrical parameters and solving the closure equations of the mechanism (Sections 6.3.3 and 6.3.4). The resulting kinematics, i.e., ab/adduction and internal/external rotations and anterior/posterior, proximal/distal and medio/lateral translations were then compared to those obtained with the OpenSim model, which relies on the Simbody engine for solving the mechanism kinematics (Sherman et al., 2011).

7.2.6 Inverse kinematics

After the OpenSim models were created for each participant, two clusters of three markers were manually placed on each model according to their position on the participant’s thigh and shank. Using the scaling tool available in OpenSim, the cluster of markers in the OpenSim models were moved to match the experimental marker location.
in the static pose, until the maximum marker and root mean square errors were below 2 cm and 1 cm, respectively, according to the OpenSim best practices (Hicks et al., 2015).

Using the inverse kinematics tool in OpenSim, each participant’s TFJ joint and ligament kinematics of five walking trials were computed in two ways. The first method (ΔL₀,implicit) employed the OpenSim model where the TFJ kinematics were described as cubic splines and, in the inverse kinematics analysis, the position and orientation of the multi-body lower-limb model were optimised to minimise the distance between measured and model-determined marker trajectories. For completeness of comparison, even if the LCL was not included in ΔL₀,implicit, its strain across the gait cycle was computed as the ratio of total LCL length variation to the initial LCL length, defined as the Euclidean distance between the centroids of the LCL attachment regions from the MRI reference pose at ~0° of TFJ flexion. Conversely, the second method (ΔL₀,min,MBO) employed the OpenSim model where the TFJ mechanism was explicitly implemented and the prismatic pairs between each proximal and distal ligament bodies were unlocked to allow for ligament elongation. In the inverse kinematic analysis, a multibody optimisation approach was used, where the position and orientation of the multi-body lower-limb model are optimised to minimise both the distance between measured and model-determined marker trajectories and the ligament elongation (Eq 4.9).

In the weighted least squares problem used in the inverse kinematic analysis, all the markers were tracked with wᵢ = 1, while the weight kⱼ used for each ligament elongation was derived from MRI as an estimation of the stiffness of each ligament. For each ligament, the axial stiffness was defined as the ratio between each ligament’s cross-sectional area (CSA) and its length from the MRI at ~0° TFJ flexion. For each ligament, the cross-sectional area was obtained by cutting the ligament in the middle (i.e., mid-point between the optimised attachment points), perpendicular to its longitudinal axis (Muneta et al., 1997), while the length was defined as the length of the centroid of the ligaments, between the optimised attachment points (Figure 4.19). Across the eight participants, highest stiffness factor (i.e., CSA/ligament length) was found for the PCL and lowest stiffness factor was found for the LCL (Table 7.1). Therefore, higher weights were assigned to ligaments expected to exhibit smaller length variations during knee flexion. However, in the multibody optimisation approach, each ligament stiffness factor was multiplied by 10 to make the two terms of the objective function (Eq. 4.9) of comparable magnitude.
7.2.7 Data analysis and statistics

For each participant, the ligament strain was computed for the four ligaments during the gait cycles. The ligament strain was defined as the ratio of total length variation to the initial ligament length, which corresponded to the Euclidean distance between the optimised ligament attachment points from the MRI reference pose at ~0° of TFJ flexion.

Kinematic data were normally distributed according to the Shapiro-Wilk test results. Therefore, Statistical Parametric Mapping (SPM) was used to assess the models’ outputs (Pataky et al., 2015). Subsequently, the resulting TFJ kinematic and ligament strain curves from the two models (i.e., $\Delta L_{0,impl\text{icite}}$ and $\Delta L_{\text{min,MBO}}$) were compared to determine if significant differences existed between the curves during gait (Pataky et al., 2013). To this end, a one-dimension two-tailed paired $t$-test was conducted on the TFJ kinematics and ligament strains, taking into consideration the dependency of all points of the gait cycle ($\alpha=0.05$) to calculate the critical threshold ($t^*$) (Penny et al., 2011). All SPM analyses were performed in Matlab using the open-source SPM1D code (version M.0.4.2, www.spm1d.org) (Pataky, 2012).

For validation purposes, we determined the experimental poses of each participant’s tibia with respect to their femur from the MRIs at approximately 0°, 7°, 15° and 25° of TFJ flexion angle (Figure 6.2). The anatomical landmarks identified in the MRI-reference 0° position, and used to create the initial SCSs, were identified on the corresponding registered bones at 7°, 15° and 25° positions (Figure 6.2b-e). These landmarks were used to create the bones’ SCSs and six degrees of freedom kinematics at the four TFJ joint angles. The transformation matrices aligning the SCSs in the MRI-reference pose to the SCSs in 7°, 15° and 25° flexion angles were computed and used to
derive the ligaments’ attachment points in all poses. Ligaments’ lengths were then computed as Euclidean distance between the attachment points at all four different poses.

7.3 Results

The two implementations (i.e., Matlab and OpenSim) of the 5-rigid-link TFJ parallel mechanism provided the same results from 0° to 90° of TFJ flexion for equivalent mechanisms, confirming that the explicit mechanism implementation was an accurate replica of the Matlab implementation.

The average and maximum marker errors obtained during inverse kinematics using the two methods were similar. Across the eight participants, the maximum marker error ranged from 3.24 to 5.88 cm when using $\Delta L_{0,\text{implicit}}$, and from 2.49 to 5.61 cm when using $\Delta L_{\text{min,MBO}}$.

\textit{Table 7.2. Comparison of the marker errors obtained for each participant using the two methods.}

<table>
<thead>
<tr>
<th>Participant</th>
<th>Mean error [cm]</th>
<th>Mean variance [cm]</th>
<th>Maximum error [cm]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\Delta L_{0,\text{implicit}}$</td>
<td>$\Delta L_{\text{min,MBO}}$</td>
<td>$\Delta L_{0,\text{implicit}}$</td>
</tr>
<tr>
<td>TD1</td>
<td>1.16</td>
<td>1.10</td>
<td>0.51</td>
</tr>
<tr>
<td>TD2</td>
<td>1.23</td>
<td>1.21</td>
<td>0.77</td>
</tr>
<tr>
<td>TD3</td>
<td>1.08</td>
<td>1.02</td>
<td>0.75</td>
</tr>
<tr>
<td>TD4</td>
<td>1.31</td>
<td>1.33</td>
<td>0.59</td>
</tr>
<tr>
<td>TD5</td>
<td>1.25</td>
<td>1.22</td>
<td>0.58</td>
</tr>
<tr>
<td>TD6</td>
<td>1.32</td>
<td>1.46</td>
<td>0.61</td>
</tr>
<tr>
<td>TD7</td>
<td>1.42</td>
<td>1.31</td>
<td>0.65</td>
</tr>
<tr>
<td>TD8</td>
<td>1.41</td>
<td>1.39</td>
<td>0.62</td>
</tr>
</tbody>
</table>

The resulting average TFJ kinematics during gait were similar between the two methods, both in terms of patterns and range (Figure 7.4). Significant differences were found only for TFJ ab/adduction, with $\Delta L_{\text{min,MBO}}$ providing a more abducted tibia with respect to $\Delta L_{0,\text{implicit}}$ from 51° to 54° of TFJ flexion angle. Compared with MRI-measured passive TFJ kinematics, both methods provided feasible kinematics during gait (Figure 7.5).
Figure 7.4. Comparison between the average TFJ kinematics during gait obtained from $\Delta L_{\text{min,MBO}}$ (blue) and $\Delta L_{0,\text{implicit}}$ (red). Curves represent the average ± standard deviation across the eight participants. Significant differences between the two methods were found at 51°-54° of TFJ flexion angle for TFJ adduction/abduction.

Figure 7.5. Comparison between the average TFJ kinematics during gait obtained from $\Delta L_{\text{min,MBO}}$ (blue) and $\Delta L_{0,\text{implicit}}$ (red). Curves represent the average ± standard deviation across the eight participants and they are compared against MRI-measured passive kinematic data (black dots).

As expected, no change in ligament length was observed with $\Delta L_{0,\text{implicit}}$, while a noticeable LCL shortening during the swing phase could be identified (Figure 7.6).
When using $\Delta L_{\text{min,MBO}}$, the ACL and the LCL exhibited average elongation and compression, respectively, during the swing phase (Figure 7.6). Average ligament strains during gait were also similar between the two methods, with significant differences found only for the ACL and the PCL at 52°-55° and 48°-52° of TFJ flexion, respectively. Moreover, compared with MRI-measured passive ligament strains, both methods provided feasible results (Figure 7.7).

**Figure 7.6.** Comparison between the average ligament strain during gait obtained from $\Delta L_{\text{min,MBO}}$ (blue) and $\Delta L_{0,\text{explicit}}$ (red). Curves represent the average ± standard deviation across the eight participants. Significant differences between the two methods were found for the ACL and PCL strains. It has to be noted that, even if the LCL was not included in the implementation of $\Delta L_{0,\text{explicit}}$, its length variation across the gait cycle was computed as the Euclidean distance between the centroids of the LCL attachment regions from the MRI reference pose at $\sim0°$ of TFJ flexion.
Subject-specific knee kinematic models with deformable ligaments in OpenSim

Figure 7.7. Comparison between the average ligament strain during gait obtained from $\Delta L_{\text{min,MBO}}$ (blue) and $\Delta L_{0,\text{implicit}}$ (red). Curves represent the average ± standard deviation across the eight participants and they are compared against MRI-measured passive ligament strain (black dots).

On average, when using $\Delta L_{\text{min,MBO}}$ the length of the ACL slightly increased as the TFJ flexion angle increased during both the stance and swing phases of gait (Figure 7.8). Contrarily, the average length of the LCL decreased as the knee flexion increased, both in $\Delta L_{\text{min,MBO}}$ and $\Delta L_{0,\text{implicit}}$. Differently from $\Delta L_{0,\text{implicit}}$, the average ligament strain curves obtained for $\Delta L_{\text{min,MBO}}$ showed different strain values at similar TFJ flexion angles (Figure 7.8).
Subject-specific knee kinematic models with deformable ligaments in OpenSim

![Figure 7.8](image.png)

**Figure 7.8.** Averaged ligament strain curves across the eight participants, as function of the TFJ flexion angle, obtained from $\Delta L_{\text{min,MBO}}$ (blue) and $\Delta L_{\text{0,implicit}}$ (red). $\Delta L_{\text{min,MBO}}$ provided different strain values, depending on whether the limb is under stance (navy blue) or swing (light blue) phase at similar TFJ flexion angles.

