Chernohorskyi D. M., Chepurnyi Y. V., Vasiliev O. S., Voller M. V., Kopchak A. V. Evaluation of the accuracy of surgical reconstruction of mandibular defects when using navigation templates and patient-specific titanium implants. Journal of Education, Health and Sport. 2021;11(2):117-132. eISSN 2391-8306. DOI <a href="http://dx.doi.org/10.12775/JEHS.2021.11.02.013">http://dx.doi.org/10.12775/JEHS.2021.11.02.013</a> <a href="https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2021.11.02.013">https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2021.11.02.013</a> <a href="https://aptsticle.com/d594307">https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2021.11.02.013</a> <a href="https://aptsticle.com/d594307">https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2021.11.02.013</a>

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8.2) and § 12. 1.2) 22.02.2019. © The Authors 2021; This article is published with open access at Icensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial Licensee which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is a nopen access article licensed under the terms of the Creative Commons.org/licenses/by-ac-sa/4.0/) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited. The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 11.01.2021. Revised: 10.02.2021. Accepted: 26.02.2021.

# Evaluation of the accuracy of surgical reconstruction of mandibular defects when using navigation templates and patient-specific titanium implants

D. M. Chernohorskyi, Y. V. Chepurnyi, O. S. Vasiliev, M. V. Voller, A. V. Kopchak

# O.O. Bogomolets National Medical University, Kyiv, Ukraine Stomatology department

### Abstract

The management of patients with post-traumatic and post-operative mandibular defects is a major challenge even for experienced surgeons. Performing traditional reconstructive interventions with the use of bone autografts is always confronted with the problem of inconsistency between the shape, architecture, a biological. An alternative to conventional bone grafting is the use of digital protocol and CAD / CAM technology, which allows fabricating different types of customised medical devices. All patients underwent reconstructive and restoring interventions with the use of patient-specific titanium implants guided by a full digital protocol.

Patients were examined in compliance with the standard scheme. To repair the defects, PSIs were fabricated with the use of selective laser sintering of titanium.

The introduction of digital technologies and computer technique of diagnosing, planning and implementation of surgical interventions has been the main direction aimed at the improving the accuracy and predictability of reconstructive restorative surgery. Among the main achievements in this direction are the improvement of software and methods of computer modeling, as well as the introduction of CAD / CAM technology.

The use of CAD / CAM technologies, in particular, navigational surgical templates and patient-specific implants for the repair of mandibular defects ensures a high level of accuracy and predictability.

Key words: Patient-specific implant; mandibular defect; mandible segmentation; mandible reconstruction; navigation templates.

#### Introduction

The management of patients with post-traumatic and post-operative mandibular defects is a major challenge even for experienced surgeons. This is primarily due to the fact that the mandible has a complex anatomical shape, architecture and conditions of functional load altering considerably with the continuity defects. When performing traditional reconstructive interventions with the use of bone autografts harvested from the iliac crest, fibula, rib or scapula, the surgeon is always confronted with the problem of inconsistency between the shape, architecture, a biological / reparative potential of the autograft and the characteristics of the patient's mandible [1-3]. Typically, to get the desired shape, bone grafts are segmented, then the fragments are fixed to each other and to the mandibular remnants with fixators placed on the bone, including reconstructive plates, meshes, gutter structures, etc., which are intraoperatively adapted (bent) to restore the natural curvature of the mandible [4]. Depending on the severity of the clinical case, the surgeon's skills and experience, this procedure can be time-consuming; some subjective factors can affect the accuracy and efficacy. Furthermore, the optimal /desired reconstruction outcome is not always obvious, as the topographic anatomy of the concerned area may be severely distorted and key anatomical landmarks can be lost. In this regard, achieving the desired aesthetic and functional routcome with the use of conventional reconstructive mandibular surgery remains challenging and often requires multi-stage surgical treatment [5].

