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● *Physics Contribution*

DOSE VARIATION AT BONE/TITANIUM INTERFACES USING TITANIUM HOLLOW SCREW OSSEOINTEGRATING RECONSTRUCTION PLATES

ABDELKARIM S. ALLAL, M.D.,* MICHEL RICHTER, M.D., D.D.S.,† MARIATERESA RUSSO, D.SC.,* MICHEL ROUZAUD, D.SC.,* PAVEL DULGUEROV, M.D.‡ AND JOHN M. KURTZ, M.D.*

Divisions of *Radiation Oncology, †Maxillo-Facial Surgery, and ‡Head and Neck Surgery, University Hospital, Geneva, Switzerland

Purpose: To evaluate dose variations at bone/titanium interfaces in an experimental model designed to simulate postoperative radiotherapy in patients with mandibular reconstructions using a titanium hollow-screw osseointegrating reconstruction plate (THORP) system.
Materials and Methods: The model consisted of a 25 × 25 × 10 mm^3 block of fresh bovine femoral diaphysis, to the surface of which a segment of THORP system reconstruction plate was fixed by means of a solid titanium screw 4 mm in diameter and 10 mm in length. Using specially designed thermoluminescent dosimeters (TLD) 2 mm in diameter and 0.13 mm in thickness, dose measurements were carried out at four distances from the screw axis (0.1, 0.3, 0.6, and 1 mm). ^{60}Co and 6-MV photon beams were used at incidences both perpendicular and parallel (''axial'') to the screw axis.
Results: For 6-MV X-ray beams incident perpendicular to the screw axis, the maximum dose enhancement (due to backscatter) and the maximum dose reduction (due to attenuation) at the bone/titanium interface were 5% (± 2%) and 6% (± 2%), respectively. The corresponding values for ^{60}Co beams were 6% (± 5%) and 10% (± 5%). For the axial incidences, a maximum dose enhancement of 5–7% was noted for both 6-MV X-rays and ^{60}Co for beams incident on the surface containing the THORP plate segment, whereas beams incident on the opposite surface induced only a very small dose enhancement (2–3%).
Conclusion: Using a new experimental model, TLD measurements showed only marginally significant dose variations at bone/titanium interfaces around THORP screws, all measured values being very close to the uncertainty limits (± 5%) associated with the method. For both ^{60}Co and 6-MV beams, dose variations appeared smaller for axial than for perpendicular incidences. Because photon beams used in head and neck cancer treatment are most often directed parallel to the screw axes, these results suggest that failures of prosthetic osseointegration are unlikely to be explained by an overdosage at the bone/titanium interface.

Reconstruction plate, Bone/titanium interface, Radiation therapy, Head and neck cancer.

INTRODUCTION

Advanced head and neck cancers are often treated with multimodality approaches combining surgery and postoperative radiotherapy. Moreover, tumors located in the oropharynx or oral cavity often require a bone resection and subsequent reconstruction procedures, particularly involving the mandible (1, 11, 20). Metal plates, designed to be screwed into the bone for reconstruction of composite mandibular defects, have come to be widely used for this purpose (11, 12, 18). Most recently, implants made of titanium and titanium alloys have gained popularity as a result of their favorable mechanical properties and greater tissue compatibility (11, 20). The problem of osseointegration failure after postoperative radiotherapy has been the subject of some debate in the literature, particularly regarding the possible mechanisms. Dose enhancement at the metal/bone interface, as reported by some investigators (3, 24), may represent a possible contributing factor.

It has long been known that, when metal inhomogeneities with high atomic number are present in the path of photon or electron beams, the dose distribution is altered and regions of over- or underdosage are produced (5, 7, 8). In clinical practice, this phenomenon can be relevant, because overdosage can lead to necrosis of the adjacent tissue, whereas underdosage can result in a decrease of the local control probability. Dose distributions in the vicinity of metal implants have been studied in several experimental models (2, 3, 8, 15, 24). Dose perturbations have been frequently documented, but with considerable variation from one study to another (3, 15, 24, 23). Most investigators have used a simple experimental model where a solid titanium plate was inserted between sheets of tissue- or bone-equivalent materials. This configuration is a crude approximation of the real anatomical conditions, making it difficult

Reprint requests to: Abdelkarim S. Allal, M.D., Division of Radiation Oncology, University Hospital, 1211 Geneva 14, Switzerland.

