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PREOPERATIVE PLANNING FOR SIMULATION OF SURGICAL MARGINS IN MAXILLECTOMY: A SYSTEMATIC REVIEW

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ABSTRACT

PURPOSE: To present the new developments in preoperative and intraoperative assessment of surgical margins in maxillectomy and highlight techniques developed for computerized simulation of surgical margins using different imaging modalities, by way of a systematic review.

MATERIALS AND METHODS: An electronic search was conducted using the terms "maxillectomy", "surgical margins", "imaging" and "surgery" in combination with the following search strategy: **Search block Maxillary Neoplasms -** ("Maxilla"[Mesh] OR "Maxillary Neoplasms"[Mesh] OR "Maxillary Sinus Neoplasms"[Mesh] OR "Maxillary Sinus"[Mesh] OR maxillectomy*[tiab] OR maxilla resection*[tiab]); **search block Margins of excision -** ("Margins of Excision"[Mesh] OR surgical margin*[tiab] OR excision margin*[tiab] OR resection margin*[tiab] OR tumor-free margin*[tiab] OR line[tiab] AND resection [tiab] AND validation[tiab]); **search block Maxillary cancer -** (maxilla*[tiab] AND ("Neoplasms"[Mesh] OR neoplasm* [tiab] OR tumor [tiab] OR tumors[tiab] OR tumorous [tiab] OR tumour* [tiab] OR cancer* [tiab] OR lymphoma* [tiab] OR malignancy* [tiab] OR oncology* [tiab] OR carcinoma* [tiab]). Clinical studies up to June 2017 were retrieved from the electronic databases of PubMed, EMBASE and SCOPUS, which provided relevant information in relation to oncological disease managed with help of preoperative surgical simulation for maxillectomy and sinonasal cancer. References of the selected articles were further searched for important relevant studies. Apart from this, a search was conducted over Google Scholar to obtain related articles.

RESULTS AND CONCLUSION: Treatment planning for major surgical procedures involving surgical intervention for cancer of the maxilla, has greatly evolved over the last few decades. Preoperative planning and surgical simulation help to decrease the incidence of positive margins after a maxillectomy, making surgical treatment more accurate. Furthermore, surgical resections have been made possible for advanced sinonasal malignancies by reducing the morbidity of injury to adjacent critical vital structures.

Keywords: Imaging, Maxillectomy, surgery, surgical margins.

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INTRODUCTION

Reports on the history of maxillectomy are very scarcely evident in the literature. There are hints that Dupuytren and Gensoul performed total maxillectomies as early as 1820 and 1824,[1] respectively. Syme performed a successful maxillectomy in 1828.[2] However, there is little detail available on the extent of operations performed or the conditions treated. According to a report by Myhre and Michaels,[1] Liston performed the typical standard maxillectomy in 1841. However, the most popular maxillectomy procedure recorded in history was that performed for treatment of President Cleveland in 1893.[3,4]

Onhgren[5] gave the classical description of "suprastructure" and "infrastructure" tumours in 1933. This classification provides efficient clinical staging for maxillary tumours in the present era as well. Elaborate studies on preservation of orbital contents were published by Larson,[6] Perry[7] and Stern.[8] Donald PJ[9] (1998) described the various extensions of the maxillectomy procedure for management of tumours demonstrating invasion towards the orbit and / or skull base.

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Malignancy of the nasal cavity and paranasal sinuses is rare, comprising 3% of the cancers of head and neck. Amongst the cases involving paranasal sinuses, maxillary sinus exhibits the highest percentage of afflictions, accounting for 35.9% of all cancers affecting the nose and paranasal sinuses. Of the remaining, about 43.9% are localized to nasal cavity, 9.5% in ethmoid sinus, 3.3% in sphenoid sinus and 1.1% in frontal sinus.[10,11] While squamous cell carcinoma is the most common malignancy affecting the maxillary sinus, several other histologic types of tumours have been reported, which include minor salivary gland malignancies, sarcomas, melanomas and undifferentiated carcinomas. Although multiple therapeutic approaches have been proposed for the management of such cases, surgical resection with postoperative radiotherapy has shown the best outcomes.