To date, an alternative to conventional bone grafting is the use of digital protocol and CAD / CAM technology, which allows fabricating different types of customised medical devices: stereolithographic and prototypical models of jaws, navigational surgical templates and patient-specific implants [6, 7]. When combined with modern diagnostic techniques (CT, MRI, 3D scanning, etc.), CAD / CAM technology is a powerful tool for three-dimensional imaging, surgical simulation and patient management. The introduction of the above technology into reconstructive maxillofacial surgery has significantly increased the predictability of surgery, diminished the impact of subjective factors on surgery results and the risk of intraoperative complications, created new opportunities for diagnosis, planning and actualization of therapeutic strategies, simplified the individual stages of surgery, and resulted in a reliable reduction in operative time, improved aesthetic and functional outcomes owing to

more accurate restoring the contour of anatomical structures and the natural shape of the jaw [8, 9].

One of the latest achievements in this direction is the creation of patient-specific implants (PSI), which are made of titanium with the use of a computer numerical controlled (CNC) milling machine or selective laser sintering (DMLS) considering a precreated virtual design [10-12]. Based on the virtual surgical simulation, selective laser sintering allows fabricating complex three-dimensional metal structures ensuring relevant parameters (geometry, size, weight, biomechanical properties) essential for the specific clinical conditions of the patient. Modern 3-D printers provide a production accuracy of 12 microns, which is much greater than the precision of any surgical manipulation, even with the use of optical magnification. The created structures do not require intraoperative bending or shape adaptation and act as templates for the proper position of jaw fragments and bone grafts. Pre-operative planning for reconstructive mandibular surgery is shifted from mechanical simulation using solid-state models to the software-based virtual simulation [11].

The clinical efficacy of this approach was demonstrated by Mazzoni (2013), Hirsch (2009), Leiggene (2009), Antony (2011), Zheng (2012a), Seruya (2013) [13-16, 2]. The major advantages of patient-specific implants were as follows: an extra increase in the accuracy of surgical interventions, greater possibilities for repairing large defects with complex geometry, reduced operative time, better fit of titanium structures to the bone surface compared to preshaped plates, decreased volume of autologous bone grafts, diminished risks and side effects associated with the harvesting, reduced number of surgical interventions for the complete patients' rehabilitation, etc. [17-18]. However, the study by Shramm (2014) showed some discrepancies in the positioning of grafts and patient-specific fixators in comparison with the virtual plan of intervention [19]. The number of such inconsistencies turned out to be much higher than expected, especially with poor quality of the baseline CT scan, lack of adequate resection and positioning templates and with large subtotal defects, extending to three or more anatomical areas [19]. According to evidence-based medicine, the issues of improved accuracy of mandibular reconstruction with PSI still lack adequate justification. Overall, the number of studies covering the efficacy of PSI in repairing mandibular defects remains limited. A significant part of them addresses the evaluation of individual clinical cases and small series, the authors use different approaches to assess the accuracy of reconstruction, which makes it difficult to compare the data obtained. Modern software systems and mathematical algorithms for contrasting and comparing three-dimensional objects as well as 3-D cephalometric analysis open up opportunities for an objective study of this issue and assessment of factors that increase the risk of errors when repairing mandibular defects.

Based on the objective criteria by the comparison of the virtual surgical plan with the achieved results confirmed by the images generated from multi-sliced spiral computed tomography, we intended to assess the accuracy of the anatomical mandibular shape restored during reconstructive interventions with the use of navigation surgical templates and patient-specific titanium implants.

Materials and Methods. Data of 40 patients who received treatment for postoperative and post-traumatic mandibular defects with continuity disruption at the Centre for Maxillofacial Surgery and Dentistry of the Kyiv Regional Clinical Hospital between 2015 and 2020 were studied. All patients underwent reconstructive and restoring interventions with the use of patient-specific titanium implants guided by a full digital protocol.

The criteria for inclusion in the stud were mandibular defects with continuity disruption, requiring reconstruction with the use of patient-specific titanium implants fabricated by DMLS. The patients gave the written informed consent to participate in the study. The exclusion criteria were as follows: age under 16, decompensated or sub-compensated concomitant somatic pathologies, mental illnesses, chronic alcoholism or drug addiction, active radiation or chemotherapy, non-compliance with medical recommendations and lack of interaction with a physician, total mandibular defects, incomplete clinical and tomographic documenting the case, the patient's refusal to participate in the study.

Among the patients included in the study, there were 32.5% of men and 67.5% of women. The age of the patients ranged from 16 to 62 years, and on average  $29.5 \pm 19.1$  years (Table 1).

