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A Postoperative Evaluation Guideline for Computer-Assisted Reconstruction of the Mandible

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Xiaoyan Cao, PhD
Review Editor JOVE
1 Alewife Center #200
Cambridge, MA 02140

Amsterdam, October 24th, 2019

Dear dr. Cao,

Please find enclosed our revised manuscript entitled *"A postoperative evaluation guideline for computer-assisted reconstruction of the mandible"*, which we would like to resubmit for publication in the *Journal of Visualized Experiments (JOVE)*. The manuscript is authored by Gustaaf J.C. van Baar, Niels P.T.J. Liberton, Henri A.H. Winters, Tymour Forouzanfar and Frank K.J. Leusink. All authors agree on the content of the manuscript.

We wish to thank the editor and reviewers for the kind comments that enabled us to improve our evaluation guideline. We have earnestly tried to clarify the unclear points that were identified.

For details about the revision, we would like to refer you to the "Rebuttal Letter" file which is attached to the submission.

Our research group strives for uniformity in the planning and evaluation approaches in computer-assisted mandibular reconstruction. This is becoming increasingly important in light of the new European Union medical device regulation (MDR) which requires standardization and Conformité Européenne (CE) certification for the entire CAS process from spring 2020 onwards. By aiming to standardize CAS in mandibular reconstruction, comparing postoperative results and facilitate future meta-analyses, we believe that this evaluation guideline will be competitive and of interest to the readers/viewers of the *JOVE.*

Kindly looking forward to your reply,

Yours sincerely, also on behalf of the other co-authors,

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TITLE:

A Postoperative Evaluation Guideline for Computer-Assisted Reconstruction of the Mandible

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oral cancer, mandibular reconstruction, free tissue flaps, surgery computer-assisted, computer-aided design, computer-aided manufacturing, data accuracy, software

SUMMARY:

Here, we propose a practical, feasible and reproducible evaluation guideline for computer-assisted reconstruction of the mandible in order to create uniformity between studies regarding postoperative accuracy evaluation. This protocol continues and specifies an earlier publication of this evaluation guideline.

ABSTRACT:

Valid comparisons of postoperative accuracy results in computer-assisted reconstruction of the mandible are difficult due to heterogeneity in imaging modalities, mandibular defect classification, and evaluation methodologies between studies. This guideline uses a step-by-step approach guiding the process of imaging, classification of mandibular defects and volume assessment of three-dimensional (3D) models, after which a legitimized quantitative accuracy evaluation method can be performed between the postoperative clinical situation and the preoperative virtual plan. The condyles and the vertical and horizontal corners of the mandible are used as bony landmarks to define virtual lines in the computer-assisted surgery (CAS) software. Between these lines the axial, coronal, and both sagittal mandibular angles are calculated on both pre- and postoperative 3D models of the (neo)mandible and subsequently the deviations are calculated. By superimposing the postoperative 3D model to the preoperative

virtually planned 3D model, which is fixed to the XYZ axis, the deviation between pre- and postoperative virtually planned dental implant positions can be calculated. This protocol continues and specifies an earlier publication of this evaluation guideline.

INTRODUCTION:

Computer-assisted surgery (CAS) in reconstructive surgery involves four consecutive phases: a virtual planning phase, a three-dimensional (3D) modeling phase, a surgical phase, and a postoperative evaluation phase[1]. The planning phase starts with the obtainment of a craniofacial computed tomography (CT) scan, and a donor site CT or CT angiography (CTA) scan. Diverse tissue types correspond to an amount of X-ray attenuation, which leads to scan voxels with a specific gray value ranged according to Hounsfield units (HU) (human bone [+1000 HU], water [0 HU], and air [-1000 HU]). These images are stored in Digital Imaging and Communications in Medicine (DICOM) file format. By selecting the regions of interest (ROIs) in segmentation software, 3D models can be generated[2]. The most popular and feasible segmentation technique is thresholding: voxels above a selected HU threshold value are enclosed in the ROI. These voxels are subsequently converted into 3D models in the Standard Tessellation Language (STL) file format[3], and uploaded into CAS software to plan the osteotomies and to design 3D devices[4]. During the modeling phase, the designed devices are 3D printed and sterilized, followed by the surgical phase. The final evaluation phase consists of a postoperative CT scan of the patient's skull, followed by an accuracy analysis comparing the postoperative result with the preoperative virtual plan.

Our recently published systematic review regarding accuracy of computer-assisted mandibular reconstructions showed heterogeneity in image acquisition, classification of mandibular defects, and evaluation methodologies. This heterogeneity limits valid comparisons of postoperative hard tissue accuracy results between studies[5]. Standardization of CAS phases in the process of mandibular reconstruction is important due to the new European Union medical device regulation (MDR), which demands Conformité Européenne (CE) certification for all different CAS processes, and which will be operational from spring 2020[6]. Here, we present a practical, feasible and reproducible evaluation guideline for computer-assisted reconstructions of the mandible in order to create uniformity between studies regarding postoperative accuracy evaluation. This protocol continues and specifies an earlier publication of this evaluation guideline[7], which is currently being tested in a large multicenter cohort study in which all different types of mandibular reconstructions will be analyzed for their accuracy aiming to discover tolerable outcome ranges regarding functionality.

PROTOCOL:

The Medical Ethics Review Committee of VU University Medical Center (registered with the US Office for Human Research Protections [OHRP] as IRB00002991) confirmed that the Medical Research Involving Human Subjects Act (WMO) does not apply to this study. The FWA number assigned to VU University Medical Center is FWA00017598.

NOTE: Validate all steps in this protocol independently by two different observers.

1. Skull and donor site imaging

1.1. Execute both pre- and postoperative scanning with a multiple detector CT (MDCT), using the same machine and scanner settings, with the parameter slice thickness (ST) set <1.25 mm. Perform the postoperative MDCT scan within six weeks after reconstruction.

NOTE: In case of adjuvant radiation therapy, use the first postoperative MDCT scan prior to the therapy.

2. Classification of the mandibular defect

2.1. Classify the mandibular defect according to the classification of Brown et al.[8].

3. Segmentation of the DICOM images of the postoperative CT scan

3.1. Open the image-based 3D medical software (e.g., Mimics inPrint 3.0). Click **File** and **New from Disk**, then a folder window will open. Select the folder that contains the DICOM images of the postoperative CT scan to import (select the whole folder), choose the right study in the list, and click **Convert**. A window will pop up for assessment of the orientation of the skull.

3.2. Change the orientation by left clicking the orientation characters; click **OK** to validate.

3.3. Perform the 5-step segmentation workflow.

3.3.1. To create ROI, click the **Thresholding** tool. Create the ROI by defining a threshold containing all the voxels of the mandibular bone within a certain interval of gray values, which is proportional to the density of the bony tissue. Manually tweak the Hounsfield range by moving the two sliders on the left and the right. Click the green button to validate the segmentation.

NOTE: The thresholding tool allows the user to select the bone within a range of density, expressed in Hounsfield Units. After this step, a new ROI appears in the ROI tab and the software jumps to the second step of the workflow.

3.3.2. To edit ROI, choose the **Isolate** tool; click the mandible in the 3D viewport, which will be automatically isolated from the cranium and becomes green. Select the option **Create result in new ROI**. Click the green button to validate the isolation and subsequently all the non-connected structures disappear. Rename the ROI (“Mandible Post-op”).

NOTE: Optionally, use the **Lasso** tool to remove scattering by editing the ROI directly on the images or in the 3D viewport. When the CT scan is of poor quality, the condyles can be connected to the skull. In that case, click the **Split** tool, which asks the user to define a foreground and a background. Select **Foreground** and select the mandible thorough the axial or coronal coupes. Select **Background** and select the maxilla and cranium thorough the axial or coronal coupes. The region corresponding with the foreground will be kept in the ROI and the region corresponding with the background will be deleted. Click the green button to validate.

3.3.3. When ROI is finished and ready to be converted into a 3D model, click the **Add Part** button of the workflow toolbar. Click the **Solid Part** tool. Select the solid part **Mandible Post-op** and select **Off** in the **Smoothing** options. Click the green button to validate.

3.3.4. When the parts are constructed, the software automatically goes to the fourth step of the workflow: edit part. With the contours of the created parts shown on the images, assess the accuracy of the parts. Skip the **Smooth** tool.

3.3.5. In the last step of the workflow (prepare print), select the **Mandible Post-op** part in the export menu, choose the output directory, select the 1,00 scale and click the green button to validate.

NOTE: The “Mandible Post-op” part is now exported as an .STL file.

4. XYZ axis orientation

NOTE: The preoperative STL model includes the cranium, (neo)mandible, and the virtually planned dental implants (if planned). Note that the evaluation works easier with separated STL files of the cranium and skull, but still in fixed position to each other. When the preoperative STL model of the cranium and the mandible are merged, use the 3D medical software (following the steps described above) to split the mandible from the cranium.