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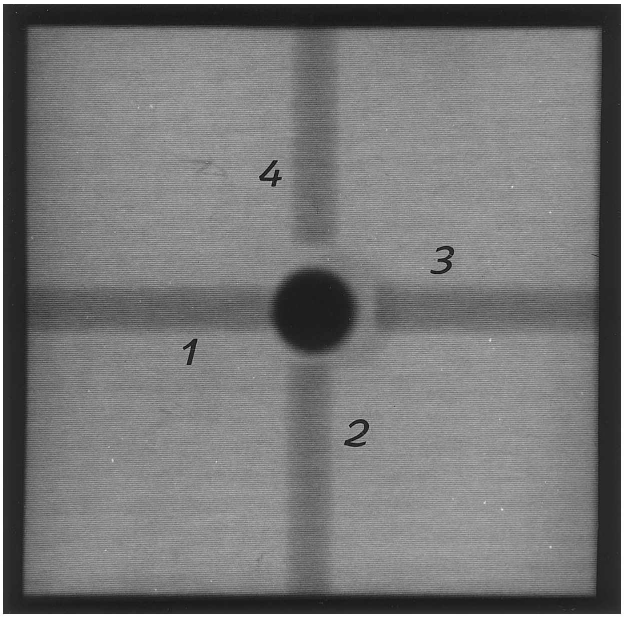

Fig. 1. Axial X-ray check of the bone block (× 4.5) demonstrating the various thicknesses of bone around the screw hole (1 = 0.1 mm; 2 = 0.3 mm; 3 = 0.6 mm; and 4 = 1 mm).

to extrapolate the dosimetric results to the clinical situation, particularly in cases employing a Titanium hollow-screw osseointegrating reconstruction plate (THORP) system. To address this particular problem, a new experimental model was developed, in which dose measurements at the titanium/bone interfaces were made under physical conditions that corresponded as closely as possible to the clinical situation. This paper reports on the results obtained with this methodology, employing photon energies and incidences commonly used in head and neck radiotherapy practice.

METHODS AND MATERIALS

Because the permanence of implants using a THORP system depends on the stability and the osseointegration of the screws inserted into the bone, we have focused our study on the measurement of dose variations in the bone surrounding the screw, rather than at the surface of solid metal plates, as in most of the studies reported in the literature (3, 15, 24). In these earlier studies, dose variation was reported to occur only in the immediate vicinity of the interfaces (0–1 mm); consequently, our measurements were limited to this range of distances.

Experimental model

To obtain a bone matrix of good homogeneity, a fragment of fresh bovine femoral diaphysis was used. To ensure plane surfaces, the bone was cut using a digital drive milling machine (MAHO 500c, Germany), thus shaping the bone segment into a rectangular block measuring 25 × 25 × 10 mm^3. Through the four lateral surfaces of the bone block and perpendicularly to the screw axis, four holes of variable depths were drilled using a 2-mm diameter flat-bottom drill. The operational tolerance of the machine used was 0.002 mm. These holes allowed various thicknesses (0.1 mm, 0.3 mm, 0.6 mm, and 1 mm) of bone to be maintained around the screw for the purpose of dosimetric measurements (Fig. 1). A solid THORP screw 4 mm in diameter and 10 mm in length (synthes THORP system, Stratec Medical, Waidenburg, Switzerland) was inserted perpendicularly to the bone surface, precisely in the center of the bone block, to allow fixation of a 25-mm long plate segment (Fig. 2). The screw was made of commercially pure titanium, containing only traces (1.5%) of other metals. Finally, four bony plugs with perfectly flat ends were manufactured from the rest of the ox bone (Fig. 2). These precisely-fitted bone plugs were designed to be inserted into each hole after the placement of the respective dosimeters, thus insuring the correct dosimeter position and avoiding the formation of interposed air cavities.

