Three dimensional virtual surgical planning for patient specific osteosynthesis and devices in oral and maxillofacial surgery. A new era.

Kraeima, Joep

CHAPTER 9

GENERAL DISCUSSION

GENERAL DISCUSSION AND FUTURE PROSPECTS

This thesis describes the optimisation and implementation of 3D virtual surgical planning (VSP) workflows for three care paths in oral and maxillofacial surgery (OMFS).

The optimisation was achieved by means of the aims of this thesis:

1. Integration of multi-modality imaging into a single 3D VSP (**chapters 2-5**).
2. Systematic comparison with conventional methods, including thorough testing and validation of new 3D VSP applications (**chapters 3, 6-8**).
3. Determination of appropriate indications for the use of 3D VSP in the selected care paths (**chapters 2, 5** and **7**).
4. Throughout this thesis the role of the technical physician was described as a valuable addition to the surgical team in OMFS. Resulting in adequate development and implementation of 3D VSP and corresponding patient specific osteosynthesis and devices.

Implementation of these aims resulted in an improvement of the workflows for 3D VSP and the corresponding surgical procedures. Improvement was found in terms of predictability of surgical outcomes, such as the accuracy of planned resections, screw positioning and positioning of bony structures (e.g. the maxilla) and surgical accuracy of application of patient specific devices.

Surgery in head and neck oncology

The oncologic-surgical challenge is to plan and perform an adequate resection with sufficient margin, based on the pre-operative information. Mandibular malignancy resections frequently include the use of 3D VSP and guided surgery techniques based on CT data only. This thesis reported a new developed and validated workflow for multi-modality image fusion in 3D VSP of mandibular resection. As was proven by the clinical cohort study (**chapter 3**) this has led to the improvement of the number of tumour free bone resection of the mandible.

The processing of the image data (e.g. CT or MRI) in order to obtain an anatomical correct 3D virtual model for 3D VSP is not self-evident. It requires a 3D software architecture that allows data fusion and segmentation for example, it requires both medical and technical expertise and can be very time consuming. A 3D VSP should include as much as possible the available information regarding the bone, tumour and other relevant characteristics such as peri neural tumour spread and relation to other structures, i.e. muscle, blood vessels, bone marrow and mucosa (1). A CT-only 3D VSP lacks this tumour related information that is required for adequate pre-operative decision making, as it cannot be seen on CT only (2, 3). The workflow for 3D VSP in our group was based mainly on a combination of already available software within the University Medical Center Groningen (UMCG). It is not restricted to the specific software packages that were used in this study, as only standardized file formats where used (e.g. STL, DICOM and RTSS). In addition, the scans used in the study where already part of the routine diagnostic work-up for head and neck oncology patients. Therefore the multi-modality workflow for 3D VSP can be easily implemented in other clinics that use 3D VSP.

One could argue that the 100% tumour free bone resections of the mandible (**chapter 3**) could also be a result of MRI based overestimation of the tumour or wider resection planning . It is reported for breast cancer that MRI estimates tumour size more accurately, however also overestimates the size (4). For oral cavity tumours it was reported that MRI decreases underestimation of the tumour in comparison to CT (5). However, especially when the MRI presents marrow edema, or suspected peri-neural extension, the exact tumour border is challenging to delineate (6, 7). Our study protocol prescribes that the tumour delineation was performed on the MRI by the technical physician, which was then checked by the radiologist that had made the clinical report of the MRI. In case areas where suspected for tumour or peri neural tumour spread, these where always included in the delineation of the tumour margins. Post-operative histopathological analysis revealed whether tumorous tissue was present at the borders of the resected bony specimen. In other to confirm histopathologically the exact tumour extension in suspected areas of bone, it would require the bony specimen to be cut into thin lamellae. These lamellae should be superimposed on the 3D virtual model of the 3D resection planning including the tumour and the bone. This is not part of current routine.