Age, completed years	Sex					
	Men		Women		Total	
	Absolute number	%	Absolute number	%	Absolute number	%
under 20	0	0	6	15	6	15
20-29	2	5	6	15	8	20
30-39	2	5	5	12.50	7	17,50
40-49	4	10.00	5	12.50	9	22,50
50-59	3	7.50	5	12.50	8	20,00
$\geq 60$	2	5	0	0	2	5,00
Total	13	32.50	27	67.50	40	100

Table 1 - Distribution of patients with mandibular defects by age and sex

The main causes of defects were as follows: mandibular resections for benign and malignant tumours - 26 patients (65%), high-energy trauma, including gunshot injuries - 3 (7.5%), osteonecrosis of various origins - 2 (5%), defects of the temporomandibular joint resulting from congenital malformations and surgical extraction of ankylosis, DOA, etc. - 9 (22.5%) (Fig. 1).



Fig.1 - Distribution by aetiology of the mandibular defect

When conducting clinical and instrumental studies, the principles of bioethics and the rights of the patient were observed in accordance with the Declaration of Helsinki and the Fundamentals of Ukrainian Legislation on Health Care (1992). The Commission on Bioethics of the Bohomolets National Medical University (Minutes No. 107 of December 29, 2017) performed the examination of the research materials.

All patients were examined in compliance with the standard scheme, which included history taking, assessing the overall and local status, employing additional research methods, followed by establishing a diagnosis and determining a treatment plan. To repair the defects, PSIs were fabricated with the use of selective laser sintering of titanium. PSIs were modeled and implanted in compliance with the digital protocol based on the guidelines.

Virtual surgical simulation and the design of patient-specific constructions were carried out according to CT data in the facilities of the laboratory of computer modeling and digital dentistry of the Dental Medical Centre of the Bogomolets National Medical University. To do this, all patients underwent a preoperative multi-slice spiral tomographic study by PHILIPS Brilliancei CTSP 128 scanner. Tomographic data presented as a series of DICOM files were imported into the D2P ver. 1.0.253 DICOM to PRINT, 3D Systems, USA. To create a three-dimensional virtual model of the bones of the facial skull, the image was segmented to create a mask in the range that corresponded to the radiological bone density. Using the Mask Editor tool, we carried out the mask editing and removing artifacts to achieve the required image quality (Fig. 2). Further, the Geomagic Freeform Plus software, 3D Systems (USA) were employed to assess the clinical situation, develop a plan, and simulate the surgery. Based on the evaluation of the defect and the donor site topography, the optimal size and shape of the graft were determined; there were simulated auxiliary devices - navigation templates for osteotomys, reconstructive templates for shaping the graft and proper bone fragments positioning, orthodontic splints and patient-specific implants of various types depending on the clinical situation.



Fig. 2 - X-ray mask editing and anatomical separation

The main types of PSI used were anatomical titanium endoprostheses, which restored the lost parts of the mandible without the additional bone autografts, patient-specific gutter-shaped fixators, and constructions combining the elements of the endoprosthesis and patient-specific fixator [20, 21].

The created virtual models were exported to the CAM software for the production of stereolithographic or prototyping models, which were "copies" of the specific anatomy of the bone structures, or reflected the desired anatomical outcome, surgical templates and splints ensuring accurate osteotomies, cuts, drilling, proper alignment of teeth and bone fragments, etc. PSIs were fabricated by additive selective laser sintering technology from titanium with a ProX 400 printer, 3D Systems (USA).

Surgical interventions were performed pursuant to the created virtual plan, observing the standards and protocols of reconstructive and restoring jaw surgery [22].

The surgery was performed under general anaesthesia using a classic submandibular approach, the length of which was determined by the size and location of the defect. When installing two-component TMJ endoprostheses, it was supplemented with a pre-auricular approach. In a "blunt" and "sharp" way, we penetrated deep into the soft tissues, skeletonized the vestibular surface of the mandible and mobilized the available bone fragments. If it was necessary to carry out the resection or osteotomy with subsequent movement of bone fragments, guiding (resection) surgical templates were placed on the vestibular surface of the mandible (Fig. 3) and fixed to the bone with mono-cortical screws in the position determined during the virtual surgical simulation (Steed, 2017).



