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Author

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Surgical Approaches to Pre-Auricular Cutaneous Squamous Cell Carcinomas Extending to the Temporal Bone

Michael Schachtel[1,2] | Mitesh Gandhi[3,4] | James Bowman[1] | Mark Midwinter[2] | Benedict Panizza[1,2]

[1]Department of Otolaryngology, Head and Neck Surgery, Princess Alexandra Hospital, Queensland Skull Base Unit, Brisbane, Queensland, Australia | [2]Faculty of Medicine, The University of Queensland, Brisbane, Queensland, Australia | [3]Department of Radiology, Princess Alexandra Hospital, Brisbane, Queensland, Australia | [4]Queensland X-Ray, Brisbane, Queensland, Australia

Correspondence: Michael Schachtel (michael.schachtel@gmail.com)

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ABSTRACT

Background: Standardized surgical approaches to advanced pre-auricular cutaneous squamous cell carcinomas (cSCC) are lacking.

Methods: Fifty–four patients who underwent lateral temporal bone resection (LTBR) for pre-auricular cSCC were grouped into "Levels" of increasing disease spread. Surgical approaches to achieve negative-margin resection were designed for each Level and replicated on cadaveric specimens.

Results: Level 1 extended to the external auditory canal, requiring LTBR ± superficial parotidectomy. Level 2 involved the retromandibular space ± temporomandibular joint, necessitating partial mandibulectomy, in addition to the above. Level 3 and 4 involved the deep parotid, being situated either away from (> 5 mm) or close (≤ 5 mm) to the anterior carotid sheath (ACS), respectively. These tumors require radical parotidectomy, with incorporation of the ACS for Level 4. Level 5 involved the ACS at the skull base and should be treated non-surgically.

Conclusion: This Level-based system will hopefully lead to further prospective studies and improvements in outcomes for advanced pre-auricular cSCC.

1 | Introduction

Surgical resection and post-operative radiotherapy (PORT) forms the mainstay of treatment for cutaneous squamous cell carcinoma (cSCC) extending to the temporal bone [1–11]. However, unlike primary temporal bone (or external auditory canal [EAC]) cSCC, there is little evidence to guide operative approaches and the extent of resection required to clear disease. This is important to address, as these tumors are more commonly encountered than primary temporal bone carcinomas and can have equally poor, if not worse, survival outcomes [1, 6, 12, 13]. Not only can these tumors directly invade the EAC, but they can also spread to crevices around the skull base and temporomandibular joint (TMJ), making *en-bloc* resection challenging. This especially holds true for pre-auricular based lesions, originating either on the skin or as a metastatic node. In our review of cSCCs requiring temporal bone resection (TBR) at our institution, compared to other subsites, pre-auricular cSCCs had the highest proportion of involved margins (39% versus 21%) and the poorest survival outcomes (5-year disease-free survival [DFS] and disease-specific survival [DSS] of 34.1% and 48.1% versus 68.8% and 85.1%, respectively) [1].

To improve operative planning and margin status for patients with advanced pre-auricular cSCC, a better knowledge of fascial planes and pathways and barriers of tumor spread is essential. Of particular interest to our group is the anterior carotid sheath (ACS), which can often serve as a convenient plane of dissection when resecting these tumors off the skull base, protecting the major vessels and lower cranial nerves from damage. In follow-up anatomical and radiological studies, we found that the ACS was a thick layer formed by multiple thin contributions from the deep cervical fascia and also appeared to form a temporary barrier to spread of malignancy [14, 15]. Furthermore, radiological involvement of this fascial layer conferred a high-risk of residual disease, with all such patients having positive margin resections, as well as poor survival outcomes despite receiving PORT. While these results suggest that the ACS is an anatomical limit of resectability, it remains unclear in the literature how tumors should be resected in relation to this fascial plane, and the extent required when other anatomical structures are involved.

This report aims to provide a standardized surgical treatment protocol for advanced pre-auricular cSCCs extending to the temporal bone, with a particular focus on the role of the ACS. This will hopefully lead to improvements in treatment planning, negative margin rates, and survival outcomes for these patients.

2 | Methods

2.1 | Patient Population

We conducted a further analysis of the 54 patients included in our previous study investigating radiological patterns of spread of pre-auricular cSCC (cutaneous or nodal origin) extending to the temporal bone [14]. Patients were grouped according to increasing anatomical structural involvement and degree of medial disease spread, and a "Level" based system was developed, from least to most advanced.

2.2 | Surgical Approaches

Surgical resections were designed for each Level to ensure clearance of tumor with adequate margins of healthy tissue. While various surgical and oncological organizations have proposed guidelines for surgical excision margins for high-risk cSCC, these are based on limited evidence and there remains no international consensus [16–18]. Recommendations for peripheral margins range between 6–10 mm, and as such, we aimed for at least 10 mm peripherally. As no clear recommendations exist regarding deep surgical excision margins, we aimed for at least 5 mm, given the close proximity of neurovascular structures to the surgical field (generally precluding a 10 mm deep margin), and that previous studies, including our own, have demonstrated higher recurrence rates for tumors with close margins compared to clear margins, using 5 mm as the cut-off measurement [1, 19]. However, as the jugular bulb/upper internal jugular vein (IJV), internal carotid artery (ICA), and lower cranial nerves are not routinely resected at our institution due to lack of proven survival benefit and high morbidity in the literature, we also accepted a deep fascial or bony margin if > 5 mm was not possible [12, 20–23].

The designed resections were then replicated on soft embalmed cadaveric specimens, demonstrating the operative steps and relevant anatomy. Specimens were donated through the Body Donor Program at the University of Queensland, and dissections were performed at the Gross Anatomy Facility. Institutional ethics approval was obtained prior to commencing (Approval No. 2019000003).

Soft embalmed specimens were prepared with vascular injections using red and blue dyed natural latex (Carolina Biological, Burlington, North Carolina, USA) using techniques as described previously by Dolci et al. [24]. Dissections were performed with the assistance of a VITOM 3D exoscope (Karl Storz SE & Co. KG, Tuttlingen, Germany), and bone dissection was performed with a πDrive Drill (Stryker, Kalamazoo, Michigan, USA). Images were captured using a Canon EOS 6D DSLR camera (Canon Inc., Ota, Tokyo, Japan) and the VITOM 3D exoscope.

3 | Results

Table 1 provides an overview of the tumor Levels, based on common patterns of spread observed, and their recommended treatment

TABLE 1 | Level-based approach to treatment of pre-auricular cSCCs extending to the temporal bone, developed through further analysis of 54 patients from Schachtel *et al.* [14].

