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Reconstructive Surgery

# Complication rates and clinical outcomes of osseous free flaps: a retrospective comparison of CAD/CAM versus conventional fixation in 128 patients

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**Abstract.** Studies evaluating plate-related complications in patient-specific versus conventional fixation systems in free flap surgery are lacking. This was a retrospective study of 128 osseous free flaps with a minimum follow-up of 12 months. Wound healing disorders, plate exposure, fixation failure, and subtotal osseous union were recorded and evaluated statistically by univariate and regression analysis. Complication rates were as follows: wound healing disorders 33.6% (computer-aided design and computer-aided manufacturing (CAD/CAM) vs. conventional: 35.1% vs. 33.0%); plate exposure 21.9% (29.7% vs. 18.7%); fixation failure 7.0% (8.1% vs. 6.6%); subtotal osseous union 36.7% (45.9% vs. 33.0%). Radiotherapy ( $P < 0.001$ ) and more than two segments ( $P = 0.026$ ) were independent variables for the overall complication rate and were negatively correlated with the dental implantation rate. The time between diagnosis and ablative surgery was increased by 11.0 days in the CAD/CAM group ( $34.2 \pm 16.2$  days vs.  $23.2 \pm 12.0$  days;  $P = 0.002$ ). Rates of dental rehabilitation were not significantly different (35.1% vs. 44.0%,  $P = 0.358$ ). On average,  $3.2 \pm 1.7$  dental implants were placed into flap segments. Plate-related complications were increased with radiotherapy and multisegment flaps. There was a non-significant trend towards increased complications with patient-specific plates in comparison to conventional reconstruction plates.

**Key words:** osseous free flaps; patient-specific implants; plate-related complications; dental rehabilitation; bone invasion.

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Mandible reconstruction with osseous free flaps is challenging and the success rate rests on several critical details, including preoperative planning, extensive anatomical knowledge, and meticulous tissue-conserving dissection. The anatomy and function of the masticatory system are complex, with several muscles acting on the mandible, and this in combination with the non-sterility of the oral cavity represents a challenge. Additionally, in the case of malignant tumours, osteoradionecrosis (ORN), and medication-related osteonecrosis of the jaws (MRONJ), conditions for osseous and soft tissue healing are often unfavourable. In a European survey among surgeons with a high level of experience, it was found that complications occurred more often when bone was included in the flap<sup>1</sup>. Recent investigations in this field have reported high rates of overall and plate-related complications, including wound healing disorders, plate exposure, and osseous non-union<sup>2-9</sup>. In this regard, it is important to consider the type of fixation as a potential independent variable for success and complication rates. Plate-related complications may affect quality of life and increase the cost of treatment<sup>7</sup>. Furthermore, dental and functional rehabilitation may be delayed.

There are currently three systems available for the fixation of free flaps in the mandible: bendable miniplates, conventional reconstruction plates, and patient-specific laser-melted Plates<sup>10</sup>. By varying the thickness and anchoring mechanisms, and using locking or non-locking screws, further refinements are possible. However, precise knowledge regarding the superiority of one of the systems over the others is lacking. While computer-aided design and computer-aided manufacturing (CAD/CAM) solutions have improved precision and cost efficiency<sup>11-14</sup>, which partly explains the increasing rates of associated surgical procedures, knowledge on the functional outcomes and complication rates of this new fixation type remains limited. Patient-specific solutions usually involve a greater expanse of solid material and a less open design (fewer holes/fenestrations), and the plates are fitted closely to the bone without gaps<sup>10</sup>. Consequently, the increased stiffness reduces inter-osteotomy gap movements and the bone-to-plate contact area is increased in comparison to conventional plating techniques. This is known to reduce cortical blood perfusion, which is a potential drawback for osseous re-union and bone remodelling<sup>15</sup>. On the other hand, patient-specific plates enable the surgeon to perform more complex and functionally im-

proved reconstructions. For instance, via individual plate design according to the virtual planning, fibula free flaps, which usually lack sufficient bone height in comparison to the mandible (if not edentulous), can easily be placed above the inferior mandible border, allowing improved implant placement and prosthetic rehabilitation. Also, perfect plate adaption can be achieved easily regardless of the flap design, which potentially reduces the tension between the plate and soft tissue coverage.

This study was performed to compare the clinical outcomes and complication rates of mandible reconstruction with conventional and patient-specific CAD/CAM reconstruction plates, with special attention to dental rehabilitation and independent risk factors.