Fig. 3 - Templates for osteotomy

Precise, minimum invasive osteotomy lines were performed using the Acteon -Piezotome Cube (Led) piezotome or oscillating surgical microsaws. The navigation template was removed and there was placed a pre-fabricated patient-specific implant that served as a reconstructive template, ensuring the correct position of the bone grafts relative to the mandible and each other, the fixation in the proper position, and restoration of the proper anatomical contour of the lower and posterior mandibular edges. For more accurate positioning of PSI in a pre-determined position, elements of macroretention were used owing to the exact matching the surface implant relief and the mandible, additional structural elements for fixation, the coincidence of the holes of the patient-specific design and the navigation template, and the like. In 40 cases, patient-specific implants were combined with free bone autografts from the iliac crest (13 (32.5%)) and with combined flaps from the fibula on microvascular anastomoses (4 (10%)) (Fig. 4). The grafts were harvested by traditional techniques. To determine the size of the graft accurately and to fragment further, we used special navigation templates made considering MSCT data of the donor site. When microvascular anastomoses were required, the PSI design ensured the convenience for this surgical stage.



Fig. 4

The patient-specific construct was fixed to the mandibular bone fragments and grafts with titanium screws of the Gamma system (Titamed, Belgium). At the surgical site, soft tissues were sutured in layers. Particular attention was paid to the careful isolation of bone grafts and elements of titanium structures from the oral cavity. In the deficiency of soft tissues, the defect was covered with local flaps, vascular pedicle flaps or soft-tissue elements of combined flaps on vascular anastomoses. Postoperatively, patients received antibacterial, anti-inflammatory and symptomatic therapy, anticoagulants and topical medicinal products.

Follow-up computed tomography of the facial skull was performed within 3 days after surgery. The correspondence of the virtual plan and the obtained postoperative outcome was assessed with the use of the Geomagic Studio 2012 software (3D Systems, Valencia, CA, USA), by superimposing the STL model of the virtually positioned mandibular fragments in the proper position on the 3D reconstruction of the postoperative CT of the facial skull (Fig. 5). The algorithm of the computer program differentiated the corresponding points of both models and calculated the mean distance between them in millimetres. The discrepancies between the superimposed images were presented as colour gradients, reflecting the existing deviations between the corresponding points of the models (Fig. 6). In addition, the maximum values of the deviation between the points of both models were measured (Ciocca et al., 2012).



Fig. 5 - Superposition of the STL model of the virtualized plan and the obtained postoperative result



Fig. 6 - Chromatographic analysis

Furthermore, in both compared models, there were evaluated cephalometric parameters characterizing mandibular symmetry and shape, including intercondylar distance (distance between Con points corresponding to the mandibular head pole; interangular distance between Go points corresponding to mandibular angles; gonial angle (an angle between the body and the mandibular ramus) in the site of reconstruction and on the contralateral intact side (Fig. 7).



Fig. 7

To determine the nature of the sample distribution, the Kolmogorov-Smirnov normality test was used. Statistical analysis of the obtained data involved the calculation of mean values, standard deviation, mean error, median and percentiles (for parameters having non-normal distribution). The assessment of the probability of discrepancies between the values was based on the non-parametric Mann-Whitney test. Statistical calculations were performed with SPSS statistic software package

## (IBM SPSS, USA).

**Results.** During surgery, patients were installed the following types of structures: anatomical endoprostheses of the mandible (9 patients (22.5%)), including complete two-component TMJ endoprostheses (8 patients (20%)), patient-specific gutter-shaped fixators combined with bone autografts (11 patients (27.5%)), our offered structures that combined elements of endoprosthesis and a patient-specific fixator (12 patients (30%)) (Fig. 8). After surgery, the anatomical shape of the mandible and its continuity were restored in all patients. However, the absolute compliance of the intended and obtained results was achieved in none of the cases.



Fig.8 - Types of titanium structures

Based on the findings of comparative analysis, six patients were found to have large discrepancies between the expected and the obtained outcomes, exceeding 10 mm (the mean deviation was 22.1 mm, and the maximum deviation was 35.7 mm). In all cases, this was due to a change in the implementation of the surgical plan and fixation of the patient-specific structure in a position that deliberately differed from the pre-determined one. The reasons for such decisions were the differences between thee mandibular anatomy, adjacent tissues and the virtual model which were associated with insufficient quality of CT scan or the course of biological regenerative processes and bone remodeling within the period between the virtual simulation and the surgery (in cases when, for one reason or another, the surgery was postponed for the considerable time). Other reasons included the need to change the position of the structure for its efficient overlap with soft tissues, the complexity of the osteotomy in accordance with virtual planning and errors in its execution, the need for displacement of the bone graft to shape a full-fledged microvascular anastomosis, the inability to reset bone fragments of the mandible in the proper position due to pronounced scarring. These cases were excluded from further analysis as outliers (Fig. 9).



