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Secondary surgical management of osteoradionecrosis using three-dimensional isodose curve visualization: a report of three cases

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J. Kraeima, R. J. H. M. Steenbakkers, F. K. L. Spijkervet, J. L. N. Roodenburg, M. J. H. Witjes: Secondary surgical management of osteoradionecrosis using three-dimensional isodose curve visualization: a report of three cases. Int. J. Oral Maxillofac. Surg. 2018; 47: 214–219.

Abstract. Osteoradionecrosis is defined as bone death secondary to radiotherapy. There is a relationship between the radiation dose received and the occurrence of osteoradionecrosis of the jaws, with the risk increasing above a dose of 60 Gy. In cases of class III mandibular osteoradionecrosis, a segmental resection can be indicated. Current practice is to completely remove the affected bone up to the point where the bone looks healthy and is bleeding. Exact resection planning and the use of guided surgery based on imaging of the bone changes have not been reported so far. This article describes a method whereby the radiotherapy dose information is incorporated into the imaging of the affected bone in order to plan a three-dimensional (3D) virtual guided resection and reconstruction of the mandible in osteoradionecrosis. The method enables 3D visualization of each desired dose field in relation to the 3D model of the affected bone. Two types of application – for resection and reconstruction – are described.

Key words: 3D planning; isodose; data fusion; osteoradionecrosis.

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Osteoradionecrosis (ORN) is defined as bone death following radiotherapy (RT), characterized by a non-healing area of exposed bone[1,2]. The deleterious and disabling side-effects of head and neck cancer radiation on bone are amongst the hardest to treat. The progression of ORN in the jaw can be difficult to control, resulting in the development of large osseous defects[3]. There is a pathophysiological relationship between the occurrence of ORN in the jaw and the radiation dose, i.e. the radiation dose is reported to be a risk factor for the development of ORN. The risk of developing ORN with a dose of 40–60 Gy is considered medium, whereas the risk at 60 Gy is frequently reported as high[4–7]. ORN often occurs within 3 years after the completion of RT and is related to trauma to the bone (tooth extractions prior to or post RT), the tumour volume treated, and the patient's health status.

This study focused on the category of patients who require surgery as a result of developing severe, or class III, ORN[8,9]. This surgical intervention includes removal of the affected bone and possibly a free-flap reconstruction as well. Determination of the resection margins of the affected bone is at present based mainly on preoperative interpretation of imaging, including computed tomography (CT) and technetium bone scans, in combination with intraoperative tissue exploration. Exact margin planning, and thereby also planned reconstruction of the defect, is not possible using these methods. Reconstructions are mostly performed without pre-treatment and exact size planning. Currently, the actual resection area of the affected bone is determined intraoperatively: the resection is continued until healthy bleeding bone is visible at the margin[10,11]. Nevertheless, as described by Zaghi et al.[12], histopathological confirmation that the necrotic bone margins have been completely resected does not always tally with the progression of ORN.

Exact intraoperative determination of the affected bone area, and thereby resection margin planning, is challenging and makes reconstruction planning unpredictable and thus suboptimal. In contrast to mandibular resections in cases of malignancy, no three-dimensional (3D) planned resection and guided surgery has been described to date for cases of ORN-related resection. Recent studies of primary oncological resections have reported successful integration of both resection planning and reconstruction based on 3D virtual planning[13–15], which might be applicable to ORN cases as well.

In order to make 3D virtual plans for the resection, the tissue affected by ORN or the tissue at risk requires adequate delineation. However, it is more difficult to derive exact margins from routine imaging in severe ORN cases. This case study introduces a method for resection planning based on 3D information of the causative radiation dose received. During 3D resection planning, the dose received can be visualized at each location of the affected bone. Moreover, this visualization technique can be applied to plan the drilling of screw holes for osteosynthesis plate fixation outside the high dose field in those cases requiring secondary reconstruction. Both applications are described below.