Level	Tumor spread	Recommended approach	*n* = 54	%
1	EAC	WLE and/or SP + LTBR	13	24.1
2	1 + RMS ± TMJ/ Mand.	1 + AM	9	16.7
3	2 + DP + ACS > 5 mm	2 + RP	6	11.1
4	3 + ACS ≤ 5 mm	3 + Sty. P. + ACS ± ITF	20	37.0
5	4 + Involving ACS	Non-surgical (i.e., immunotherapy, RT)	6	11.1

Abbreviations: ACS, anterior carotid sheath; AM, ascending mandibulectomy; DP, deep parotid gland; EAC, external auditory canal; ITF, infratemporal fossa resection; LTBR, lateral temporal bone resection; Mand., mandible; RMS, retromandibular space; RP, radical parotidectomy; RT, radiotherapy; SP, superficial parotidectomy; Sty. P., styloid process; TMJ, temporomandibular joint; WLE, wide local excision.

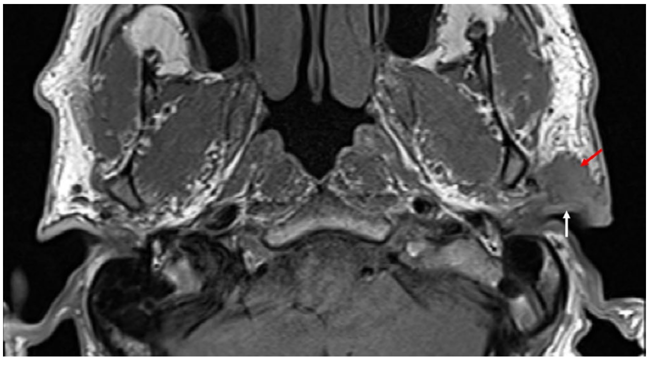

FIGURE 1 | Example of a Level 1 tumor. Axial T1 imaging depicting a recurrent left pre-auricular cutaneous squamous cell carcinoma (*red arrow*) extending posteriorly to involve only the cartilaginous external auditory canal (*white arrow*). [Color figure can be viewed at wileyonlinelibrary.com]

paradigms—outlined in further detail below (Figures 1–9). For each Level, incision planning and incorporation of skin and soft tissue is handled case-by-case and can vary greatly depending on the site of origin (cutaneous or nodal) and extent of involvement. Attempts should be made to preserve cosmesis where possible, while also ensuring at least a 10 mm peripheral margin. For most pre-auricular based lesions, the pinna (or part of) can usually be spared, and vascularity is likely best preserved through

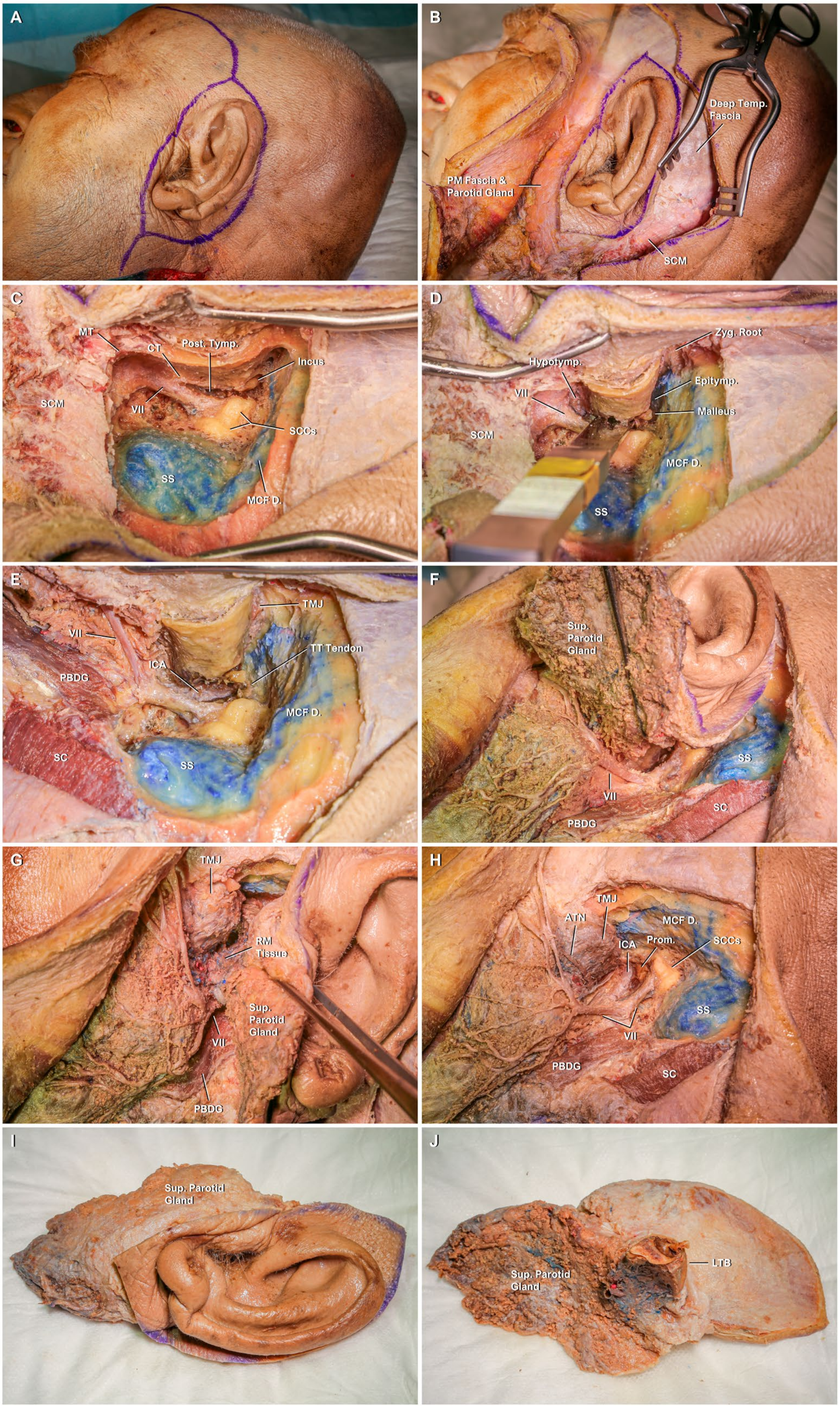

FIGURE 2 | Legend on next page.

a pre-auricular incision (usually incorporating the tragus) and a posteriorly based flap (Figures 6 and 8). Note that in the following examples, clearance of the medial disease extent is the main focus of the dissections, and the incisions and soft tissue resection may not necessarily correlate to the radiological example provided.

3.1 | Level 1

Tumor spread (Figure 1): Involvement or close extension (≤5 mm) to the EAC, without invasion of other anatomical structures.

Recommended approach (Figure 2): Depending on the location of the main tumor mass, (LTBR) is combined with a wide local excision of skin and/or superficial parotidectomy, preserving the facial nerve (VII) branches. For tumors that abut the EAC, an *en-bloc* partial LTBR may be sufficient (i.e., excision of the anterior bony EAC wall). However, if tumor invades the EAC, a formal *en-bloc* LTBR is required (i.e., excision of the entire cartilaginous and bony EAC).

