Margin status (Core)

Reason/Evidentiary Support

Ideally, the resection specimen would be handed over from surgeon to pathologist directly for orientation and clarification of surgical margins. Failing this, the margins should be labelled by the surgeon and/or illustrated with a diagram. Specimens from endoscopic tumour resections should also be labelled. If the margins are sent separately, for frozen section or otherwise, identification of their site in relation to the resection specimen should be clarified by the surgeon. The surgical margins, both mucosal and deep, should be thoroughly sampled. A positive or close margin will usually result in postoperative radiotherapy and treatment associated morbidity at this site may be severe. Skin and bone margins may also require documentation depending upon the type of resection.

Evidence relating to margins at this specific site is lacking and therefore extrapolated from other head and neck sites, the oral cavity being the most studied. The literature would generally support 5 mm as a prognostically relevant pathologic **clear** margin.[1,2] This is best considered the minimum acceptable margin and is not a guarantee of lack of local recurrence which can be up to 25% with a clear margin.[2,3] Values ranging from 3 mm to 7 mm have been put forward.[1,4] In lower stage tumours, without other adverse variables, a margin less than 5 mm may be adequate[5,6] so that in considering adjuvant therapy, other features of the tumour must be taken into account. The evaluation of margins and the treatment choices should also be made considering the complex anatomy of this area. For example, a sinonasal adenocarcinoma can have pushing margins at the periorbital tissues without infiltration, and in this case no orbital exenteration is needed to achieve clear margins >5 mm.

There is no agreed-upon definition of what constitutes a **close** margin, as the effective cut off varies between studies depending upon anatomic subsite, tumour stage and other adverse pathologic variables.[7] Tumours with close margins carry an increased risk for local recurrence[1,7,8] but there is significantly better overall survival than for involved margins.[9]

Several studies support the definition of a **positive** margin to be invasive carcinoma at the margin[1,6,9] although <1 mm is also used.[10] Most studies also consider carcinoma in situ/high-grade dysplasia as a positive margin.[1] The presence of dysplasia at the margin is associated with a significant risk of local recurrence[11] and development of a second primary.[12] Information regarding the distance of invasive carcinoma, carcinoma in situ, or high-grade dysplasia from the nearest margin should be recorded where possible.

While there is no standard recommendation for the other histologic types of carcinoma, adherence to the recommendations for squamous cell carcinoma is acceptable.

References

1 Hinni ML, Ferlito A, Brandwein-Gensler MS, Takes RP, Silver CE, Westra WH, Seethala RR, Rodrigo JP, Corry J, Bradford CR, Hunt JL, Strojan P, Devaney KO, Gnepp DR, Hartl DM, Kowalski LP, Rinaldo A and Barnes L (2013). Surgical margins in head and neck cancer: a contemporary review. *Head Neck* 35(9):1362-1370.

2 Anderson CR, Sisson K and Moncrieff M (2015). A meta-analysis of margin size and local recurrence in oral squamous cell carcinoma. *Oral Oncol* 51(5):464-469.

3 Brandwein-Gensler M, Teixeira MS, Lewis CM, Lee B, Rolnitzky L, Hille JJ, Genden E, Urken ML and Wang BY (2005). Oral squamous cell carcinoma: histologic risk assessment, but not margin status, is strongly predictive of local disease-free and overall survival. *Am J Surg Pathol* 29(2):167-178.

4 Liao CT, Chang JT, Wang HM, Ng SH, Hsueh C, Lee LY, Lin CH, Chen IH, Huang SF, Cheng AJ and Yen TC (2008). Analysis of risk factors of predictive local tumor control in oral cavity cancer. *Ann Surg Oncol* 15(3):915-922.

5 Dik EA, Willems SM, Ipenburg NA, Adriaansens SO, Rosenberg AJ and van Es RJ (2014). Resection of early oral squamous cell carcinoma with positive or close margins: relevance of adjuvant treatment in relation to local recurrence: margins of 3 mm as safe as 5 mm. *Oral Oncol* 50(6):611-615.

6 Ch'ng S, Corbett-Burns S, Stanton N, Gao K, Shannon K, Clifford A, Gupta R and Clark JR (2013). Close margin alone does not warrant postoperative adjuvant radiotherapy in oral squamous cell carcinoma. *Cancer* 119(13):2427-2437.

7 Alicandri-Ciufelli M, Bonali M, Piccinini A, Marra L, Ghidini A, Cunsolo EM, Maiorana A, Presutti L and Conte PF (2013). Surgical margins in head and neck squamous cell carcinoma: what is 'close'? *Eur Arch Otorhinolaryngol* 270(10):2603-2609.

8 Bradley PJ, MacLennan K, Brakenhoff RH and Leemans CR (2007). Status of primary tumour surgical margins in squamous head and neck cancer: prognostic implications. *Curr Opin Otolaryngol Head Neck Surg* 15(2):74-81.

9 Sutton DN, Brown JS, Rogers SN, Vaughan ED and Woolgar JA (2003). The prognostic implications of the surgical margin in oral squamous cell carcinoma. *Int J Oral Maxillofac Surg* 32(1):30-34.

10 Dillon JK, Brown CB, McDonald TM, Ludwig DC, Clark PJ, Leroux BG and Futran ND (2015). How does the close surgical margin impact recurrence and survival when treating oral squamous cell carcinoma? *J Oral Maxillofac Surg* 73(6):1182-1188.

11 Jerjes W, Upile T, Petrie A, Riskalla A, Hamdoon Z, Vourvachis M, Karavidas K, Jay A, Sandison A, Thomas GJ, Kalavrezos N and Hopper C (2010). Clinicopathological parameters, recurrence, locoregional and distant metastasis in 115 T1-T2 oral squamous cell carcinoma patients. *Head Neck Oncol* 2:9.

12 Slootweg PJ, Hordijk GJ, Schade Y, van Es RJ and Koole R (2002). Treatment failure and margin status in head and neck cancer. A critical view on the potential value of molecular pathology. *Oral Oncol* 38(5):500-503.