Materials and methods

Workflow

In order to plan and evaluate resections in relation to a selected isodose curve, a workflow was developed using a combination of radiation oncology planning software (Mirada Medical, Oxford, UK) and surgical planning software (ProPlan CMF 3.0; Materialise, Leuven, Belgium). Visualization and 3D planning requires access to the CT dataset showing the patient's current situation, as well as the RT planning, including the isodose curves.

This workflow was applied to three example cases, which are described below. In all cases, after consulting the radiation oncologist, the correct isodose lines of the planned target volume (PTV) (e.g. 56 Gy) were selected and exported as a radiotherapy structure set (RTSS) together with the CT dataset of the RT. The CT and RTSS were combined using a conversion method described by Kraeima et al. 2015[16]. In short, a conversion tool written in MATLAB (MathWorks, Natick, MA, USA) introduces a voxel highlight on the CT image for every coordinate corresponding to the RTSS file. In short, the RTSS is projected onto and combined with the CT, resulting in an enhanced DICOM file containing both the CT and isodose information.

The combined RT dose and CT information was imported into the 3D surgical planning software ProPlan 2.1 (Materialise, Leuven, Belgium). The isodose information was segmented into a 3D model, as well as all relevant bony structures. This combined 3D visualization was then used to discuss and determine the osteotomies for the resection of the affected bone. The workflow is described and presented in Fig. 1, including an example image for each software step.

In the case of previously performed surgical resections (for example patient 1A described below), the 3D model was supplemented with 3D visualizations of the osteotomies performed in the earlier surgical intervention. These were derived from the postoperative imaging of the previous intervention.

Patient 1A—retrospective analysis of resection vs. radiotherapy field

The first patient (patient 1A) was treated using conventional methods, as the 3D visualization methods were not available at that time. A retrospective analysis of the ORN in relation to the 3D visualization of the RT field was performed.

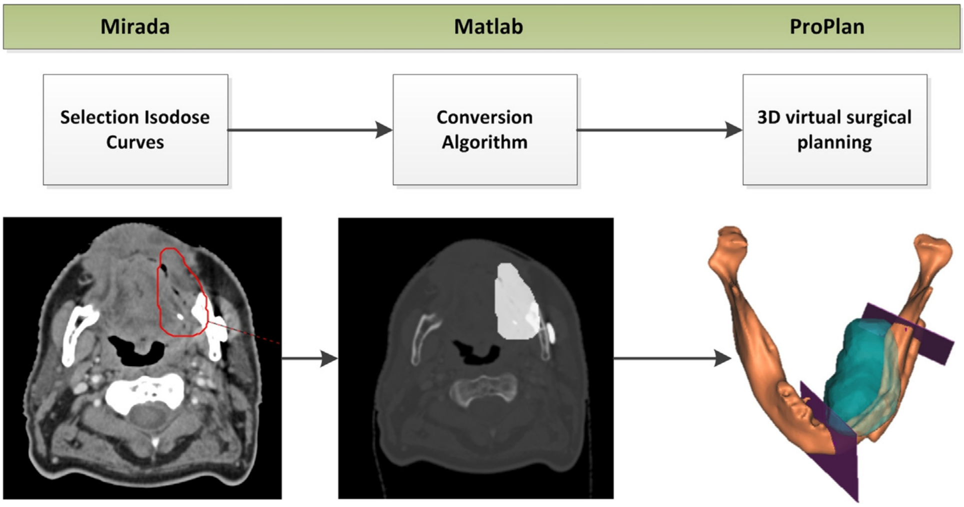

Fig. 1. Schematic overview of the workflow from isodose curve selection to 3D visualization and surgical planning.

This patient was diagnosed with squamous cell carcinoma in the floor of the mouth, stage pT4N0, in April 2009. The carcinoma was subsequently removed surgically by means of a marginal mandibular resection. Histopathology confirmed tumour-free margins of 5 mm, but bone invasion, perineural spread, and an invasive tumour front were observed. The patient underwent intensity modulated radiation therapy (IMRT) to the mandible postoperatively, with a maximum dose of 56 Gy within the PTV.