3.2 | Level 2

Tumor spread (Figure 3): In addition to the EAC, involvement of the retromandibular space between the tympanic plate and upper mandibular neck, with or without invasion of the TMJ or mandible.

Recommended approach (Figure 4): LTBR, superficial parotidectomy, and partial excision of the ascending mandible is required to clear disease. In situations where the mandibular cut can be made more superiorly, preservation of the temporal branch of VII is possible through gentle inferior retraction. However, this branch may require sacrifice in other cases to gain appropriate access.

3.3 | Level 3

Tumor spread (Figure 5): Further medial spread of disease to the deep parotid lobe (in addition to the structures above), but away (> 5 mm) from the styloid process and ACS. In all cases, the intra-parotid VII is either directly involved or encased by tumor.

Recommended approach (Figure 6): Radical parotidectomy is required in addition to LTBR and partial ascending mandibulectomy. Given the ACS is away from the tumor mass, this thick plane can be followed when dissecting the soft tissue off the skull base, protecting the underlying ICA, IJV, and lower cranial nerves. If required for perineural spread (PNS), VII can be readily chased back to the geniculate ganglion given the wide surgical access from LTBR. Otherwise, the nerve can be resected at the stylomastoid foramen as usual, and a sample can be sent for frozen section analysis if suspicion for PNS exists.

3.4 | Level 4

Tumor spread (Figure 7): As for Level 3, although with tumor spread close (≤5 mm) to or abutting the ACS (styloid process), without more medial extension through the fascial plane to encase the styloid process, IJV, or ICA.

FIGURE 3 | Example of a Level 2 tumor. Axial CT demonstrating a left pre-auricular cutaneous squamous cell carcinoma (*red arrow*) involving the cartilaginous external auditory canal (*white arrow*) and retromandibular space (*blue arrow*). [Color figure can be viewed at wileyonlinelibrary.com]

FIGURE 2 | Level 1 surgical approach. (A) An appropriate skin incision is planned, depending on the site of the main tumor mass (*Note:* The tumor depicted in Figure 1 could be excised with skin and pinna preservation as demonstrated in Figure 4). (B) Skin flaps are raised above the deep temporal and parotidomasseteric fascia. (C) A standard mastoidectomy is performed, exposing the sigmoid sinus and middle cranial fossa dura. A posterior tympanotomy is then created. (D) The incudostapedial joint is disarticulated and the incus is removed. The posterior tympanotomy is extended into the hypotympanum, sacrificing the chorda tympani, and the epitympanum is opened further through drilling of the zygomatic root. Drilling is extended antero-inferiorly and superiorly to reach the parotid gland and temporomandibular joint. The lateral temporal bone can then be fractured forward through either gentle anterior pressure or, if resistance is encountered, cautious use of a 2 mm osteotome. (E) Once fractured forward, the posterior tympanotomy is widened, allowing completion of anterior drilling lateral to the internal carotid artery, liberating the lateral temporal bone. The facial nerve is followed anteriorly to the parotid gland from the stylomastoid foramen. As pictured, drilling of the mastoid tip and posterior reflection of the sternocleidomastoid muscle can also be performed to improve exposure. (F) A superficial parotidectomy is performed, preserving the facial nerve branches. (G) The specimen is then freed from the retromandibular tissue, which contains branches of the auriculotemporal nerve. Care should be taken here to avoid injury to the maxillary artery and vein, which enter the masticator space behind the mandibular neck. (H) The resulting defect post resection. (I) Lateral and (J) medial views of the excised specimen. ATN, auriculotemporal nerve; CT, chorda tympani; D., dura; Epitymp., epitympanum; Hypotymp., hypotympanum; ICA, internal carotid artery; LTB, lateral temporal bone; MCF, middle cranial fossa; MT, mastoid tip; PBDG, posterior belly of digastric muscle; PM, parotidomasseteric; Post., posterior; Prom., promontory; RM, retromandibular; SC; splenius capitis muscle; SCM, sternocleidomastoid muscle; SS, sigmoid sinus; SCCs, semicircular canals; Sup., superficial; Temp., temporal; TMJ, temporomandibular joint; TT, tensor tympani; Tymp., tympanotomy; VII, facial nerve; Zyg., zygomatic. [Color figure can be viewed at wileyonlinelibrary.com]

Recommended approach (Figure 8): In addition to the Level 3 clearance, given the proximity of the styloid process and ACS to the tumor mass, LTBR should also include the styloid process, and dissection should proceed below the ACS to incorporate a deep fascial margin in the resection. This can be achieved through resection of VII in its mastoid portion to widen access, and further drilling of the hypotympanum between the upper IJV and styloid process attachment at the skull base. This

FIGURE 4 | Legend on next page.

mobilizes the styloid process and its muscles, and helps delineate the superficial layers of the anterior carotid sheath (tensor-vascular-styloid fascia [TVSF]/stylopharyngeal fascia [SPF]) from its deeper layers (buccopharyngeal fascia [BPF]/longus capitis fascia [LCF]), which travel deep to the styloid process. Dissection can then advance medially either between the layers of the sheath, with the glossopharyngeal nerve (IX) remaining protected by the underlying fascia (as illustrated), or under the plane entirely, resecting IX at the point in which it enters the sheath. Although not pictured, resection can also extend to include the infratemporal fossa for cases of direct tumor invasion or zone 1 trigeminal nerve mandibular branch (V_3) PNS, and the Gasserian ganglion via a lateral craniotomy for zone 2 disease.

3.5 | Level 5

Tumor spread (Figure 9): In addition to the Level 1–4 structures, tumor extension beyond the anterior carotid sheath at the skull base to encase or erode the styloid process.

Recommended approach: As previously shown, these tumors carry high risk of residual disease (100% involved margin rate) and poor survival outcomes despite radical surgical resection and PORT (Figure 10) [14]. As such, alternative treatment options should be considered (i.e., immunotherapy or radiotherapy).