### Patients and methods

A retrospective single-centre cohort study was designed at the University Medical Centre Hamburg-Eppendorf, Germany. Study approval was obtained from the local ethics committee. The study population comprised all adult patients (>18 years of age) who underwent microsurgical mandible reconstruction between January 2011 and December 2015. A minimum documented follow-up period of 12 months was necessary for study enrolment. Patients with initial flap loss due to thrombosis, infection, or anastomosis failure and those with a follow-up period of less than 12 months were excluded from the study.

The medical charts of all patients were screened for demographic, disease- and surgery-related data, including age, sex, indication, presence of diabetes, presence of vascular disease, donor site, type of reconstruction, number of segments, flap revision due to microvascular thrombosis, preoperative or adjuvant radiotherapy (RT), surgery time, type of fixation, and dental status. Plate removal and dental rehabilitation were recorded and postoperative radiographs (panoramic views, cone beam computed tomography (CBCT) or computed tomography (CT) scans) obtained at 12 months postoperative were evaluated by two investigators (C.R., C.S.), with particular focus on re-ossification in the inter-osteotomy gaps. When both two-dimensional (2D) and three-dimensional (3D) datasets were available, only the 3D dataset was evaluated. Osseous union was classified as subtotal when the investigators rated at least one of the gaps between flap segments or between the mandible and flap

to have an osseous contact area of less than 50%. Wound healing disorders (including infection), plate exposure, fixation failure due to screw loosening or plate breakage, and subtotal osseous union (defined as <50% osseous contact area in the inter-osteotomy gap) were defined as plate-related complications. Fig. 1 illustrates typical examples of osseous unions and subtotal unions in panoramic views and CBCT.

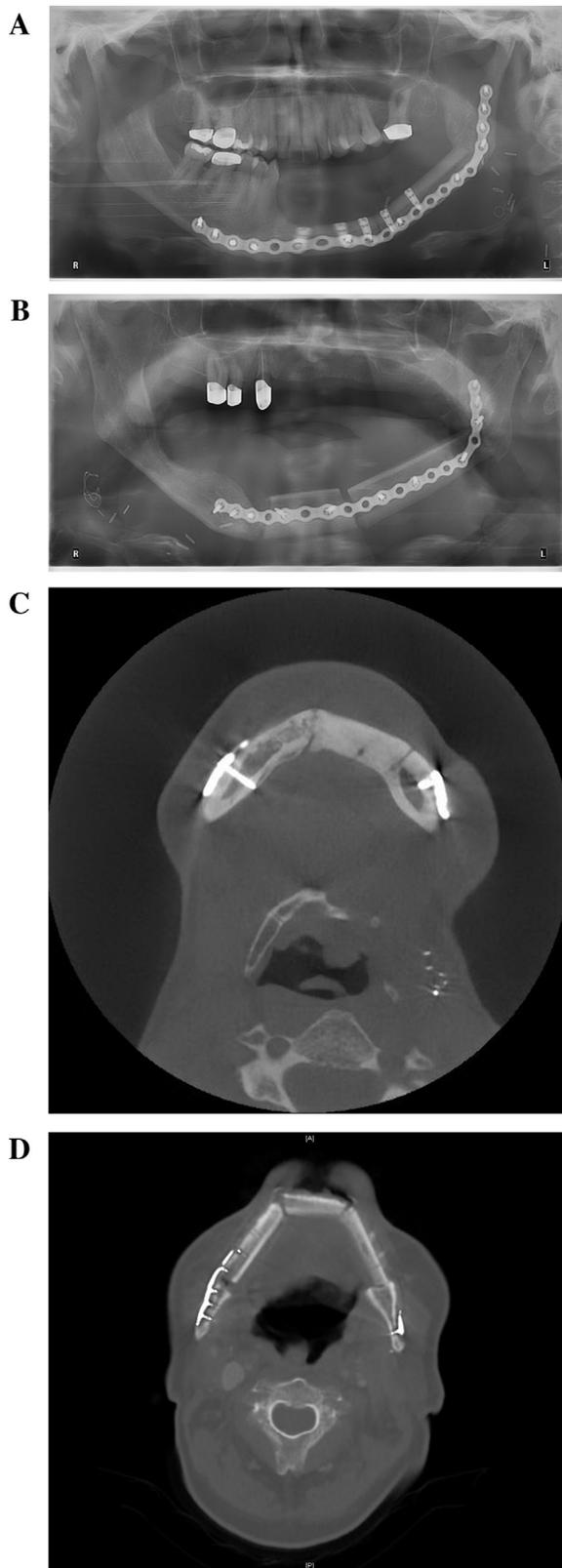
The study population was divided into two groups in order to compare reconstruction characteristics and complication rates between patients with conventional and patient-specific CAD/CAM plates. Flap fixation was performed with intraoperatively bent conventional reconstruction plates (bars) of 2.0–2.5 mm thickness or patient-specific laser-melted plates derived from CAD/CAM planning procedures of different manufacturers (DePuy Synthes, Umkirch, Germany; KLS Martin Group, Tuttlingen, Germany). Cutting guides for flap harvesting at the donor site were only used in the CAD/CAM group. All plates were fixed with bicortical locking screws at the mandible and with monocortical non-locking screws at the free flap segments in order to prevent vessel damage during drilling or screw placement. The treating surgeon made the decision regarding conventional or patient-specific plating on an individual basis as part of routine practice. More complex cases and those requiring multisegment flaps were in general more often indicated for CAD/CAM planning and plate usage. Due to the retrospective study design, no clearly definable variables were evident in this regard.

