



REVIEW

The uncertainty of the surgical margin in the treatment of head and neck cancer

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Received 10 July 2006; accepted 1 August 2006

Available online 16 November 2006

KEYWORDS

Surgical margin;
Head and neck cancer;
Decision making;
Oncology;
Philosophy;
Surgery;
Head and neck surgery;
Maxillofacial surgery;
Plastic surgery

Summary We discuss our surgical philosophy concerning the subtle interplay between the size of the surgical margin taken and the resultant morbidity from ablative oncological procedures, which is ever more evident in the treatment of head and neck malignancy. The extent of tissue resection is determined by the "trade off" between cancer control and the perioperative, functional and aesthetic morbidity and mortality of the surgery. We also discuss our dilemmas concerning recent minimally invasive endoscopic microsurgical techniques for the trans-oral laser removal or co-ablation of aero-digestive tract tumours, which result in a minimal surgical margin of oncological clearance. By a process of inductive argument as to the nature of the surgical margin, we consider whether the risks of taking a lesser margin with adjuvant therapy is justified by the attendant gain in reduced surgical morbidity and the possible costs in tumour control.

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Introduction

In the past resection of head and neck malignancy was often limited by the difficulties of reconstruction using pedicled tissue flaps. With the advent of free tissue transfer and

reconstructive capability, this situation has changed and the limiting factor is overwhelmingly oncological clearance with regard to morbidity.

The fundamental surgical goal is that of complete tumour resection. How does the surgeon ensure this? It is a common and convenient assumption that tumours are homogeneous and have a rectilinear edge. It was supposed that malignancy stopped at a visibly defined border and the surgeon simply had to cut along the 'dots', whilst leaving an adequate margin for error. This philosophy belies several flaws including two-dimensional thinking but contains an underlying empirical truism that tumours should be removed as completely as possible. With empiricism in mind, we shall discuss the 'all important' issue of the uncertainty of the 'surgical margin'.

The purpose of curative oncological surgery is primarily to remove all local malignant disease and leave no residual viable tumour cells.¹ However, excision implies a distinction between regions, a discontinuity; unfortunately, tumours may exist along continuous lines. Given the need for the surgical removal of a solid tumour it has long been accepted that local control is better if the removal of surrounding tissue is maximized i.e. "more is better".²

In general terms, the indicator of the completeness of surgical removal is the margin of uninvolved tissue around an exposed neoplasm. The enigma of this surgical margin applies to nearly all solid tumours and their management. How generous this margin should be has not been defined for all forms of cancer or selected classes of malignancy. Tumour site, anatomical restrictions, presumed biological characteristics of the cancer, the respective advantages of conservation and extended surgery affect the adequacy of surgical resection. There is little doubt, that residual cancer will yield local persistence and nearly always an increased mortality.³⁻⁶ Despite the use of post-operative adjuvant therapy the risk of recurrence associated with an initially positive margin is always greater than that of a negative margin. However, the effect of leaving positive margins is not entirely predictable.

In one study with head and neck cancer, patients with positive margins were followed up and at 5 years, over a third were alive and disease free and over half of these patients did not have local recurrence perhaps due to local tissue ischemia as a result of post-operative scarring or micro-environmental immune changes in favour of the tumour host.^{7,8}

The "positive/negative" status of the margin is the most significant histo-pathological predictor of recurrence at the primary site. In clinical practice, the true histological limit of the tumour is unknown, as the specimen would have to be sampled many times to be confident of absolute histological clearance.

The minimalist approach using very narrow surgical margins which are at least histologically clear has resulted in equal if not better oncological control rates as compared with more radical resections.⁹⁻¹¹ It has been postulated this effect is the result of both minimizing the impairment of endogenous tumour inhibitors (such as the immune response) and reducing the effect of surgically induced release of tumour facilitators (such as wound healing growth factors e.g. EGF, tissue plane breaches). Such minimalist resection is also associated with less impairment of global

function. This work challenges the "more is better" approach of excision.

The upper aero-digestive tract is bathed in a milieu including carcinogens.^{12,10,13} It may not be accurate to assume that malignancy develops in just one cell. There may be several foci of cancer giving some mucosal cancers multi-centricity i.e. multiple primaries. However, one cell line or clone will become dominant through natural clonal selection and have a suppressive effect on other clones, which may then not develop full malignant potential. Hence, a malignancy may be surrounded by a corona of potentially malignant heterogeneous sub-clones that during suppressive entrainment by the main mass do not exhibit all the phenotypic characteristics or histological appearances of malignancy. There may even be a gradient of malignancy.¹⁴⁻¹⁷ This is borne out by the fact that immunohistochemical studies have revealed positive staining for markers of genomic alteration associated with malignancy (P53, eIF4.etc) in histologically negative surgical margins which are later correlated with a high recurrence rate.^{3,14,18-23}

For the above reasons, the edge of a malignancy is difficult to define and far from being a rectilinear 'all or nothing phenomenon' its nature is more probabilistic (along a one tailed Gaussian distribution). At its simplest a tumour can be regarded as being surrounded by a three dimensional "atmosphere" of malignancy. The more 'standard deviations' of distance the surgical margin is from the tumour bulk the lower the probability of remaining viable tumour cells. This margin is further blurred by three dimensional stereometric sampling errors in observations and the presence of favored and unfavored anatomicophysiological sites allowing rapid or slow tumour progression or sequestration, e.g. tumour skip lesions (mucosal surfaces) and embolisation (along nerves or vessels), or 'outliers' in statistical terms.²⁴⁻²⁶

Discussion

Factors affecting the surgical margin

The effect of the size of the primary tumour on the margin and metastasis: The larger the primary lesion (T stage) the higher local recurrence rates and mortality even with surgically free margins.^{27,28} Despite this 5-10% of carcinomas resist the goal of clear margins regardless of T stage at surgery. This may be due to the fact that positive tissue (severe dysplasia, in-situ carcinoma, invasive carcinoma) within 0.5 cm of a surgical margin places a patient at nearly equal risk for local recurrence which is associated with almost 80% incidence of recurrent disease at the primary site compared with 32% of patients with negative margins.²³

The surgical margins for upper aero-digestive tract squamous cell carcinomas vary widely because there is both a site dependency on the ability of the surgeons to obtain tumour free margins and a site specific significance of involved or uninvolved limits of the excision. This variation relates more to the biological and anatomical environment of the tumour site at macroscopic and microscopic levels, than due to purely intrinsic biological differences in the

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