4 | Discussion

Advanced pre-auricular cSCCs, originating either primarily on the skin or as a metastatic nodal deposit, are challenging to treat, with relatively high rates of involved surgical margins and poor survival outcomes, as demonstrated in our previous report of cSCCs requiring TBR [1]. Similarly, in their study of primary and peri-temporal bone malignancies, Gidley et al. found that tumors of the peri-auricular skin had some of the worst outcomes compared to other subsites, with a 5-year DFS and overall survival of 33.6% and 42.7%, compared to 77.3% and 82.3% for EAC primaries [6]. Contributing to this disparity in survival outcomes and the difficulties in managing pre-auricular cSCCs is the fact that there is a paucity of evidence guiding treatment of these tumors and there remains a lack of standardized surgical approaches. While attempts have been made to create stage-based treatment protocols, the utility of such systems are questionable, given most, if not all, tumors are classified as T4 or N3b according to the American Joint Committee on Cancer system [5]. As such,

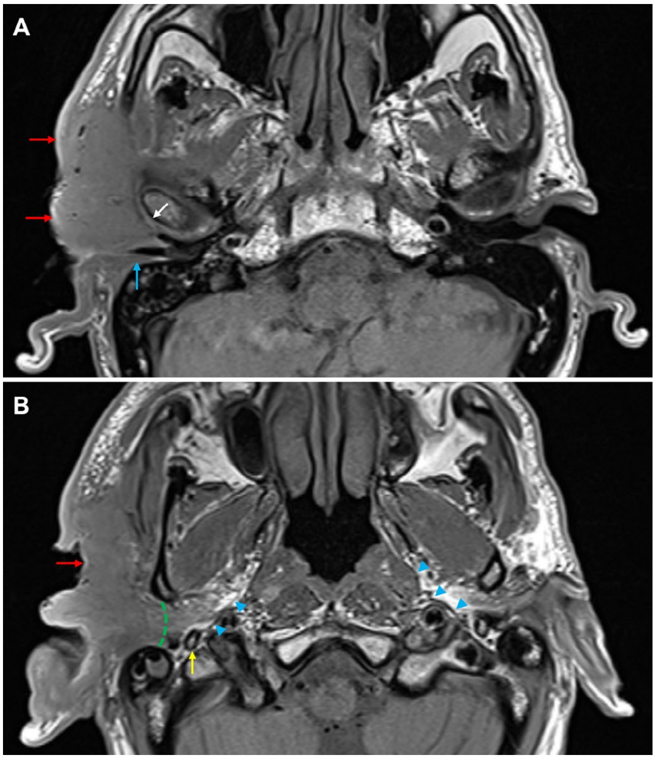

FIGURE 5 | Example of a Level 3 tumor. Axial T1 imaging of a right metastatic parotid nodal deposit of cutaneous squamous cell carcinoma (*red arrows*). Superiorly (A), tumor involves the external auditory canal (blue arrow) and retromandibular space (*white arrow*). More inferiorly (B), tumor extends to the deep parotid lobe (*green hashes*) but remains away (> 5 mm) from the styloid process (*yellow arrow*) and anterior carotid sheath (*blue triangles*), seen as a hypointense line extending medially from the styloid process. [Color figure can be viewed at wileyonlinelibrary.com]

FIGURE 4 | Level 2 surgical approach. (A) Skin incisions are planned. In cases where wide local excision of skin is not required, a post-auricular C-shaped incision can be utilized (*Note:* For the tumor in Figure 3, excision of the pre-auricular skin and anterior pinna would be required—as seen in Figures 6 and 8). (B) The external auditory canal is transected and skin flaps are raised above the deep temporal and parotidomasseteric fascia. At this point, a blind sac closure can be performed if the lateral canal is not involved. (C) Mastoidectomy and an extended posterior tympanotomy are then performed, and the incus is removed. (D) Inferior, superior, and anterior bony cuts are completed as performed in Level 1. The facial nerve is then followed toward the parotid gland. (E) Dissection of the superficial parotid gland is performed, which is rolled superiorly. Gentle inferior retraction of the temporal branch of the facial nerve (*yellow triangles*) can facilitate exposure of the mandibular neck to perform the bony cut. However, this branch may require resection in cases of aberrant facial nerve anatomy or when the mandibular cut need to be made more inferiorly. The *en-bloc* specimen can then be delivered after ligation of the maxillary artery and vein and freeing of the lateral pterygoid muscle from its attachments to the temporomandibular joint and mandible. There should be caution in avoiding damage to the inferior alveolar nerve, which travels deep to the lateral pterygoid muscle. (F) The resulting surgical defect, with a patient example provided for comparison (G). (H) Lateral and (I) medial views of the excised specimen. A., artery; CT, chorda tympani; D., dura; EAC, external auditory canal; Ext., extended; IAN, inferior alveolar nerve; ICA, internal carotid artery; IJV, internal jugular vein; LP, lateral pterygoid muscle; LSCC, lateral semicircular canal; LTB, lateral temporal bone; Mand., mandible; Max., maxillary; MCF, middle cranial fossa; MT, mastoid tip; PBDG, posterior belly of digastric muscle; PM, parotidomasseteric; Post., posterior; RM, retromandibular; SCM, sternocleidomastoid muscle; Sph. Sp., sphenoid spine; SS, sigmoid sinus; Sup., superficial; Temp., temporal; TMJ, temporomandibular joint; Tymp., tympanotomy; V., vein; VII, facial nerve; XI, accessory nerve; Zyg., zygomatic. [Color figure can be viewed at wileyonlinelibrary.com] different approaches may be warranted for same-staged tumors, as treatment tends to be individualized based on the direction of spread and structures involved. Thus, we aimed to provide examples of surgical resections and approaches that can be used to manage pre-auricular cSCCs extending to the temporal bone, based on common patterns of spread observed, as opposed to their prognostic staging group. We also aimed to draw attention