### 7.4 Discussion

In this study we developed subject-specific rigid-body lower limb models including fully personalised TFJ kinematic models based on parallel mechanisms. The TFJ mechanism featured rigid articular contacts and four minimally deformable ligaments (i.e., ACL, PCL, MCL and LCL), the geometry of which was measured off the MRI and then optimised to minimise Equations 6.1-6.3. The developed models were used to assess the TFJ and ligament kinematics during gait of eight healthy children and adolescents with a multibody optimisation approach tracking experimental markers and minimising ligament elongations ($\Delta L_{\text{min,MBO}}$). For comparison purposes, TFJ and ligament kinematics during gait were also computed employing 5-rigid-link parallel mechanisms with three isometric ligaments and an inverse kinematics approach that just tracked experimental markers ($\Delta L_{\text{0,implicit}}$). The two models (i.e., $\Delta L_{\text{min,MBO}}$ and $\Delta L_{\text{0,implicit}}$) provided similar knee and ligament kinematics, with significant differences found only
in small ranges of the knee flexion range of motion for TFJ ab/adduction, ACL and PCL strains.

The adopted TFJ parallel mechanism was presented and validated in previous studies (Chapter 6) (Brito da Luz et al., 2017). The addition of deformable ligaments to parallel mechanism TFJ models for multibody optimisation was also previously introduced (Clément et al., 2015; Gasparutto et al., 2012; Sancisi et al., 2017) and validated (Gasparutto et al., 2015). However, a similar approach has never been implemented in OpenSim before. The present study presents a simple and fast multibody optimisation approach that expands the functionality of the least squares multibody optimisation tool available in OpenSim.

Relative weight definition for markers and ligaments is one of the main challenges of the multibody optimisation approach ($\Delta L_{\text{min,MBO}}$). Previous studies (Gasparutto et al., 2012; Gasparutto et al., 2015; Sancisi et al., 2017) defined the weights for each ligament (Table 7.3) consistently with the maximum lengthening found in the literature in the TFJ flexion range of motion during gait (i.e., 0°-60° of TFJ flexion) (Bergamini et al., 2011; Hsich et al., 1997; Rovick et al., 1991) and assigned a weight of 1 to all the markers. In this study a weight of 1 was also assigned to all markers but, contrarily to previous studies, subject-specific ligament weights were defined, based on each ligament’s length and cross-sectional area measured from MRI. The relative magnitude of the average ligament stiffness factors (i.e., CSA/ligament length) across the eight participants was in agreement with literature (Bergamini et al., 2011; Hsich et al., 1997; Rovick et al., 1991), with highest stiffness found for the PCL and lowest stiffness found for the LCL.

**Table 7.3. Ligament weights defined in previous studies (Gasparutto et al., 2012; Gasparutto et al., 2015; Sancisi et al., 2017) for the penalty-based method.**

<table>
<thead>
<tr>
<th>Weight</th>
<th>ACL</th>
<th>PCL</th>
<th>MCL</th>
<th>LCL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1000</td>
<td>10000</td>
<td>10</td>
<td>1</td>
</tr>
</tbody>
</table>

For the first time, this study reported metrics of marker errors in a multibody optimisation approach that computes kinematics while minimising ligament elongation. According to the OpenSim best practices (Hicks et al., 2015), mean marker errors were acceptable both for $\Delta L_{\text{min,MBO}}$ and $\Delta L_{\text{0,implicit}}$, and the maximum marker errors were generally below the recommended threshold of 4cm. The presence of few maximum marker errors > 4cm in $\Delta L_{\text{min,MBO}}$ can derive from the incorporation of the TFJ mechanism.
Contrarily to our hypothesis, joint kinematics pattern and magnitude were similar between the two models, with only few noticeable differences. Contrarily to $\Delta L_{0, \text{implicit}}$, when using $\Delta L_{\text{min,MBO}}$, participants exhibited an average adducted tibia during the swing phase of gait. Moreover, $\Delta L_{\text{min,MBO}}$ presented a reduced variability in TFJ external rotation compared to $\Delta L_{0, \text{implicit}}$. Based on the comparison with passive MRI-measure kinematic data, the resulting TFJ kinematics were feasible and the ranges of motion were in agreement with bone-pin marker data during gait (Benoit et al., 2006). However, differently from healthy adult participants (Sancisi et al., 2017), the gait of all the children and adolescents involved in this study was characterised by an externally rotated tibia, in agreement with Leardini et al. (2007). The external rotation of the tibia with respect to the femur during gait might depend on the TFJ mechanism, which is solved by using the geometry of the knee in the MRI-reference pose. It has been shown (Section 6.5) that, when compared to published adult cadaveric data, paediatric participants exhibited a more externally rotated tibia during passive knee flexion, which might be a consequence of knee laxity in children (Baxter, 1988; Flynn et al., 2000; Hinton et al., 2008) in passive supine position (i.e., during MRI acquisition).

Ligament strain values were also similar between the two models, with only significant differences found for the ACL and PCL. When compared to passive MRI-measured ligament strain data, the resulting ligament strain values were reasonable. Moreover, the ranges of ACL and MCL elongation during gait obtained with $\Delta L_{\text{min,MBO}}$ were comparable to those computed in previous studies (Liu et al., 2011; Wu et al., 2010). The average ligament strain patterns obtained from $\Delta L_{\text{min,MBO}}$ were similar to those obtained by Sancisi et al. (2017) when minimising ligament length variations in a multibody optimisation approach. Contrastingly to in vivo measurements of ACL length and relative strain during gait (Taylor et al., 2013), the average ACL strain curve obtained with $\Delta L_{\text{min,MBO}}$ revealed ACL elongation during the swing phase of gait (Figure 7.6), rather than shortening. However, the large variation of the ACL strain during the swing phase highlights the presence of both elongation and shortening patterns. Interestingly, the LCL exhibited a considerable shortening during the swing phase of gait when using $\Delta L_{0, \text{implicit}}$, necessary to maintain the other three ligaments isometric.

The developed method based on multibody optimisation approach allowed some model adaptation to different loading condition (Figure 7.8), corresponding to different phases of the gait cycle. This model adaptation was prevented when employing the model with isometric ligaments. Moreover, the proposed subject-specific rigid-body models,
Despite requiring initial tuning, are a good compromise between simplistic non-
physiological joint kinematic models and complex and computationally expensive
deformable models (e.g., finite element or elastic foundation models).

The personalised TFJ and PFJ kinematic models developed in this study can also
be used as a platform for forward dynamics simulations, where external (i.e., ground
reaction forces) and/or muscle forces produce motion. OpenSim offers multiple tools to
generate forward dynamics simulations of human motion, for example the residual
reduction algorithm (RRA). This tool permits the kinematics of the model, obtained from
the inverse kinematics analysis, to vary to be more consistent with the ground reaction
forces collected during walking. Another example of forward dynamics simulation
available in OpenSim is the concurrent optimization of muscle activations and kinematics
(COMAK) tool (Lenhart et al., 2015; Smith et al., 2016a). After incorporating the muscles
into the developed lower-limb models, the COMAK simulation tool can be used to
simultaneously optimize muscle activations and secondary TFJ and PFJ kinematics. This
simulation approach satisfies both whole-body and joint-level movement dynamics, while
minimizing a weighted squared muscle activation objective function. The multibody TFJ
and PFJ models proposed in this study, with bodies connected by 6 degree of freedom
joint and constrained by ligaments and articular contact, represent unique model
configurations that, when incorporated into the COMAK workflow, would be able to
provide load-dependent secondary TFJ and PFJ kinematics. Knowing the effect of ground
reaction forces and muscle loading on the underlying TFJ and PFJ kinematics can be
extremely instructive in the assessment of patellar dislocation during dynamic tasks.

The proposed lower limb kinematic models have some limitations. First, the same
weight was assigned to each marker, therefore no differentiation was made between
different marker locations. Second, the accuracy of the segmentation might affect the
computation of the ligament stiffness factors. Third, no direct way of validating the TFJ
and ligament kinematic results from the two models was available. In fact, radiation
exposure (Clément et al., 2015; Lu et al., 2008; Marra et al., 2015) or invasive procedures
(Benoit et al., 2006; Bonci et al., 2014; Reinschmidt et al., 1997) used to measure in vivo
knee kinematics, limit the use of these validation methods in paediatric populations.

7.4.1 Future work

As previously mentioned, one of the main challenges of the multibody
optimisation approach \(\Delta L_{\text{min,MO}}\) consists in the definition of the relative weights for
markers and ligaments. To provide more realistic estimations of knee and ligament
kinematics during gait, future work will focus on the development of an optimisation
algorithm that will optimise both marker and coordinate weights to minimise ligament length elongation. Preliminary work has been done to optimise only the weight assigned to the four coordinates (i.e., ligament elongations), in order to minimise the mean of the four ligaments’ elongation ranges. To this end, a bound constraint optimisation was implemented in Matlab, using the *fminsearchbnd* function, and applied to the $\Delta L_{min,MBO}$ models of the eight TD participants involved in this study. Consequently, the weight of each ligament could vary between an upper and a lower bounds, which were defined as the average MRI-based ligament stiffness factors across the eight TD participants, plus or minus its standard deviation, respectively (Table 7.2). However, when using the optimised coordinate weights in $\Delta L_{min,MBO}$, no significant differences were found in TFJ and ligament kinematics compared to the approach described in this chapter, which used individualised MRI-based stiffness factors. These preliminary results suggested that, to potentially improve the estimation of knee and ligament kinematics, not only the optimisation of the marker weights is required, but also the optimisation of the marker weights.

Moreover, we plan to perform a sensitivity analysis to evaluate how the TFJ kinematics and ligament elongation are affected by the ligament weights used in $\Delta L_{min,MBO}$. By assessing the sensitivity of $\Delta L_{min,MBO}$ to the ligament weight variation, we could determine which TFJ motion components are more sensitive to the ligament weight definition, as previously described (Sancisi et al., 2017).

Future work will also focus on the implementation of a 6-link TFJ mechanism with prescribed ligament length variation in OpenSim (Section 6.3). In study 3 (Chapter 6), comparable knee and ligament kinematics were found using a passive 5-rigid-link TFJ parallel mechanism and a 6-link TFJ mechanism with prescribed ligament length variation (Section 6.4). Therefore, we plan to use the 6-link TFJ mechanism with prescribed ligament length variation in a multibody optimisation approach in OpenSim to estimate knee and ligament kinematics during gait. Preliminary work has been done to implement the 6-link TFJ mechanism with prescribed ligament length variation in OpenSim for the same eight participants, using the same approach used for the 5-rigid-link mechanism. However, the mechanism could not be correctly built in three participants out of eight, suggesting that the mechanism parameters obtained in Matlab do not implement a parallel mechanism that can be assembled within the accuracy required by the Simbody engine. Future work is then required to enhance the approach of parameter optimisation used to build models employing the 6-link TFJ mechanism with prescribed ligament length variation.
Once the implementation of the models is robust and the weights of the markers and coordinates are optimised, we plan to extend this approach to the analysis of gait of pathological populations, such as children and adolescents with recurrent patellar dislocation.

Finally, future research could also investigate the use of vertical open-bore MRI scanners to track the movement of the TFJ under loading conditions across the TFJ flexion range of motion (Macri et al., 2018), which would allow model validation.