The fusion of CT and MRI itself is subject to alignment errors. These errors are described to be > 1mm (8-10). Further optimisation of this 3D VSP is explored in **chapter 4** which describes the MRI only workflow for mandibular resection. MRI can be used to derive bone information as well as tumour information, making a CT-MRI fusion superfluous. However current available sequences for MRI based bone segmentation of the mandible still have drawbacks. MRI requires, in our own experience, substantially longer data processing time and difficulties for exact segmentation of cortical borders in anatomical relevant areas (e.g. mental region) as is described in **chapter 4**. Further optimisation of the selected sequences, as well as inclusion of new developed MRI sequences may provide better contrast of bone in MRI images. As an example, the ultrashort echo time (UTE) sequences can be used to obtain black bone images. This UTE utilizes TE of only microseconds which enables the bone to have a dark signal intensity in the MRI image (11, 12).

The ability to combine different image modalities in one 3D VSP has proven to be of value for other applications, such as secondary surgical management of osteoradionecrosis (ORN) as well. This thesis did not aim to provide a clinical cut-off value for which value of received radiation dose should be used in case of surgical resection of ORN. In order to find such cut-off value, a large dataset must be analysed using the described method of isodose visualisation. It does however present the use of multimodality image fusion in these cases, which again can easily be adapted and used in centres that use other software for 3D VSP.

Orthognathic Surgery

This thesis reports the optimisation of the 3D VSP workflow in orthognathic surgery, by the development and application of patient specific osteosyntheses (PSOs). By means of **chapters 6** and **7**, it was found that surgical accuracy of maxillary translations was improved by the use of PSOs. **Chapter 7** defines indications for use in relation to the planned translation of the maxilla. In both the pilot study (**chapter 6**) and the randomised controlled multi-centre trial (**chapter 7**) it is shown that the use of PSOs result in a smaller deviation from the 3D VSP, compared to the application of conventional osteosynthesis material (OSM) in combination with the use of an 3D VSP based intraoperative splint. Already the use of PSO was reported to improve accuracy, to be potentially time-saving and not to introduce any difference in required plate removal compared to conventional OSM (13-15). Current studies lacked a systematic comparison with conventional methods by means of a randomised controlled multi-center trial. As this thesis aimed to optimise the workflow for 3D VSP in terms of accuracy, the question rises up to what level optimisation is required? A study of Proffit et al. 2007 reports that a deviation from the planned position of the maxilla of 2mm or more is considered clinically significant and 4mm or more is considered to be above the post-operative orthodontic achievable range of correction (16). Even though this study was reported already in 2007, before the use of 3D VSP was integrated in the routine of orthognathic surgery, it still provides a reference for comparing methods. The use of conventional OSM was reported to result in deviations of >2mm from the planned position (17-21). As was presented in the result section of **chapter 7** indications for using PSOs where defined based on this 2mm cut-off value. As an example, an anteroposterior translation of 3.7mm or more while using the conventional OSM leads to 2mm deviation from planning, whereas the PSO method leads to only 1.4mm deviation from planning on average. If another cut-off value, than 2mm, is preferred for using PSOs or application of conventional splint-based methods, the regression functions obtained in **chapter 7** can be solved accordingly. Further, detailed, analysis of subgroups is required in order to obtain indications for use of PSOs in case of e.g. segmental osteotomies.

The message is that by using PSO for orthognathic surgery the accuracy of maxillary translation is improved, and specific indications for use can be derived based on clinical preferences. Long term stability effects of PSOs are still to be evaluated. For example it is hypothesized that there can be a difference in the amount of (one year) relapse between PSO and conventional OSM treated maxilla's.