Hordijk et al[12] (1985) presented a retrospective study of 96 patients in order to evaluate the indications for massive surgery (maxillectomy and orbital exenteration) in malignancies of maxillary sinus. The absolute 5-year survival in patients treated for cure was 51%. The authors recommended that if patients are treated for cure in order to achieve clear surgical margins, major surgery is necessary which may be combined with radiotherapy. Correspondingly, Choi et al[13] (2004) conducted a retrospective analysis for investigating the surgical outcomes of radical maxillectomy in advanced cancers of maxillary sinus invading through the posterior wall. 28 patients were included, who were suffering from squamous cell carcinoma of the maxillary sinus. 9 cases were T3 and 19 were T4. The surgical management involved total maxillectomy in 12 cases (42.9%) and radical maxillectomy in 16 cases (57%). Radical maxillectomy was performed regardless of staging whenever the cancers invaded through the posterior wall. 2-year disease-free survival rate was 75% for both total and radical maxillectomy, while the local recurrence rates were 8.3% and 18.7% respectively. The authors concluded that radical maxillectomy is the best treatment for all cases of advanced maxillary cancers which exhibit invasion through the posterior wall because this procedure can provide sufficient resection margins and hence lower recurrence rates.

Similar results were reported by Kohler et al[14] (2010) who conducted a retrospective analysis of 96 patients to define prognostic factors for maxillary squamous cell carcinomas and to propose a new surgical staging. These patients were treated at a single institution between 1985 and 2005. 24 patients underwent surgery alone, 43 underwent surgery with postoperative radiotherapy and 29 were treated by radiotherapy alone. In the surgically treated patients, a multivariate analysis revealed that only the involved surgical margins remained significant for survival. No significant association was found in the radiotherapy group. However, patients in surgery group demonstrated a better survival as compared to radiotherapy group (p=0.0032). The authors concluded that surgical treatment should be considered the first line option for management of sinonasal malignancies. In congruence, Poeschl et al[15] presented a retrospective study in 2011. Records of 95 patients with squamous cell carcinoma of maxillary sinus were analyzed to evaluate the influence of T staging, grading and surgical margins on survival outcomes. Most patients (66%) exhibited a T4 staging while the nodal staging was N0 in 42% of cases. The histopathological grading was G2 in 57% of cases, G3 in 22% and G1 in 21%. The 5-year overall survival rate was 71% while the rate of recurrence was 37%. The authors concluded that advanced stage T4 and grading did not significantly influence the cumulative survival rates. However, the most critical factor for prevention of recurrence was negative resection margins.

Nonetheless, local recurrence is the most persistent factor responsible for failure of treatment, the risk ranging from 35% to 80%. This is due to the high rates of positive surgical margins associated with maxillectomy.[16] Although obtaining negative surgical margins is the goal of all oncosurgery, it is not feasible in some cases of head and neck. This is especially true in relation to maxillectomy, due to the proximity of many vital anatomical structures such as the cranial nerves, the eye and the brain. It has been this underlying reason, which precludes achievement of negative margins for cancer of maxillary sinus.

The answer to this problem lies in accurate preoperative planning. Various techniques of preoperative surgical simulation have been reported from high-volume oncology centers throughout the world. The factor common to all is the resultant decrease in percentage of positive margins. The planning could be based on different imaging techniques but the overall goal remains the same, i.e., accurate delineation of the line of resection. The following discussion will focus on the preoperative imaging technique for planning the line of resection in cases of maxillectomy.

PREOPERATIVE PLANNING FOR PLANE OF RESECTION:

3D virtual planning is based on preoperatively acquired CT and/or MRI images. While CT imaging provides accurate segmentation of bony

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structures, MR images are required to reveal soft tissue details, such as tumour expansion and invasion information, i.e. tumour delineation. These images are subjected to multimodality image fusion with the help of especially constructed softwares (Eg. The Mirada, by Mirada Medical, Oxford Centre for Innovation, United Kingdom).
After storing all imaging data into acquisition softwares such as Mirada, 3D virtual planning is performed with help of 3D planning software (eg. ProPlan CMF 2.0 – Materialise, Leuven). If MR imaging data has been obtained preoperatively for soft tissue delineation, then the 3D tumour volume calculated by MR imaging is translated to 3D plan based on the CT file, using a compatibility algorithm (for eg. Matlab – Mathworks, Natick, MA, USA). After all image processing, the final information can be stored and used as DICOM digital dataset for surgical planning and execution.
An alternative to using the three software technique is commercially available, ready-to-use navigation systems such as iPLAN (Brainlab, Medtronic; Germany) or Eclipse (Varian Medical Systems).