4.1. Open the evaluation software (**Table of Materials**). Drag the preoperative STL file (including virtual plan) in the popped-up screen.

4.2. Determine the Frankfurt plane, midsagittal plane, and the nasion for uniform orientation of the preoperative STL model of the skull on the XYZ axis.

4.2.1. Click **Construct** | **Plane** | **3-Point Plane** and create a virtual point by using Ctrl + left click both the internal acoustic foramina and the left infraorbital margin (Frankfurt plane)[9]. Click **Create and close** after pointing on the STL model.

4.2.2. Click **Construct** | **Line** | **2-Point Line** and create a virtual point by using Ctrl + left click the nasion and the incisive foramen (midsagittal plane)[10].

4.2.3. Click **Construct** | **Point** | **Point** and create a virtual point by using Ctrl + left click the nasion.

4.2.4. Click **Operations** | **Main Alignment** | **Plane-Line-Point**. Combine the actual parameter “Plane 1” with the nominal parameter “Plane Z”, the actual parameter “Line 1” with the nominal parameter “Line Y”, and the actual parameter “Point 1” with the nominal parameter “Global coordinate system”.

NOTE: The preoperative STL models of the cranium and (neo)mandible are now fixed to the XYZ axis (**Figure 1**).

5. Volume assessment of the pre- and postoperative STL models

NOTE: Examine pre- and postoperative STL models on volume similarity to rule out volume inaccuracies between the two models as much as possible, since they can influence accuracy measurements.

5.1. Select the STL file of only the preoperative (neo)mandible under **Actual Elements**, where all "Meshes" are shown. Click **Operations** | **CAD** | **Actual Mesh To CAD**. Select **New CAD data** in the popped-up menu, rename the file (e.g., "Mandible Pre-op") and click **OK**.

NOTE: The preoperative STL model is now visible under **Nominal Elements** | **CAD** in the left explorer menu.

5.2. Drag the postoperative STL model into the software (created during section 3 of the protocol). Rename the file (e.g., "Mandible Post-op"). Select the STL file under **Actual Elements** in the left explorer menu where all "Meshes" are shown. Click **Operations** | **Alignment** | **Single Element Transformation** | **3-Point Alignment**.

5.3. In the popped-up menu, combine 3 "Nominal points" on the "Mandible Pre-op" (e.g., condyle superior, horizontal, and vertical corner of the mandible) with 3 similar "Actual points" on the "Mandible Post-op" by ctrl + left clicking. Validate with **Apply and Close**.

NOTE: The STL models will be roughly superimposed on each other based on these 3 landmarks. This will speed up the calculations of the software during the next steps.

5.4. Deselect the **Mandible Pre-op** and select the **Mandible Post-op** in the left explorer menu. Click the **Select/Deselect on Surface** tool in the bottom toolbar. Select a surface on the remnant mandible on both the lateral and medial sides (not in touch with the osteosynthesis material).

5.5. Click **Operations** | **Alignment** | **Single Element Transformation** | **Local Best Fit**. Select **All CAD groups** as the targeted element in the popped-up menu. Take a maximum distance of 10.000 mm. Validate with **Apply and Close**.

NOTE: The selected part of the remnant mandible of the "Mandible Post-op" will be accurately superimposed on the similar part of the "Mandible Pre-op". Now both models are ready for the STL volume assessment.

5.6. Click the **Select/Deselect on Surface** tool in the bottom toolbar. Select a surface on only the lateral side within the surface of the previous step. Click **Inspection** | **CAD Comparison** | **Surface Comparison on Actual**.

5.7. Use a maximum distance of 10.00 mm in the popped-up menu and validate with **OK**. Click with the right mouse button on this surface, choose **Select Patch**. Click the magnifying glass on the toolbar above. A round toolbar pops up in the screen. Click **Check | Deviation Label Arithmetic Mean** and the arithmetic mean in mm will be shown (**Figure 2**).

5.8. In case of an arithmetic mean <0.5 mm, continue to section 6 of this protocol. In case of an arithmetic mean >0.5 mm, repeat the postoperative CT scan (DICOM file) segmentation in the 3D medical software by adjusting the threshold values. Repeat the segmentation and superimposition until an arithmetic mean <0.5mm is achieved.

NOTE: The two STL volumes are now ready for valid accuracy comparisons.

6. Superimposition of the condylar processes

6.1. Deselect the **Mandible Pre-op** and select the **Mandible Post-op** in the left explorer menu. Click the **Select/Deselect on Surface** tool in the bottom toolbar. Select the whole surfaces of both condyles by drawing planes (lateral and medial side) from the most caudal point of the incisura mandibulae (mandibular notch) perpendicular to the posterior edge of the border between condyle and the vertical corner.

6.2. Click **Operations | Alignment | Single Element Transformation | Local Best Fit**. Select **All CAD groups** as the targeted element in the popped-up menu. Take a maximum distance of 10.000 mm. Validate with **Apply and Close**.

NOTE: The selected condyles of the "Mandible Post-op" will be accurately superimposed on condyles of the "Mandible Pre-op" (**Figure 3**).

7. Calculation of the coronal, axial, and sagittal mandibular angles

NOTE: The identification of bony landmarks is performed separately on the "Mandible Pre-op" and "Mandible Post-op" STL models. Deselect the **Mandible Post-op** while identifying bony landmarks in the "Mandible Pre-op", and vice versa.

7.1. Select the **Mandible Pre-op** in the left explorer menu. Click **Construct | Point | Surface Point** to determine virtual points on the condyle superior (CS), condyle posterior (CP), vertical corner (VC), and horizontal corner (HC) according to the classification of Brown et al.[8].

7.2. Select the **Mandible Post-op** in the left explorer menu. Click **Construct | Point | Projection Point** to determine virtual points on the CS, CP, VC, and HC according to the classification of Brown et al.[8].

NOTE: For Brown class Ic, IIc or IVc defects, determine virtual points on the most superior and posterior part of the vertical segment of bone graft or the titanium/prosthetic condyle. If the mandibular resection includes one or more corners, select the most inferior point of the osteotomy plane between the two segments of bone graft. When the mandibular resection includes only half of a horizontal or vertical corner (remnant mandible next to a segment of bone graft), determine a virtual point on the segment of bone graft on the most inferior part of the osteotomy plane. In case of a Brown class I mandibular defect, determine a virtual point on the most anterior and inferior part of the horizontal segment of bone graft and consider this virtual point as the horizontal corner. In case of (extra) osteotomies outside the anatomical vertical or horizontal corner, determine the osteotomy closest to these corners as vertical or horizontal corner.

7.3. To create a line between 2 virtual points, click **Construct** | **Line** | **2-Point Line**. Select 2 points under **construction elements** in the popped-up menu to connect them with a line. Click **Create and close**.

7.4. To create an angle between 2 lines, click **Construct** | **Angle** | **3-Point Angle**. Subsequently select **Point 1**, **Angle Point** and **Point 2** in the popped-up menu. Click **Create and close**.

NOTE: The angle between the 2 lines is calculated and shown.

7.5. With this knowledge, determine the right and left coronal mandibular angles between the lines from CS to VC and the midsagittal line (ML).

7.5.1. Determine the right and left axial mandibular angles between the lines from VC to HC and ML.

7.5.2. Determine the sagittal mandibular angles between the lines from CP to VC and the lines from VC to HC.

7.5.3. Calculate and report the deviations in degrees (°) between the postoperative angles and the virtual planned angles.

8. Calculation of the XYZ deviations and distance XYZ of the virtually planned dental implants

NOTE: Use the correct dental implant diameter and height (including cover screw) during the preoperative planning for correct comparison.

8.1. Click **Construct** | **Point** | **Point** and create a virtual point by using Ctrl + left click in the middle and top of the cover screws of the dental implants in the “Mandible Pre-op” file.

8.2. Click **Construct** | **Point** | **Surface Point** and create a virtual point by using Ctrl + left click in the middle and top of the cover screws of the dental implants in the “Mandible Post-op” file.

8.3. Click **Construct** | **Distance** | **2-Point Distance** and connect all points on the dental implants with each other in the popped-up menu.

8.4. Select all the points on the dental implants in both the "Mandible Pre-op" and the "Mandible Post-op" files in the left explorer menu. Click the magnifying glass on the toolbar above. A round toolbar pops up in the screen. Click **Check** and select **dXYZ** to show the distance XYZ in mm per dental implant using the formula:

$$dXYZ = \sqrt{(x^2 - x^1)^2 + (y^2 - y^1)^2 + (z^2 - z^1)^2}$$

REPRESENTATIVE RESULTS:

A James Brown class III mandibular defect was reconstructed at our department with the fibula free flap as a donor site. Direct guided dental implant placement was performed with the use of a fibula cutting guide which also included dental implant guides. The reconstruction was evaluated with the presented guideline. The coronal, axial and sagittal mandibular angle deviations (°) and six dental implant XYZ distances (mm) were calculated and reported (**Figure 4** and **Figure 5**).