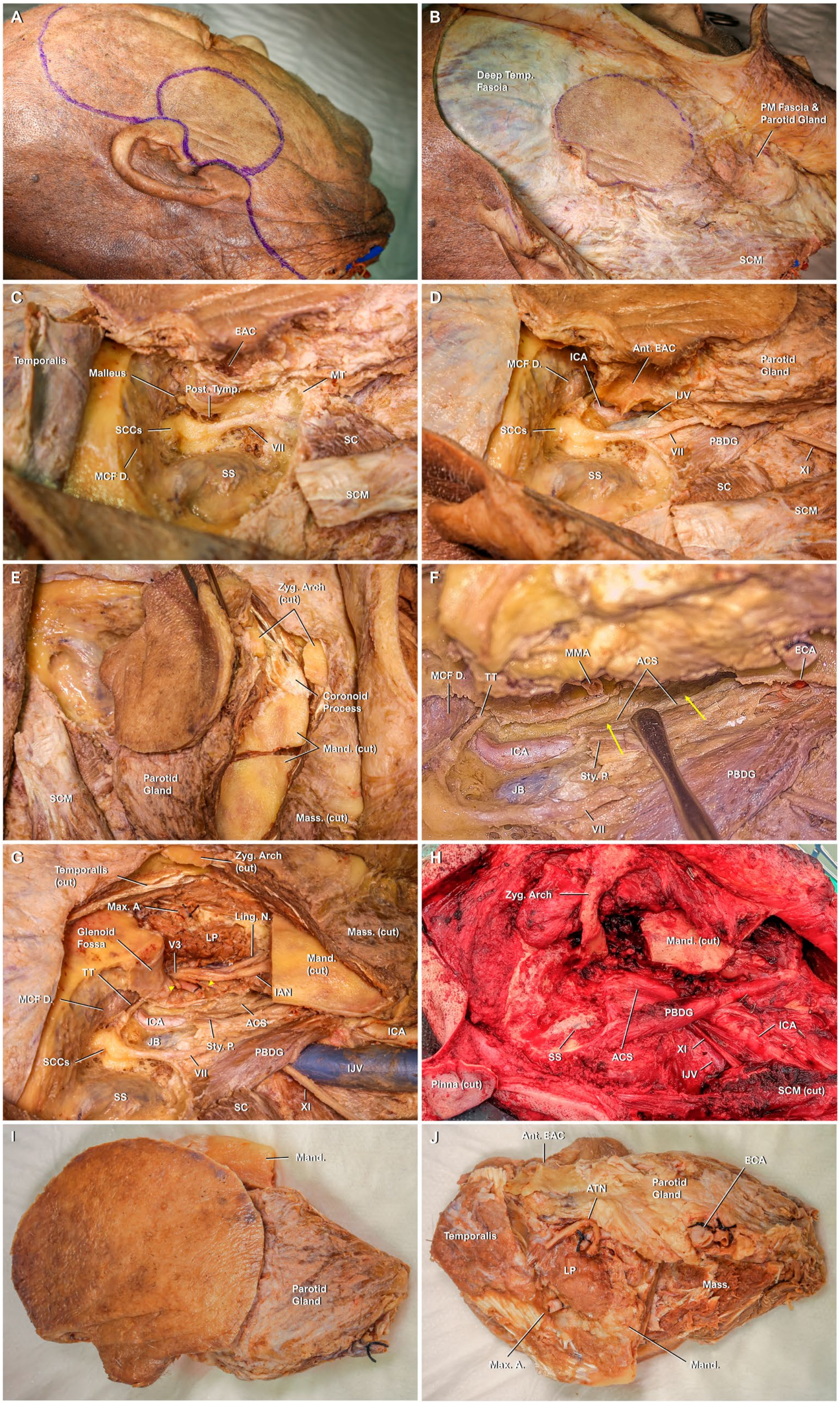

FIGURE 6 | Legend on next page.

to the utility and role of the ACS as a fascial plane of dissection and anatomical limit of resectability.

Through further analyzing our previous case-series, we developed a Level-based system of treatment, with each Level increase correlating with further medial spread of disease and a more radical surgical resection [14]. Level 1 represented the least advanced tumors which either extended close (≤ 5 mm) to or involved the EAC. While treatment of tumors involving the EAC is generally straightforward and in line with that of primary EAC carcinomas, it remains more unclear for those abutting the temporal bone or EAC. The approach for these tumors has traditionally been soft tissue resection alone, possibly in efforts to preserve function and cosmesis [11]. However, achieving an *en-bloc* clear margin resection in this setting is very challenging. As such, we also perform TBR when tumors are abutting to improve access and ensure clearance of the posterior and medial margin, even in the absence of direct EAC or temporal bone invasion. In these situations, a partial LTBR, such as excision of the anterior EAC wall, as opposed to a formal *en-bloc* LTBR, would likely suffice as an appropriate bony margin. We have found that this type of resection is more time efficient than a LTBR and has less risk of an inadvertent VII injury.

This more aggressive approach appears justified when comparing our long-term outcomes (2- and 5-year DSS 70.2% and 48.1%, respectively) to studies which utilized a soft tissue approach only (2-year DSS 33%) and considering the significant impact margin status has on survival outcomes (Hazard ratio [HR] > 3 for recurrence, $p < 0.01$) [1, 25]. Furthermore, most patients who underwent such operations generally tolerated it well and reported acceptable levels of post-operative morbidity, as detailed in our previous complications analysis [1]. An additional benefit we have observed is that the risk of developing temporal bone osteoradionecrosis is much less when LTBR is performed compared to soft tissue resection or mastoidectomy alone. Longer-term analyses of morbidity and quality of life outcomes post-surgery are required to fully determine the risk versus benefit balance in these cases.

Support for the ancillary use of TBR has also emerged particularly in studies of primary and/or secondary parotid tumors [11, 26–30]. Gidley et al. demonstrated that the addition of

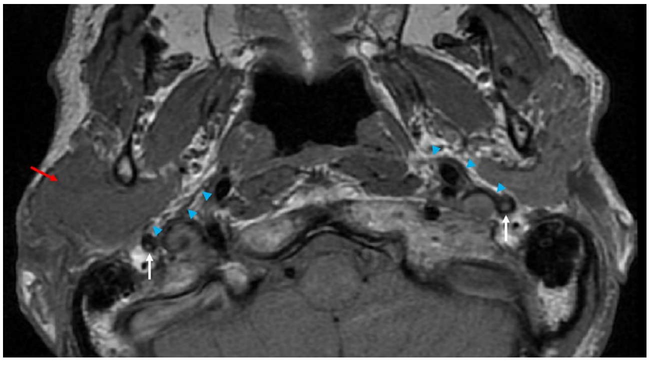

FIGURE 7 | Example of a Level 4 tumor. Axial T1 imaging of a nodal deposit of cutaneous squamous cell carcinoma in the right parotid gland. Tumor (*red arrow*) involves the deep parotid lobe and extends close (≤ 5 mm) to the styloid process (*white arrows*) and anterior carotid sheath (*blue arrows*), without obvious extension through the fascial plane. [Color figure can be viewed at wileyonlinelibrary.com]