Irradiation and dose measurement

Dose measurements were carried out by means of specially designed thermoluminescent dosimeters (TLD) of 2-mm diameter and 0.13 mm thick (Teledyne Isotopes, Westwood, NJ). All TLDs were calibrated with a ^{60}Co beam at 2 Gy reference dose. Dose readings were done by a TLD reader (Toledo 654, Vinten Instruments) with ± 3% precision, corrected for nonlinearity in response. ^{60}Co and 6-MV

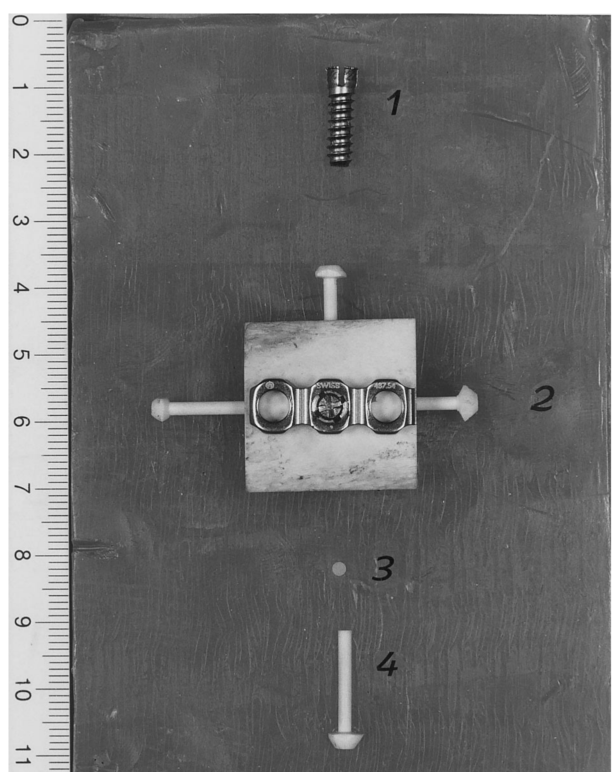

Fig. 2. The experimental model (1 = type of screw used; 2 = the bone block with a fixed plate segment and plugs inserted; 3 = TLD, and 4 = bone plug).

Table 1. Results of dose enhancement measurements at tissue-titanium interface (simple model)

Dosimeter	Dose enhancement for ^{60}Co	Dose enhancement for 6-MV photons
TLD	28 ± 5%	29 ± 5%
Ionization chamber	25 ± 1%	23 ± 1%
Film	22 ± 5%	22 ± 5%

photon beams were used, representing the energies most commonly used in head and neck cancer treatment. ^{60}Co and 6-MV irradiations were performed at 80 cm and 100 cm SSD and doses specified at a depth of 0.5 cm and 1.5 cm, respectively, using field sizes of 15 × 15 cm.

Different photon beam incidences were studied. Irradiation using incidences perpendicular to the screw axis allowed evaluation of backscatter radiation and the maximum dose attenuation due to the metal plate. Opposed ''axial'' incidences (parallel to the screw axis) represent the main beam incidences used in the clinical situation. The dose was always measured for the four different distances mentioned above.

Before using the new model, a set of dose measurements were made using a simple model consisting of a 10 × 10 × 0.5 cm^3 pure titanium plate embedded in a polystyrene phantom. The backscatter radiation was measured for the same photon beam energies, using the same SSDs and depth of dose specification, but with a field size of 25 × 25 cm. For this model, in addition to the TLD measurements, the dose measurements were also carried out by means of XV-2 Kodak films (± 5% precision) and a PTW-Freiburg parallel-plate ionization chamber (window thickness = 2.3 mg/cm^2, ± 1% precision). Film responses were converted to dose values using a calibration curve stored in the film-reading program of the photodensitometer.

RESULTS

Dose measurements in the simple model

Dose variations, calculated as the ratio of doses measured with and without the titanium plate, are displayed in the form of percentages in Table 1. All measurements at the titanium polystyrene interface showed a dose enhancement due to the backscattered radiation (22–28% for ^{60}Co and 22–29% for 6 MV). The three different measurement techniques gave consistent results.

Dose measurements in the new model

The dose variations represent the ratio of doses measured at different distances from the screw to the value at a distance of 0.1 mm (hereafter referred to as the dose at the bone/titanium interface). The dose variations are expressed in percentage form. The choice of 0.1 mm distance instead of 0 mm as the bone/titanium interface was motivated by the fact that the THORP system screw (Fig. 2) has an irregular lateral surface, that prevents an adequate direct contact with the TLD. Thus, air cavity interposition and a slanting of the dosimeter with respect to the interface were avoided and the reproducibility of the TLD position assured.