The hypothesis of the study was that rates of plate-related complications differ between conventional and patient-specific CAD/CAM fixation plates.

The statistical analysis was performed using IBM SPSS Statistics version 21.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics and frequencies were calculated for each parameter. Correlation analyses were calculated using the  $\chi^2$  test or Fisher's exact test. Multivariate analysis was performed by logistic regression and odds ratios (OR) were computed. The level of significance was set at 5% ( $P < 0.05$ ).

### Results

One hundred and seventy-four successful free flap mandible reconstructions were performed during the study period. One hundred and twenty-eight patients met the inclusion criteria of initial flap survival



**Fig. 1.** Examples of inter-osteotomy gap ossification: (A) panoramic view of sufficient osseous union in three gaps after a two-segment fibula free flap reconstruction; (B) panoramic view of subtotal osseous union in the right distal and intermediate gap; (C) cone beam computed tomography of sufficient osseous union in two gaps in a patient with a one-segment fibula free flap; (D) cone beam computed tomography of a subtotal osseous union in the right distal and right intermediate gap versus sufficient ossification in the left distal and left intermediate gap.

and a minimum follow-up period of 12 months after surgery. Patients were excluded in the event of early flap loss or clinical and/or radiological loss of follow-up. Successful flap revision due to microvascular thrombosis was not an exclusion criterion.

Demographic, pathological, and therapy-related characteristics of the study population are listed in Table S1. The patients were 82 men and 46 women, with an average age of  $59.2 \pm 12.4$  years. The average follow-up was 15.5 months. The indication for mandible resection was oral squamous cell carcinoma (OSCC) of the floor of the mouth or mandible in 85 cases, ORN in 18 cases, MRONJ in eight cases, and a benign tumour in 17 cases (ameloblastoma, myxofibroma, ossifying fibroma). The fibula was the most common donor site ( $n = 107$ ). The majority of patients ( $n = 95$ ) received a multisegment osseous free flap and 26.6% ( $n = 34$ ) were composed of more than two segments. Three-quarters (75.0%,  $n = 96$ ) of all cases were primary reconstructions. Thirty-nine patients (30.5%) received adjuvant RT, while 32 (25.0%) had undergone RT of the head and neck region in recent years before mandible reconstruction. On comparison of the study groups (conventional fixation vs. CAD/CAM plate), there was a statistically significant difference regarding the time delay between diagnosis and ablative surgery among OSCC patients undergoing primary reconstruction (increase of 11.0 days in the CAD/CAM group;  $P = 0.002$ ). The relative proportion of multisegment flaps was higher in the CAD/CAM group (37.8% vs. 22.0%;  $P = 0.066$ ). The rate of plates with a thickness of more than 2.0 mm was 36.2% in the conventional group, whereas all CAD/CAM plates were designed with a thickness of 2.0 mm ( $P < 0.001$ ). Also, the proportion of flaps including the ramus was higher in the CAD/CAM group (43.2% vs. 24.2%;  $P = 0.003$ ). No further differences regarding case characteristics were found between the groups.