FIGURE 6 | Level 3 surgical approach. (A) In this example, incisions are planned based on a pre-auricular cutaneous lesion requiring wide local excision. In situations when the pinna (or part of) can be preserved and there are large portions of the pre-auricular skin or concha involved with tumor, incisions should extend in a pre-auricular fashion with the pinna taken posteriorly to preserve some vascularity. (B) Skin flaps are raised as standard. (C) Mastoidectomy and posterior tympanotomy are performed, and the incudostapedial joint is disarticulated. (D) The epitympanum and hypotympanum is drilled lateral to the internal jugular vein and carotid artery, and the parotid gland's inferior border is freed from surrounding soft tissue. In this case, the posterior ear canal wall has also been drilled and the annulus and malleus have been excised. These additional steps set up a partial lateral temporal bone resection, which can be used for tumors that abut the temporal bone, with the anterior ear canal wall providing a bony margin. This approach also has benefit in providing wider exposure for anterior drilling to occur. In cases where the posterior canal wall must remain intact (i.e., formal lateral temporal bone resection), facial nerve transection high in its mastoid segment at this step can widen the posterior tympanotomy to ~4 mm, which is usually sufficient for a 1-2 mm diamond burr to complete anterior drilling. This can also be widened further through gentle anterior pressure and fracturing of the lateral temporal bone forward. Note that wide exposure of the internal carotid artery is usually not required, but has been depicted here to demonstrate relevant anatomy. (E) Anteriorly, soft tissue dissection proceeds at the anterior edge of the parotid gland and through the masseter muscle, to expose the mandibular ramus. Bony cuts are then made in the ascending mandible, with care not to enter the oral cavity. If required for additional superior bony and soft tissue margins, the zygomatic arch and a cuff of temporalis muscle can be resected. Otherwise, the attaching temporalis fibers are freed from the coronoid process. (F) The facial nerve is then transected at the stylomastoid foramen (or more proximally if required for perineural spread), and dissection proceeds in a lateral to medial direction, freeing the soft tissue from the skull base. The plane of dissection (*yellow arrows*) remains superficial to the styloid process and the thick fascia of the anterior carotid sheath. The ascending mandible is then freed from its soft tissue and muscular attachments. The maxillary and external carotid arteries are ligated as required to liberate the *en-bloc* specimen. If mandibular cuts are made superior to the mandibular foramen, attempts should be made to preserve the inferior alveolar nerve in the infratemporal fossa. (G) The resultant defect, with the *yellow triangles* corresponding to the cut ends of the two roots of the auriculotemporal nerve encircling the middle meningeal artery. (H) Surgical defect of a patient who has undergone a Level 3 resection, however, the zygomatic arch has been preserved. (I) Lateral and (J) medial views of the excised specimen. A., artery; ACS, anterior carotid sheath; Ant., anterior; ATN, auriculotemporal nerve; D., dura; EAC, external auditory canal; ECA, external carotid artery; IAN, inferior alveolar nerve; ICA, internal carotid artery; IJV, internal jugular vein; JB, jugular bulb; Ling., lingual; LP, lateral pterygoid muscle; Mand., mandible; Mass., masseter muscle; Max., maxillary; MCF, middle cranial fossa; MMA, middle meningeal artery; MT, mastoid tip; N., nerve; PBDG, posterior belly of digastric muscle; PM, parotidomasseteric; Post., posterior; SC, splenius capitis; SCCs, semicircular canals; SCM, sternocleidomastoid muscle; SS, sigmoid sinus; Sty. P., styloid process; Temp., temporal; TT, tensor tympani muscle; Tymp., tympanotomy; V., vein; V3, mandibular branch of the trigeminal nerve; VII, facial nerve; XI, accessory nerve; Zyg., zygomatic. [Color figure can be viewed at wileyonlinelibrary.com]

TBR to parotidectomy resulted in clear margins in more than 80% of their 49 patients with advanced parotid tumors [27]. In previous series, this has been reported to be as low as 37% [31, 32].

A similar treatment philosophy applies to Level 2 tumors which involved or were in close proximity to the TMJ and/or mandibular neck. Thus, to clear disease, an ascending mandibulectomy is required in addition to LTBR, superficial parotidectomy and/or

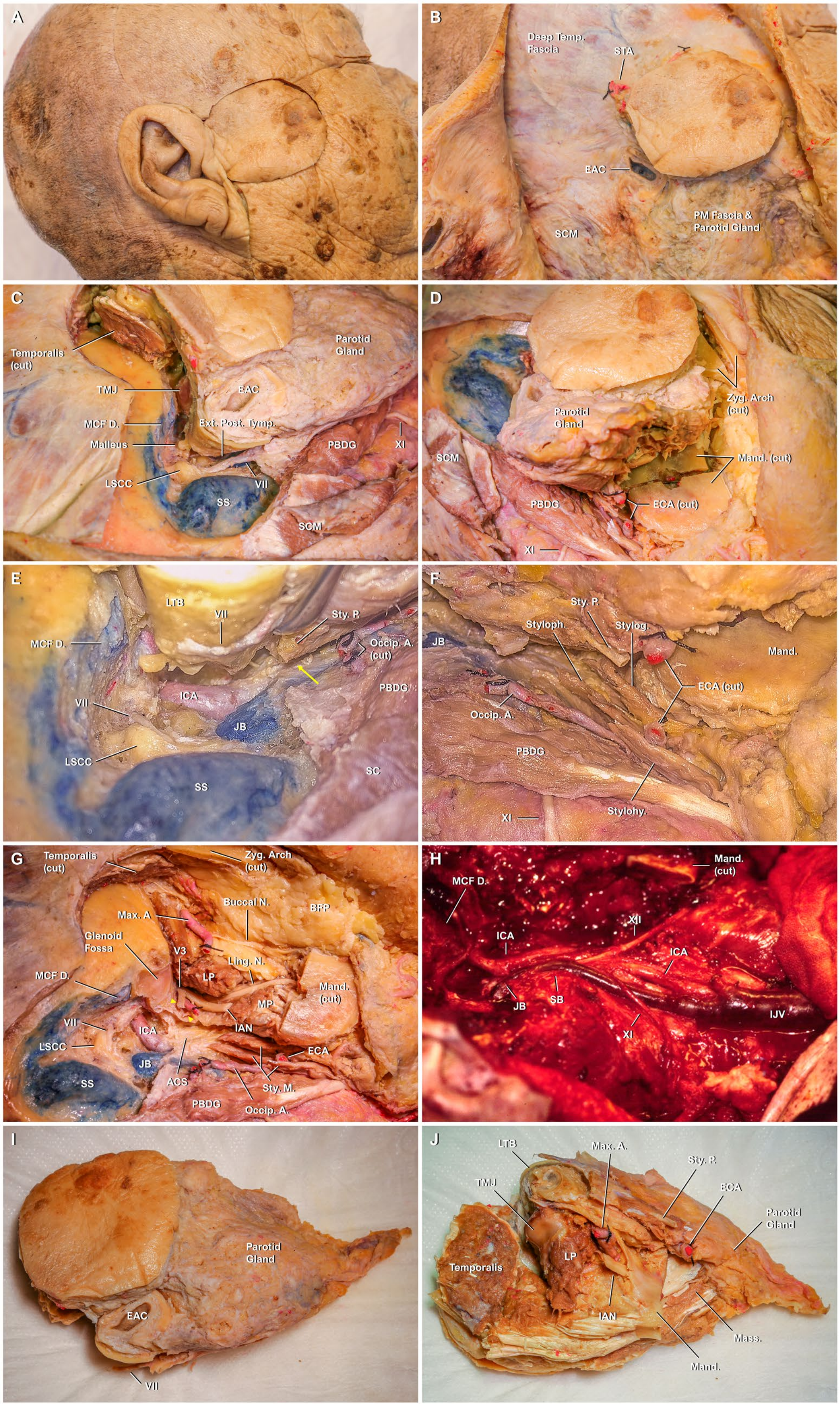

FIGURE 8 | Legend on next page.

wide local excision. Level 3 and 4 tumors only differed by their proximity to the styloid process and ACS. We previously used the styloid process as a surrogate marker for this fascial plane, given their known anatomical relationship and that the plane could only be visualized on MRIs performed more recently with higher resolution [14]. For tumors situated away (> 5 mm) from this plane (Level 3), dissection can proceed superficial to this thick fascia when resecting the soft tissue off the skull base, which protects the underlying major neurovascular structures from inadvertent damage. However, for tumors extending close (≤ 5 mm) to this plane (Level 4), the ACS should be resected to provide a deep fascial margin.