7.5 Conclusion

Three-dimensional subject-specific TFJ kinematic models, with individualised bone geometry and ligaments, are promising tools to investigate the gait biomechanics of healthy children and future studies will extend their use to analyses of pathological gait.
CHAPTER 8

Development and validation of subject-specific patellofemoral joint kinematic models for children and adolescents with recurrent patellar dislocation

This chapter describes four different modelling approaches used to estimate passive PFJ kinematics in children and adolescents with recurrent patellar dislocation. Each approach represents a step towards a more accurate representation of the PFJ kinematics in this patient population. The estimated kinematics from the last modelling approach will be compared against in vivo PFJ kinematics measured from MRIs collected at four knee flexion angles. The manuscript describing the results from the last approach will be submitted as Barzan, M., Maine, S., Brito da Luz, S., Modenese, L., Stockton, C.A., Conconi, M., Sancisi, N., Lloyd, D.G., & Carty, C.P. Development and validation of subject-specific patellofemoral joint kinematic models for children and adolescents with recurrent patellar dislocation. Journal of Orthopaedic Research.

8.1 Introduction

Patellar dislocation is a common and disabling injury in the paediatric population. The risk of first-time dislocation is particularly high in female patients aged ten to 17 years, with a reported annual incidence of 30-108 per 100000 individuals (Fithian et al., 2004; Gravesen et al., 2017). First time patellar dislocation commonly leads to recurrent instability, with the redislocation rate in patients younger than 18 years of age reported as high as 71% following non-operative treatment (Jaquith et al., 2017; Lewallen et al., 2013b; Palmu et al., 2008) and 67% following medial patellofemoral ligament reconstruction (Palmu et al., 2008). Poor long-term outcomes of current treatments
Subject-specific patellofemoral joint kinematic models for recurrent patellar dislocators

highlight the necessity for a better understanding of the patellar dislocation injury mechanism.

Different clinical tests and radiographical measurements have been used to describe patellar kinematics in the assessment of patellar instability. The *J*-sign is a common diagnostic test used to identify patellar maltracking (Post, 1999), i.e. the deviation of the patella from the trajectory of the trochlear groove. A positive *J*-sign describes an exaggerated lateral to medial translation of the patella into the trochlear groove in early tibiofemoral joint (TFJ) passive flexion. However, grading of a positive *J*-sign is subjective, its examination lacks inter-observer accuracy (Smith et al., 2012) and merely focuses on the lateral patellar translation, without considering any lateral patellar tilt. Common radiographical measurements of patellar maltracking include patellar tilt, bisect offset ratio and lateral patellar displacement (Pal et al., 2013; Ward et al., 2007b). While these two-dimensional radiographical measurements can quantify abnormal patellar position, they generally refer to one single static position and, therefore, they are unable to describe the patellar dislocation injury mechanism during dynamic tasks.

Recently, some authors have attempted to describe patellar tracking by measuring patellofemoral kinematic parameters at different TFJ flexion angles. Bisect offset ratio and lateral patellar displacement were calculated at different TFJ flexion angles in adult (Elias et al., 2016; Tanaka et al., 2016) and paediatric (Biyani et al., 2014; Regalado et al., 2014) patients with patellar instability, using three-dimensional knee bone reconstructions from dynamic computed tomography (CT) and magnetic resonance imaging (MRI), respectively. Regalado et al. (2014) performed the same measurements also in an age-matched healthy cohort and found that patients with dislocation had higher bisect offset ratio, a more lateralisated patella and a lower patellar tilt angle than controls, especially close to full TFJ extension. However, despite providing objective measurements of patellar maltracking at multiple TFJ flexion angles, these studies did not fully characterise the motion of the patella relative to the femur throughout the entire TFJ flexion range of motion.

Therefore, the first aim of this study was to use MRIs to generate patellofemoral (PFJ) models to estimate three dimensional passive PFJ kinematics in children and adolescents with recurrent patellar dislocation (RPD) and typically developing (TD) age-matched controls. While a single PFJ hinge model was developed for TD participants, four sequential modelling approaches (*A*<sub>1</sub>, *A*<sub>2</sub>, *A*<sub>3</sub> and *A*<sub>4</sub>), with varying complexity (i.e., have different number of joints, geometrical parameters and optimisation constraints), were implemented for RPD patients. The second aim was to validate the kinematic results
Subject-specific patellofemoral joint kinematic models for recurrent patellar dislocators

from the models implemented for recurrent patellar dislocators against PFJ kinematics measured from MRIs collected at four different TFJ flexion angles. Finally, the third aim was to compare the estimated PFJ kinematics between RPD patients and TD participants. It was hypothesised that, compared to the first modelling approach where the PFJ was modelled as a single hinge joint, the three modelling approaches with increased complexity, obtained by adding a second hinge joint and different optimisation constraints, would provide better estimates of MRI-measured PFJ kinematics across the four knee flexion angles. Moreover, it was hypothesised that, compared to TD participants, RPD patients would exhibit a more externally rotated and lateralised patella, especially between 0° and 30° of TFJ flexion.

8.2 Methods

8.2.1 Participants

Four RPD patients and eight TD children and adolescents were recruited (Table 8.1). RPD patients were offered enrolment following outpatient orthopaedic consultations at the Lady Cilento Children’s Hospital (LCCH) (Brisbane, Australia). Patients were considered eligible for the study if they were between six and 18 years old and experienced multiple (two or more) dislocations of minimal energy. Patients were excluded if they experienced congenital patellar dislocations. All the RPD patients recruited for this study experienced recurrent dislocations on their left knee. TD participants, free from musculoskeletal or neurological impairment or lower limb injury within the prior six months, were recruited from the local community. Additional exclusion criteria for both groups included congenital limb abnormalities, previous surgical intervention affecting the anatomy of the knee or extensor mechanism, any past medical history of bony or soft tissue trauma or infection that may have affected bony or soft tissue anatomy, and inability to tolerate or deemed unsafe for MRI. Ethics approval was obtained from the Children’s Health Queensland Hospital and Health Services human research ethics committee (HREC/13/QRCH/197) and the Griffith University human research ethics committee (AHS/42/14/HREC), and participants’ guardians provided their written informed consent.

Table 8.1. Participants’ characteristics. Age, mass and height are expressed as average and standard deviation.

<table>
<thead>
<tr>
<th></th>
<th>RPD (n=4)</th>
<th>TD (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/female)</td>
<td>2/2</td>
<td>4/4</td>
</tr>
<tr>
<td>Age (years)</td>
<td>13.0 [2.5]</td>
<td>14.0 [2.6]</td>
</tr>
<tr>
<td>Height [m]</td>
<td>1.6 [0.1]</td>
<td>1.6 [0.1]</td>
</tr>
</tbody>
</table>
8.2.2 Medical image acquisition and processing

Two sets of MRIs were collected at the LCCH from each participant. First, an MRI scan (1.5T, SIEMENS MAGNETOM Avanto_fit syngo MR VE11B, Germany) of both lower limbs (3D PD SPACE, slice thickness: 1.0 mm, voxel size: 0.83 x 0.83 x 1.0 mm³) was performed with the participant in a supine position. Second, a regional MRI scan (3T, SIEMENS MAGNETOM Skyra, Germany) of the participant’s knee (left knee for RPD patients, right knee for TD participants) (3D SPC T2, slice thickness: 0.53 mm, voxel size: 0.53 x 0.53 x 0.53 mm³) was performed with the knee close to 0° TFJ flexion using a dedicated knee coil. This position will be called MRI reference pose. Moreover, for each RPD patient, three additional dedicated left knee scans were acquired at approximately 10°, 20° and 30° of tibiofemoral joint (TFJ) flexion by using a flexible array coil wrapped around the knee.

Three-dimensional lower limb bones, knee ligaments and cartilages were segmented in Mimics Research 20.0 (Materialise, Belgium). Segmented bones included the femur, patella, tibia and fibula, while ligaments included the anterior cruciate (ACL), posterior cruciate (PCL), medial collateral (MCL) and lateral collateral (LCL) ligaments and patellar tendon. Femoral, tibial and patellar cartilages were also segmented. Three-dimensional full-length bones were registered onto the three-dimensional knee reconstructions at approximately 0° TFJ flexion through an iterative closest point algorithm (Besl et al., 1992) in 3-matic (Materialise, Belgium) to obtain a comprehensive three-dimensional reconstruction of each participant’s anatomy. Furthermore, for each RPD patient, full-length bones were also registered onto the additional left knee reconstructions at each considered TFJ flexion angle.

8.2.3 Subject-specific TFJ and PFJ kinematic models

Three segment coordinate systems (SCSs) were defined for the femur, patella and tibia using anatomical landmarks manually located on the bone segmented meshes to obtain the relative pose of the bones (Belvedere et al., 2007; Cappozzo et al., 1995b).

8.2.3.1 TFJ kinematic model for TD and RPD participants

For all the participants, the TFJ was modelled as a 6-link parallel mechanism, including two sphere-on-sphere contacts (representing the medial and lateral contacts between the femoral condyles and the tibial plateaus) and four ligaments (ACL, PCL, MCL and LCL). The geometry of the contact surfaces (i.e., sphere centres and radii) was obtained from MRI by approximating the femoral condyles and tibial plateaus by best-
fitting spheres (Matlab R2014b, MathWorks). The geometry of the ligaments (i.e., ligament lengths, attachment points) was derived from the MRI close to 0° TFJ flexion by computing the centroids of the segmented ligament attachment regions on the corresponding bones. In this TFJ model, while the two articular contacts were considered rigid, the ACL, PCL, MCL and LCL length changes tracked the pattern of published experimental ligament length changes (Belvedere et al., 2012; Bergamini et al., 2011; Blankevoort et al., 1991) over the TFJ flexion range of motion (section 6.3.3 and 6.3.4).

After each subject-specific TFJ was created, each participant’s MRI-measured parameters (i.e., sphere centres and ligament attachment points) were optimised to solve the closure equations of the TFJ mechanism (section 6.3.4).

8.2.3.2 PFJ kinematic model for TD participants

For TD participants, the PFJ was modelled as a hinge joint, where the patella was constrained to rotate about and at a constant distance from an axis while maintaining constant patellar tendon length (Sancisi et al., 2011a). The axis of rotation was defined by the centre of two spheres fitted to the medial and lateral patellofemoral articular surfaces (Brito da Luz et al., 2017). For each participant, the geometry of the PFJ contact surfaces and the attachment regions of the patellar tendon were manually identified on the comprehensive three-dimensional representation of the participant’s leg. Subsequently, the PFJ articulating surfaces were approximated by best fitting spheres in custom Matlab scripts and the geometry of the patellar tendon (i.e., attachment points and length) was defined with the same procedure used for the other TFJ ligaments.

The model’s geometrical parameters were then optimised to ensure that the PFJ mechanism could be solved. The optimisation algorithm included an outer loop, that optimised each participant’s MRI-measured geometrical parameters (i.e., sphere centres and patellar tendon attachment points), and an inner loop, that solved the PFJ mechanism. In the outer loop, the three-dimensional coordinates of the sphere centres could deviate up to 5 mm from their initial MRI-measured position. The radii of these spheres were also updated by minimising the summed least square residuals between fitted spheres and MRI-segmented cartilages, while ensuring that the residuals were <5% of the optimised radii. Finally, the optimised attachment points of the patellar tendon were maintained within their respective bone attachment regions.