Three months after primary treatment, and 1 month after IMRT, the patient was diagnosed with intraoral exposed necrotic bone (ORN) and a fractured mandible with an orocutaneous fistula. The fistula healed following hyperbaric oxygen (HBO) treatment (30 sessions) and the intraoral mucosa remained intact. In agreement with the patient, it was decided to reconstruct the mandibular defect with a free cancellous bone graft from the iliac crest, in lieu of using a free vascularized flap[16]. The affected bone was cut from the mandible up to the point where the sequestra had been removed and the bone was bleeding from the marrow. The free bone from the iliac crest was inserted as a block and fixed with a 2.3-mm reconstruction plate. The patient then received 14 additional sessions of HBO treatment and a daily dose of amoxicillin–clavulanic acid for a period of 14 days.

Three weeks later, the patient developed a cutaneous fistula whereby the osteosynthesis plate was exposed but the intraoral mucosa remained intact. Second surgery included resection of the exposed anterior part of the native mandible, which had developed ORN around the osteosynthesis screws. The iliac graft, although vital, was removed, and the defect was reconstructed with a free vascularized fibula flap. This was done because bone was exposed through the skin and there was substantial lysis of the bone around the exposed screws. Moreover it needed replacement with bone and soft tissue to overcome the tissue loss, thus it was determined that a free vascularized fibula flap was the best option. The graft healed without further complications and is in situ to this day.

As described above, the patient suffered from ORN twice and underwent two corrective surgeries. In order to determine whether the second surgery could have been avoided, as well as the areas subjected to RT and at what doses, a retrospective 3D analysis was performed. The RT dose information and the CT data were combined in order to visualize both the 3D dose information and the bony structures. The RT dose received in the PTV was 56 Gy. After consulting the radiation oncologist, the correct isodose lines of the PTV (56 Gy) were selected and visualized according to the described workflow[17]. The final 3D model included the visualization of the 56 Gy field, the mandible, and the previously performed osteotomy planes in the mandible.

Patient 1B—prospective 3D analysis and surgical treatment of ORN

The method described above for the retrospective assessment of patient 1A was applied to an additional patient case (patient 1B). In this case, the visualized RT dose field was used prospectively for resection margin planning. This patient had developed squamous cell carcinoma in the floor of the mouth and had undergone surgical resection including a marginal resection of the mandible as primary treatment, and additional RT (56 Gy). The patient developed ORN within 11 months after the primary treatment. The high-dose 56 Gy and 50 Gy areas were visualized according to the workflow described above.

Patient 2—determination of osteosynthesis screw locations

This 84-year-old male patient was diagnosed with squamous cell carcinoma (pT4N1) in the buccal mucosa of the left mandible in January 2014. The malignancy was removed by 3D guided surgical resection, including neck dissection, and the defect was reconstructed with a free vascularized fibula flap. Postoperative IMRT-based RT was delivered to the PTV at a dose of 66 Gy. An intraoral fistula occurred within 20 months after the completion of RT, in which the bone was exposed. HBO was applied, following which the outer cortex of the exposed bone was removed until the bone started to bleed. The bone was then covered with a soft tissue nasolabial rotational flap. Of note, the fibula graft was not removed, and therefore continuity of the mandible was retained.

The fistula persisted after the attempt to cover it using local tissue grafting. Also, the osteosynthesis plate holding the fibula graft in place had migrated in the condyle region, as can be seen in the panoramic radiograph in Fig. 2a. The osteosynthesis plate was removed, along with the necrotic fibula graft. In order to preserve the contour and provide the patient with a stable occlusion, a new 2.7-mm osteosynthesis reconstruction plate was inserted, includ-