As the ACS is a thick layer with multiple fascial contributions, it may be adequate in some situations to only perform a partial resection, such as for tumors close to, but not abutting, the sheath. This is possible to achieve, as shown in Figure 8G, where resection of only its superficial TVSF/SPF layers has been performed. These layers were separatable from the deeper LCF/BPF layers on lifting the styloid process, which was also consistent with our previous experience dissecting frozen unembalmed cadavers [15]. This has the advantage of preserving IX which remains protected by the LCF/BPF until it emerges from the sheath 4 cm below the skull base [15]. However, this approach may not be oncologically safe for tumors abutting the ACS, and as such, resection of the entire fascial plane may be required. While the IJV, ICA, and the other lower cranial nerves can still be preserved with this approach, as IX pierces the fascia 9 mm below the skull base, this nerve will need to be sacrificed [15]. Nonetheless, before definitive recommendations can be made, further histopathological investigations need to be performed regarding the ACS, and its individual layers, forming an effective barrier to spread of malignancy.

Functional outcomes post iatrogenic or intentional IX transection have not been documented in the literature. However, post-operative dysphagia, dysgeusia, reduced oropharyngeal sensation/gag reflex, and aspiration have been reported in smaller studies and case reports of IX palsy post tonsillectomy

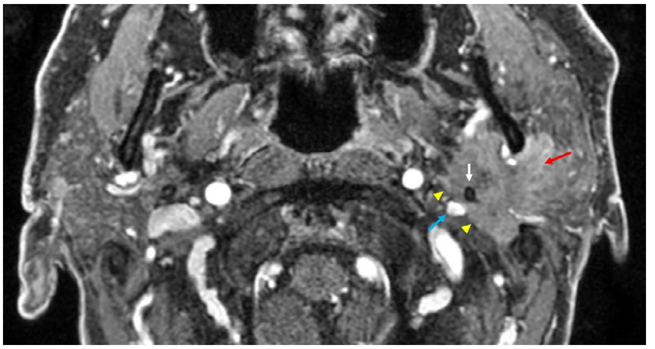

FIGURE 9 | Example of a Level 5 tumor. Axial T1 fat–suppressed post-gadolinium imaging demonstrating a left metastatic parotid cutaneous squamous cell carcinoma (*red arrow*) encasing the styloid process (*white arrow*) and extending through the anterior carotid sheath (*yellow triangles*) to abut the internal jugular vein (*blue arrow*). [Color figure can be viewed at wileyonlinelibrary.com]

FIGURE 8 | Level 4 surgical approach. (A, B) Skin incisions are made and flaps are raised as described in the above approaches. (C) A mastoidectomy and an extended posterior tympanotomy are performed. The epitympanum is opened through drilling of the zygomatic root and extended anteriorly until the temporomandibular joint is reached. The parotid gland is dissected along its inferior border, freeing it from the surrounding soft tissue. Superiorly, the temporalis muscle is divided low in the temporal fossa. (D) The anterior and inferior edges of the mandible are isolated by cutting through the masseter muscle. The periosteum covering the ramus and angle of the mandible is elevated, together with the overlying masseter and parotid gland. The external carotid artery is ligated at the point in which it emerges between the stylohyoid and styloglossus muscles, posterior to the mandible. Bony cuts are then made in the mandibular ramus, and if required, the zygomatic arch. (E) The facial nerve is transected in its mastoid portion, which widens exposure (as detailed in Figure 6) to allow completion of anterior drilling and liberation of the anterior tympanic plate. If required for access, further extension of the superior tympanotomy via drilling of the middle cranial fossa floor and elevation of intact dura can also be performed. Note that wide exposure of the petrous internal carotid artery, as demonstrated here, is not required. The jugular bulb and internal jugular vein are followed inferiorly toward the skull base through further drilling of the retrofacial air cells and hypotympanum. Depression of the vein can be performed to avoid inadvertent injury during this step. The anteriorly located styloid process is then freed from the vein and dissection proceeds medially (*yellow arrow*) deep to the styloid process and under the anterior carotid sheath. In this example, only the layers attaching to the styloid process (tensor-vascular-styloid and stylopharyngeal fascia) were resected. This allows for preservation of the glossopharyngeal nerve, which remains protected by the underlying longus capitis and buccopharyngeal fascial layers. (F) Antero-inferiorly, the stylohyoid, styloglossus, and stylopharyngeus are divided. The ascending mandible is freed from the lateral pterygoid and soft tissue, and branches of the maxillary artery are ligated, delivering the *en-bloc* specimen. If required, the infratemporal fossa can be incorporated into the resection for direct tumor invasion or perineural spread involving the auriculotemporal nerve, and combined with a craniotomy to resect the Gasserian ganglion for zone 2 perineural spread involving the mandibular branch of the trigeminal nerve. (G) The defect after resection (*yellow triangles* demonstrating the cut roots of the auriculotemporal nerve). Note that the two deep layers of the anterior carotid sheath remain in situ. (H) Resection can extend to include the entire anterior carotid sheath in cases of tumor abutment, as demonstrated in this patient example. The glossopharyngeal nerve has been sacrificed, which enters this fascia just below the skull base. (I) Lateral and (J) medial views of the excised specimen. A., artery; ACS, anterior carotid sheath; BFP, buccal fat pad; CS, carotid sheath; D., dura; EAC, external auditory canal; ECA, external carotid artery; Ext., extended; IAN, inferior alveolar nerve; ICA, internal carotid artery; IJV, internal jugular vein; JB, jugular bulb; Ling., lingual; LSCC, lateral semicircular canal; LP, lateral pterygoid muscle; LTB, lateral temporal bone; Mand., mandible; Mass., masseter; Max., maxillary; MCF, middle cranial fossa; MP, medial pterygoid muscle; N., nerve; Occip., occipital; PBDG, posterior belly of digastric muscle; PM, parotidomasseteric; Post., posterior; SB, skull base; SC, splenius capitis; SCM, sternocleidomastoid muscle; SS, sigmoid sinus; STA, superficial temporal artery; Sty. P., styloid process; Sty. M., styloid muscles; Stylohy., stylohyoid muscle; Stylog., styloglossus muscle; Styloph., stylopharyngeus muscle; Temp., temporal; TMJ, temporomandibular joint; Tymp., tympanotomy; V., vein; V3, mandibular branch of the trigeminal nerve; VII, facial nerve; XI, accessory nerve; XII, hypoglossal nerve; Zyg., zygomatic. [Color figure can be viewed at wileyonlinelibrary.com]