TECHNIQUES FOR SURGICAL SIMULATION AND COMPUTER ASSISTED SURGERY:

A - ICTGS - intraoperative computed tomographic guidance system :

Homma et al[17] (2008) described the use of intraoperative computed tomographic guidance system (ICTGS) for maxillectomy. The ICTGS is a real-time correlation of the operative field with a preoperative imaging dataset, which shows the precise location of a surgical instrument in relation to the surrounding structures. The study involved five patients with malignancies of maxillary sinus – three with squamous cell carcinoma, one with adenoid cystic carcinoma and another one with lieomyosarcoma. CT scans were obtained for all these patients, comprising non-overlapping axial cuts of 1 mm thickness. Fiducial markers were used during the scanning process, but headsets were not worn. These images were transferred to Stealth Station® ICTGS system (Medtronic) with help of an optical disk. After induction of anaesthesia, a headset was placed. The calibration of surgical hand piece was done by placing the tip of the instrument into a divot on the headset light emitting diode (LED) array while the foot pedal was depressed. The registration was made by correlating the anatomic surface fiducials and fiducial markers with the corresponding points on CT images. The registration process spanned over an average of 10.2 minutes (range 10 -12 min.). The average accuracy for the entire series was 0.95 mm (range – 0.6 -1.19 mm). Such accuracy was maintained in all cases throughout the operation. This helped the surgeon to decide upon the extent of removal in real time.
The ICTGS system showed extraordinary benefits when the resection was done at level of zygoma, frontal process of maxilla, orbital floor and the pterygoid process. All these patients exhibited disease-free survival during the follow-up period (median of 28 months, range = 19-57 months). The ICTGS reveals 3D anatomy of normal facial structure, as well as the location of tumour intraoperatively, thus aiding to determine the accurate line of dissection and resection.

Comments and Description:

It is pertinent to elaborate the technique employed in ICTGS. The line of resection for cases requiring a maxillectomy is marked on the preoperative CT or MRI scans. In the operating theatre, after the completion of surgical procedure for maxillectomy, the surgical defect is packed with a bolus of gauze and a CT image of the surgical site is obtained. The area of surgical defect is compared with the originally planned line of resection. If the margins seem to be close or positive, the surgical procedure can be extended to obtain definite negative margins. Such comparison of data within the operation theatre, requires digital software for extrapolation of preoperative versus postoperative margin status, over a high resolution CT image. Intriguing, as it may be perceived, the surgeon can easily identify on the monitor, the distance between the surgical margins and the preoperatively planned line of resection.

B Nishio et al[18] (2017) proposed a similar technique for preoperative surgical simulation and validation of the line of resection in surgical resection of advanced sinonasal cancer. Seven patients with advanced sinonasal cancer who underwent treatment between 2011 and 2013, were included in this study. The authors compared preoperative 3D virtual simulation of surgical resection with the actual intraoperative surgical status and examined the differences between planned and actual lines of resection (osteotomy) using post-simulation and postoperative CT scans, with the help of iPLAN software (BrainLab). The imaging protocol involved preoperative CT images obtained within 2 weeks prior to surgery, post-simulation CT images obtained after 3D virtual surgical simulation and postoperative CT images obtained at 6 months postoperatively. There were no perioperative mortalities. The authors concluded that virtual simulation of en bloc resection for advanced sinonasal malignancy, provides a highly effective means of surgical planning. The major difference between this technique and that described by Homma was that Nishio et al established the utility of surgical simulation in very advanced surgical resections for highly invasive sinonasal malignancies which are operated upon at few tertiary care hospitals in the world.

C Guijarro-Martinez et al[19] (2014) published a study describing the optimization of the interface between radiology, surgery, radiotherapy and pathology in head and neck tumour surgery based on a navigation-assisted multidisciplinary network. All implicated fields were integrated by a common server platform (iPLAN® Net Server, Brainlab AG, Germany) and had remote data access in a ready to use format. The resection margins and exact locations for biopsies were mapped intraoperatively. The pathologist was able to use the numerical coordinates of these samples to precisely trace each specimen in the anatomical field. Subsequent to this, map-guided radiotherapy could be planned. Thus, apart from the benefits of image-guided resection, this model enabled radiotherapy planning according to the specific coordinates of the resection defect and any residually affected sites identified by the pathologist. The irradiation of adjacent healthy structures was thus minimized.

D Rana et al[20] (2012) presented a study on role of computer-assisted surgery for primary and secondary treatment of head and neck malignancies. The study involved 5 categories of oncologic surgical procedures in which computer-assisted surgery was applied, from 2005 to 2011 – preplanned trajectorial-guided tumour biopsy, intraoperative image controlled tumour resection, tumour mapping, reconstruction after tumour surgery (true to planning) and oral rehabilitation (backward planning). Data was obtained for all 5 categories in relation to preoperative planning, import of image data suitable for navigation and intra-operative precise infrared-based navigation. The authors were able to develop and clinically evaluate a novel 3-dimensional planning and navigation software solution for treatment of craniofacial tumours. This study provided description of surgical simulation technology as applied to biopsies from deep seated tumours, apart from applications towards surgery.

