Microendoscopy: a clinical reality in intra-operative margin analysis of head & neck lesions

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Abstract

Introduction
The tumour margin is an important surgical concept that significantly affects morbidity and mortality. We describe the clinical application of intraoperative microendoscopy in defining the surgical margins during head and neck surgery.

Method
A clinical margin is first marked by the operator followed by microendoscopic assessment of this margin. Biopsies are taken from areas suggestive of close or positive margins on microendoscopy. The histological margins are further analysed formally and the resection revised accordingly if necessary.

Discussion
The advantages of this technique is that a large area of mucosa can be sampled whose histomorphological changes can be visualised in real time allowing the operator to make important informed decisions regarding the resection margins at the time of surgery. Shrinkage, thermal and orientation artefacts are also avoided.

Conclusion
We have developed the use of the microendoscope to aid intra-operative decision making during surgery.

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Methodology

Background (Cont.)

A microendoscope is used to obtain an accurate microscopic assessment at the time of clinical examination, to inform the surgical decision as to the nature of the cellular characteristics of the mucosal lesion and its edge aiding biopsy yield and excision margin. Microendoscopy allows "in vivo" and "in situ" examination of the epithelium. The scope allows the monitoring of the whole mucosal surface both normal and pathological, and allows the detection of patterns specific for pathology e.g. inflammation, metaplasia, dysplasia, and neoplasia. The advantages of the scope are that once the microendoscope is acquired at relatively low initial cost it is used like any autoclavable Hopkins rod, and maintenance costs are similarly low. The scope can be used to guide further surgery, biopsy or simple surveillance of large areas of suspect mucosa. The microendoscope enables on table analysis to inform one’s choices of further surgery even when biopsy (frozen section) is not available.

We present the head & neck surgical oncologist with a workable protocol for the use of the microendoscope in the assessment of the margins of excised lesions.

Method

“Written informed consent was obtained from the patient for publication of this report and any accompanying images.” Institutional ethical approval was obtained. The operating Storz Hopkins II autoclavable microendoscope (Figure 1), is attached via an adapter to a camera system (3 chip Olympus\Sony) linked via a video recorder with outputs to a monitor and photo-printer. Video encoding was done, in the main by, using a Xenon-light source (Karl Storz 300 attached via a Storz fibre optic cable), a 3 CCD camera (Karl Storz Tricam) and a Sony DV Cam system (DSR-20P) that enable a high resolution playback. Static documentation was performed in the form of simple photography (sony printer/dpi) as well as dynamic (in the form of a video-clip, stored in a DV magnetic tape, which required editing). High quality photographic images can also be extracted from the edited video. The scope is available in different sizes which can be used for different anatomical sites; the dimensions of the microendoscope were 5.5 mm diameter and 23 cm long and the vital stain used is Methylene blue. The microendoscope scope has a fitted rotating screw which allows magnification to be changed from 0x to 60x to 150x, minor movements permit focussing and de-focussing at specific depths of field. The clinician would, having prepared the patient, mark out his proposed margin for excision (Figure 2). The generalised area would be surveyed at 0x magnification, until an area of abnormality is found; this would then be examined at 60x and then 150x. Examination would always proceed from an area of normality (Figure 3) to abnormality (Figure 4); the whole of the surface of the lesion would be reviewed to determine any heterogeneity. The microendoscopic margin of the lesion would then be delineated and any areas of discrepancy between the clinical and microendoscopic margin were photo-documented. The clinician would excise the lesion, which would be sent for frozen section analysis as would be the noted areas of discrepancy between the clinical and microendoscopic margin. A later analysis is made between the histological photomicrograph and microendoscopic image. When frozen section is not available a microendoscopic margin is taken and the biopsy sent for formal histological analysis.

Figure 1: Storz HopAkins II autoclavable microendoscope

Figure 2: Clinical margin of oral lesion

Figure 3: Normal mucosal histology of previous lower margin (200x)

Figure 4: Abnormal histological features in right mucosal margin (150x)
Methodology

After suction clearance, the tip of the microendoscope is firmly applied to the pre-stained (0.1% Methylene blue) area of interest to obtain an occlusive contact and then moved for dynamic assessment of the lesion (Figure 5), its margins, the local tissue and the underlying mucosal vasculature and blood flow. The examination is found to be reproducible between operators. Staining is repeated if further assessment is required (Figures 6 and 7).