The outer loop minimised for two objective functions (Eq. 8.1-8.2), where the first best matched the pattern, i.e. correlation \( \rho_i \), between estimated and published experimental \( i \)-th motion component of PFJ kinematics (Anglin et al., 2008; Sancisi et
Subject-specific patellofemoral joint kinematic models for recurrent patellar dislocators

al., 2011b), while the second minimised the difference between MRI-measured \( g_{m,k} \) and optimised \( g_{o,k} \) k-th geometrical parameter (i.e., sphere centres and patellar tendon attachment points).

\[
J_1 = (1 - \rho_i)^2 \quad i = 1, \ldots, 6 \quad (8.1)
\]
\[
J_2 = (g_{m,k} - g_{o,k})^2 \quad k = 1, \ldots, 12 \quad (8.2)
\]

A Multiple Objective Particle Swarm Optimisation (MOPSO) algorithm was used in Matlab to optimise the geometrical parameters to minimise the two objective functions in the outer loop. Within the multiple MOPSO solutions, the solution that achieved the best match between the patterns of the estimated and published experimental PFJ kinematics (i.e., solution with minimum \( J_1 \)) was chosen, given that the geometrical parameters were always within the limits of reasonable anatomical variability (i.e., the tree-dimensional coordinates of the spheres could only deviate up to 5 mm from their initial position).

Subsequently, the inner loop used the optimised geometrical parameters to solve the closure equations of the PFJ mechanisms for 1° increments of the TFJ flexion angle while ensuring that the estimated kinematic curves were continuous.

### 8.2.3.3 PFJ kinematic models for RPD patients

The previously described modelling approach have been validated for TD participants (section 6.4 ), although, it is unclear if it can accurately replicate the PFJ kinematics in RPD patients, where the patella exhibited an exaggerated lateral to medial translation into the trochlear groove during early stages of passive TFJ flexion (approximately between 0°-30°) (Figure 8.1).

![Figure 8.1](image-url)

*Figure 8.1. Axial left knee MRIs of a RPD patient at approximately 0° (a), 10° (b), 20° (c) and 30° (d) of TFJ flexion. The patella translates medially (M) into the trochlear groove as the knee flexes from a lateral (L) position at extended knee posture (from a to d).*
Therefore, four different sequential approaches ($A_1$, $A_2$, $A_3$ and $A_4$) were implemented to model the PFJ in RPD patients. The first approach ($A_1$) consisted of the same hinge mechanism used for TD participants, where the axis of rotation of the patella was defined by the centre of two spheres fitted to the medial and lateral patellofemoral articular surfaces (section 8.1.3.1). The following approaches ($A_2$, $A_3$ and $A_4$) consisted of a combination of two separate PFJ hinge mechanisms, which had different axes of rotation. Specifically, the first hinge mechanism described the lateral to medial translation of the patella into the trochlear groove between $0^\circ$ and approximately $30^\circ$ of TFJ flexion, while the second described the motion of the patella after it reached a more congruent position into the trochlear groove and until $90^\circ$ of TFJ flexion. To derive the axis of rotation of the first mechanism, the reconstructed volume of the patella from the knee scan at $\sim 30^\circ$ of TFJ flexion was registered onto the three-dimensional reconstruction of the knee at $\sim 0^\circ$ TFJ flexion. This way, the amount of lateral to medial translation of the patella during the first $\sim 30^\circ$ of TFJ flexion could be visualised. For the first PFJ mechanism, a surface connecting the two poses of the patella (i.e., at $0^\circ$ and $30^\circ$ of TFJ flexion) was manually delineated on the reconstructed femoral cartilage, as an approximation of the region where the patella was likely to articulate between $0^\circ$ and $30^\circ$ of TFJ flexion. A cylinder was best fitted in 3-matic to this articulating surface and its axis was then used to define the hinge axis of rotation of the first PFJ mechanism. For the second PFJ mechanism, the articulating surfaces were defined as implemented for TD participants. In both PFJ mechanisms, the patellar tendon was considered isometric over the TFJ flexion range of motion.

The differences between the three PFJ modelling approaches ($A_2$, $A_3$ and $A_4$) were the patella poses used as initial guesses and the objective functions minimised in the outer loop. Specifically, $A_2$ used the poses of the patella in the reference MRI pose and at $\sim 30^\circ$ of TFJ flexion as initial guesses for the first and second mechanisms, respectively. Contrastingly, $A_3$ and $A_4$ used the pose of the patella at $\sim 30^\circ$ of TFJ flexion as initial guess for both the first and the second mechanisms (Figure 8.2). Regarding outer loop objective functions, $A_2$ and $A_3$ only minimised the difference between MRI-measured and optimised geometrical parameters (Eq. 8.2), while the correlation between estimated and published experimental PFJ kinematics (Eq. 8.1) was not considered, given the abnormal patellar tracking in this patient group. On the other hand, $A_4$ minimised i) the mean difference between mechanism-estimated ($T_{me}$) and MRI-measured medio/lateral translation ($T_{ml}$) at approximately $0^\circ$ and $30^\circ$ of TFJ flexion (Eq. 8.3) and ii) the mean range of the second order derivatives ($D^2$) of the PFJ kinematic curves ($f_j$) (Eq. 8.4). These functions were
chosen to approximate the lateral to medial translation of the patella between 0° and 30° of TFJ flexion, while ensuring continuous and smooth kinematics. Within the multiple MOPSO solutions obtained from $A_4$, the solution that provided minimum $J_3$ was chosen, as it suggested better tracking of the MRI-registered medio/lateral patellar translation while ensuring continuous PFJ kinematics.

\[
J_3 = \text{mean}(\sqrt{(T_{le} - T_{im})^2}) \quad i = \sim 0^\circ \text{ and } 30^\circ \text{ of TFJ flexion} \quad (8.3)
\]

\[
J_4 = \text{mean}[\text{max} \ (D^2(f_j) - \text{min} \ (D^2(f_j)))] \quad j = 1, \ldots, 6 \quad (8.4)
\]

\[N_i = abcd(e^V, f^V)\]

\[V_i = \sim 0^\circ \text{ and } 30^\circ \text{ of TFJ flexion}\] (8.3)

\[N_u = abcd(acw)\]

\[V_x = y^V, azd(V_x)\]

\[j = 1, \ldots, 6\] (8.4)

**Figure 8.2.** Description of the four modelling approaches ($A_1, A_2, A_3$ and $A_4$) implemented to estimate the PFJ kinematics in RPD patients. $A_1$ used a single hinge mechanism, where the axis of rotation (black dotted line) was defined as the vector connecting the centre of the spheres (blue) fitted to the medial and lateral patellofemoral articulating surfaces in the trochlea (aqua). The initial pose of the patella was computed from the MRI reference pose (purple). Contrastingly, $A_2$, $A_3$ and $A_4$ used two hinge mechanisms: the first axis of rotation (black dotted line) was the axis of the cylinder fitted to the region (orange) where the patella was likely to articulate between 0° and 30° of TFJ flexion, while the second axis of rotation (black dotted line) was defined as for $A_1$. In $A_2$ the initial pose of the patella for the first mechanism was derived from the MRI reference pose at $\sim 0^\circ$ of TFJ flexion (purple), while the initial pose for the second mechanism was the pose of the patella at $\sim 30^\circ$ of TFJ flexion (dark green). $A_3$ and $A_4$ used the same initial pose of the patella at $\sim 30^\circ$ of TFJ flexion (dark green) for both mechanisms.
In $A_2$ and $A_3$ the two PFJ mechanisms were solved independently, in the *inner* and *outer* loops, and then combined into a single solution. This comprised the results from the *first* PFJ mechanism from 0° to 30° of TFJ flexion and the results from the second PFJ mechanism from 30° to 90° of TFJ flexion. The two solutions were merged by using cubic splines in Matlab. The cut-off of 30° was chosen because 0°-30° of TFJ flexion is believed to be the range at which patellar dislocation occurs clinically (Burks et al., 1998; Desio et al., 1998; Hautamaa et al., 1998), due to a lack of congruence between the articulating surfaces of the femur and of the patella. In contrast, in $A_4$ the two PFJ mechanisms were solved sequentially in the same algorithm.

### 8.2.4 Data analysis and statistics

Within the four modelling approaches previously described, the approach that provided the best match with MRI-registered medio/lateral position of the patella and also continuous PFJ kinematic curves was chosen to model the PFJ in RPD patients. For the four RPD patients, the Root-Mean-Square Errors (RMSEs) between each patient’s predicted and MRI-measured PFJ kinematics were computed and averaged across the four TFJ flexion angles. Ninety-five percent confidence intervals (CI) were also computed. Furthermore, Statistical Parametric Mapping (SPM) was used to determine if there were significant differences between the kinematic curves of RPD patients and TD participants at any TFJ flexion angle (Pataky et al., 2013).

### 8.3 Results

One single PFJ hinge model and four different PFJ hinge models were produced and optimised for each TD participant and RPD patient, respectively. The four approaches implemented for RPD patients ($A_1$, $A_2$, $A_3$ and $A_4$) led to gradual improvements in the estimation of MRI-registered data and continuity of the PFJ kinematic curves (Figure 8.3 and videos at: [https://www.youtube.com/channel/UCRalXpnctnTEyYwkyMPILaLw/playlists](https://www.youtube.com/channel/UCRalXpnctnTEyYwkyMPILaLw/playlists)). Specifically, $A_1$ provided continuous and smooth kinematic curves but kept the patella in a lateral position with respect to the femur (Video 8.1) throughout the TFJ flexion range of motion. Contrastingly, $A_2$ was able to estimate the lateral to medial translation of the patella between 0° and 30° of TFJ flexion but provided discontinuous kinematic curves (Video 8.2). In contrast, $A_3$ provided continuous kinematic curves while estimating the lateral to medial translation of the patella from 0° to 30° of TFJ flexion and also the patella motion in the trochlear groove from 30° to 90° of TFJ flexion. However, the amount of lateral to medial translation of the patella in the first 30° of TFJ flexion was low compared to MRI-registered data (Video 8.3). Finally, $A_4$ well estimated the lateral to medial
translation of the patella from 0° to 30° of TFJ flexion, as well as the patella motion in the trochlear groove from 30 to 90° of TFJ flexion, while providing continuous PFJ kinematics (Video 8.4). Therefore, A4 was chosen as the best approach to model the PFJ in RPD patients.

**Figure 8.3.** Comparison of PFJ kinematics obtained from the four approaches (A1, A2, A3 and A4) as function of the TFJ flexion angle for one RPD patient (RPD1). Gradual improvements in the estimation of MRI-registered data and continuity of the PFJ kinematic curves were obtained from A1 (light green) to A4 (navy blue).

