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## The validity of surgical clips as radiographic markers for the tumour resection cavity in head and neck cancer treatment

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#### A R T I C L E I N F O

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#### ABSTRACT

*Background:* A prerequisite of irradiation after advanced head and neck tumour resection is the accurate localization of the tumour resection margin. The purpose of the following study is to evaluate the use of surgical clips placed in the tumour resection margins for use as radiographic markers to facilitate focussed adjuvant radiation therapy.

*Materials*: To evaluate whether the clips remain predictive for the resection margin, we analysed the deviation of each clip in two postoperative CT scans on different days. Bone registration points were used to fuse the two CT scans in the region of the primary tumour and the distances between corresponding clips were measured.

*Results:* The tumour resection margins were labelled with an average of 18 titanium clips. In total 282 clips were evaluated. Metric analysis of clip deviation between the two postoperative CT scans found a mean distance of 4.5 mm  $\pm$  2.5 mm with a range of 0.5–11.8 mm. No significant statistical relationship of the clip differences as a function of time, the method of reconstruction or administered radiotherapy could be demonstrated.

*Conclusion:* Placement of surgical clips in the cavity walls after complete tumour resection provides an easy and inexpensive approach for defining resection margins and allows for increased accuracy of adjuvant treatment.

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#### 1. Introduction

The treatment of malignant tumours of the head and neck requires an interdisciplinary approach combining surgery and radiotherapy. After complete tumour resection of advanced oral squamous cell carcinoma (SCC), defect coverage relies heavily on microsurgical free flap techniques (Hohlweg-Majert et al., 2012). Furthermore, therapy of SCC frequently mandates the use of adjuvant irradiation. Postoperative radiotherapy of head and neck malignancies improves local tumour control but is associated with increased morbidity due to irradiation of non-target tissue (Lavaf et al., 2008; Geretschlager et al., 2012). An essential prerequisite for adjuvant radiation is accurate localization of the surgical excision cavity, the former tumour bed. Visualization and delineation of the tumour resection margins are crucial to adjuvant radiation planning, because treatment can then be confined to a limited volume of head and neck tissue adjacent to the tumour cavity.

Generally, tumour bed localization is performed using preoperative and postoperative radiological imaging, surgical annotation, clinical investigation of the surgical defect, and pathohistological annotations. Additionally, identification of the tumour bed using computer tomography (CT) and magnetic resonance imaging by delineating the interface between native tissue and free flap grafts has been attempted, but boundaries are often difficult to identify and do not allow the precise localization of the former tumour bed in the majority of patients (Nemeth et al., 2000; Coles et al., 2009;

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Yang et al., 2013). In this situation, labelling the tumour bed with titanium ligature clips has been found to be useful (Bittermann et al., 2013).

Radio-opaque markers attached to the excision cavity walls in combination with 3D imaging techniques overcome some of the difficulties in tumour bed delineation and are most commonly reported in breast cancer surgery since 1993 (Bedwinek, 1993). A consensus exists for the use of surgical markers, regardless of whether titanium clips or gold seeds are used, to improve the quality of postoperative radiotherapy of the breast (Coles et al., 2009; Kirby et al., 2013).

Markers of the surgical cavity provide additional local information compared with CT images alone, and can lead to modification of field borders in irradiated patients (Coles et al., 2009; Kirby et al., 2010a, 2010b). Several authors have demonstrated the importance of demarcating the resection cavity with surgical clips in order to reduce the risks of a geographical miss and unnecessary normal tissue irradiation (Bedwinek, 1993; Krawczyk and Engel, 1999). However, whether surgical clips remain predictive of the head and neck tumour resection cavity throughout therapy is not yet established.

We hypothesise that surgical clips placed in the excision cavity after tumour resection can be used as radiographic markers to facilitate improved adjuvant radiation therapy. The objective of this study is to analyse possible clip migration, in a prospective study, in 16 patients as part of their cancer follow-up.

### 2. Material and methods

A total of 16 patients with surgically placed clips outlining the tumour excision cavity were prospectively evaluated at the University of Freiburg, Germany, in the Department of Oral and Maxillofacial Surgery and Regional Plastic Surgery. Ethical approval was obtained before undertaking this study. Written informed consent was obtained from all study patients.

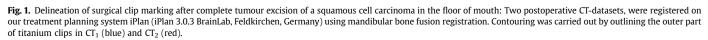
All patients underwent tumour resection, neck lymph node dissection and tumour bed marking with titanium ligature clips in one stage by the same oral and maxillofacial surgical team.

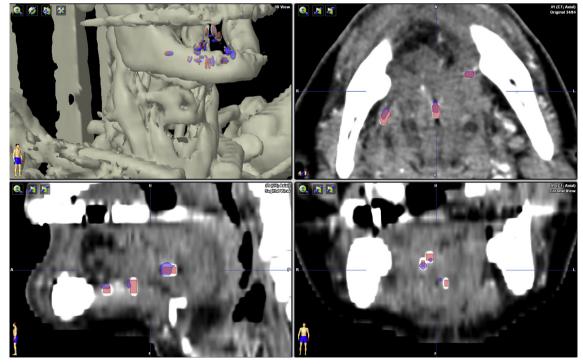
Following complete local excision of the primary tumour, the tumour bed was marked with radio-opaque titanium ligature clips (Ethicon Endo-Surgery, Ligaclip Extra Titanium Medium, Cincinnati, OH, USA). All patients had titanium clips placed immediately after tumour ablation and before tissue reconstruction; each excision cavity boundary was defined by clips positioned at the deep, superficial, medial, lateral, inferior and superior boundaries. In cases of extensive tumour growth or irregularly formed tumour delineation, additional clips were placed in the cavity walls before plastic remodelling. The number of inserted clips was recorded for each patient. The first postoperative CT scan  $(CT_1)$  was performed at least 3 weeks after surgery to avoid postoperative changes. The number of titanium clips identified on CT scan and their x, y and zcoordinates were recorded. Successful use of the clips was defined as unique identification of all clips with their location expressed in x, y and z-coordinates. Segmentation was carried out by outlining the outer part of titanium clips on each CT slice.

An additional CT scan ( $CT_2$ ) was carried out due to regular postoperative follow-up or radiation planning and the entire contouring process was repeated.  $CT_2$  was performed in the treatment position determined during the first CT scan. The time between  $CT_1$ and  $CT_2$  was recorded.

The two sets of images, were registered on our treatment planning system, iPlan (iPlan 3.0.3 BrainLab, Feldkirchen, Germany), for each patient, using bone fusion registration based on mutual information in the region of the primary tumour (Fig. 1).

The segmented and registered clips of  $CT_1$  and  $CT_2$  were imported in a common coordinate system (Rapidform XOR; Inus





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