FIGURE LEGENDS:

Figure 1: Uniform orientation of the preoperative STL model of the skull on the XYZ axis with the Frankfurt plane projected to the Z axis (red line), the midsagittal plane projected to the Y axis (green line), and the nasion projected to the X axis (blue line).

Figure 2: A part of the right side of the mandible (without involvement of osteosynthesis material which causes scattering) of the preoperative virtually planned STL model is superimposed on the postoperative STL model. Subsequently the CAS software is used to calculate the arithmetic mean. The 0.02 mm deviation between both volumes in this example falls within the norm (<0.5 mm) to proceed to the next step of the evaluation guideline.

Figure 3: Superimposition of the postoperative STL model (grey) on the preoperative STL model, revised to the virtual plan (blue). Only both condylar processes are selected for the iterative closest-point algorithm (red).

Figure 4: Reconstruction of a Brown class III defect using the fibula free flap as a donor site. In this example, six virtually planned dental implants are primary placed during the reconstruction using a 3D guide. The coronal, axial and sagittal angles are calculated on both the preoperative virtually planned 3D model and the postoperative 3D model. The deviations between the angles in degrees (°) are shown. CS, condyle superior; CP, condyle posterior; VC, vertical corner; HC, horizontal corner; ML, midsagittal line; FFF, fibula free flap.

Figure 5: Dental implant deviations on the X, Y and Z axis and the distance XYZ (dXYZ) of the six guided placed dental implants.

DISCUSSION:

This postoperative evaluation guideline aims to facilitate increased uniformity of accuracy analysis of computer-assisted mandibular reconstructions. The focus is on four components determining the success of mandibular reconstruction: (1) the position of both condyles, (2) the angles of the osteotomy planes, (3) the size, position and fixation of the bone graft segments, and (4) the position of the guided dental implants (if immediate performed and included in the virtual planning).

In the first step of our proposed protocol, we recommend MDCT scanning for both pre- and postoperative imaging, because the quality of CT images affects the volume accuracy of segmented STL models. The largest volume deviations are found in STL models segmented out of cone beam computed tomography (CBCT) scanner DICOM data[11]. These volume deviations influence accuracy and fitting of 3D printed templates and guides, and thus also influences postoperative accuracy measurements between pre- and postoperative STL models. Therefore, we recommend the use of MDCT scanners in both pre- and postoperative imaging for mandibular reconstruction using CAS. Slice thickness is the most influencing factor in STL volume accuracy and should be set <1.25 mm. A higher slice thickness yields to loss of detail in the STL models and affects accuracy measurements[12,13]. A recently published systematic review on accuracy in mandibular reconstruction using CAS showed poor description in the materials and methods section of CT scanner parameters used by authors[5]. In our opinion, CAS studies should always specify the type and parameters of pre- and postoperative imaging modalities in the materials and methods section. In order to avoid long term changes in the volume, shape, and position of the segments of the bone graft, the postoperative MDCT scan should be performed within six weeks after reconstruction[14]. In case of adjuvant radiation therapy, use the first postoperative MDCT scan prior to the therapy to avoid radiation related pathology in the mandibular bone[15].

Classification of mandibular defects is needed to compare reconstructions with similar complexity. In 2016, Brown et al.[8] proposed a mandibular defect classification describing four classes, with a relationship between the class number and the complexity of the reconstruction. The alignment of pre- and postoperative STL models in the CAS software to evaluate the accuracy of the reconstruction introduces some difficulties. The superimposition software tool moves a selected part of an STL model (the source) to best match a fixed part of an STL model (the reference) using an iterative closest-point algorithm. However, superimposition of the entire (neo)mandible is inaccurate due to scattering of the reconstruction plate(s), which will lead to shifts of the entire reconstruction, not representing the postoperative clinical position of the mandible[16]. The same problem is introduced while superimposing isolated parts of the reconstruction[17]. Superimposition of the mandible including the maxilla and cranium is inaccurate because mouth opening will always be different during the pre- and postoperative scanning. Therefore, to evaluate the postoperative position of the (neo)mandible we decided to create mandibular angles (pioneered by De Maesschalck et al.[18]) on both pre-and postoperative STL models separately to bypass the superimposition problems. However, to evaluate the dental implant positions we necessarily needed to align both models, using the superimposition software tool. To align pre- and postoperative STL models with the closest approach to the clinical postoperative intermaxillary relation, we believe that superimposition of only both condylar processes is the most feasible, standardized and reproducible method. Although the postoperative position of both condyles can be affected by inaccurate neomandible reconstruction, the intermaxillary relation will accommodate to the midline and thus averages the position of both condyles around the midsagittal plane[19]. In our protocol, only the preoperative STL model is quickly fixed to the XYZ axis using a plane-line-point tool in the CAS software, representing a benchmark from which the postoperative deviations of the dental implants can be determined. The fixed skull position on the XYZ axis can lead to small cephalometric differences between cases. However, this has no influence on the dental implant measurements, because it has no consequences for the distance XYZ in mm between dental implant positions when the postoperative 3D model is superimposed onto the fixed preoperative 3D model with only both condyles selected for the iterative closest point algorithm.

As described above, De Maesschalck et al.[18] pioneered an evaluation method for hard tissue accuracy of mandibular reconstruction using CAS, bypassing the need for osteotomy plane determination and bypassing the use of a superimposition tool. The most serious disadvantage of this method is that it failed to specify the method used to determine the midsagittal plane, which needs to be standardized and reproducible. Also, no virtually planned dental implants are included and a differentiation between complexity of mandibular reconstructions is lacking. We included the evaluation of postoperative positions of virtually planned dental implants in our protocol because the number of authors applying guided dental implants in the future is likely to increase. In 2016, Schepers et al.[20] proposed an excellent postoperative evaluation method for virtually planned dental implants in mandibular reconstruction using CAS by measuring the center point deviation (mm) and angular deviation (°) per dental implant. The main limitation of this method is the quantity of measurements per implant which decreases the feasibility and results in loss of overview of accuracy of the entire reconstruction. We propose a more simplified method by determining one recapitulatory number per dental implant by measuring the distance XYZ (dXYZ in mm). With regard to dental rehabilitation, the position of the neck of the dental implant is decisive for future prosthetics. Therefore, our evaluation protocol recommends creating virtual points on the neck of the dental implants in the pre- and postoperative STL models. To keep the evaluation of the dental implants feasible we decided to skip angular deviation measurements, because angular deviations up to 15° can be corrected with angled implant abutments.

Our proposed guideline is applicable for all types of donor sites and allows for different bone graft fixation possibilities. Also, CT scattering of metal fixation parts in the postoperative imaging will not influence measurements of the guideline[5]. In this evaluation guideline, we used Mimics inPrint 3.0 and GOM Inspect Professional 2019. However, the protocol describes software tools which are available in all CAS software packages. This guideline aims to contribute to a much more standardized and uniform approach to objectify relationships between accuracy and all different approaches during the CAS phases. There is abundant room for further progress in determining acceptable mandibular angle deviations per Brown class, their relationship with the postoperative positions of virtually planned dental implants, and acceptable dental implant deviations (dXYZ) for future prosthetics. Currently, our department is conducting a multicenter study to validate this guideline in a large cohort, which also takes all the above-mentioned variables into account.

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DISCLOSURES:
The authors have nothing to disclose.