Consequently, the PFJ kinematics for each of the four RPD patients were estimated using A4 and compared against their respective MRI-registered data (Figure 8.4, Figure 8.5, Figure 8.6, Figure 8.7). From the MRI-registered data it can be noted that, while for three RPD patients (RPD1, RPD2 and RPD3) the patella exhibited a lateral to medial translation in the first 30° of TFJ flexion (J-sign pattern), RPD4 had increased lateral translation of the patella in TFJ flexion (Figure 8.7). Overall, for the four RPD patients, A4 provided continuous curves and well approximated the MRI-registered data.
Subject-specific patellofemoral joint kinematic models for recurrent patellar dislocators

Figure 8.4. Comparison between $A_4$-estimated (blue) and MRI-registered (black dots) PFJ kinematics, as function of the TFJ flexion angle, for one RPD patient (RPD_1).

Figure 8.5. Comparison between $A_4$-estimated (blue) and MRI-registered (black dots) PFJ kinematics, as function of the TFJ flexion angle, for one RPD patient (RPD_2).
Figure 8.6. Comparison between $A_t$-estimated (blue) and MRI-registered (black dots) PFJ kinematics, as function of the TFJ flexion angle, for one RPD patient (RPD$_3$).

Figure 8.7. Comparison between $A_t$-estimated (blue) and MRI-registered (black dots) PFJ kinematics, as function of the TFJ flexion angle, for one RPD patient (RPD$_4$).

Average RMSEs between $A_t$-estimated and MRI-measured PFJ kinematics were below 7.7° and 4.7 mm for PFJ rotations and translations, respectively (Figure 8.8). Moreover, no significant RMSE differences between $A_t$-estimated and MRI-measured patellar ab/adduction and internal/external rotation were found.
**Subject-specific patellofemoral joint kinematic models for recurrent patellar dislocators**

**Figure 8.8.** Average RMSEs and 95% CI for each motion component of the PFJ kinematics for RPD patients.

Compared to TD participants, RPD patients exhibited larger variability in PFJ kinematics (Figure 8.9). Generally, RPD patients exhibited a more extended, externally rotated and lateraled patella with respect to TD participants throughout the TFJ range of motion. Moreover, significant differences in these three motion components between the two population groups were found at early stages of TFJ flexion (0°-20° for extension/flexion, 0°-28° for internal/external rotation and 0°-26° for medio/lateral displacement) (Figure 8.9).

**Figure 8.9.** Comparison of the average PFJ kinematics, as function of the TFJ flexion angle, between RPD patients (blue) and TD participants (grey). Curves represent the average ± standard deviation across the eight TD participants and four RPD patients. Significant differences between the two groups were found for PFJ extension/flexion, external/internal rotation and medio/lateral translation.
Subject-specific patellofemoral joint kinematic models for recurrent patellar dislocators

8.4 Discussion

For the first time we developed subject-specific paediatric PFJ mechanisms from MRIs to estimate passive three-dimensional PFJ kinematics in RPD patients and TD controls. Four different approaches ($A_1$, $A_2$, $A_3$ and $A_4$) were implemented for RPD patients and the kinematics obtained from the last approach ($A_4$) were validated against in vivo kinematics obtained from MRIs at four different TFJ flexion angles. The estimated PFJ kinematics were similar to those measured from MRIs, with generally low RMSEs. Moreover, we compared the estimated PFJ kinematics between RPD patients and TD participants. Compared to TD participants, RPD patients exhibited a more extended, externally rotated and lateralled patella over the TFJ flexion range of motion.

When compared to MRI-registered data, $A_4$ well estimated the medio/lateral translation of the patella from 0° to 30° of TFJ flexion while providing continuous PFJ kinematics, therefore it was chosen as the best approach to describe patellar tracking in this patient population. With the use of two different MRIs, one close to 0° and one close to 30° of TFJ flexion, this approach allowed to dynamically quantify potential J-sign tracking and lateral patellar tilt (i.e., patellar external rotation) on an individual basis. Moreover, similarly to dynamic kinematic computed tomography (Tanaka et al., 2016), this mechanism was able to characterise different patterns of patellar maltracking, identifying increased lateral translation in extension (i.e., J-sign pattern) in three RPD patients and an increased lateral patellar translation in flexion for one RPD patient. Therefore, this methodology has the potential to correlate anatomical and functional findings with the currently used clinical examinations. Moreover, the high variability in patterns of patellar maltracking found in RPD patients confirms the importance of using subject-specific tools to assess each patient’s characteristics of instability.

In agreement with our hypothesis, RPD patients presented with a more externally rotated and lateralled patella than TD participants at early stages of TFJ flexion (i.e., <28°). These findings are in agreement with Regalado et al. (2014), who reported higher lateral patellar displacement, bisect offset ratio and lower patellar tilt angle (indicating a more externally rotated patella) values at 0°, 10°, 20° and 30° of TFJ flexion in adolescent patients with patellar instability compared to healthy controls.

The proposed PFJ kinematic models have some limitations, among which the low number of RPD patients included in this study. This choice was dictated by the availability, for the same RPD patient, of two MRIs, which allowed us to build two different PFJ mechanisms. Moreover, due to the lack of a standardised position of the
patient’s leg position during MRI acquisition, in the development of PFJ models we assumed that the congruence between the patella and the trochlear groove was reached at the knee position captured by the MRI with the highest TFJ flexion angle available. However, for some RPD patients, congruence between the patella and the trochlear groove might occur at a lower or higher TFJ flexion angle. Finally, due to the restraining size of the MRI bore, validation data were acquired only at TFJ flexion angles <33°, which hindered validation at larger ranges of motion.

8.4.1 Future work

To extend the application of the proposed PFJ model to other RPD patients, future MRI collection should include two different MRIs for each RPD patient at standardised TFJ flexion angles. Considering that 0°-30° of TFJ flexion is believed to be the range at which patellar dislocation occurs clinically (Burks et al., 1998; Desio et al., 1998; Hautamaa et al., 1998), and that large inter-subject variability exists in this patient group, the two MRIs should be taken at 0° and 40° of TFJ flexion to ensure that both the poses of the patella at knee extension and in congruence with the trochlear groove are captured.

Conversely, to extend the application of the proposed PFJ model to other RPD patients for whom a second MRI at a more flexed TFJ angle is not available (e.g., for the other 20 RPD patients recruited for the current PhD project), the pose of the patella engaged in the trochlear groove could be estimated. To this end, we have performed pilot testing of a congruence model of the PFJ to our patient group. This is similar to the previously developed (Conconi et al., 2012) and validated (Conconi et al., 2015) kinematic model of the tibio-talar joint. This congruence model of the tibio-talar joint only required the knowledge of the morphology of the articular surfaces to estimate the passive joint motion. The passive motion of the tibio-talar joint was predicted by searching for the motion that maximised the joint congruence, this being defined by a measure based on the Winkler elastic foundation contact model (Conconi et al., 2014). This model has been recently extended to the TFJ, with promising results (Conconi et al., 2018), but it has not been applied to the evaluation of the PFJ motion yet.

Our pilot testing of this approach estimated the passive PFJ kinematics in our cohorts of TD participants and RPD patients. From visual inspection of the MRIs at the reference pose, the patellar tendon did not appear to be in full tension, therefore, an adjustment of its length was necessary. To this end, the initial patellar tendon length, computed as Euclidean distance between the centroids of the attachment regions of the tendon on the patella and on the tibia, was projected onto the segmented surface of the tendon on its central plane (Figure 8.10). The adjusted patellar tendon length was
computed as average of the lengths of the two projected curves. The patella was then translated, from its initial position in the MRI reference pose, in the proximal/distal direction until obtaining a patellar tendon length equal to the adjusted length. For each participant, the TFJ kinematics was obtained from the 6-link parallel mechanism with prescribed ligament length variation (section 4.4.1). With this approach, the congruence model produced encouraging results for TD participants (Video 8.5).

![Figure 8.10](image)

**Figure 8.10.** Projection of initial patellar tendon length onto the reconstructed patellar tendon volume (pink). The adjusted patellar tendon length was obtained as the average of the lengths of the two projected curves.

However, the same approach produced an unstable patellar motion at low TFJ flexion angles (i.e., from 0° to ~40° of TFJ flexion) for RPD patients, possibly due to a lack of congruence between the surfaces of the patella and the trochlea. Moreover, when RPD patients presented with a dysplastic patella, the congruence model drastically modified the initial position of the patella (e.g., ab/adduction values > 90°), in the attempt to maximise the congruence between patella and trochlea. To address this issue, we decided to lock the patellar ab/adduction to the value computed from the MRI reference pose. This choice avoided considerable changes of patellar orientation at low TFJ flexion.
angles and provided a good estimation of the patellar motion at higher TFJ flexion angles (Video 8.6). Despite the fact that the patella remained unstable at low TFJ flexion angles for all four RPD patients, from the inspection of the videos and graphs describing the patellar kinematics (Figure 8.11), the patella was in a stable position, for all the RPD patients, at 60° of TFJ flexion. Therefore, the position of the patella at 60° of TFJ flexion can be used as initial position for the a PFJ hinge mechanism, where the articulating surfaces are defined as the medial and lateral articular surfaces in the trochlea and the patellar length remains constant over the TFJ flexion range of motion (i.e., second PFJ mechanism in $A_2$ and $A_3$ approaches). From this hinge mechanism, the position of the patella at 30° of TFJ flexion can be estimated and assumed as the first congruent position of the patella in the trochlear groove (Burks et al., 1998; Desio et al., 1998; Hautamaa et al., 1998). This latest position of the patella, together with its position at the MRI reference pose, can be then used to solve the PFJ mechanisms described in $A_4$.

**Figure 8.11.** PFJ kinematics obtained for the four RPD patients (RPD$_1$, RPD$_2$, RPD$_3$, RPD$_4$) using the congruence model. For each patient, the patella ab/adduction was locked at the value derived from the MRI reference pose. For all the four patients, the patella reached a stable position in the trochlea at ~60° of TFJ flexion (dotted vertical line).

Finally, future research could also use vertical open-bore MRI scanner to track the movement of the patella relative to the femur under loaded conditions across TFJ flexion range of motion (Macri et al., 2018). These approaches would expand the model validation to larger TFJ flexion range of motion.
8.5 Conclusion

In conclusion, this study presented a methodology to create subject-specific PFJ rigid body models to estimate three-dimensional passive patellar kinematics in paediatric RPD patients and TD controls. When compared to MRI-measured data of RPD patients, the proposed approach provided encouraging results, given its ability to dynamically quantify potential J-sign and lateral patellar tilt on an individual basis. Moreover, the developed PFJ models provide a platform for muscle force integration, enabling the calculation of PFJ contact forces, which can be extremely instructive in the understanding of the patellar dislocation injury mechanism and might inform surgical prescription.
CHAPTER 9

General discussion

This chapter will discuss how the thesis findings can be used to inform clinical decision making in the treatment of recurrent patellar dislocation in children and adolescents. A summary of the thesis is firstly presented (Section 9.1), highlighting the main findings of each study. Modelling (Section 9.2) and clinical (Section 9.3) implications of the proposed methods and findings of each study are then introduced. Finally, limitations (Section 9.4) and future research directions (Section 9.5) are discussed.