The most common complication was subtotal osseous union, which occurred in 47 cases overall (36.7%) (CAD/CAM vs. conventional: 45.9% vs. 33.0%;  $P = 0.167$ ). The location was the distal gap in 17 patients; there were eight isolated mesial non-unions and 22 patients had subtotal osseous union at more than one location. Wound healing disorders at the recipient site occurred in 43 cases overall (33.6%) (CAD/CAM vs. conventional: 35.1% vs. 33.0%;  $P = 0.814$ ). There were 28 cases (21.9%) of plate exposure (CAD/CAM vs. conventional: 29.7% vs. 18.7%;  $P = 0.170$ ) and nine cases (7.0%) of fixation failure (CAD/CAM vs. conventional:

8.1% vs. 6.6%;  $P = 0.761$ ). Details of the numbers of complications and related variables are given in Table S2.

The overall complication rate was increased among patients with more than two segments (76.5% vs. 54.3%;  $P = 0.023$ ) and among patients with recent or adjuvant RT (preoperative 84.4%, adjuvant 66.7%, none 42.1%;  $P < 0.001$ , Table S2), with a significant difference between preoperative and adjuvant RT ( $P = 0.033$ ). Accordingly, ORN as an indication for mandible resection was also a significant variable (ORN 94.4%, malignant 58.8%, MRONJ 50.0%, benign 35.3%;  $P = 0.003$ ).

Non-significant trends (>10% difference) were found for diabetes (71.4% vs. 58.8%;  $P = 0.361$ ), osteomyocutaneous flaps (63.8% vs. 43.5% myo-osseous flaps;  $P = 0.071$ ), postoperative non-occlusion (67.2% vs. 52.5%;  $P = 0.090$ ), chemotherapy (74.1% vs. 56.4%;  $P = 0.096$ ), and type of fixation (CAD/CAM 67.6% vs. conventional 57.1%;  $P = 0.275$ ).

The individual analyses of each of the four types of complication revealed that secondary reconstructions (34.4% vs. 17.7% for primary reconstructions;  $P = 0.048$ ), postoperative non-occlusion (no contact points between teeth of the upper and lower jaw, 31.3% vs. 11.5%;  $P = 0.007$ ), defects including the symphysis (28.4% vs. 13.0%;  $P = 0.037$ ), and RT in general (preoperative RT 50.0%, adjuvant RT 23.1%, no RT 5.3%;  $P < 0.001$ ) were associated with increased rates of plate exposure. Detailed analysis revealed that both a history of RT prior to mandible reconstruction (50.0%;  $P < 0.001$ ) and adjuvant RT (23.1%;  $P = 0.012$ ) significantly increased the rate of this complication. The difference between preoperative and adjuvant RT was also significant ( $P = 0.002$ ). Accordingly, ORN was correlated with significantly increased plate exposure rates compared to the other indications for free flap reconstruction (ORN 50.0%, malignant tumour 22.4%, benign tumour 0.0%, MRONJ 0.0%;  $P = 0.002$ ).

Non-significant trends regarding plate exposure were noted for number of segments (>2, 32.4%; ≤2, 18.1%;  $P = 0.085$ ), re-resection due to residual tumour (66.7% vs. 20.8%;  $P = 0.058$ ), and type of fixation (CAD/CAM 29.7% vs. conventional 18.7%;  $P = 0.170$ ). The comparison of flaps with and without a skin island revealed no significant difference (myo-osseous vs. osteomyocutaneous: 17.4% vs. 22.9%;  $P = 0.566$ ).

Wound healing disorders were promoted by the administration of chemotherapy

(63.0% vs. 25.7%;  $P < 0.001$ ) and preoperative RT (preoperative RT 53.1%, adjuvant RT 35.9%, no RT 21.1%;  $P = 0.008$ ). Accordingly, this complication occurred more often in the case of mandible resection due to osteoradionecrosis (ORN 61.1%, MRONJ 50.0%, malignant tumour 29.4%, benign tumour 17.6%;  $P = 0.008$ ). A non-significant trend towards increased rates of wound healing disorders was noted in patients who underwent flap revision due to microvascular thrombosis (46.1% vs. 32.2%;  $P = 0.312$ ) and those containing more than two segments (41.2% vs. 30.9%;  $P = 0.275$ ).

Fixation failure ( $n = 9$ ) only occurred in patients with a 2.0 mm plate. Plate failure only occurred with conventional plates, while screw loosening and screw fracture were found to be mechanisms of failure in the CAD/CAM group. Preoperative RT significantly increased the rate of material failure (preoperative RT 15.6%, adjuvant RT 5.1%, no RT 3.5%;  $P = 0.011$ ).