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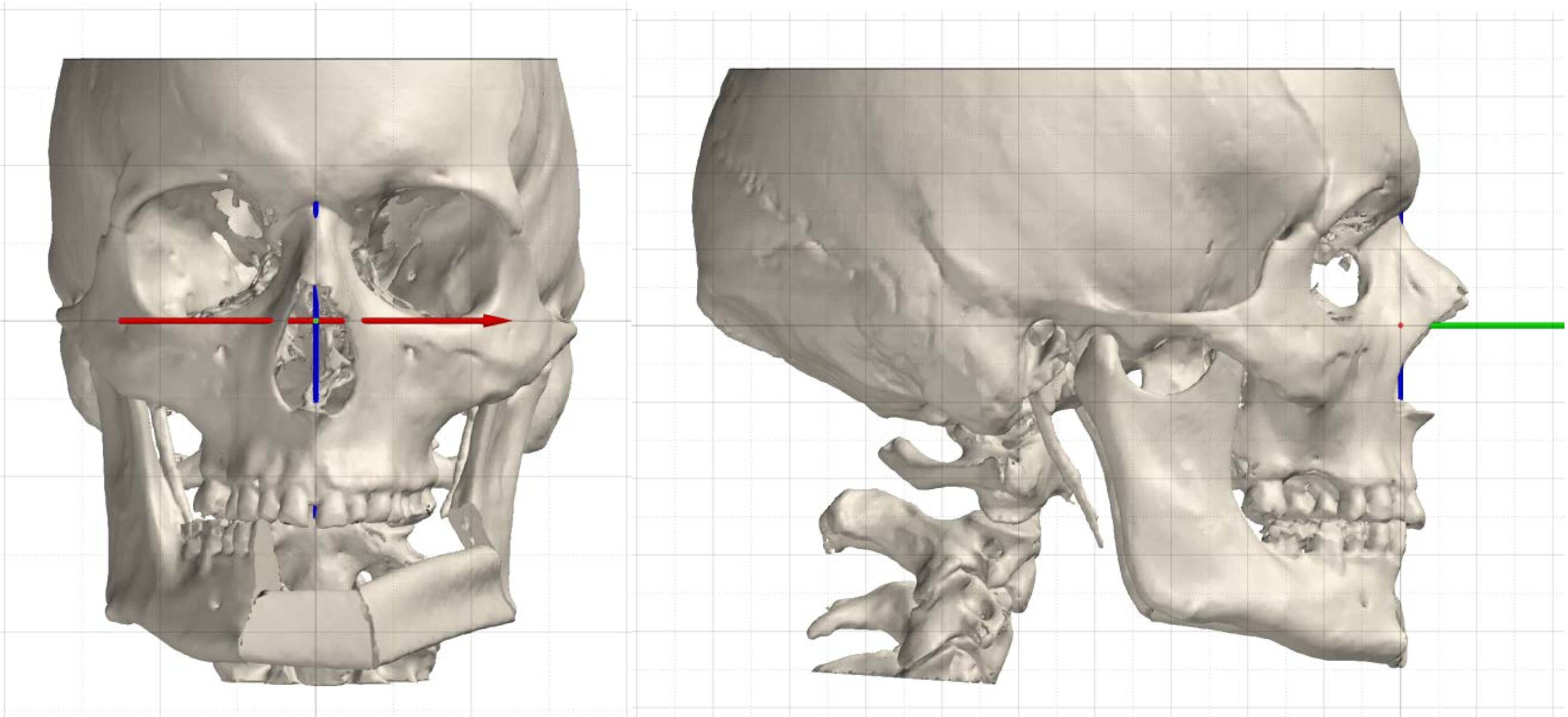


Figure 2

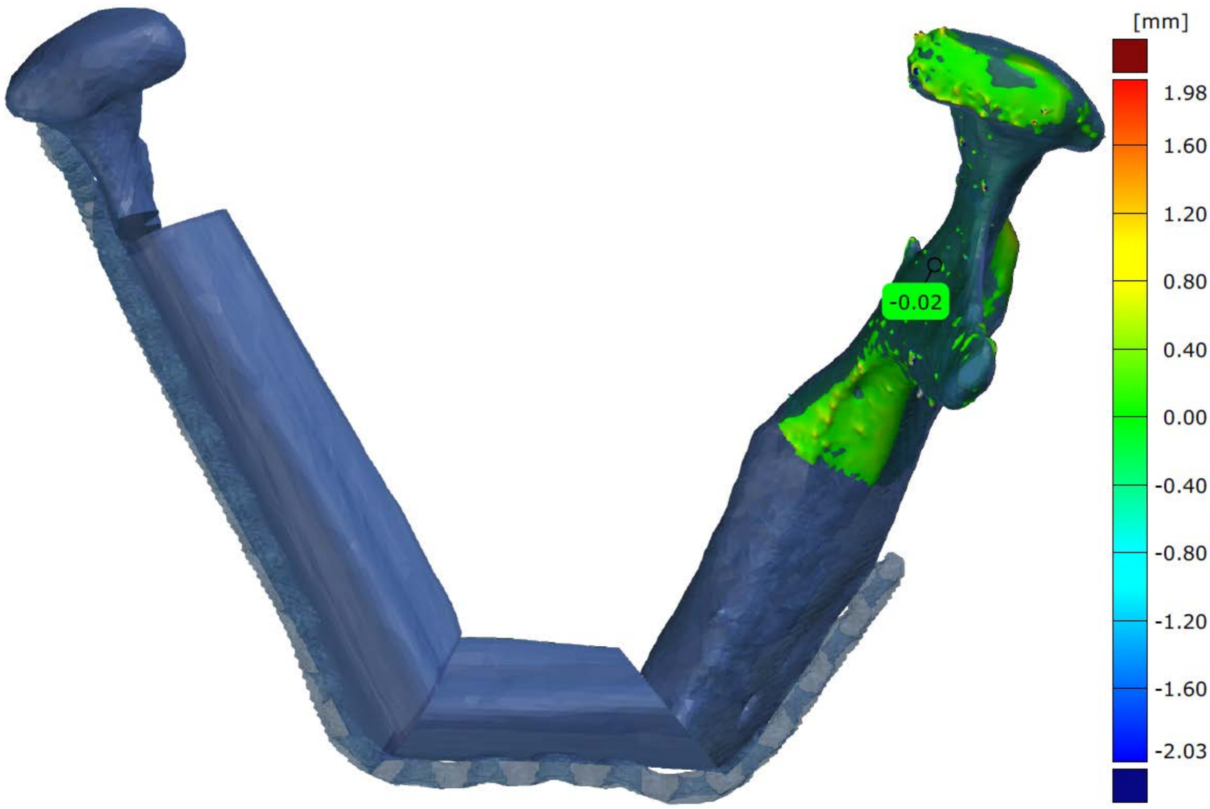


Figure 3 Click here to access/download;Figure;Figure 3.pdf

Figure 4

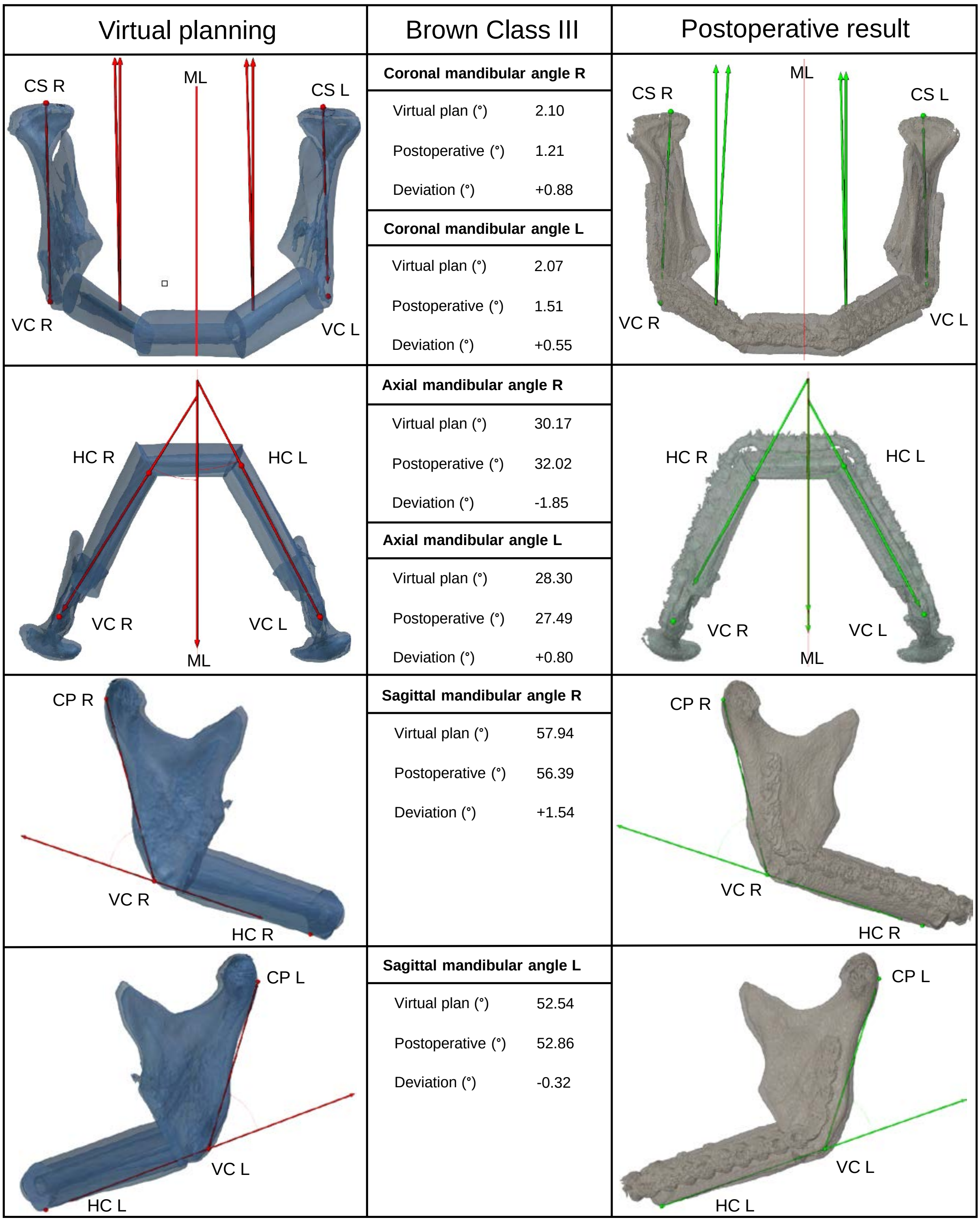
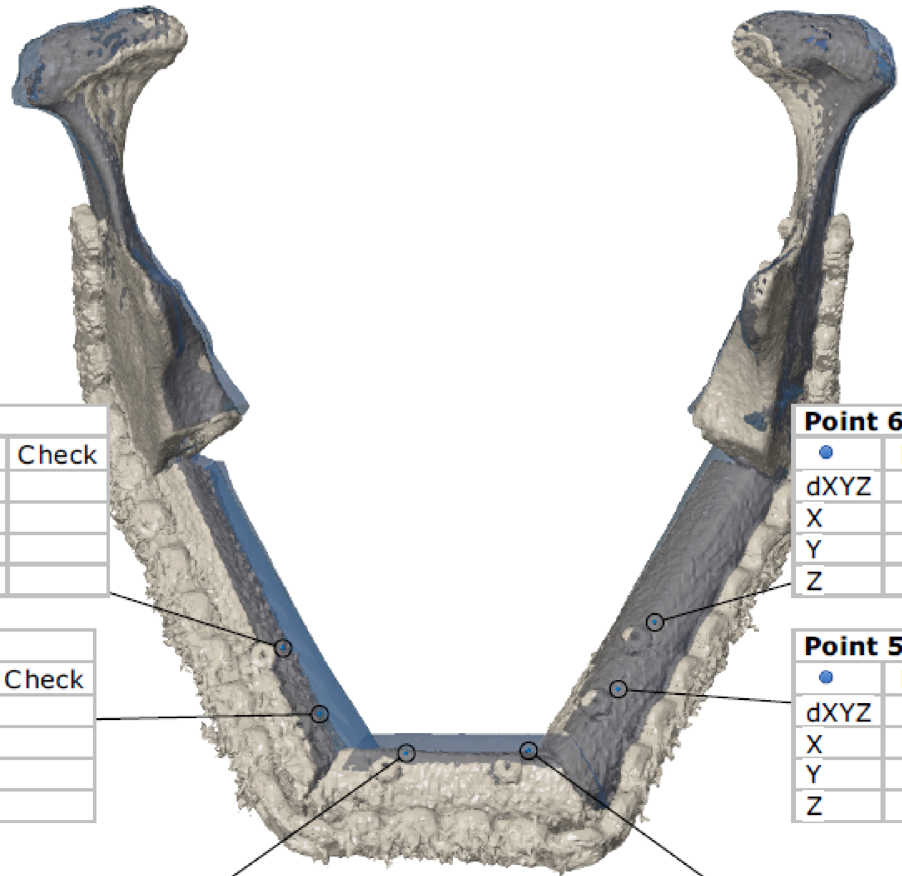