9.1 Thesis summary

The general aim of this thesis was to develop and validate subject-specific rigid-body models of the tibiofemoral and patellofemoral joints in children and adolescents with recurrent patellar dislocation. To this end, this thesis was divided into five studies, each relating to a specific aim. The first two studies aimed to characterise anatomical differences between paediatric patients with recurrent patellar dislocation and age-matched controls, while the last three studies focused on the development and validation of rigid-body kinematic models of the TFJ and PFJ to elucidate any kinematic differences between pathological and healthy paediatric cohorts. Interpretation of the findings specific to each study has been described within of the relative chapters. This final chapter first provides brief summaries of each study, but then provides an integrated interpretation of the thesis findings within the context of the current available literature.
In study one (Chapter 3) we systematically and critically reviewed the current literature to characterise lower limb alignment, patellofemoral morphology and soft tissue restraints of the PFJ through static medical imaging measurements in paediatric recurrent patellar dislocators (RPD) and age-matched typically developing (TD) participants. Moreover, the data were synthesised to stratify the factors that influence patellofemoral joint (PFJ) stability and recommendations on the assessment and reporting of PFJ parameters in this patient population were provided. Results from the meta-analysis showed that the tibial tuberosity to trochlear groove (TT-TG) distance and bony sulcus angle could be confidently used to predict the risk of recurrence in the paediatric population, and therefore are measures that should be included in patient evaluation. Nonetheless, the systematic review revealed a paucity of data comparing paediatric RPD and TD participants for many commonly implemented static medical imaging measures and this lack of available literature was the motivation for study 2.

In study two (Chapter 5) we analysed the differences in lower limb alignment, PFJ alignment and trochlea dysplasia between paediatric RPD patients and TD participants using magnetic resonance imaging (MRI). This comparison was essential as results from the systematic review revealed that there is a paucity of reported radiological parameters to define normal and pathoanatomical paediatric cohorts. A prospective cross-sectional study was conducted on 24 RPD children and adolescents and 25 age-matched TD participants. Significant differences between the two groups were found for acetabular inclination, tibial-femoral torsion, TT-TG distance, lateral patellar tilt, congruence angle and cartilaginous sulcus angle. In agreement with the meta-analysis conducted in study one, TT-TG distance and cartilaginous sulcus angle were included in the final predictive model, which correctly classified 84.4% of cases of recurrent patellar dislocation. The ability of the TT-TG distance and cartilaginous sulcus angle to dissociate between RPD and TD participants suggest that the alignment of the tibiofemoral joint (TFJ) and the morphology of the trochlear groove are important factors to consider in any evaluation of recurrent patellar dislocation. Therefore, if we want to develop kinematic models of the TFJ and PFJ in this patient population, subject-specific anatomy must be incorporated in the construction of the models. However, prior to the development of kinematic models for recurrent patellar dislocators, we need to ensure that we can accurately model the TFJ and PFJ in healthy children and adolescents, and this was therefore the aim of study three.

In study three (Chapter 6) we developed three subject-specific TFJ kinematic models, with either rigid or extensible ligament constraints, and a subject-specific PFJ
model for eight healthy paediatric participants. The estimated joint and ligament kinematics from the three models were also validated against in vivo kinematics measured from MRIs at four different TFJ flexion angles. The three TFJ models were created from MRIs and used to solve the TFJ kinematics: (i) 5-rigid-link parallel mechanism with rigid surface contact and isometric anterior cruciate (ACL), posterior cruciate (PCL) and medial collateral (MCL) ligaments ($\Delta L_0$), (ii) 6-link parallel mechanism with minimised ACL, PCL, MCL and lateral collateral ligament (LCL) length changes ($\Delta L_{\text{min}}$) and (iii) 6-link parallel mechanism with prescribed ACL, PCL, MCL and LCL length variations ($\Delta L_{\text{match}}$). The $\Delta L_0$ and $\Delta L_{\text{match}}$ models compared best against MRI-measured data, with errors below 6.93° and 4.23 mm for joint angles and displacements, respectively, and below 2.01 mm for ligament lengths. The comparison of the resulting RMSEs and kinematics with previously validated studies and published experimental kinematics evidences that $\Delta L_0$ and $\Delta L_{\text{match}}$ can describe joint and ligament kinematics in healthy paediatric individuals with satisfying accuracy. The conclusion from this study was that $\Delta L_0$ and $\Delta L_{\text{match}}$ can be used to estimate passive three-dimensional paediatric TFJ, PFJ and ligament kinematics and can be incorporated into lower-limb models to estimate joint kinematics and kinetics during dynamic tasks.

In study four (Chapter 7) we assessed the TFJ and ligament kinematics during gait using a rigid-body lower limb model incorporating a fully subject-specific paediatric kinematic TFJ model with articular contacts and minimally deformable ligaments. This was essential to extend the findings of the previous study to dynamic tasks. To address this aim, eight healthy participants underwent MRI and three-dimensional gait analysis. For these participants, the TFJ was implemented in OpenSim, based on optimised MRI-measured geometrical parameters, as a 5-rigid-link parallel mechanism with spherical articular contacts and three knee ligaments (ACL, PCL and MCL). For each participant, TFJ angles and ligament lengths were calculated by tracking experimental markers while minimising ligament elongation using the least squares multibody optimisation (MBO) tool available in OpenSim. The kinematic results from MBO were compared against those obtained using the implicit 5-rigid-link mechanism $\Delta L_0$, with significant differences found for TFJ ab/adduction, ACL and PCL strains. The developed subject-specific TFJ kinematic models are promising tools to investigate the gait biomechanics of healthy children and future studies will extend their use to the analyses of pathological gait.

In study five (Chapter 8) we developed subject-specific PFJ kinematic models to evaluate passive patellar tracking in paediatric RPD patients and TD controls. The resulting PFJ kinematics for RPD patients were also validated against in vivo kinematics
measured from MRIs at four different TFJ flexion angles. Finally, the estimated PFJ kinematics between RPD patients and TD participants were compared. For RPD patients, we modelled the PFJ from MRIs using two different hinge mechanisms, which described (i) the lateral to medial translation of the patella into the trochlear groove from approximately 0° to 30° of TFJ flexion, and (ii) the motion of the patella after it reached a more congruent position in the trochlear groove. When compared to MRI data, the proposed PFJ models were able to characterise different patterns of patellar maltracking in RPD patients. Moreover, RPD patients exhibited a more externally rotated and lateralisated patella than TD participants between 0° and 30° of TFJ flexion. We concluded that these models provided accurate estimations of pathological PFJ kinematics that could be used to inform surgery planning and evaluation.

9.2 Modelling implications

Existing musculoskeletal TFJ and PFJ models have different levels of complexity (Figure 9.1). At one end of the spectrum, researchers simplify the TFJ, for example, to a simple hinge or spherical joint (Anderson et al., 2001; Fregly et al., 2007; Klein Horsman et al., 2007; Richard et al., 2017). More realistic TFJ models include coupling constraints that allow for additional TFJ sliding and rolling motion based on TFJ flexion (Delp et al., 1990; Donnelly et al., 2012; Tsai et al., 2014) and parallel mechanisms (Di Gregorio et al., 2003; Feikes et al., 2003; Ottoboni et al., 2010; Parenti-Castelli et al., 2000; Sancisi et al., 2011a; Wilson et al., 1997). These rigid-body parallel mechanisms allow to estimate primary (i.e., flexion/extension) and secondary (i.e., internal/external rotation, ab/adduction and anterior/posterior, proximal/distal and medio/lateral translations) TFJ kinematics. At the other end of the spectrum, there are more complex models that, besides allowing estimation of secondary TFJ kinematics, can also provide estimates of tissue stresses and strains (i.e., tertiary kinematics) in the TFJ. These continuum models include 11-12 DoF multibody elastic foundation contact TFJ models (Guess et al., 2014; Hast et al., 2013; Lenhart et al., 2015; Marra et al., 2017; Marra et al., 2015; Smith et al., 2016b; Thelen et al., 2014) and finite element models (Adouni et al., 2012; Halonen et al., 2017; Kiapour et al., 2014; Mootanah et al., 2014). Depending on the research question (Hicks et al., 2015), both TFJ (and PFJ) rigid-body models and continuum models can have different levels of personalisation.
Figure 9.1 Different levels of complexity and subject-specificity within the spectrum of TFJ musculoskeletal models. The red arrow lists the level of subject-specificity that can be achieved in the implementation of rigid-body models, while the green arrow lists the level of subject-specificity that can be achieved in the implementation of continuum models. The figure highlights where the developed rigid-body knee kinematic models fit within the spectrum of TFJ musculoskeletal models. This figure focuses on the TFJ, but the same concept can be applied to other joints.

Personalisation of musculoskeletal TFJ and PFJ models can vary from scaled-generic models to fully subject-specific medical image informed models. However, based on the model application and data availability, different intermediate levels of subject-specificity can be achieved. Personalisation of TFJ rigid-body models includes, for example, the definition of the TFJ axis of rotation from medical images (Martelli et al., 2015; Valente et al., 2014) or the linear adjustment of cadaveric-based TFJ and PFJ motion components according to the dimensions of the femur and the tibia measured from medical images (Arnold et al., 2000; Scheys et al., 2011b). The TFJ and PFJ anatomy can also be personalised using data mining methods (Steger et al., 2012; Zhang et al., 2014a; Zhang et al., 2014b) or via segmentation of medical images (Brito da Luz et al., 2017; Kainz et al., 2016; Valente et al., 2014).

The proposed personalised rigid-body TFJ and PFJ kinematic models, compared to simplified joint models (i.e., hinge, spherical), besides very well estimating secondary joint kinematics (Begon et al., 2018; Clément et al., 2015), have other associated advantages. For instance, personalised parallel mechanism models have the potential to improve other dependent quantities of interest in musculoskeletal modelling (Arnold et al., 2000; Navacchia et al., 2017). The action of muscles and muscle force estimates in
neuromuscular skeletal models rely on the joint anatomy and secondary joint kinematics (Arnold et al., 2000; Draganich et al., 1987; Gerus et al., 2013; Marouane et al., 2017; Navacchia et al., 2017; Pandy et al., 1998; Tsai et al., 2012), and personalisation (Arnold et al., 2000; Gerus et al., 2013; Tsai et al., 2012). Furthermore, it has been recently argued that accurate muscle force estimation is crucial in the creation of multiscale models, which can combine rigid-body models and more complex continuum models (Fernandez et al., 2014; Fernandez et al., 2016; Fernandez et al., 2018; Sartori et al., 2017). Moreover, muscle forces estimated in personalised rigid-body musculoskeletal models can provide muscle force boundary conditions for personalised finite element models of the knee, built off the same medical images and rigid-body model foundations (Fernandez et al., 2016; Fernandez et al., 2018; Fondren et al., 1985). Importantly, the developed subject-specific kinematic models well predicted in vivo passive TFJ, PFJ and ligament kinematics while allowing for computational convenience and not needing to resort to continuum models (Chapter 6). The corollary of this is that these personalised rigid-body models clearly show that secondary kinematics have a strong dependence on joint three-dimensional anatomical geometry and may not necessary rely on soft tissue restraints. Finally, the proposed rigid-body models rely on computationally tractable implementations, compared to continuum joint models, and could be widely used in opensource software such as OpenSim to produce estimates of muscle forces and contributions to joint moments.