Fig. 9

In cases where the surgical plan was implemented in compliance with the created virtual model, the mean deviations of the points were 1.16 + 0.56 mm, and the maximum - 6.9 + 2 mm. Maximum deviations in most cases ranged from 3 to 9 mm and affected the aesthetic outcome to a lesser extent than the condition of soft tissues and the need for additional plastic surgery to overlap bone grafts and endoprostheses. The values of the maximum and mean deviation did not reliably depend on the size of the defect and the type of structure used.

When comparing the inter-condylar distances of the intended models with obtained results, no reliable differences were found (103 + 6.9 mm vs. 104.3 + 7 mm; p> 0.05). The

intended inter-angular distance was 93.4 + 74 versus 93.4 + 6.9 in postoperative CT (p> 0.05); differences in gonial angles were also insignificant both when comparing the intended and obtained results, the right and left sides.

#### Discussion

The main objectives of mandibular defects management are the continuity and contour restoration, positioning of the jaw in space with reproduction of normal occlusion and correct relationships in TMJ, the creation of conditions for adequate prosthetic rehabilitation and replacement of soft tissue defects without affected mobility of anatomical structures of the lower third of the face. Solving these objectives ensures an acceptable aesthetic result and adequate masticatory function but requires a precise restoration of symmetry and threedimensional shape of the lost anatomical structures. Traditional methods of mandibular reconstruction, relying on the intraoperative adaptation of the shape of bone grafts and metal fixators under the surgeon's visual control, were based largely on subjective spatial representations, the simplest linear and angular measurements and the use of anatomical landmarks that may be partially lost or distorted by the pathological process. The accuracy of such interventions depended significantly on the surgeon's experience, professional skills, and as the creativity and intuition. Consequently, the level of predictability remained low. The resulting spatial inconsistencies led to the pronounced facial asymmetry, changes in the facial profile, malocclusion and masticatory disorders, the development of pain syndromes, which necessitated the additional corrective interventions (sometimes numerous).

In recent decades, the introduction of digital technologies and computer technique of diagnosing, planning and implementation of surgical interventions has been the main direction aimed at the improving the accuracy and predictability of reconstructive restorative surgery. Among the main achievements in this direction are the improvement of software and methods of computer modeling, as well as the introduction of CAD / CAM technology, which allowed implementing a virtual plan with high precision directly during the surgery. In this regard, according to the literature, the main innovations that has increased the accuracy of the restored anatomical shape of the mandible are as follows: 1) tereolithographic models for pre-and intraoperative adaptation of fixators and bone grafts; 2) navigational surgical templates for graft harvesting and proper positioning of bone fragments; 3) specific implants, including anatomical endoprostheses of jaws; 4) intraoperative computer navigation. The combination of all (or several) these techniques in the framework of a complete digital protocol (so-called computer-assisted surgery - CAS) is the most effective approach.

The authors point out that digital technologies increase the accuracy of mandibular - reconstruction Nevertheless, a postoperative result never fully corresponds to the virtual surgical plan; linear deviations reported by various studies are from 0 to 12.5 mm and angular deviations are from 0.9 ° to 17.5 °. It should be noted, however, that determining the accuracy and precision of surgery, the authors mainly relied on inhomogeneous series with a small number of observations and used different criteria to assess the symmetry and degree of recovery of the anatomical shape of the mandible, which significantly complicates the interpretation and comparison. Based on the findings of meta-analysis, Van Baar shows that the overall quality of scientific publications and accumulated experience is insufficient to obtain convincing evidence and statistically significant confirmation of the benefits of PSIs in terms of their accuracy [23].