Virtual planning
Brown Class III
Postoperative result
CS R
ML
CS L
VC R
VC L
Coronal mandibular angle R
Virtual plan (°) 2.10
Postoperative (°) 1.21
Deviation (°) +0.88
Coronal mandibular angle L
Virtual plan (°) 2.07
Postoperative (°) 1.51
Deviation (°) +0.55
HC R
HC L
VC R
VC L
ML
Axial mandibular angle R
Virtual plan (°) 30.17
Postoperative (°) 32.02
Deviation (°) -1.85
Axial mandibular angle L
Virtual plan (°) 28.30
Postoperative (°) 27.49
Deviation (°) +0.80
CP R
VC R
HC R
Sagittal mandibular angle R
Virtual plan (°) 57.94
Postoperative (°) 56.39
Deviation (°) +1.54
CP L
VC L
HC L
Sagittal mandibular angle L
Virtual plan (°) 52.54
Postoperative (°) 52.86
Deviation (°) -0.32

Figure 5



Point 1

●	Nominal	Actual	Dev.	Check
dXYZ			+3.00	
X	-25.39	-28.18	-2.79	
Y	+19.94	+18.96	-0.98	
Z	+3.31	+2.80	-0.51	

Point 2

●	Nominal	Actual	Dev.	Check
dXYZ			+3.09	
X	-20.11	-22.89	-2.78	
Y	+9.65	+8.86	-0.79	
Z	+0.11	-0.98	-1.09	

Point 3

●	Nominal	Actual	Dev.	Check
dXYZ			+3.43	
X	-7.54	-10.42	-2.88	
Y	+2.50	+0.91	-1.59	
Z	-0.73	-1.70	-0.97	

Point 4

●	Nominal	Actual	Dev.	Check
dXYZ			+3.71	
X	+10.18	+7.25	-2.93	
Y	+2.54	+0.76	-1.78	
Z	-0.27	-1.69	-1.42	

Point 5

●	Nominal	Actual	Dev.	Check
dXYZ			+3.71	
X	+23.13	+19.99	-3.14	
Y	+11.76	+11.00	-0.76	
Z	+3.12	+1.30	-1.82	

Point 6

●	Nominal	Actual	Dev.	Check
dXYZ			+3.55	
X	+28.42	+25.70	-2.72	
Y	+21.96	+20.67	-1.29	
Z	+6.60	+4.72	-1.88	

Name of Material/Equipment	Company	Catalog Number	Comments/Description
GOM Inspect Professional 2019	GOM		Evaluation software
Mimics inPrint 3.0	Materialise		Image-based 3D medical software

Responses to comments of reviewers

A postoperative evaluation guideline for computer-assisted reconstruction of the mandible

Manuscript number: JoVE60363R1

We wish to thank the editor and reviewers for the kind comments that enabled us to improve our evaluation guideline. We have earnestly tried to clarify the unclear points that were identified.

Responses to comments of the Editor:

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues. The JoVE editor will not copy-edit your manuscript and any errors in the submitted revision may be present in the published version.

We performed a final check on the paper. We believe that the English language used throughout this paper is correct, clear and concise. The grammar has been extensively reviewed by a native speaker.

2. Please revise lines 53-56, 62-64, 194-198, 208-210, 256-259, 271-272, 282-284 to avoid textual overlap with previously published work.

We revised the lines which were mentioned by the editor:

Lines 53-56:

Lines are determined between the condyle, vertical- and horizontal corner (according to the mandibular defect classification of Brown et al.) and subsequently the axial, coronal, and sagittal mandibular angles are calculated. The evaluation of postoperative positions of virtually planned dental implants is included, because the number of authors applying guided dental implants in the future is likely to increase.

Has been changed to:

The condyles and the vertical- and horizontal corners of the mandible are used as bony landmarks to define virtual lines in the CAS software. Between these lines the axial, coronal, and both sagittal mandibular angles are calculated on both pre- and postoperative 3D models, and subsequently the deviations are calculated. By superimposing the postoperative 3D model to the preoperative virtually planned 3D model, which is fixed to the XYZ-axis, the deviation between pre- and postoperative virtually planned dental implant positions can be calculated.

Lines 62-64:

Computer-assisted surgery (CAS) in mandibular reconstruction includes a planning, modeling, surgical, and evaluation phase[1]. The planning phase starts with a computed tomography (CT) scan of the skull, and a CT or CT angiography of the donor site.

Has been changed to:

Computer-assisted surgery (CAS) in reconstructive surgery involves four consecutive phases; a virtual planning phase, a 3D modeling phase, a surgical phase, and a postoperative evaluation phase[1]. The planning phase starts with the obtainment of a craniofacial computed tomography (CT) scan, and a donor site CT or CT angiography (CTA) scan.

Lines 194-198:

Fig. 1 Guideline step 3: an example given of the STL volume assessment. A part of the remnant mandible (not in touch with the osteosynthesis material because of scattering) of the preoperative STL model is superimposed on the postoperative STL model. The arithmetic mean in this example is 0.02 mm, which is accurate enough (< 0.5 mm) to continue to the next step in the evaluation guideline.

Has been changed to:

Fig. 1 Guideline step 3: A part of the right side of the mandible (without involvement of osteosynthesis material which causes scattering) of the preoperative virtually planned STL model is superimposed on the postoperative STL model. Subsequently the CAS software is used to calculate the arithmetic mean. The 0.02mm deviation between both volumes in this example falls within the norm (< 0.5mm) to proceed to the next step of the evaluation guideline.

Lines 208-210:

Fig. 4 A Brown class III defect reconstructed with the FFF including six virtually planned dental implants and evaluated with the guideline. Coronal, axial and sagittal angles of the virtual planning and the postoperative result are shown and compared.