9.3 Clinical implications

9.3.1 Understanding the patellar dislocation mechanism

The first two studies of this thesis focused on static medical imaging and identified anatomical differences between paediatric patients with recurrent patellar dislocation and age-matched controls. Findings from the systematic review (Study 1) were consistent with the findings obtained from the comparison of anatomical parameters in our pathological and healthy paediatric cohorts (Study 2). In both studies, we showed that patients with recurrent patellar dislocation exhibited a higher sulcus angle and TT-TG distance compared to TD controls, suggesting that these two measurements may be used to predict the risk of recurrent patellar dislocation in children and adolescents. Moreover, we identified anatomical thresholds for characterising paediatric patients with recurrent patellar dislocation and this information could be used to streamline clinical patient evaluation. However, despite providing valuable insights into the PFJ anatomy and lower limb alignment, we suggest that these two-dimensional measurements computed from a
General discussion

static pose are insufficient to determine cause effect-relationships between PFJ anatomy and function. Often, assumptions on how these anatomical risk factors affect the PFJ function guide clinicians towards the choice of surgical treatments. The possibility to model the TFJ and PFJ with personalised anatomical information might uncover how these static measurements contribute to the dynamic function of the TFJ and PFJ.

A high sulcus angle indicates a shallow and flattened trochlear groove. This is thought to place the patient at risk of patellar dislocation at TFJ flexion angles >30°, because the trochlea is the most important patellar stabiliser during this TFJ flexion range (Lee et al., 2014). As the knee flexes beyond 30°, the slope and depth of the trochlea affect patellar stability, while the slope and the height of the lateral trochlear facet constrain lateral patellar translation (Ahmed et al., 2000; Jafari et al., 2008). In the kinematic PFJ models proposed in this thesis for patients with recurrent dislocation, a shallow trochlear groove would affect the size of the spheres fitted to the medial and lateral patellofemoral articulating surfaces in the second PFJ mechanism (i.e., from ~30° to 90° of TFJ flexion). Specifically, a flatter lateral trochlear facet would increase the radius of its fitted sphere with respect to the medial facet and, consequently, tilt the hinge axis of rotation laterally thereby causing the patella to track laterally and, potentially, dislocate.

An increased TT-TG distance is a measure of the relative misalignment between the femoral trochlea and the tibial tuberosity. The misalignment between the distal femur and the proximal tibia can be related to a combination of excessive femoral anteversion and external tibial torsion, which can lead to a more lateralised quadriceps line of pull due to the quadriceps internally rotating. A lateralised quadriceps line of pull can increase the magnitude of lateral force application from the quadriceps mechanism on the patella (Huberti et al., 1984). Specifically, in the TFJ model proposed in this thesis, an increased TT-TG distance would result in an increased external TFJ rotation and, when assessing gait using a full lower limb musculoskeletal model, would increase hip internal rotation compared to healthy controls. Moreover, the proposed kinematic models can be used to quantify how the TT-TG distance varies with TFJ flexion across the gait cycle. Indeed, an elevated TT-TG distance during the stance phase of gait, where the TFJ flexion angle is generally < 30°, might predispose an individual to patellar dislocation.

Characterising how the anatomy of the knee affects PFJ function across the TFJ range of motion will allow clinicians to make informed surgical decisions and provide objective measures to evaluate the effectiveness of their surgical interventions.
Specifically, the kinematic models proposed in this thesis (Studies 3, 4 and 5) can quantify how anatomical risk factors, such as a flattened trochl ear groove and/or an increased TT-TG distance, would affect lower limb joint function. The comparison of 6-DoF TFJ and PFJ kinematics between patients with recurrent patellar dislocation and healthy controls can reveal atypical joint kinematics in recurrent patellar dislocators and highlight the most affected motion components. Consequently, the PFJ function could be restored by tailoring the surgery to correct the most affected TFJ and/or PFJ motion components.

9.3.2 Tailored surgeries to correct for patellar dislocation

Of all the different types of surgical interventions, bony surgical procedures are most commonly used to correct a dysplastic trochlea or lower limb rotational misalignment. Trochleoplasty involves deepening the groove by removing subchondral bone (Dejour et al., 2010) and might be used to reshape the trochlea in skeletally mature patients with extreme dysplasia. Conversely, medialisation and/or advancement of the tibial tubercle and/or femoral derotation osteotomy can restore proper alignment between the femoral trochlea and the tibial tubercle (Weber et al., 2016a), and compensate for a deficient trochlea (Bollier et al., 2011). In skeletally immature patients, for whom tibial tubercle transfer is contraindicated due to the high risk of violating bone growth, patellar tendon transfer is preferred to achieve distal alignment of the extensor mechanism. To this end, the Roux-Goldthwaith procedure (Fondren et al., 1985), which consists in the medial translation of the lateral part of the patellar tendon, can be used, often in combination with medial retinacular plication or MPFL reconstruction (Deie et al., 2003) to additionally correct the lateral position of the patella. However, while these surgeries can reduce anatomic imaging risk factors, it remains unclear whether and to what extent these corrections would affect post-operative PFJ function.

In addition to describing the primary and secondary TFJ and PFJ kinematics, the technology developed in this thesis can potentially be used to predict post-operative joint function on an individual basis. The proposed kinematic models could allow the surgeon to perform in silico surgeries and, as a result, quantify the cause effect-relationships between corrected anatomical risk factors and PFJ function, and help verifying if the hypothesised dislocation mechanism for the individual patient has been mitigated. For example, deepening of the trochlear groove can be replicated in silico by removing subchondral bone from the three-dimensional reconstruction of the femur in 3-matic. This would increase the curvature of the medial and lateral patellofemoral articulating surfaces and, therefore, reduce the radii of the spheres fitted to those surfaces and make these radii of comparable magnitude. Evenly-sized fitted spheres would improve alignment between
General discussion

the hinge axis of rotation in the second PFJ mechanism developed for recurrent dislocators (i.e., from ~30° to 90° of TFJ flexion) and the axis defined by the medial and lateral femoral epicondyles, thereby reducing the amount of lateral patellar tracking during TFJ flexion.

Correction of the distal alignment of the extensor mechanism, either with antero/medialisation of the tibial tubercle or with medialisation of the patellar tendon, can also be replicated in silico. The tibial tubercle or the lateral part of the patellar tendon can be cut from the respective three-dimensional reconstruction of the tibia and patellar tendon in 3-matic (Materialise, Belgium) and translated it more medially and/or anteriorly on the tibia bone. While the simulated procedures would not modify the relative orientation between the femur and the tibia in the proposed models, as the TFJ coordinate systems would remain the same (Table 4.4), this correction would affect patellar tracking. In fact, as the patellar tendon is considered isometric in the PFJ mechanisms, a lateralised insertion of the patellar tendon on the tibia would favour lateral patellar tracking during TFJ flexion. Conversely, medialisation of the patellar tendon attachment, either via tibial tubercle or patellar tendon transfer, would correct the distal alignment of the extensor mechanism and favour the tracking of the patella in the trochlear groove. Moreover, even if the current PFJ kinematic models do not include retinacula and MPFL, the effects of medial retinacular plication or MPFL reconstruction can be reproduced in silico by medially translating the patella. This correction would improve the alignment of the patella in the trochlear groove, contributing to improve the overall distal alignment of the extensor mechanism. Specifically, compared to a lateral initial patellar position, a more medial initial position with respect to the femur would change the selection of the patellofemoral articulating surface in the first PFJ mechanism developed for recurrent dislocators, possibly reducing the misalignment between the two PFJ mechanisms (i.e., from 0° to 30° and from 30° to 90° of TFJ flexion) hinge axes of rotation. This could reduce the initial medio/lateral patellar displacement and favour a smooth transition between the two PFJ mechanisms.

Using the developed models, proximal or distal femoral derotation osteotomy can also be performed in silico by cutting and rotating the three-dimensional reconstruction of the femur in 3-matic. Using this procedure, the relative alignment between the femoral trochlea and the tibial tuberosity would be restored, with a consequent reduction of the TFJ external rotation across the TFJ flexion range of motion. If the quadriceps muscles were incorporated in the kinematic models, proximal and distal femoral derotation osteotomies would also rotate the quadriceps origin and insertion, respectively, reducing
the lateralisation of the quadriceps line of pull which would result in a reduction of the magnitude of lateral force applied on the patella. However, the incorporation of the muscles in the developed kinematic models was beyond the scope of this thesis.

Besides allowing the surgeons to virtually replicate commonly used surgical procedures, the developed models could also be used to test new procedures in silico. After assessing cause effect-relationships between PFJ anatomy and function for the individual patient, the surgeon could virtually assess the functional outcomes of different available procedures, taking into account skeletal maturity. If none of these surgeries would improve patellar stability (i.e., reduce patellar maltracking), the surgeon could virtually test new and more optimal procedures before implementing them in theatre.

9.4 Limitations

Although individual study limitations were presented within each respective thesis chapter, general limitations applying to the methods and assumptions used to create and validate personalised paediatric kinematic models require further discussion.