Temporomandibular joint surgery

This thesis presented the development of a custom 3D VSP based temporomandibular joint total joint replacement (TMJ-TJR) device, as it being one of the most advance applications of 3D VSP. This Groningen TMJ-TJR, was developed according to the Groningen principle, which includes a 15mm lowered centre of rotation (22). The G-TMJ-TJR is a multi-material, multi component prosthesis of which 2 parts where customized compared to the original stock design. The design aims to minimize wear between the moving parts by an interaction of the zirconia condylar sphere and translation plate with an ultra-high molecular weight polyethylene disk part. In addition custom surgical placement guides where developed and applied in order to translate the 3D planned position of the G-TMJ-TJR towards the actual bony structures with high accuracy. A humane cadaver series (N = 10 prostheses) received the custom G-TMJ-TJR based on routine surgical approaches. The accuracy of the positioning of the custom G-TMJ-TJR was confirmed based on post-operative CT data an 3D data analysis. The benefit of custom fitter parts in relation to bone (mandible and fossa part) was reported to be beneficial for stability and improvement of osseo-integration (23-25). Application of a custom TMJ-TJR device requires less perioperative trimming an re-contouring of the bone, especially when patients suffer from large mandibular angles or asymmetries (25). The G-TMJ-TJR has meanwhile been applied successfully in 5 patients. Follow-up in terms of pain reduction and improvement of function will be reported in future studies.

FUTURE PROSPECTS

Image processing and Deep Learning

This thesis has described several applications for optimization of 3D VSP, however especially **chapter 4** underlines that this does not always result in improvement of user friendliness or in time efficiency. The anatomical and pathological information for a 3D VSP is available in the obtained imaging, but it requires to be segmented manually by an employee involved in the 3D VSP workflow. This employee can make mistakes or choose a certain interpretation. This employee is trained and will progressively improve in performing the segmentations or other interpretations of the data. However, another approach would be to use a *deep learning* application that can segment and/or interpret the image data.

Deep learning is a method of machine learning that enables a computer program to learn in a progressive way from its own experience, in order to continuously improve its ability to perform the (3D segmentation) task (26). Artificial neural networks, a type of deep learning architecture, are computing systems that can learn and progressively improve their ability to learn (27). When applying this concept to segmentation of anatomical structures in medical image data (e.g. CT or MRI), this could provide further optimization of the workflow by automation, decrease of the inter observer variability and improvement of the accuracy (28, 29). Potentially it would enable accurate and fast segmentation of the required anatomical structures from each modality that the neural network is trained to process.

In our group already the first series of automated mandibular segmentation based on CT data was performed. This was based on a neural network approach in which manually segmented 3D mandible data was used for training of the network. Hereafter, a series of new CT data containing the mandible was imported in the network and automatically segmented. A visualization of a typical result is presented in Figure 1 below, in which 1A presents a manual segmentation, 1B a result of the neural network algorithm and 1C is the 3D superimposed image of both A and B, including a colourmap representing the differences in millimeters. Further studies are required in order to apply these concepts into the daily practice of 3D VSP and to assure compatibility with additional image modalities (i.e. MRI and PET). The aim is to further optimize 3D VSP applications and to use the information that is available in the imaging technology even better.

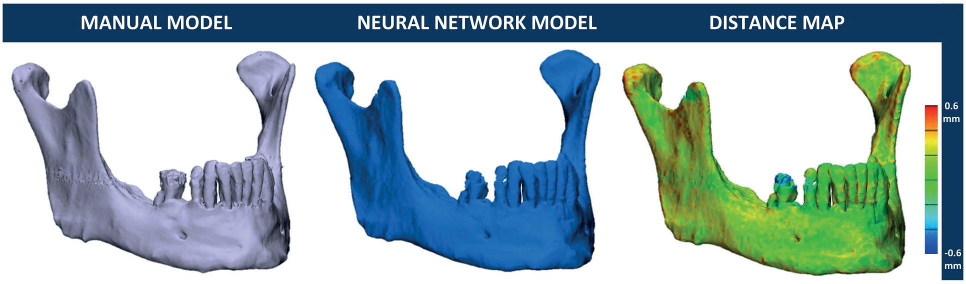

Figure 1: A comparison between the manual segmentation methods (A) of the mandible and the neural network algorithm (B) based on CT data. The distance map (C) presents the differences in milimeter between both models.