Has been changed to:

Fig. 4 Reconstruction of a Brown class III defect using the fibula free flap as a donor site. In this example, six virtually planned dental implants are primary placed during the reconstruction using a 3D guide. The coronal, axial and sagittal angles are calculated on both the preoperative virtually planned 3D model and the postoperative 3D model. The deviations between the angles in degrees (°) are shown.

Lines 256-259 (mentioned by the editor), including the order of the whole paragraph has been changed to clarify the argumentation to use both condyles for superimposition.

To align pre- and postoperative STL models with the closest approach of the postoperative clinical situation, superimposition of both condylar processes is the most simple and reproducible method. The superimposition tool in the CAS software calculates the 'best fit' of two clouds of points with an iterative closest-point algorithm. Although the postoperative position of both condyles will be affected by inaccurate neomandible reconstruction, the intermaxillary relation will accommodate to the midline and thus averages the position of both condyles around the midsagittal plane[17]. Superimposition of the entire (neo)mandible is inaccurate due to scattering of the reconstruction plate(s), which will lead to shifts of the entire reconstruction, not representing the postoperative clinical position of the mandible[18]. The same problem is introduced while superimposing isolated parts of the reconstruction[19].

Superimposition of the mandible including the maxilla and cranium is inaccurate because mouth opening will always be different during the pre- and postoperative scanning.

Has been changed to:

The alignment of pre- and postoperative STL models in the CAS software to evaluate the accuracy of the reconstruction introduces some difficulties. The superimposition software tool moves a selected part of an STL model (the source) to best match a fixed part of an STL model (the reference) using an iterative closest-point algorithm. However, superimposition of the entire (neo)mandible is inaccurate due to scattering of the reconstruction plate(s), which will lead to shifts of the entire reconstruction, not representing the postoperative clinical position of the mandible[16]. The same problem is introduced while superimposing isolated parts of the reconstruction[17]. Superimposition of the mandible including the maxilla and cranium is inaccurate because mouth opening will always be different during the pre- and postoperative scanning. Therefore, to evaluate the postoperative position of the (neo)mandible we decided to create mandibular angles (pioneered by De Maesschalck et al.[18]) on both pre-and postoperative STL models separately to bypass the superimposition problems. However, to evaluate the dental implant positions we necessarily needed to align both models, using the superimposition software tool. To align pre- and postoperative STL models with the closest approach to the clinical postoperative intermaxillary relation, we believe that superimposition of only both condylar processes is the most feasible, standardized and reproducible method. Although the postoperative position of both condyles can be affected by inaccurate neomandible reconstruction, the intermaxillary relation will accommodate to the midline and thus averages the position of both condyles around the midsagittal plane[19].

Lines 271-272:

De Maesschalck does not use a standardized and reproducible method to determine the midsagittal plane.

Has been changed to:

De Maesschalck failed to specify the method used to determine the midsagittal plane, which needs to be standardized and reproducible.

Lines 282-284:

The virtual points are created on the neck of the dental implant, which is most important with regard to the future dental rehabilitation. Angular deviations (up to 15°) are not a major burden because angled abutments are able to correct these deviations. Therefore, angular deviation of the dental implants is not taken into account.

Has been changed to:

With regard to dental rehabilitation, the position of the neck of the dental implant is decisive for future prosthetics. Therefore, our evaluation guideline recommends to create virtual points on the neck of the dental implants in the pre- and postoperative STL models. To keep the evaluation of the dental implants feasible we decided to skip angular deviation measurements, because angular deviations up to 15° can be corrected with angled implant abutments.

3. All methods that involve the use of human or vertebrate subjects and/or tissue sampling must include an ethics statement. Please provide an ethics statement at the beginning of the protocol section indicating that the protocol follows the guidelines of your institution.

We added the following sentences at the beginning of the protocol:

The Medical Ethics Review Committee of VU University Medical Center (registered with the US Office for Human Research Protections (OHRP) as IRB00002991) confirmed that the Medical Research Involving Human Subjects Act (WMO) does not apply to this study. The FWA number assigned to VU University Medical Center is FWA00017598.

4. Please revise the Protocol to contain only action items that direct the reader to do something (e.g., "Do this," "Ensure that," etc.). The actions should be described in the imperative tense in complete sentences wherever possible. Avoid usage of phrases such as "could be," "should be," and "would be" throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a "NOTE." Please include all safety procedures and use of hoods, etc. However, notes should be used sparingly and actions should be described in the imperative tense wherever possible. Please move the discussion about the protocol to the Discussion.

Line 93:

NOTE: All steps in this protocol should be independently validated by two different observers.

Has been changed in:

NOTE: Validate all steps in this protocol independently by two different observers.

Lines 96-100:

1.1. Execute both pre- and postoperative scanning with a multiple detector CT (MDCT), using the same machine and scanner settings. Slice thickness affects the STL volume accuracy and should be set <1.25mm. A higher slice thickness yields to loss of detail in the STL models[8,9]. Perform the postoperative MDCT scan within six weeks after reconstruction to bypass long term changes in the volume, shape and position of the segments of the bone graft[10].

Has been changed to:

1.1. Execute both pre- and postoperative scanning with a multiple detector CT (MDCT), using the same machine and scanner settings, with the parameter slice thickness set <1.25mm. Perform the postoperative MDCT scan within six weeks after reconstruction.

The sentence (lines 98-100):

"Perform the postoperative MDCT scan within six weeks after reconstruction to bypass long term changes in the volume, shape and position of the segments of the bone graft[10]."

Has been moved to the end of the second paragraph of the discussion, because it discusses the protocol.

Lines 101-102:

NOTE: In case of adjuvant radiation therapy, use the first postoperative MDCT scan prior to the therapy to avoid radiation related pathology in the mandibular bone[11].

Has been changed to:

NOTE: In case of adjuvant radiation therapy, use the first postoperative MDCT scan prior to the therapy.

The sentence (lines 101-102):

"In case of adjuvant radiation therapy, use the first postoperative MDCT scan prior to the therapy to avoid radiation related pathology in the mandibular bone[11]."

Has been moved to the end of the second paragraph of the discussion, because it discusses the protocol.

Lines 104-105:

2.1. Classify the mandibular defect according to the classification of Brown et al. to facilitate valid postoperative comparisons between reconstructions with similar complexity[8].

Has been changed to:

2.1. Classify the mandibular defect according to the classification of Brown et al.[8].

5. Please organize the sections/steps properly so that the protocol can be followed in chronological order.

6. Please add more details to your protocol steps. There should be enough detail in each step to supplement the actions seen in the video so that viewers can easily replicate the protocol. Please ensure you answer the "how" question, i.e., how is the step performed? Alternatively, add references to published material specifying how to perform the protocol action. For actions involving software usage, please provide all specific details (e.g., button clicks, software commands, any user inputs, etc.) needed to execute the actions.

7. 3.1: It is unclear how this is done.

8. 3.2: Please describe how to perform this step in the software.

9. 3.3: Please specify how to calculate.

10. 3.4: How is the segmentation done?

11. Sections 4-7: Please specify the software actions (button clicks, etc.).

We changed the protocol according to the comments 5-11 of the editor:

3. Segmentation of the DICOM images of the postoperative CT scan

3.1. Open Mimics inPrint 3.0. By clicking on "File" and "New from Disk", a folder-selection window will open. Select the folder that contain the DICOM images of the postoperative CT scan to import (select the whole folder); choose the right study in the list, then click on "Convert". A window will pop up for assessment of the orientation. Change the orientation by left clicking on the orientation characters; click on "OK" to validate.

3.2.1. The first step of the 5-step workflow is called "Create Region of Interest". Click on the "Thresholding" tool. Create the region of interest (ROI) by defining a threshold containing all the voxels of the mandibular bone within a certain interval of gray values, which is proportional to the density of the bony tissue. The tool allows you to select the bone within a range of density, expressed in Hounsfield Units. Manually tweak the Hounsfield range by moving the two sliders. Click on the green button to validate the segmentation. A new ROI appears in the ROI tab.

3.2.2. The software automatically jumps to the second step of the workflow, called "Edit ROI". Choose the "Isolate" tool; click on the mandible in the 3D viewport, which will be automatically isolated from the cranium and becomes green. Select the option "Create result in new ROI". Click on the green button to validate the isolation and see all the non-connected structures disappear. You can rename the ROI ("Mandible Post-op"). Optionally, use the "Lasso" tool to remove scattering by editing the ROI directly on the images or in the 3D viewport.

NOTE: When the CT scan is of poor quality, the condyles can be connected to the skull. In that case, click on the "Split" tool, which asks you to define a foreground and a background. Select "Foreground" and select the mandible thorough the axial or coronal coupes. Select "Background" and select the maxilla and cranium thorough the axial or coronal coupes. The region corresponding with the foreground will be kept in the ROI and the region corresponding with the background will be deleted. Click on the green button to validate.