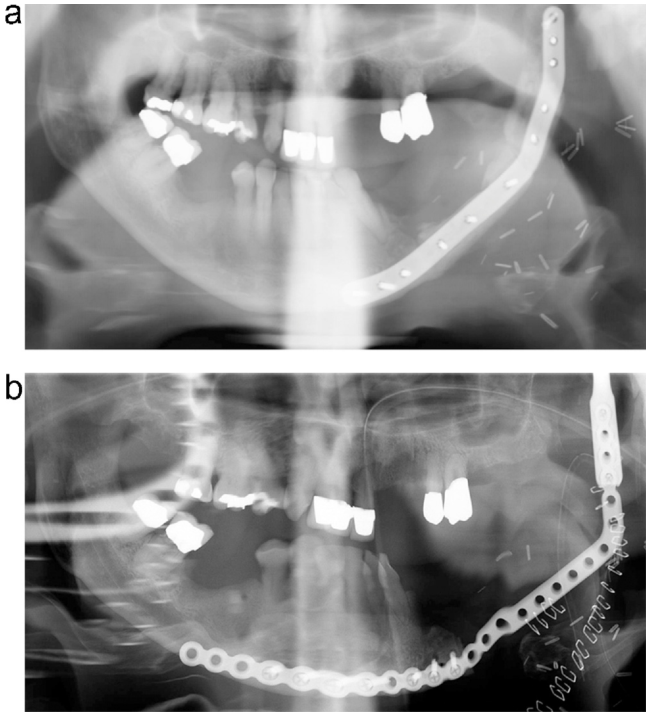

Fig. 2. (A) Panoramic radiograph showing plate migration at the left condyle. (B) Panoramic radiograph after plate reconstruction with screw placement based on visualization of the radiotherapy dose.

ing a condylar add-on. At the same time, the orocutaneous fistula was closed from the outside using a pedicled temporal fascia flap with skin. No additional bone graft was used in this procedure because the patient refused bony reconstruction at that time. The patient accepted the risk of plate exposure without bone insertion.

The screw locations for the reconstruction plate were planned according to the 3D visualization. This planning was based on the radiation dose received in order to prevent unnecessary screw insertion in the high-dose areas.

All required screw locations were planned outside the high-dose field of 66 Gy. At least three of the screws were planned outside the low-dose 50 Gy area, in order to maintain plate stability and to prevent screw movement. A 3D visualization of the RT dose received was made. This visualization included both the 66 Gy and the entire 50 Gy area, which was agreed to be a potential area at risk of developing ORN[18]. Both the 66 Gy and 50 Gy volumes were selected and imported into the virtual planning software using the methods reported above.