Finite Element Analysis and Implant Design

This thesis describes several applications of patient specific osteosynthesis and devices (**chapters 6**, **7** and **8**). The shape and fitting of these products was tailored to the contour of the bone of the individual case. The locations of the screws were planned based on the thickness of the bone and the expected cortical grip. However the design and locations of the screws where all off-shelf based and thereby similar to the previously used conventional alternatives. Although not part of the primary research questions in this thesis, the mandibular resection cases (**chapters 3** and **4**) all required application of reconstructive osteosynthesis, optionally combined with a free vascularized fibular flap. It is reported that especially this osteosynthesis can be subject to failure in terms of plate fracture or screw loosening (30, 31).

The application of biomechanical models in order to design osteosynthesis materials and implants was reported using the finite element (FE) method (31-33). These FE models are not uniform and have a variation in required input factors such as constraints, load, mechanical properties of the bone, muscle forces and vectors. The application of a FE model can predict the behavior of e.g. osteosynthesis plates or implants. In search of further optimization of the design of 3D VSP based osteosynthesis and implants, the output of a FE model should be applied in the design process by means of a topology optimization (TO) process. Topology optimization is a mathematical method that, given certain boundary conditions, can optimize the design or layout of an object. In our group the first experiments are performed in which a mandibular defect after planned tumour resection is reconstructed with TO based design of reconstructive osteosynthesis materials. An example of a freeform design result is presented in Figure 2. In Figure 2A an example of a TO-based design with a fibular graft is presented. Figure 2B presents the application of a TO based reconstructive OSM only.

Application of TO will be explored in future study, using a FE model, applied to the design of osteosynthesis and implants and optimal locations for screws in OMFS. Not only will this enable the evaluation of different designs, also the use of different materials with different characteristics (e.g. wear rate or stiffness) can be evaluated.

Augmented reality

This thesis has described 3D VSP applications that mainly use patient specific 3D printed surgical guides for translation towards the surgical procedure. The use of intra operative navigation is frequently reported as an alternative translation method of 3D VSP into surgical procedure(34-37). Using intra operative navigation has reported drawbacks, which are mainly that the surgeon has to look away from the surgical field in order to receive feedback from the system (38) and absence of haptic feedback received by the surgeon during the cutting or drilling, which is the case when using 3D printed guides. When the 3D information could be projected onto the surgical field, with good stability and accuracy, this could optimize the translation from 3DVSP to the actual surgical procedure. The use of augmented reality (AR) via head mounted devices (HMDs) has been reported as a potential technique for translating 3D VSP to the actual surgical procedure (39). Figure 3 presents a schematic overview of a typical set-up when using intra operative navigation without (Figure 3A) and with (Figure 3B) AR via a HMD.

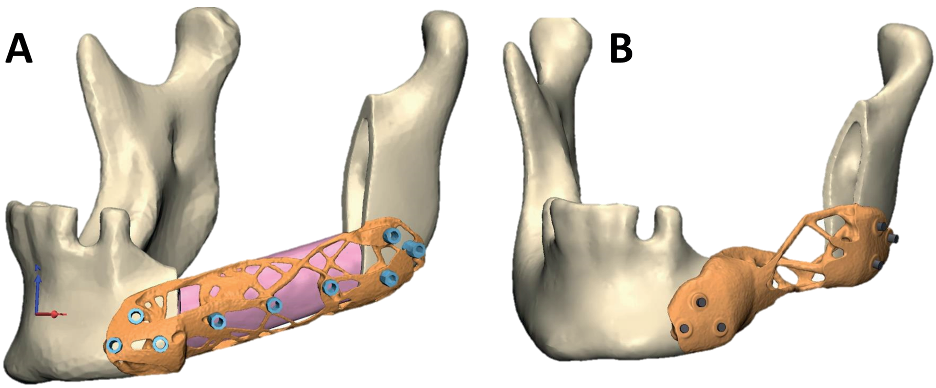

Figure 2: A. An example of a topology optimised design for OSM with a fibula graft. B. An example of a topology optimised design for reconstructive OSM without a fibula graft.