E Feichtinger et al[21] (2010) reported a study describing a new method of assessing resection margins intraoperatively using image-guided surgery based on positron emission tomography / computed tomography (PET/CT) image fusion. The image fusion was done on the workstation of a 3D-navigation system in six patients who underwent surgical treatment of advanced head and neck carcinomas. Intraoperative navigation of the ablative defect showed an unsafe resection margin in four patients. Additional image-guided resection in three of these patients allowed local control of tumour to be achieved.

F Rasmussen et al[22] (2007) presented their report on functional neuronavigation combined with intra-operative 3D ultrasound in the setting of surgical resections close to eloquent areas of brain. The objective was to evaluate the usefulness of functional magnetic resonance imaging (fMRI) and DTI (diffusion tensor imaging) data in an ultrasound-based neuronavigation system. fMRI data was obtained preoperatively in twelve patients while DTI data was obtained in six patients. This preoperative data was transferred to a commercial ultrasound-based navigation system and used for surgical planning and guidance. During surgery, intraoperative ultrasound volumes were acquired when needed and multimodal data was used for guidance and resection control. An automatic voxel-based registration method between preoperative MRA (MR-angiography) and intraoperative 3D ultrasound angiography (Power Doppler) was developed and evaluated preoperatively. Furthermore, this study demonstrated that automatic ultrasound-based updates of important preoperative MRI data are feasible and can be used to compensate for brain shift. For related reference, McKenzie et al[23] (2014) have provided a detailed evaluation of medical modelling and simulation as applied to various fields of surgery and medicine.

DISCUSSION

Many patients with malignancies of maxillary sinus present with advanced stage of disease with direct extension to adjacent critical areas. Incidence of locoregional recurrence is high due to specific anatomical characteristics of this area. The air filled sinuses and adjoining nasal cavity permit occult growth of these tumours. Appearance of any diagnostic signs and symptoms is late, until the lesion has reached considerable volume. Hence, the invasion of critical structures is rapid with consequent difficulties in planning of treatment. In order to overcome uncertainties in surgical planning and minimize chances of recurrence, preoperative imaging with CT and MRI is pivotal to the successful execution of surgical attack.

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Imaging by way of computerized tomography (CT) provides accurate delineation of the bony invasion, while MRI reveals a detailed evaluation of soft tissue infiltration. For successful resection of maxillary tumours, in an effort to preclude the probability of recurrence, various techniques have been developed and validated in human subjects which involve preoperative surgical simulation and intraoperative computer-assisted surgery to define the line of resection with impeccable precision. This translates into a new dimension of “Precision Oncology” which can be perceived as a major paradigm shift. All this has been possible because of the sincere and diligent efforts of highly dedicated people who have the zeal for innovation and research. It is evident from the outcomes of this exhaustive study that these techniques help to analyze the surgical margins in great detail and hence reduce the probability of positive margins in order to prevent locoregional recurrence.

Treatment planning for major surgical procedures involving surgical intervention for cancer of the maxilla, has greatly evolved over the last few decades. Various important landmark studies have been cited in the foregoing text. The major studies which presented results of preoperative surgical simulation as applied exclusively to the procedure of maxillectomy, were published by Homma[17] and Nishio[18]. While Homma et al described application of the technique to cancer of the maxilla, Nishio further extended the indication of surgical simulation to cancers of the maxilla exhibiting local invasion towards the orbit and skull base. Rana et al[20] described additional indications of the technique such as biopsy from deep seated tumours and three-dimensional tumour mapping for reconstruction of the ablative defect. Feichtinger et al[21] added the new imaging modality of PET/CT fusion for assessment of surgical margins and preoperative planning. This allowed evaluation of locally involved tissue which could not be detected on CT and MRI scans. Rasmussen et al[22] provided a description of the technique in relation to tumours located close to eloquent areas of brain. The authors presented validated results of intraoperative ultrasound based navigation in real-time, correlating the data with preoperative simulation based on images of functional MRI and diffusion tensor imaging. All these studies described the indications and results of preoperative simulation as would be pertinent to the surgeons. However, the possibilities and applications of these innovative techniques go much beyond the perceptions of many. Guijarro-Martinez et al[19] have explained that the same images and data could be utilized by the radiotherapists for accurate delineation of the radiation field. Also, it serves as a three-dimensional map for the pathologists who examine the frozen sections and postoperative specimens. If the data is made accessible to the surgeons, the radiation oncologists and pathologists through a common digital platform, planning and communication between these three groups would be much more accurate.

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CONFLICT OF INTERESTS:

The authors declare that there is no conflict of interests that could influence this work.

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