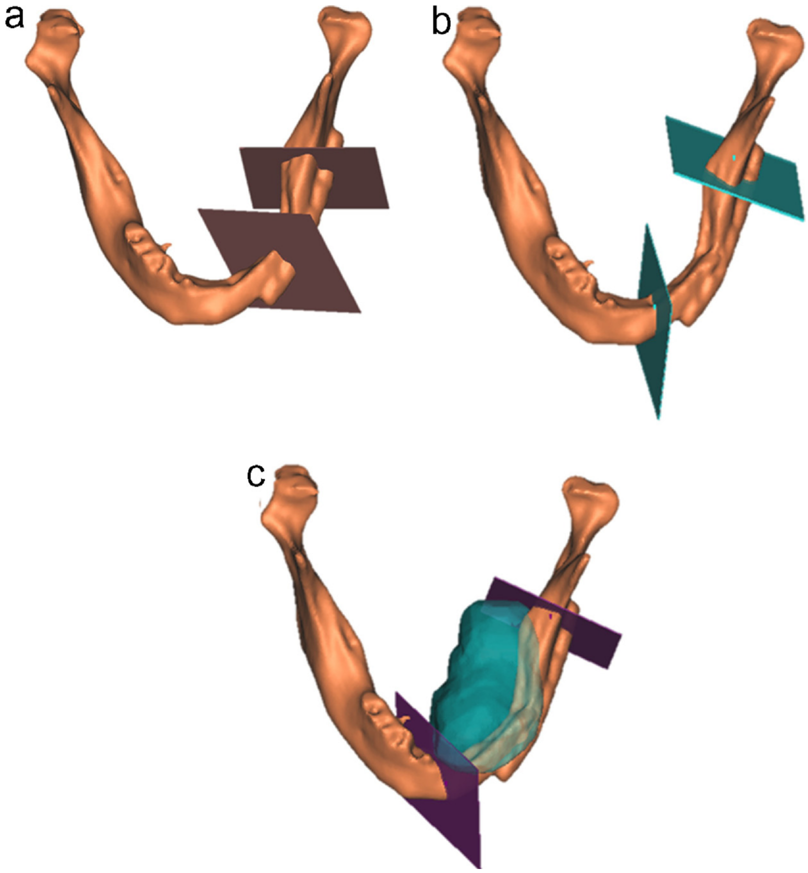

Fig. 3. Stepwise 3D representation of the retrospective evaluation of the resection in patient 1A. (A) The initial resection following ORN, including reconstruction with an iliac crest graft. (B) The resection after the second occurrence of ORN, including reconstruction with a fibula graft. (C) Proposed resection based on visualization of the radiotherapy dose administered.

Results

Patients 1A and 1B

The 3D visualizations of patients 1A and 1B were completed according to the workflow presented in Fig. 1. 3D visualization of all osteotomies performed in patient 1A and the suggested osteotomies based on RT showed that the resection margins of the first surgical correction, including the iliac crest graft, were within the 56 Gy field (Fig. 3). In addition, the osteotomies of the second surgical intervention, including the fibula graft, were around the margins of the high-dose field, as seen in Fig. 3b. Visualization of the 56 Gy area is presented in Fig. 3c.

Figure 4b shows the visualization of the 50 Gy isodose field in relation to the mandible for patient 1B. A dose of 50 Gy was chosen because the risk of developing ORN with this RT dose is low[18]. Surgical guides were designed and fabricated for resection of the affected bone, according to the 3D surgical plan. The resections were performed according to the guides, and bleeding of the bone was observed after resection. Pathological examination of the resected bone fragments confirmed ORN. No recurrence of the ORN has been seen during the follow-up period to date.

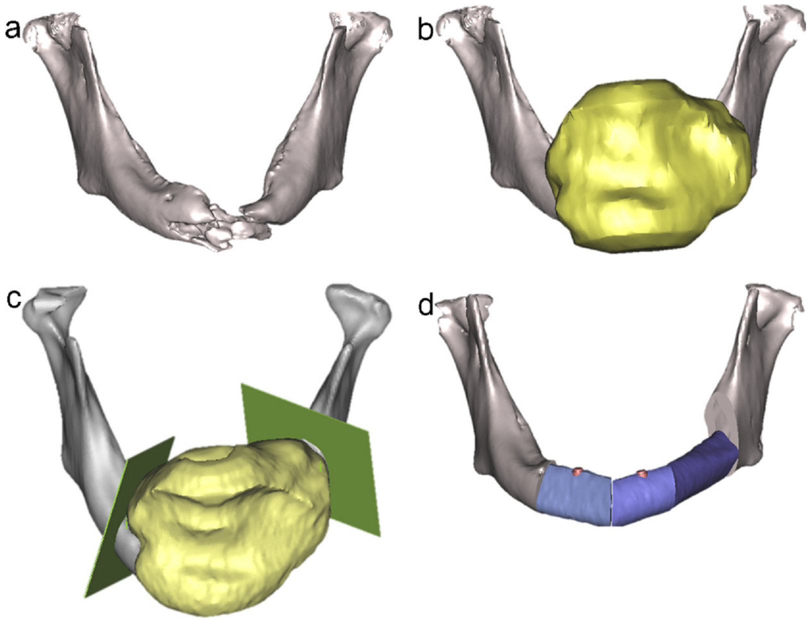

Fig. 4. Stepwise representation of the 3D planning workflow for patient 1B. (A) ORN had led to mandibular fracture. (B) Projection of the 50 Gy radiotherapy field. (C) Resection planning, with planned osteotomies outside the 50 Gy field. (D) Reconstruction planning including a fibula graft and dental implants.