In this regard, we studied 40 patients operated in the single centre in compliance with the unified principles and protocols for installing PSIs. The purpose of the study was to perform an objective assessment of the precision of surgical interventions based on computer modeling and 3-D cephalometry. Our studies have shown that the maximum deviations of the points of the model are in the range of 3-9 mm, which virtually does not affect the integral aesthetic outcome. In this case, the mean deviation of points in the studied series was less than 2 mm. The maximum and mean deviations did not depend on the type of construction and the size of the defect.

It is obvious that various parts of the mandible have different aesthetic significance. Accordingly, changes in the symmetry of the angles and chin are usually more noticeable than deviations in the area of the mandibular body and rami. We have confirmed that the reproduction of the required bone symmetry by key points (the inter-condylar and interangular distances) was precise (the mean deviation is less than 1 mm) during the PSI installation.

Noteworthy is the fact that deviations were present in all cases and they always turned out to be larger than the calculated total error of CT, modeling and PSI fabrication. This is primarily due to the elastic properties of the bone, navigation templates and PSI, the possible displacement of the structure while screwing the locking screws, minor angular deviations and errors at the surgical stage of the structure installation.

Of particular note are six cases (15%) excluded from the general analysis, where the maximum and average displacements were significantly higher (at the level of 35.7 mm and 22.1 mm, respectively), due to a change in the surgical plan implementation. In those cases, the PSIs were deliberately placed in a position different from the intended one, which led to

the significant linear and angular deviation and significantly affected the aesthetic outcomes of the surgery. The major reasons for this were errors caused at 1) the planning stage, 2) the implementation of the surgical plan, 3) a considerable period of time from the moment of the structure modeling to the installation (with a change in anatomical relationships resulting from various biological processes), and 4) low-quality CT. In our opinion, the main ways to prevent such errors and complications are careful planning of surgical interventions with the involvement of a biomedical engineer and surgeon, strict adherence to the protocol of surgical intervention, the availability of appropriate technical support, and the use of only high-quality CT with a resolution of 150 microns, 50 lp / cm.

**Conclusions.** The use of CAD / CAM technologies, in particular, navigational surgical templates and patient-specific implants for the repair of mandibular defects ensures a high level of accuracy and predictability. The maximum deviation of the obtained result from the intended one is 9.86 mm, and the mean deviation is 6.9 mm. In this case, the value of the deviations does not reliably depend on the size of the defect or the type of patient-specific design used.

# References

1. Metzler P, Geiger EJ, Alcon A, Ma X, Steinbacher DM. Three-dimensional virtual surgery accuracy for free fibula mandibular reconstruction: planned versus actual results. J Oral Maxillofac Surg. 2014 Dec;72(12):2601-12.

2. Zheng L, Lv X, Zhang J, Liu S, Zhang J, Zhang Y. Translating Computer-Aided Design and Surgical Planning Into Successful Mandibular Reconstruction Using a Vascularized Iliac-Crest Flap. J Oral Maxillofac Surg. 2018 Apr;76(4):886-893.

3. Chim H, Salgado CJ, Mardini S, Chen HC. Reconstruction of mandibular defects. Semin Plast Surg. 2010 May;24(2):188-97.

4. Lee WB, Choi WH, Lee HG, Choi NR, Hwang DS, Kim UK. Mandibular reconstruction with a ready-made type and a custom-made type titanium mesh after mandibular resection in patients with oral cancer. Maxillofac Plast Reconstr Surg. 2018 Nov 25;40(1):35.

5. Foley BD, Thayer WP, Honeybrook A, McKenna S, Press S. Mandibular reconstruction using computer-aided design and computer-aided manufacturing: an analysis of surgical results. J Oral Maxillofac Surg. 2013 Feb;71(2):e111-9.

6. Stirling Craig E, Yuhasz M, Shah A, Blumberg J, Salomon J, Lowlicht R, Fusi S, Steinbacher DM. Simulated surgery and cutting guides enhance spatial positioning in free fibular mandibular reconstruction. Microsurgery. 2015 Jan;35(1):29-33.

7. Antony AK, Chen WF, Kolokythas A, Weimer KA, Cohen MN. Use of virtual surgery and stereolithography-guided osteotomy for mandibular reconstruction with the free fibula. Plast Reconstr Surg. 2011 Nov;128(5):1080-4.

8. Tarsitano A, Battaglia S, Crimi S, Ciocca L, Scotti R, Marchetti C. Is a computer-assisted design and computer-assisted manufacturing method for mandibular reconstruction economically viable? J Craniomaxillofac Surg. 2016 Jul;44(7):795-9.