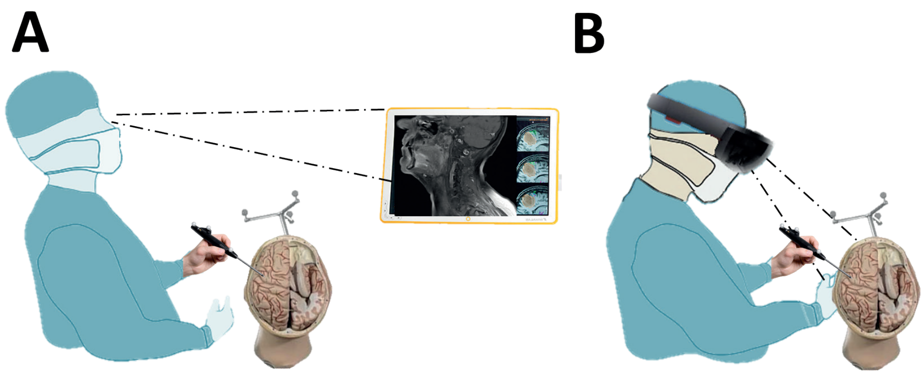

Figure3: A. The use of intraoperative navigation with a wall mounted screen. B. The use of intra operative navigation with a HMD an AR projection

In our group we have developed a method that integrates the use of both intra operative navigation and a HMD which projects AR content (Figure 3B). This workflow was validated by means of an user performance evaluation on a phantom object. This resulted in a significant improvement of both speed and accuracy in navigational tasks, when the AR HMD was applied (Glas et al. submitted at *PloS One, at the time of preparing this thesis*). Overall completion of the navigational tasks where performed 1.7 times faster and 0.8mm more accurate when using AR via an HMD, compared to the use of the intra operative system only. The next step is to implement this workflow into clinical practice. The multi-modality 3D VSP as described in this thesis, will be the base of the surgical procedure. The translation towards this procedure can be performed with the AR on a HMD. Future studies should compare this method to the use of 3D printed guides or intraoperative navigation solely, and reveal the added value and indications for use of AR in OMFS.

Technical Physician

The expectations described in the *future prospects* section above, as well as the results described in this thesis underline that technology and engineering expertise are increasingly important in OMFS. Current routines already rely on the use of 3D VSP and related technologies. In the coming years it is likely that the use of imaging techniques, 3D VSP and PSOs will be used more frequently and in other, new, applications as it becomes more readily available and the advantages are systematically reported in literature. This requires the systematical embedding of medical-technical expertise within the OMFS. As was pointed out within this thesis a new health professional, the technical physician, is a professional that combines both medical and technical expertise in the field of OMFS. This professional can independently perform clinical tasks and perform the 3D VSP workflows required for the applications described in this thesis.

Integration of a technical physician, trained within the field of OMFS, to the team of practitioners assures efficient use of 3D technology. In addition, it enables early signaling of new technology and development and validation of new 3D workflows. This makes the technical physician a valuable addition for the field of OMFS in the new era of 3D VSP.

CONCLUSION

The new strategies for 3D VSP in OMFS, provided by this thesis, improve the treatments in terms of predictability, accuracy and provides detailed possibilities for postoperative evaluation. This thesis optimizes the workflows, systematically compares the 3D VSP methods to conventional methods and objectifies the indications for use of 3D VSP. In the new era of 3D VSP the 3D technology will be applied for every patient, not when we can, but when we should.

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