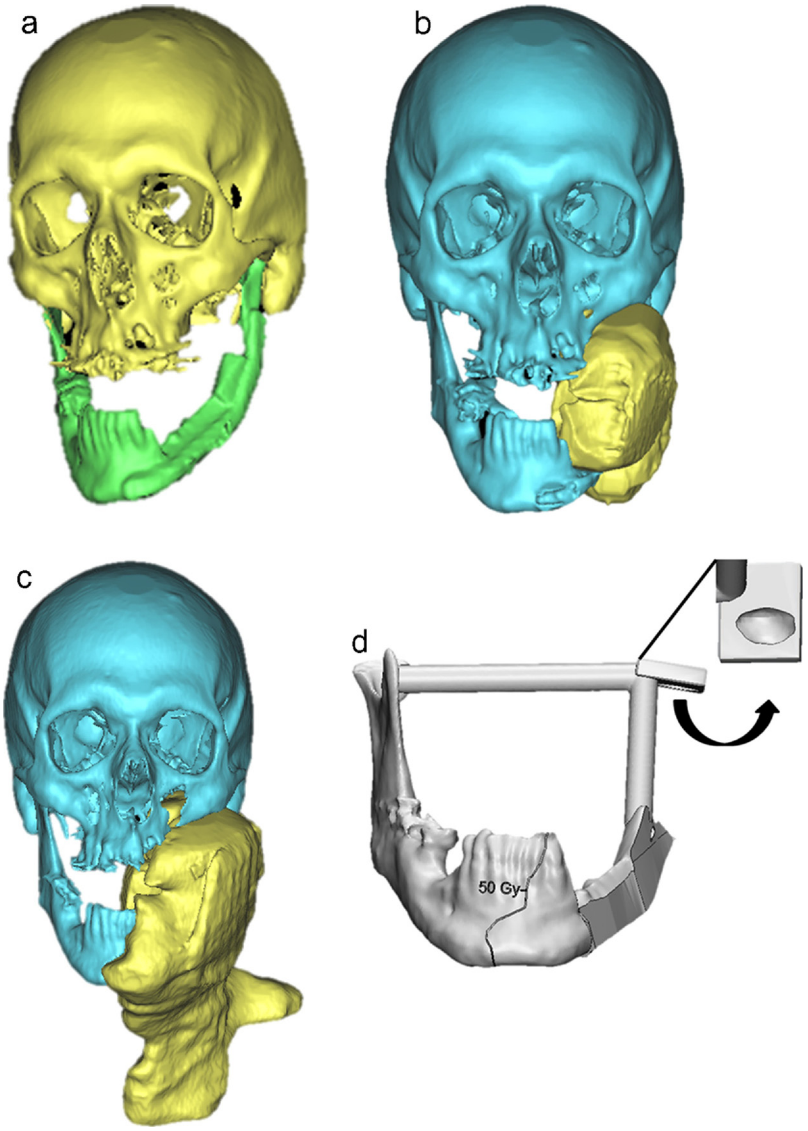

Fig. 5. Stepwise representation of the 3D planning workflow. (A) Current ORN situation, with a fibula reconstruction in situ. (B) Visualization of the area that received a dose of 66 Gy. (C) Visualization of the area that received a dose of a maximum of 50 Gy. (D) 3D print model of the mandible used to pre-shape the osteosynthesis plate, including an extension to direct the condylar add-on, as indicated by the arrow under the insert.

Patient 2

The planning of the screw locations in patient 2, based on isodose lines, is shown in Fig. 5. Figure 5a shows the situation at baseline, Fig. 5b shows the visualization of the 66 Gy field, Fig. 5c shows the visualization of the 50 Gy field, and Fig. 5d shows the 3D print model for plate bending including the aimed position of the condylar add-on of the plate.