3.2.3. Your ROI is now clear and ready to be converted into a 3D model. Click on the "Add Part" button of the workflow toolbar. Click on the "Solid Part" tool. Select the solid part "Mandible Post-op" and select "Off" in the "Smoothing" options. Click on the green button to validate.

3.2.4. When the parts are constructed, the software automatically goes to the fourth step of the workflow: "Edit Part". The contours of the created parts are shown on the images, which allows for a last assessment of the accuracy of the parts. Skip the "Smooth" tool.

3.2.5. In the last step of the workflow "Prepare Print", select the "Mandible Post-op" part in the export menu, choose your output directory, select the 1,00 scale and click on the green button to validate. The "Mandible Post-op" part is now exported as an .STL file.

4. XYZ axis orientation

NOTE: The preoperative STL model includes the cranium, (neo)mandible and the virtually planned dental implants (if planned). Please note that the evaluation works easier with separated STL files of the cranium and skull, but still in fixed position to each other. When the preoperative STL model of the cranium and the mandible are merged, use the Mimics *inPrint 3.0. software following the steps described above to split the mandible from the cranium.*

4.1. Open GOM Inspect Professional 2019. Drag the preoperative STL file (including virtual plan) in the popped up screen.

4.2. Determine the Frankfurt plane, midsagittal plane, and the nasion for uniform orientation of the preoperative STL model of the skull on the XYZ axis:

4.2.1. Click on "Construct", "Plane", "3-Point Plane" and create a virtual point by using Ctrl + left click on both the internal acoustic foramina and the left infraorbital margin (Frankfurt plane)[9]. Click on "Create and close" after pointing on the STL model.

4.2.2. Click on "Construct", "Line", "2-Point Line" and create a virtual point by using Ctrl + left click on the nasion and the incisive foramen (midsagittal plane)[10].

4.2.3. Click on "Construct", "Point", "Point" and create a virtual point by using Ctrl + left click on the nasion.

4.2.4. Click on "Operations", "Main Alignment", "Plane-Line-Point". Combine the actual parameter "Plane 1" with the nominal parameter "Plane Z", the actual parameter "Line 1" with the nominal parameter "Line Y", and the actual parameter "Point 1" with the nominal parameter "Global coordinate system". The preoperative STL models of the cranium and (neo)mandible are now fixed to the XYZ axis.

5. Volume assessment of the pre- and postoperative STL models

5.1. Select the STL file of only the preoperative (neo)mandible under "Actual Elements", where all "Meshes" are shown. Click on "Operations", "CAD", "Actual Mesh To CAD". Select "New CAD data" in the popped up menu, rename the file to your preference (e.g. "Mandible Pre-op") and click "OK". The preoperative STL model is now visible under "Nominal Elements", "CAD" in the left explorer menu.

5.2. Drag the postoperative STL model into the software (created during step 3 of the guideline). Rename the file to your preference (e.g. "Mandible Post-op"). Select the STL file under "Actual Elements", in the left explorer menu where all "Meshes" are shown. Click on "Operations", "Alignment", "Single Element Transformation", "3-Point Alignment".

5.3. In the popped up menu, combine 3 "Nominal points" on the "Mandible Pre-op" (e.g. condyle superior, horizontal- and vertical corner of the mandible) with 3 similar "Actual points" on the "Mandible Post-op" by ctrl + left clicking. Validate with "Apply And Close". The STL models will be roughly superimposed on each other based on these 3 landmarks. This will speed up the calculations of the software during the next steps.

5.4. Deselect the "Mandible Pre-op" and select the "Mandible Post-op" in the left explorer menu. Click on the "Select/Deselect On Surface" tool in the bottom toolbar. Select a surface on the remnant mandible on both the lateral and medial side (not in touch with the osteosynthesis material). Click on "Operations", "Alignment", "Single Element Transformation", "Local Best Fit". Select "All CAD groups" as the targeted element in the popped up menu. Take a maximum distance of 10.000mm. Validate with "Apply And Close".

The selected part of the remnant mandible of the "Mandible Post-op" will be accurately superimposed on the similar part of the "Mandible Pre-op".

5.5. Now both models are ready for the STL volume assessment. Click on the "Select/Deselect On Surface" tool in the bottom toolbar. Select a surface on only the lateral side within the surface of the previous step. Click on "Inspection", "CAD Comparison", "Surface Comparison On Actual". Use a Max. distance of 10.00mm in the popped up menu, and validate with "OK". Click with the right mouse button on this surface, choose "Select Patch". Click on the magnifying glass on the toolbar above. A round toolbar pops up in the screen. Click on "Check", "Deviation Label Arithmetic Mean". The arithmetic mean in mm will be shown.

5.6. In case of an arithmetic mean <0.5 mm, continue to step 6 of this guideline. In case of an arithmetic mean >0.5 mm, repeat the postoperative CT scan (DICOM file) segmentation in the Mimics inPrint 3.0. software by adjusting the threshold values. Repeat the segmentation and superimposition until an arithmetic mean <0.5mm is achieved. The two STL volumes are now ready for valid accuracy comparisons.

6. Superimposition of the condylar processes

6.1. Deselect the "Mandible Pre-op" and select the "Mandible Post-op" in the left explorer menu. Click on the "Select/Deselect On Surface" tool in the bottom toolbar. Select the whole surfaces of both condyles by drawing planes (lateral and medial side) from the most caudal point of the incisura mandibulae (mandibular notch) perpendicular to the posterior edge of the border between condyle and the vertical corner.

6.2. Click on "Operations", "Alignment", "Single Element Transformation", "Local Best Fit". Select "All CAD groups" as the targeted element in the popped up menu. Take a maximum distance of 10.000mm. Validate with "Apply And Close". The selected condyles of the "Mandible Post-op" will be accurately superimposed on condyles of the "Mandible Pre-op".

7. Calculation of the coronal, axial and sagittal mandibular angles

NOTE: The identification of bony landmarks is performed separately on the "Mandible Pre-op" and "Mandible Post-op" STL models. Deselect the "Mandible Post-op" while identifying bony landmarks in the "Mandible Pre-op", and vice versa.

7.1. Select the "Mandible Pre-op" in the left explorer menu. Click on "Construct", "Point", "Surface Point", to determine virtual points on the condyle superior (CS), condyle posterior (CP), vertical corner (VC) and horizontal corner (HC) (according to the classification of Brown et al.).

7.2. Select the "Mandible Post-op" in the left explorer menu. Click on "Construct", "Point", "Projection Point", to determine virtual points on the condyle superior (CS), condyle posterior (CP), vertical corner (VC) and horizontal corner (HC) (according to the classification of Brown et al.).

NOTE: For Brown class Ic, IIc or IVc defects; determine virtual points on the most superior- and posterior part of the vertical segment of bone graft or the titanium/prosthetic condyle.

NOTE: If the mandibular resection includes one or more corners, select the most inferior point of the osteotomy plane between the two segments of bone graft. When the mandibular *resection includes only half of a horizontal or vertical corner (remnant mandible next to a segment of bone graft), determine a virtual point on the segment of bone graft on the most inferior part of the osteotomy plane.*

NOTE: In case of a Brown class I mandibular defect; determine a virtual point on the most anterior and inferior part of the horizontal segment of bone graft, and consider this virtual point as the horizontal corner (HC).

NOTE: In case of (extra) osteotomies outside the anatomical vertical- or horizontal corner, determine the osteotomy closest to these corners as vertical- or horizontal corner.

7.3. To create a line between 2 virtual points, click on "Construct", "Line", "2-Point Line". Select 2 points under "construction elements" in the popped up menu to connect them with a line. Click on "Create and close".

7.4. To create an angle between 2 lines, click on "Construct", "Angle", "3-Point Angle". Subsequently select "Point 1", the "Angle Point" and "Point 2" in the popped up menu. Click on "Create and close". The angle between the 2 lines is calculated and shown.

7.5. With this knowledge, determine the right and left coronal mandibular angles between the lines from condyle superior (CS) to vertical corner (VC) and the midsagittal line (ML).

7.5.1. Determine the right and left axial mandibular angles between the lines from vertical corner (VC) to horizontal corner (HC) and the midsagittal line (ML).

7.5.2. Determine the sagittal mandibular angles between the lines from condyle posterior (CP) to vertical corner (VC) and the lines from vertical corner (VC) to horizontal corner (HC).

7.5.3. Calculate and report the deviations in degrees (°) between the postoperative angles and the virtual planned angles.

8. Calculation of the XYZ deviations and distance XYZ of the virtually planned dental implants

NOTE: Use the correct dental implant diameter and height (including cover screw) during the preoperative planning for correct comparison.

8.1. Click on "Construct", "Point", "Point" and create a virtual point by using Ctrl + left click in the middle and top of the cover screws of the dental implants in the "Mandible Pre-op" file.

8.2. Click on "Construct", "Point", "Surface Point" and create a virtual point by using Ctrl + left click in the middle and top of the cover screws of the dental implants in the "Mandible Post-op" file.