9. Schepers RH, Raghoebar GM, Vissink A, Stenekes MW, Kraeima J, Roodenburg JL, Reintsema H, Witjes MJ. Accuracy of fibula reconstruction using patient-specific CAD/CAM reconstruction plates and dental implants: A new modality for functional reconstruction of mandibular defects. J Craniomaxillofac Surg. 2015 Jun;43(5):649-57.

10. Huang JW, Shan XF, Lu XG, Cai ZG. Preliminary clinic study on computer assisted mandibular reconstruction: the positive role of surgical navigation technique. Maxillofac Plast Reconstr Surg. 2015 Jul 30;37(1):20.

11. Mascha F, Winter K, Pietzka S, Heufelder M, Schramm A, Wilde F. Accuracy of computer-assisted mandibular reconstructions using patient-specific implants in combination with CAD/CAM fabricated transfer keys. J Craniomaxillofac Surg. 2017 Nov;45(11):1884-1897.

12. Rana M, Chin SJ, Muecke T, Kesting M, Groebe A, Riecke B, Heiland M, Gellrich NC. Increasing the accuracy of mandibular reconstruction with free fibula flaps using functionalized selective laser-melted patient-specific implants: A retrospective multicenter analysis. J Craniomaxillofac Surg. 2017 Aug;45(8):1212-1219.

13. Mazzoni S, Marchetti C, Sgarzani R, Cipriani R, Scotti R, Ciocca L. Prosthetically guided maxillofacial surgery: evaluation of the accuracy of a surgical guide and custom-made bone plate in oncology patients after mandibular reconstruction. Plast Reconstr Surg. 2013 Jun;131(6):1376-85.

14. Dérand P, Hirsch JM. Virtual bending of mandibular reconstruction plates using a computer-aided design. J Oral Maxillofac Surg. 2009 Aug;67(8):1640-3.

15. Leiggener C, Messo E, Thor A, Zeilhofer HF, Hirsch JM. A selective laser sintering guide for transferring a virtual plan to real time surgery in composite mandibular reconstruction with free fibula osseous flaps. Int J Oral Maxillofac Surg. 2009 Feb;38(2):187-92.

16. Seruya M, Fisher M, Rodriguez ED. Computer-assisted versus conventional free fibula flap technique for craniofacial reconstruction: an outcomes comparison. Plast Reconstr Surg. 2013 Nov;132(5):1219-28.

131

17. Peel S, Bhatia S, Eggbeer D, Morris DS, Hayhurst C. Evolution of design considerations in complex craniofacial reconstruction using patient-specific implants. Proc Inst Mech Eng H. 2017 Jun;231(6):509-524.

18. Kang SH, Kim MK, Lee JY. Single-tooth dento-osseous osteotomy with a computer-aided design/computer-aided manufacturing surgical guide. J Korean Assoc Oral Maxillofac Surg. 2016 Apr;42(2):127-30.

19. Wilde F, Winter K, Kletsch K, Lorenz K, Schramm A. Mandible reconstruction using patient-specific pre-bent reconstruction plates: comparison of standard and transfer key methods. Int J Comput Assist Radiol Surg. 2015 Feb;10(2):129-40.

20. Ciocca L, Mazzoni S, Fantini M, Persiani F, Baldissara P, Marchetti C, Scotti R. A CAD/CAM-prototyped anatomical condylar prosthesis connected to a custom-made bone plate to support a fibula free flap. Med Biol Eng Comput. 2012 Jul;50(7):743-9.

21. Ciocca L, Mazzoni S, Marchetti C, Scotti R. Technical aspects of prosthetically guided maxillofacial surgery of the mandible. A pilot test study. Acta Bioeng Biomech. 2014;16(2):21-9.

22. Steed M. Advances in the Management of Mandibular Condylar Fractures, An Issue of Atlas of the Oral & Maxillofacial Surgery Clinics, Volume 25-1 Elsevier 9th February 2017.

23. Van Baar GJC, Forouzanfar T, Liberton NPTJ, Winters HAH, Leusink FKJ. Accuracy of computer-assisted surgery in mandibular reconstruction: A systematic review. Oral Oncol. 2018 Sep;84:52-60.