More than two segments (52.9% vs. 30.9%;  $P = 0.022$ ) and both adjuvant and preoperative RT were associated with increased rates of subtotal union (preoperative RT 46.9%, adjuvant RT 48.7%, no RT 22.8%;  $P = 0.014$ ). Non-significant trends (>10% difference) were found in patients with diabetes (50.0% vs. 35.1%;  $P = 0.275$ ), flap revision (53.8% vs. 34.8%;  $P = 0.177$ ), vascular disease (42.1% vs. 35.8%;  $P = 0.598$ ), postoperative non-occlusion (43.3% vs. 29.5%;  $P = 0.106$ ), reconstructions including the mandible body (38.5% vs. 18.2%;  $P = 0.182$ ), and type of fixation (CAD/CAM 45.9% vs. conventional 33.0%;  $P = 0.167$ ).

Cox regression revealed that multisegment free flaps (2.740-fold increased risk;  $P = 0.026$ ), inclusion of the mandible body (4.589-fold increased risk;  $P = 0.030$ ), RT in general (preoperative or adjuvant vs. no RT 2.730-fold increased risk;  $P < 0.001$ ), and indication (ORN vs. others 14.167-fold increased risk;  $P = 0.011$ ) were independent risk factors for the occurrence of plate-related complications (Table S3). In comparison to preoperative RT, the risk of complications was reduced when administering adjuvant RT (0.296-fold;  $P = 0.038$ ).

Dental rehabilitation with implants was performed earlier in the CAD/CAM group ( $59.0 \pm 22.6$  weeks vs.  $79.0 \pm 38.9$  weeks, difference = 20.0 weeks;  $P = 0.001$ ), although the relative proportion of dental rehabilitation did not differ between the groups ( $P = 0.358$ , Table S4). A significant impact on dental rehabilitation was only found for number of seg-

ments (>2 vs. ≤2: 23.5% vs. 47.9%;  $P = 0.014$ ) and RT (yes vs. no: 32.3% vs. 52.6%;  $P = 0.002$ ). Further, a tendency towards less implantation was registered in patients with a plate-related complication (yes/no: 34.6% vs. 49.0%;  $P = 0.155$ ), chemotherapy (yes/no: 25.9% vs. 45.5%;  $P = 0.066$ ), and scapula donor site (scapula vs. DCIA/fibula: 12.5% vs. 43.3%;  $P = 0.085$ ). Regression analysis confirmed only an increased number of segments (>2) to be significantly associated with a reduced dental rehabilitation rate (0.335-fold;  $P = 0.016$ , Table S5).

On average,  $3.2 \pm 1.7$  dental implants were placed into flap segments and there was no significant difference in the rates of dental rehabilitation between the CAD/CAM and conventional groups (35.1% vs. 44.0%;  $P = 0.358$ ).

## Discussion

The fixation of osseous free flaps at the mandible can be performed with titanium miniplates, reconstruction plates, or patient-specific plates. The latter are increasingly popular, however their clinical superiority has not yet been clearly demonstrated<sup>16,17</sup>. The aim of the current study was to compare clinical outcomes and complication rates between fixation performed with milled reconstruction bars that are manually bent to the mandible (conventional) and laser-melted patient-specific reconstruction plates derived from CAD/CAM procedures designed with maximum bone-plate contact area and increased plate height<sup>10</sup>.

In a previous study, increased stiffness and reduced vertical displacement were demonstrated for CAD/CAM plates, a mechanical characteristic that is known to reduce interfragmentary movements<sup>10,18,19</sup>. In contrast to the long bones, for which optimal ranges of axial and shear movements are defined and thus manufacturers are theoretically able to optimize their plating systems to obtain ideal interfragmentary movement in order to promote osseous union, no such study for maxillofacial surgery has been conducted to date<sup>18,19</sup>.

Osseous union is usually expected within 6–8 weeks postoperative and radiographic continuity of the bone can be visualized by then<sup>7,20</sup>. With a subtotal osseous union rate of 33.0% in the conventional group, the present study results are in accordance with those of previous studies that have reported relatively high percentages of impaired bone healing in free flap surgery<sup>6,7</sup>. Differences in percentages may be explained by the fact that, in

addition to total non-unions, subtotal ossified gaps with less than 50% bone contact area were also considered a complication in the present study.