Only the 50 Gy dose line was included in the 3D printed model of the mandible, because the 66 Gy border lay within the part that would definitely be removed during the procedure. The printed model was used to pre-shape the osteosynthesis plate and to provide direct feedback as to where to drill the screw holes in the <50 Gy dose area. Intraoperatively, bleeding of the bone was observed after drilling the screw holes. The osteosynthesis plate was shaped and placed, including a condylar add-on, which replaced the condyle. This has been in situ for 10 months so far. The final result is shown in the panoramic radiograph in Fig. 2b. Note that the 3D visualization method described in this study was not available during the previous interventions that this patient had received. In other words, this was the first time that the method to visualize the RT fields and plan the screw locations had been used.

Discussion

This case study presents a novel method for 3D visualization of RT isodose lines in relation to 3D bone models derived from CT data at the time of ORN occurrence. This method enables the evaluation of ORN risk areas, exact resection planning of ORN-affected bone, and the planning of screw locations for reconstruction plates outside the high-dose area. The current methods for resecting affected ORN bone consist of the interpretation of CT data and intraoperative exploration of the tissue. As described by Zaghi et al., histopathological confirmation of necrosis-free bone margins after identifying bleeding healthy bone intraoperatively does not assure cessation of the progression of the disease[12].

This method of 3D visualization and planning of resection/screw positions does not assure or guarantee a course of improvement after treatment (compared to conventional surgical treatment), as ORN is a multifactorial problem. However there is a correlation between the RT dose received and the occurrence of ORN, which should be considered and incorporated into the planning of surgical treatment[19,20]. In addition, comparable visualization could be used in decision-making with regard to tooth extraction or implant insertion in irradiated areas.

This case study does not provide advice regarding cut-off values for radiation doses and planning of resection margins. Any dose can be visualized, as reported here. Hence, this method could serve the individual surgeon's preference.

It is recommended that cut-off doses or the probability dose mapping is determined, by correlating the dose received and the occurrence of ORN. In order to derive such a predictive model, a large database analysis is required[20].

A functional trade-off between loss of function and preventive bone resection is difficult if no exact cut-off doses are defined. For example, a resection based on a 50 Gy dose field could include resecting an intact mandibular nerve, the mandibular condyle, or temporomandibular joint, thereby decreasing a stable occlusion. Additional evidence is required in order to adequately define the risk of recurrence of ORN and the trade-off with loss of function in the case of a preventive resection. Moreover the advised resection planning remains unclear and is founded on the individual surgeon's choice at this stage.

Pautke et al. described a method for intraoperative guidance for resection margins[21]. They suggested using tetracycline bone fluorescence-guided resection to identify the region affected by ORN. This technique appears to have improved the surgical therapy of ORN; however no large trials using this method have been described. Moreover, preoperative planning that includes the restoration of defects is not enabled by this method. An advantage of the method described in this article is that it does not require the administration of additional pharmaceuticals.

ORN can manifest as a progressive disease, whereby necrosis can continue even after surgical removal of the affected bone at a later stage. In the conventional surgical treatment of severe ORN, the affected bone is removed up to the point where healthy bleeding bone is identified at the margin. Usually, no additional margins are included in the resection in anticipation of potential relapse of the disease. The method developed in this study could provide a single-stage solution for those cases in which the relationship between the radiation dose and situations that require second surgical resection can be determined.

In conclusion, this article reports a decision supportive method that visualizes the selected isodose fields together with the 3D bone models. The use of this method in clinical practice has been demonstrated. Despite the absence of a strict relationship between the RT dose received and the risk of ORN, related to the cut-off dose, pre-planned resection margins or screw-location planning can help in accurate surgical planning. By which the required (traumatic) surgical manipulation of the bone can be directed to the area of bone that has received a low radiation dose. The tool developed in this study, at this stage, could be added to current decision-making options for the treatment of severe ORN.

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None.

Competing interests

No competing interests.

Ethical approval

Although this was a retrospective study, the ethics board approved the use of the visualization techniques, based on routine imaging in the hospital. This approval is also applicable to the manuscript (M14.160224).

Patient consent

Not required.

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