8.3. Click on "Construct", "Distance", "2-Point Distance", and connect all points on the dental implants with each other in the popped up menu.

8.4. Select all the points on the dental implants in both the "Mandible Pre-op" and the "Mandible Post-op" files in the left explorer menu. Click on the magnifying glass on the toolbar above. A round toolbar pops up in the screen. Click on "Check" and select "dXYZ". The distance XYZ in mm is shown per dental implant using the formula:

$$dXYZ = \sqrt{(\mathrm{x}^2 - \mathrm{x}^1)^2 + (\mathrm{y}^2 - \mathrm{y}^1)^2 + (\mathrm{z}^2 - \mathrm{z}^1)^2}$$

12. After you have made all the recommended changes to your protocol section (listed above), please highlight in yellow up to 2.75 pages (no less than 1 page) of protocol text (including headers and spacing) to be featured in the video. Bear in mind the goal of the protocol and highlight the critical steps to be filmed. Our scriptwriters will derive the video script directly from the highlighted text.

Done.

13. References: Please do not abbreviate journal titles; use full journal name.

Done.

14. Table of Materials: Please ensure that it has information on all relevant supplies, reagents, equipment and software used, especially those mentioned in the Protocol. Please sort the materials alphabetically by material name.

We added Mimics inPrint 3.0 and GOM Inspect Professional 2019 to the table of materials.

Responses to comments of Reviewer 1:

Reviewer #1:

Manuscript Summary:

The Authors present an evaluation guideline for computer-assisted reconstructions of the mandible in order to increased uniformity of accuracy analysis of computer-assisted mandibular reconstructions, based on the position of the condyles, the angles of the osteotomy planes, the size, position and fixation of the bone graft segments and the position of the guided dental implants.

We want to thank the reviewer for the time that has been taken to read the manuscript and for the comments to improve our manuscript.

Concerns:

Authors say that "To align pre- and postoperative STL models with the closest approach of the postoperative clinical situation, superimposition of both condylar processes is the most simple and reproducible method": in this case I think that another reliable and accurate method to assess the accuracy of the reconstruction is to superimpose the pre and post-op STL models by taking into consideration fixed reference landmarks on the virtual planning and postoperative CT scan (such as the screw holes on the plate or plate surface), to obtain the most accurate 3D overlap.

We agree with the reviewer that multiple superimposition methods are available and described in the literature. However, in the evaluation we are not looking for a "best 3D model fit" in the software, but we are looking for a realistic "best clinical fit", representing the clinical postoperative (neo)mandible position, and thus the correct intermaxillary relation which is important for future dental rehabilitation. The superimposition software tool moves a selected part of an STL model (the source) to best match a fixed part of an STL model (the reference) using an iterative closest-point algorithm. As stated in the discussion section; superimposition of (parts of) the reconstruction plate(s) is discouraged due to scattering of the metal, causing volume differences of the postoperative STL models versus the preoperative virtual plan. This will lead to shifts of the entire reconstruction while using the iterative closest point algorithm, and thus this will not represent the postoperative clinical position of the mandible. The same problem is introduced while superimposing isolated parts of the reconstruction; for example alignment of the bony segments only; the pre- and postop segments will "best fit" but no account is taken for the rest of the mandible including the condyles, so the entire mandible can shift during superimposition of the bony segments, not representing the postop situation. Superimposition of the mandible including the maxilla and cranium is also inaccurate because mouth opening will always be different during the pre- and postoperative scanning. Taking all the above into account, we believe that superimposition of both condylar processes is the most simple and reproducible method, representing the postoperative clinical situation.

Authors say that: "Although the postoperative position of both condyles will be affected by inaccurate neomandible reconstruction, the intermaxillary relation will accommodate to the midline and thus averages the position of both condyles around the midsagittal plane": I agree with the Authors but the use of a plane-line-point tool in the CAS software to uniform orientation of the skull on the XYZ-axis may represent a pitfall, because it depends by the set-up of the head natural position and by the selected cephalometric points and planes, with the consequent effect on the superimposition of the condylar processes, although the accommodation of the intermaxillary relation to the midline.

To evaluate the dental implant positions we necessarily needed to align both 3D models, using the superimposition software tool. However, to avoid misunderstandings, we want to clarify that only the preoperative 3D model of the skull is fixed to the XYZ axis, using a plane-line-point tool. This fixation is useful for 3D orientation during evaluation and represents a benchmark from which the deviations of the dental implants can be determined. We agree with the fact that the fixed skull position on the XYZ axis will be a little different between cases. However, this has no consequences for the measurements, because it has no consequences for the distance XYZ in mm between dental implant positions when the postoperative 3D model is superimposed onto the fixed preoperative 3D model with only both condyles selected for the iterative closest point algorithm. So the orientation of the skull on the XYZ axis does not influence the superimposition of the condylar processes.

Responses to comments of Reviewer 2:

Manuscript Summary:

The Authors describe an evaluation guideline for computer-assisted reconstructions of the mandible in order to increased uniformity of accuracy analysis of CAS.

We want to thank the reviewer for the time that has been taken to read the manuscript and for the comments to improve our manuscript.

Major Concerns:

None

Minor Concerns:

Authors state that "To align pre- and postoperative STL models with the closest approach of the postoperative clinical situation, superimposition of both condylar processes is the most simple and reproducible method": The existing literature on this topic describes other alternative methods as reliable and accurate. The most utilised is to superimpose the pre and post-op STL models by taking into consideration fixed reference 'external' landmarks on the virtual planning and postoperative CT scan (such as plate surface), to obtain the most accurate 3D overlap. Please, discuss this aspect.

As stated before in our response to the comments of Reviewer 1, we agree with the reviewer that multiple superimposition methods are available and described in the literature. However, in the evaluation we are not looking for a “best 3D model fit” in the software, but we are looking for a realistic “best clinical fit”, representing the clinical postoperative (neo)mandible position, and thus the correct intermaxillary relation which is important for future dental rehabilitation. The superimposition software tool moves a selected part of an STL model (the source) to best match a fixed part of an STL model (the reference) using an iterative closest-point algorithm. As stated in the discussion section; superimposition of (parts of) the reconstruction plate(s) is discouraged due to scattering of the metal, causing volume differences of the postoperative STL models versus the preoperative virtual plan. This will lead to shifts of the entire reconstruction while using the iterative closest point algorithm, and thus this will not represent the postoperative clinical position of the mandible. The same problem is introduced while superimposing isolated parts of the reconstruction; for example alignment of the bony segments only; the pre- and postop segments will “best fit” but no account is taken for the rest of the mandible including the condyles, so the entire mandible can shift during superimposition of the bony segments, not representing the postop situation. Superimposition of the mandible including the maxilla and cranium is also inaccurate because mouth opening will always be different during the pre- and postoperative scanning. Taking all the above into account, we believe that superimposition of both condylar processes is the most simple and reproducible method, representing the postoperative clinical situation.

Based on the comments of the editor, and Reviewer 1 and 2, we revised and added some sentences to the following paragraph in the discussion:

The alignment of pre- and postoperative STL models in the CAS software to evaluate the accuracy of the reconstruction introduces some difficulties. The superimposition software tool *moves a selected part of an STL model (the source) to best match a fixed part of an STL model (the reference) using an iterative closest-point algorithm. However, superimposition of the entire (neo)mandible is inaccurate due to scattering of the reconstruction plate(s), which will lead to shifts of the entire reconstruction, not representing the postoperative clinical position of the mandible16. The same problem is introduced while superimposing isolated parts of the reconstruction17. Superimposition of the mandible including the maxilla and cranium is inaccurate because mouth opening will always be different during the pre- and postoperative scanning. Therefore, to evaluate the postoperative position of the (neo)mandible we decided to create mandibular angles (pioneered by De Maesschalck et al.18) on both pre-and postoperative STL models separately to bypass the superimposition problems. However, to evaluate the dental implant positions we necessarily needed to align both models, using the superimposition software tool. To align pre- and postoperative STL models with the closest approach to the clinical postoperative intermaxillary relation, we believe that superimposition of only both condylar processes is the most feasible, standardized and reproducible method. Although the postoperative position of both condyles can be affected by inaccurate neomandible reconstruction, the intermaxillary relation will accommodate to the midline and thus averages the position of both condyles around the midsagittal plane19. In our guideline, only the preoperative STL model is quickly fixed to the XYZ axis using a plane-line-point tool in the CAS software, representing a benchmark from which the postoperative deviations of the dental implants can be determined. The fixed skull position on the XYZ axis can lead to small cephalometric differences between cases. However, this has no influence on the dental implant measurements, because it has no consequences for the distance XYZ in mm between dental implant positions when the postoperative 3D model is superimposed onto the fixed preoperative 3D model with only both condyles selected for the iterative closest point algorithm.*

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