Despite the lack of significance, a trend towards increased rates of subtotal osseous union in the inter-osteotomy gaps was registered in the CAD/CAM group. Increased plate stiffness and a reduction of inter-osteotomy movements below the critical minimum may have contributed to this outcome. The greater expanse of solid material and less open design due to missing notches between screw holes, as well as the increased vertical plate height in general, may also explain the tendency towards increased rates of wound healing disorders and plate exposure. The greatly increased bone-plate contact area due to the perfectly adapted design of the patient-specific plates, along with the increased vertical dimension, consequently lead to reduced cortical bone perfusion<sup>15</sup>, which may play a critical role in osseous union and wound healing in general.

Increased material thickness in any dimension may also cause radiation dose variability and scattering artefacts during adjuvant therapy, potentially increasing the dose 'in front of' and decreasing it 'behind' the Plate<sup>7,21-24</sup>. Despite modern protocols with multidirectional irradiation aimed at reducing this effect, the definitive prevention of over- or under-dosage is difficult, not least because the planning procedure with CT or CBCT scans is drastically impaired through the presence of metal artefacts in postoperative imaging caused by titanium in general<sup>25</sup>. However, since the relative proportion of patients undergoing adjuvant RT was slightly higher in the CAD/CAM group, the relative increase in postoperative plate-related complications and impaired osseous union may not be fully explained by differences in plate design, stiffness, and adaptation.

This trend may be explained further by the fact that the total number of segments was found to be an independent variable and there was an increased proportion of multisegment free flaps in the CAD/CAM group. Nevertheless, because CAD/CAM planning is believed to deliver very precise results, it is surprising that despite the supposedly optimized gap width that can be achieved via the combination of virtual planning and cutting guides compared to free-hand harvesting, re-ossification does not occur at higher rates. Without cutting guides, especially for multisegment flaps, it is more challenging to create a flap design that reduces the gaps to an absolute minimum. A gap width of more than 1 mm

prevents primary bone healing, and for secondary healing with callus formation, mechanical underloading, which results from the use of locking plates with bicortical screws, is unfavourable. The increased rate of non-union in patients without postoperative occlusion and thus minimized axial loading on the bone, further underlines the importance of mechanical stimuli for bone healing<sup>18,19,26</sup>. The increased rates of complications for multisegment free flaps confirm data recently published by Okura et al., who found a 2.8-fold increased risk for flaps with at least three gaps<sup>5</sup>.

While multisegment free flaps and adjuvant RT were primarily associated with increased rates of non-union and plate exposure, a history of RT prior to mandible reconstruction increased the rates of all complications in comparison to patients without any type of RT, and differences between adjuvant and preoperative RT were only significant for plate exposure and the overall complication rate. RT reduces the number of haematopoietic stem cells and osteoblast activity<sup>27</sup>. Recent studies have demonstrated a history of irradiation to be a major risk factor for postoperative complications in reconstructive surgery, especially when the time lapse between surgery and RT is more than 6 weeks<sup>5,28</sup>. The findings of the present study are in accordance with those of recent studies on plate-related complications, all indicating RT as the major independent variable, especially when administered preoperatively or in combination with chemotherapy<sup>4,5,7,29</sup>.

As for subtotal union, the rates of plate exposure and wound healing disorder found in the present study are also within the ranges of rates published recently, with these complications reported to occur in 27-69% of all patients<sup>2,4-8,29,30</sup>. Besides the association with adjuvant and recent RT, plate exposure also occurred significantly more often in patients with secondary mandibular reconstructions. This is not surprising, because soft tissue coverage tends to become more difficult in patients undergoing surgical re-intervention, which is further amplified by a non-significant increased rate in patients undergoing re-operation due to residual tumour. Increased rates of plate exposure were also found in patients with multisegment free flaps and reconstructions including the mandible body (non-significant) and symphysis region (significant), which may be explained by more difficult soft tissue coverage in this group of patients. With multisegment free flaps and especially naturally more acute inter-

segmental flap angles between the symphysis and body region, plate pressure on the skin, especially during jaw movements, may be increased and cause reduced perfusion, followed by necrosis and finally penetration. Targeted mild retrognathia of the neomandible and sufficient soft tissue coverage via the inclusion of a skin island could be helpful to reduce the number of plate exposures in these patients. Of note, flaps including a skin island were not associated with increased soft tissue complication rates in the current study.