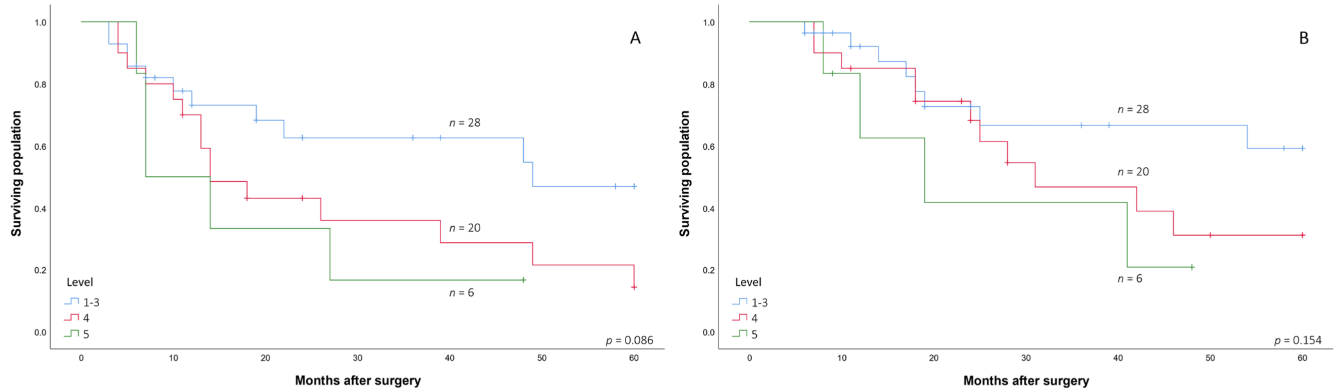

FIGURE 10 | Disease-free survival (A) and disease-specific survival (B) stratified by tumor Level, adapted from Schachtel et al. [14] [Color figure can be viewed at wileyonlinelibrary.com]

or carotid endarterectomy [33, 34]. As the underlying etiology in these cases was largely neuropraxia, most patients had spontaneous resolution of their symptoms with time, and thus it remains unknown whether the same functional outcomes would occur when the nerve is transected. However, in our experience, of the few patients who had intentional IX sacrifice, none developed any noticeable dysphagia or a requirement for enteral feeding.

The final group of patients (Level 5) were tumors involving or extending beyond the ACS. To achieve a clear surgical margin resection in this setting requires excision of the upper IJV, ICA, and/or lower cranial nerves. This is not performed at our institution, or others, due to the associated morbidity and lack of proven survival benefit [12, 20–23]. Because of this, as demonstrated in our previous study, all patients in this group had involved deep (or medial) surgical margins and trended toward higher recurrence and mortality rates (HR >2.5) (Figure 10) [14]. Additionally, PORT was not effective in controlling disease, with five out of six patients recurring despite all receiving their full prescribed dosage. The ACS can thus be considered an anatomical limit of resectability, and it may be in the best interest of these patients to not surgically resect and for alternative treatment options to be considered. This may be in the form of immunotherapy, which is being more routinely offered as a first line treatment for patients with advanced or unresectable disease. A recent phase 2 study investigating neoadjuvant cemiplimab for resectable cSCC revealed a complete pathological response in 51% of patients [35]. Given promising results also seen in other studies, we anticipate that immunotherapy will soon form an integral role in the treatment protocol of cSCC [36–41]. Combinations of definitive radiotherapy, EGFR inhibitors (i.e., cetuximab), and chemotherapy (i.e., platinum agents, 5-fluorouracil, taxanes, bleomycin) can also be considered in inoperable cases if contraindications to immunotherapy exist or there is a failure to respond [42]. Proton therapy may also play a role in these patients in the future, with the advantage of sparing adjacent structures from collateral dose, compared to traditional photon therapy [43, 44]. However, access to this technology is limited, and there remains no direct head-to-head trial comparing clinical outcomes for locally advanced unresectable cSCC.

In addition to the ACS, we also consider involvement of the upper IJV/jugular bulb, ICA, lower cranial nerves, zone 3 PNS, and extensive dural or brain invasion as unresectable disease, which is consistent with studies of primary temporal bone SCC [5, 12, 21–23, 45]. There should also be caution in treating patients with more extensive skull base erosion, as the temporal bone can act as a medium for often undetectable microscopic spread through bony canals and intra-osseous vessels. We have previously shown that all patients with bony EAC invasion had involved margins and significantly higher rates of recurrence (HR >4) than those with intact bone [14]. Zanoletti et al. also found that despite clear margins, 44% of patients with primary temporal bone SCC developed recurrences [46]. Thus, adequate oncological results may only be feasible for tumors that have limited, or no, bony involvement.

The limitations of this study are the relatively small number of cases examined, owing to the rarity of the disease process. Furthermore, these surgical approaches were based on radiological patterns of spread observed, and correlation to histopathological findings has not yet been performed. However, in our experience and of other authors, imaging is usually very accurate with a high degree of concordance for involvement of soft tissue, bone, and PNS, especially when CT and MRI are combined [4, 21, 23, 45, 47–51]. Additionally, as these proposed surgical approaches are based on retrospective analyses and anecdotal experience only, prospective studies implementing this protocol are required to demonstrate its true effectiveness at improving overall margin status and survival outcomes for these patients.

5 | Conclusion

Pre-auricular cSCCs extending to the temporal bone are advanced and aggressive tumors, with high rates of involved margins and poor survival outcomes. We have created a Level-based approach to the treatment of these malignancies, based on anatomical structural involvement and the medial spread of disease. This ranges from Level 1, which are tumors involving or abutting the EAC requiring LTBR ± superficial parotidectomy, to Level 4, which extend close to or abut the ACS necessitating resection of this fascial plane, in addition to a LTBR (and styloid process), radical parotidectomy, and partial ascending mandibulectomy. We also identified Level 5 tumors which involve the ACS at the skull base and carry high risk of residual disease and poor outcomes despite extensive surgery and PORT. Given this, these patients may be best treated with non-surgical interventions, such as immunotherapy or radiotherapy. We hope the proposed management protocol and surgical approaches can be instituted in further prospective studies, and improvements in prognosis are observed for these difficult to treat cancers.

Author Contributions

Michael Schachtel: conceptualisation, methodology, formal analysis, investigation, methodology, data curation, writing – original draft, writing – review and editing, visualization, project administration. **Mitesh Gandhi:** conceptualisation, methodology, investigation, writing – review and editing, supervision, project administration. **James Bowman:** conceptualisation, methodology, writing – review and editing, supervision, project administration. **Mark Midwinter:** conceptualisation, methodology, writing – review and editing, supervision, project administration. **Benedict Panizza:** conceptualisation, methodology, writing – review and editing, supervision, project administration.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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