First, creating subject-specific rigid-body models is a time-consuming process that can take up to 19 hours per patient, including data acquisition, data processing, optimisation of geometrical parameters and model creation (Figure 9.2). While 19 hours is acceptable for research purposes, it is unacceptable for clinical applications. Of these 19 hours, three hours correspond to patient and staff time (i.e., patient’s data collection), while 11 hours correspond to staff time only (i.e., data processing, creation of full lower limb models). Five of the 19 hours correspond to computational time required to create the knee joint models. These 5 hours do not have a big impact on the application of the developed methods in the clinical setting as the knee joint models can be created overnight and the time required for this task is likely to reduce in the future with the availability of faster computers. Most of the time required to build personalised models relies on manual segmentation of medical images (~8.5 hours per patient for a single limb model). Provided a medical imaging dataset is available for children and adolescents, statistical shape modelling (Zhang et al., 2016a) and/or other machine learning methods could be used in the future to accelerate medical images segmentation (Erickson et al., 2017; Wang et al., 2018) and generation of three-dimensional lower limb bones in healthy participants. However, the use of subject-specific anatomy may still be necessary to capture abnormal anatomical features (e.g., dysplastic trochlea) and to prescribe individualised treatments for paediatric patients with recurrent patellar dislocation.
**General discussion**

<table>
<thead>
<tr>
<th>Resources</th>
<th>TD participants</th>
<th>Additions for RPD patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motion capture data</td>
<td>~90 minutes</td>
<td>+ Knee MRI at ~30° TFL flexion</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data processing</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone, ligaments and cartilage segmentation &amp; registration</td>
<td>~8 hours</td>
<td>+</td>
</tr>
<tr>
<td>Selection of TFL, PFL articulating surfaces, ligament attachments &amp; anatomical landmarks</td>
<td>~30 minutes</td>
<td>+</td>
</tr>
<tr>
<td>Quit data processing</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Creating full-lower limb models</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TFJ &amp; PFL models creation</td>
<td>~5 hours</td>
<td>+</td>
</tr>
<tr>
<td>TFJ &amp; PFL geometrical parameters’ optimization through MOPSO</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Solution of TFJ &amp; PFL passive mechanisms</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Creation of full-lower limb model in OpenSim</td>
<td>~20 minutes</td>
<td>+</td>
</tr>
<tr>
<td>Definition of explicit TFJ mechanism in OpenSim</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

**Figure 9.2.** Workflow to create subject-specific lower limb kinematic models for TD participants (left) and RPD patients (right). Red watches correspond to patient and staff time, green watches to staff time only and blue watches to computational time.
Second, the amount of imaging resource used to develop and validate the kinematic models is considerable (Figure 9.2). The acquisition of a full lower-limb scan and a detailed knee scan for each patient with recurrent patellar dislocation is advantageous, as it enables characterisation of both lower limb alignment and PFJ morphology within time limits that are comparable to those in a clinical service (~60 minutes). However, the addition of a second knee scan to model the PFJ in this patient group, with consequent increased acquisition time and costs, may limit the clinical translation of this method. The acquisition of a second knee scan for patients with recurrent patellar dislocation could be avoided by estimating the position of the patella at ~30° of TFJ flexion using a previously developed and validated congruence model (Conconi et al., 2012) applied to the PFJ.

Third, the developed TFJ and PFJ kinematic models estimate the joints’ passive kinematics, therefore not taking into account the effect of joint loading. While previous studies suggested that the joint kinematics during gait might differ from passive joint kinematics (Dyrby et al., 2004; Westphal et al., 2013), other studies reported similarities between unloaded and physiologically loaded joints (Lu et al., 2008; Myers et al., 2012). Therefore, passive joint kinematic models might be sufficient to provide accurate estimations of secondary knee kinematics and provide a platform for muscle force integration.

Fourth, due to the lack of published paediatric knee and ligament kinematic data, the developed TFJ models were tuned using adult cadaveric data, presupposing comparable knee and ligament kinematics. While the agreement between MRI-measured and cadaveric data in Study 3 (Figures 6.4-6.5) made this assumption reasonable for most TFJ motion components and ligaments, guidance from published kinematic data from adults might not capture, for example, a greater (compared to adults) TFJ laxity typical of the paediatric population (Flynn et al., 2000; Hinton et al., 2008).

Lastly, due to the restraining size of the MRI bore, validation data were acquired only at TFJ flexion angles < 30°, which hindered validation of the proposed models at a larger TFJ range of motion. However, as patellar dislocation is believed to occur between 0° and 30° of TFJ flexion (Burks et al., 1998; Desio et al., 1998; Hautamaa et al., 1998), it is likely that the developed models captured the most important TFJ flexion range for RPD patients. The lack of validation data at TFJ flexion angles > 30° could be addressed by using vertical open-bore MRI scanner to dynamically track the movement of soft tissues and bones under loading conditions across the TFJ flexion range of motion (Macri et al., 2018). These technologies, besides expanding the model validation to a larger TFJ
General discussion

flexion range of motion, would also extend the applications of the models to tasks such as running and jumping.

9.5 Future research directions

Several directions for future research have emerged from the findings of this thesis and the previously identified limitations. While some recommendations have been highlighted in the respective thesis chapters, important directions for future research, which can improve clinical translation of the technology developed within this thesis, require further discussion.

Future experimental studies that aim at developing paediatric knee kinematic models should include experimental knee and ligament kinematic data collected at TFJ flexion angles between 0° and 90°. The availability of this dataset would allow to tune the developed TFJ and PFJ models to kinematic data specific of the paediatric population, which might result in a more accurate estimation of each individual’s kinematics and might capture unique anatomical characteristics typical of the paediatric population, such as high knee ligamentous laxity (Flynn et al., 2000; Hinton et al., 2008). Moreover, this paediatric dataset would extend the model validation presented in this study to higher TFJ flexion angles.

The proposed implementation of fully personalised rigid-body kinematic models of the TFJ and PFJ will also allow the creation of a paediatric database. The future database will include the anatomy of paediatric lower limb bones, knee cartilage and ligaments, as well as the knee and ligament kinematics estimated both during passive TFJ flexion and during gait. Machine learning methods can then use the information contained in the database to generate anatomical (Erickson et al., 2017; Wang et al., 2018) and kinematic data more rapidly, therefore additionally reducing the computational time and the amount of resources needed to generate personalised kinematic models in the paediatric population.

After providing a robust method to develop and validate TFJ and PFJ kinematic models in a subset of children and adolescents with and without recurrent patellar dislocation, we plan to extend this method to the other participants recruited for this project. Subject-specific lower limb models, incorporating fully personalised TFJ and PFJ mechanisms, will be developed for the other 21 recurrent dislocators and 16 healthy participants recruited for this project. To build the PFJ mechanism in the 21 patients with recurrent patellar dislocation, the position of the patella at 30° of TFJ flexion will be estimated by using a joint congruence model developed at the University of Bologna.
(Conconi et al., 2015; Conconi et al., 2012, 2014; Conconi et al., 2018), that will be applied to the PFJ. The development of these additional models would allow investigation of functional differences at the knee between the two population groups and substantiate the preliminary findings of this thesis. Moreover, the magnitude of the kinematic differences between the two population groups would allow to recommend if the errors between MRI-registered and model-based kinematics reported in Chapter 7 are acceptable for clinical applications. In fact, if the magnitude of the reported errors is lower than the kinematic differences between the two groups we can confidently classify patients based on their most affected motion component. As discussed in Section 9.3.1, the surgery can then be tailored to correct the most affected TFJ or PFJ motion component for the individual patient and, as a result, restore PFJ function.

Additionally, we plan to use the developed rigid-body kinematic models to assess how static anatomical measures of lower limb and PFJ alignment from imaging (e.g., Q-angle, TT-TG distance) vary dynamically. For example, the TT-TG distance has been measured from MRI (Becher et al., 2017; Seitlinger et al., 2014) or CT (Hirschmann et al., 2017; Williams et al., 2016) at isolated TFJ flexion angles, but it has never been measured or estimated across the gait cycle. The implementation of the models to investigate the entire gait cycle has the potential to increase our understanding of the patellar dislocation injury mechanism during dynamic tasks and provide more informed indications for surgical treatments and/or rehabilitation techniques.

In the future, it will be necessary to incorporate muscles into the personalised knee kinematic models to create rigid body musculoskeletal knee models. Indeed, the forces from quadriceps muscles are thought to contribute substantially to the patellar dislocation injury mechanism. In fact, an imbalance in muscles forces generated by the four quadriceps muscles, especially between the vastus medialis and lateralis, and a rotational misalignment of the quadriceps muscle group can generate a lateral line of pull of the muscles, with a consequent increase of the magnitude of the lateral force applied on the patella. The incorporation of the quadriceps muscles into subject-specific lower limb models require the definition of muscle origins, insertions and pathways on an individual basis. While the quadriceps origins and insertions can be selected from MRIs, subject-specific muscle paths can be defined, for example, using optimisation-based approaches (Killen et al., 2018) that generate muscle wrapping surfaces based on each individual’s bone anatomy.

Once the muscles are incorporated into the subject-specific lower limb model, PFJ contact forces (i.e., internal loads) can be estimated by using either inverse or forward
dynamics approaches (Figure 9.3). In the inverse approach, which solves the forces from the motion, the secondary knee kinematics estimated extending passive knee kinematics to dynamic tasks (Chapter 7) can be used to compute PFJ moments via the inverse dynamic tool in OpenSim. Muscle forces can be computed using static optimisation (Erdemir et al., 2007) or a calibrated EMG-informed approach (Pizzolato et al., 2015). Contrarily, in the forward dynamic approach, which solves the motion from the forces, the TFJ and PFJ kinematic models proposed in Chapter 7 can be used in the residual reduction algorithm or in the concurrent optimization of muscle activations and kinematics (COMAK) tool (Brandon et al., 2017; Lenhart et al., 2015; Smith et al., 2016a) to assess how external forces and muscle loading in dynamic tasks would alter the underlying secondary TFJ and PFJ kinematics. Muscle forces can be directly obtained using the COMAK tool or with the computed muscle control approach (Thelen et al., 2003). The estimation of the magnitude and direction of the quadriceps muscle forces will enable quantification of the magnitude of the lateral force applied on the patella, which could help identifying the risk of dislocation. Finally, estimated quadriceps muscle forces can be combined with patellar tendon forces, derived by solving the static equilibrium of forces, to estimate PFJ contact forces during gait.

Knowing the magnitude of PFJ contact forces can be extremely useful for assessing patients with recurrent patellar dislocation as abnormal contact forces may perturb tissue homeostasis within the joint (Goudakos et al., 2010) and lead to increased risk of developing PFJ osteoarthritis (Wu et al., 2000). Identifying factors that 1) increase PFJ contact forces and 2) reduce PFJ stability for each individual patient allows for personalised surgical planning and/or rehabilitation. Once all the force boundary conditions are known for the PFJ, personalised continuum-based modelling may be employed to establish the role of soft tissue restraint in recurrent patellar dislocation and its surgical management. Ultimately, this personalisation should improve long-term treatment outcomes and patient quality of life.
Figure 9.3. Different pathways (i.e., inverse and forward dynamic approaches) to estimate PFJ contact forces using the subject-specific models developed in this thesis. Dotted blue lines represent the main outputs.

9.6 Conclusion

In conclusion, this thesis evaluated the anatomical and functional differences at the knee between children and adolescents with recurrent patellar dislocation and age-matched typically developed controls. The developed TFJ and PFJ kinematic models well estimated *in vivo* secondary kinematics measured from MRI and captured different patterns of patellar maltracking in patients with recurrent patellar dislocation. This technology can be used to identify the major contributors (i.e., most affected TFJ or PFJ motion components) for dynamic patellar maltracking and, consequently, plan a surgical treatment that aims to correct them. This could help identify surgical approaches that are most likely to improve patellar tracking and stability on an individual basis, which should then result in better long-term surgical outcomes, such as reduced costs from surgical revision and improved patient quality of life.
References


References


References


Campbell, A. C., Alderson, J., Lloyd, D., & Elliott, B. (2009). Effects of different technical coordinate system definitions on the three dimensional representation of
the glenohumeral joint centre. *Medical & biological engineering & computing, 47*(5), 543.


References


References
References


References


References


References


References


References


References


References


tasks of increasing demand using biplane fluoroscopy. The American journal of sports medicine, 40(1), 170-178.


References


References


References


References

Image-Specific Fine Tuning. *IEEE Transactions on Medical Imaging, 37*(7), 1562-1573.


References