**Table 1** Diagnostic criteria assessed to determine abnormality

<table>
<thead>
<tr>
<th>Level</th>
<th>Criteria</th>
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<tbody>
<tr>
<td>Cellular</td>
<td>Cell: seen in longitudinal tissue plane rather than transverse/depth</td>
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<tr>
<td></td>
<td>Cellular morphology, expected histology</td>
</tr>
<tr>
<td></td>
<td>Nuclear staining pattern: orientation, size, shape, limits</td>
</tr>
<tr>
<td></td>
<td>Nucleolar staining morphological pattern, orientation</td>
</tr>
<tr>
<td>Tissue</td>
<td>Cell-cell regularity</td>
</tr>
<tr>
<td></td>
<td>Extracellular matrix: homogenous, heterogeneous</td>
</tr>
<tr>
<td></td>
<td>Margin: discrete, blurred</td>
</tr>
<tr>
<td></td>
<td>Underlying cells, micro-vessel density</td>
</tr>
</tbody>
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Adverse microendoscopic predictors of abnormality (Table 1) would include the presence of a large nuclear to cytoplasmic ratio in cells together with evident bizarre shaped nuclear staining and the presence of numerous mitotic figures per field, punctate staining of cells and the heaping up of bizarre sheets of stained cells suggesting rapid cell turnover. There may even be pseudo-tissue borders in unexpected sites e.g. not at traditional squamo-columnar junction sites. By using these criteria, it should be possible to obtain a high sensitivity and specificity in determining abnormal mucosa compared to formal histopathological examination.

Forty patients undergoing resection of oral squamous cell carcinoma were recruited by Upile et al. The surgical margin was first marked by the operator followed by microendoscopic assessment. Biopsies were taken from areas suggestive of close or positive margins after microendoscopic examination. These histological samples were later scrutinized formally and the resection margins revisited accordingly when necessary. Using the microendoscope, Upile et al. reported their experience in the determination of surgical margins at operation and later comparison with frozen section and paraffin section margins “gold standard”. They were able to obtain a sensitivity of 95% and a specificity of 90%. Inter-observer Kappa scores comparing the microendoscope with formal histological analysis of normal and abnormal mucosa were 0.85.

The same group used microendoscopic technique for microvascular monitoring of free autologous jejunal flap by the direct visualisation of the flow of erythrocytes through the capillary vasculature on both the mucosal and serosal surfaces. Blood flow was seen to be pulsatile, with individual erythrocytes visible in the capillaries. The best view was obtained when the scope was focussed directly on the capillary rather than the graft surface. The view of the unstained mucosal surface was bland apart from the fine capillary loops which were seen to fill with each pulsatile event. The microendoscopic examination of the

**Discussion**

Microendoscopic assessment of mucosal lesions can act to inform the surgical decision regarding the nature of the cellular characteristics of a lesion and its edge, aiding biopsy yield and the adequacy of the laser excision margin.

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serosal surface revealed much larger calibre vessels with obvious blood flow.

A fundamental knowledge of regional histology and pathology is obviously assumed on part of the clinician. We feel there must be a high degree of cooperation between the surgeon and histopathologist. Perhaps initially correlating microendoscopic still or video footage with formal histology slides until confidence is gained. This correlative exercise should continue until a measure of proficiency is gained in topographical histopathologic interpretation. Local specificity and sensitivity in detecting areas of abnormality should be ascertained to develop skills of having a raised index of suspicion of when to biopsy.

The potential pitfalls of the technique are that it is a new skill and the equipment is still relatively expensive (although costs could be offset against the saving of potentially residual disease and failed grafts). Costs can be reduced by the local manufacture of the various adaptors necessary to connect the microendoscope to existing camera systems (Laparoscopic, Cystoscopic, Otolaryngological).

The disadvantages of this technique are that the microendoscope does not provide three dimensional information to provide depth of invasion however this may be ascertained by a series of ‘MOHR’S’-like 2 dimensional analyses using the microendoscope. A degree of depth field information may be obtained by varying the focus to allow visualisation of underlying structures cells or blood vessels. Despite this, cellular details can be determined up to tens of cell layers deep depending on illumination. Intra-wound interpretation using the microendoscope for assessing deep margins is difficult and requires a thorough understanding of the topographical histopathological appearance of the area especially when observing the oblique cuts made with excision. It also requires the surgeon to have an intimate knowledge of the histology of the area on which they are operating.

The technique of microendoscopy will no doubt be improved by advances in optical systems, illumination, recording and image processing. The microendoscope has a range of exciting applications in Oral Medicine, Otolaryngology, Oral & Maxillofacial Surgery and Plastic Surgery; however the main advance with the scope is that we have more informed choice of the state of the in situ epithelial margin taken when excising squamous cell carcinoma. We found that the microendoscopic examination of lesions had great utility in the excision of mucosal lesions. This combined with the recent advancement of vital or immunologically tagged antibody targeted staining will advance the type of surgical margin we take from the standard clinically visible margin to that of a histopathological margin during surgery.

Conclusion

We describe the clinical application of this once orphan technology and provided a practical guide to its everyday use by the surgeon both in the clinical and surgical fields. The advantages of this technique is that a large area of mucosa can be sampled whose histomorphological changes can be visualised in real time allowing the operator to make important informed decisions with regards the intra-operative resection margin at the time of the operation. Shrinkage, thermal and orientation artifacts are also avoided. For the technique to be successful the surgeon, pathologist and cytopathologist will need to be familiar with the subtleties of microendoscopy and this will require close collaboration between specialties.

References