The use of CAD/CAM plates seems to increase plate-related complication rates and, to date, there is no evidence for improved postoperative function in axiographic analyses<sup>16,17</sup>. However, the reduced surgical time (as confirmed by the results of the current study), high precision procedures, and improved cost efficiency in comparison to conventional plating systems have shown this new generation of plates to be advantageous for multisegment cases<sup>12,13,31,32</sup>. Accordingly, the reduced duration of surgery and hospital length of stay seem to offset the increased cost of plate production. However, increased rates of complications with currently available CAD/CAM plates in general and the consequent need to return for additional procedures, i.e. hardware replacement, hardware removal, modelling osteotomy, or soft tissue coverage, must also be taken into account when analyzing the cost-effectiveness of these systems in future investigations.

In particular, for the less experienced surgeon and for complex 3D cases, the use of patient-specific plates, taking into account correct repositioning via preoperative planning, is beneficial. Additionally, material failure due to mechanical overloading of the plate is relatively unlikely, considering in vitro and mathematical biomechanical data, as well as the greatly reduced bite forces after mandible reconstruction<sup>10,33-35</sup>. According to the results of the current study, dental rehabilitation is performed earlier in those with CAD/CAM plates than in those with conventional plates, although the rate of dental rehabilitation is not increased. Considering the similar characteristics of the two study groups (Table S1), it is difficult to define reasons for this trend. However, since the overall time period between reconstructive surgery and implantation is more than 12 months on average, a certain bias may be included and a longer follow-up period may have further increased the duration until dental rehabilitation and the rate of dental im-

plantation in the CAD/CAM group. The same applies for the reduced rates of implantation among patients with adjuvant RT, whose general rehabilitation may take longer and thus the rates of successful implantation may further change.

A disadvantage of CAD/CAM plating is that therapy planning takes time and extends the period between diagnosis and surgical treatment. A recent investigation of 21,263 patients showed that longer time intervals between diagnosis and therapy were associated with a poorer prognosis in head and neck squamous cell carcinoma<sup>36</sup>. In theory, although 11 days difference may not sound very long, tumour growth and bone invasion may develop further with this treatment delay.

This study has some limitations. Only reconstruction plates were compared to CAD/CAM plates and no conclusions can be drawn regarding CAD/CAM plates versus miniplates. However, several studies have indicated the superiority of reconstruction plates (bars) over miniplates regarding plate-related complications<sup>3,4</sup>, whereas others have found no difference between bendable miniplates and conventional reconstruction plates for free flap fixation<sup>6,8</sup>. The exclusion of patients with early flap loss or incomplete clinical and radiological follow-up limits the interpretation of the results to patients who have survived the first year after the surgical intervention. Additionally, the retrospective study design limits the statistical and scientific merit of the study; therefore, future prospective investigations are needed to draw reliable conclusions.

The classification of intersegmental gaps into union vs. subtotal union was performed in an unblinded manner and was not controlled with volumetric 3D analysis, hence this outcome measure may be subject to an examination bias. Further, the clinical relevance of subtotal union as a predictor of dental rehabilitation as a final outcome parameter may be questioned, since no difference in dental implantation rates was found between patients with and without rated subtotal union. This may be due to the fact that subtotal union of less than 50% contact area may still be a sufficient basis for dental rehabilitation. In addition, in the event that no plate removal is performed prior to dental implantation, insufficient osseous bridging may even be disregarded and functionally irrelevant. However, the critical reflection of osseous union as an outcome measure of mandible reconstruction is an important aspect and should be further examined in future studies that

more closely investigate the effects of functional loading and unloading of the bone and intersegmental gap area via mechanobiological transmission, especially with regards to load-bearing and load-sharing fixation and variables affecting inter-osteotomy movements.

In conclusion, this study indicated a non-significant trend towards increased complication rates in patients with CAD/CAM plates for free flap fixation at the mandible compared to conventional plates. Preoperative RT, multisegment reconstructions, and mandible body reconstructions were found to be independent variables related to increased rates of soft tissue complications and subtotal osseous union. Future studies should focus on technical and mechanobiological aspects in order to improve the clinical outcomes of patients undergoing free flap mandible reconstruction.

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#### Competing interests

No competing interests of the authors.

#### Ethical approval

Ethical approval was given by the local ethics committee (Ethikkommission der Ärztekammer Hamburg; PV5032).

#### Patient consent

Not required.

#### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.ijom.2019.01.029>.

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