Table 2. Dose variation for incidences perpendicular to the screw axis (TLD measurements in the new model)

Depth (mm)	Dose enhancement ^{60}Co / 6-MV photons	Dose reduction ^{60}Co / 6-MV photons
0.1 (ref.)	1	1
0.3	4 ± 6%/5 ± 5%	8.7 ± 5%/0 ± 2%
0.6	2 ± 6%/5 ± 2%	7.4 ± 5%/6 ± 2%
1	6 ± 5%/3 ± 2%	10 ± 5%/5 ± 1%

Measurements performed with the reconstruction plate segment in place showed a certain dependence of dose on radiation geometry. Thus, for incidences perpendicular to the screw axis using 6-MV X-rays, the maximum dose enhancement (due to backscatter) and the maximum dose reduction (due to attenuation) at the bone/titanium interface were 5% (± 2%) and 6% (± 2%), respectively (Table 2). For ^{60}Co, these values were 6% (± 5) and 10% (± 5) for dose enhancement and dose reduction, respectively. However, for axial incidences using 6-MV X-rays, a dose enhancement (maximum 5%, ± 2%) was noted only when the THORP segment was on the same side as the incident beam (''upstream''), irradiation from the opposite direction (''downstream'') induced no significant dose enhancement, with the dose variation remaining in the range of 2% (Table 3). Similar results have been obtained using ^{60}Co (maximum of 7% and 3% for the plate segment positioned upstream and downstream, respectively).

DISCUSSION

During the last two decades, titanium implants have become widely used in mandibular reconstruction, anchorage of tooth prostheses, and in the construction or fixation of other maxillofacial prostheses. When these implants are used in patients with advanced head and neck cancers, the reconstruction procedures frequently involve the mandible, and postoperative irradiation is often administered. Several factors have been incriminated in osseointegration failures of these prostheses; these include the portion of the mandible removed, the type of the recovering flap, and the use of postoperative radiotherapy (1, 4, 12, 20, 21). Although the mechanisms of these failures remain complex and may be multifactorial, for patients receiving radiotherapy, osteora-

Table 3. Dose variation for axial incidences (TLD measurements in the new model)

Depth (mm)	^{60}Co, THORP plate US / DS	6-MV photons, THORP plate US / DS
0.1 (ref.)	1	1
0.3	−3 ± 3%/−3 ± 3%	−5 ± 2%/+1 ± 4%
0.6	−1 ± 3%/−2 ± 2%	−3 ± 2%/+1 ± 3%
1	−7 ± 7%/−3 ± 1%	−2 ± 1%/+2 ± 4%

US = upstream; DS = downstream.

dionecrosis surrounding the inserted screws may represent a possible cause of failure.

Although conventionally fractionated irradiation at doses of 60 Gy or less is unlikely to cause spontaneous radionecrosis in the intact mandible (9, 25), a localized bone necrosis around the inserted screws might result from a significant dose enhancement at the metal/bone interface. Dose variations in the vicinity of metal implants have been well documented by several investigators (2, 3, 15, 24), but with results varying widely among different studies. Thus, for soft tissue or bone/titanium interfaces, increases in dose varying from 10% to as much as 30% were noted using ^{60}Co (3, 15, 24), whereas data from studies using higher photon energies showed either similar (2, 3), slightly lower (15) or higher (22) values. Most of the investigators used a simple experimental model where a solid titanium plate was inserted between sheets of tissue- or bone-equivalent materials. This configuration bears only superficial resemblance to the real clinical situation, because the THORP plate has multiple holes and is secured to the bone by screws.

Taking these considerations into account, we developed an original experimental model whereby dose measurements at the titanium/bone interface were made using the same materials commonly employed in the clinical situation. A preliminary study using a simple model showed dose-enhancement values due to the backscattered radiation similar to those reported in the literature (3, 16, 24), either for ^{60}Co (22–28%) or 6 MV (22–29%). Moreover, three different measurement techniques were documented to give similar results, justifying the decision to use TLDs as a sole measurement tool for the new model.

Using the new model, only marginally significant dose variations could be documented at the bone/titanium interface around the screw, because almost all measured values remained very close to the limits of uncertainty of the method ($\pm$ 5%). This finding underlines the importance of using a model that approximates the clinical situation as closely as possible, and suggests that results previously obtained using simple models should be interpreted with caution.

The dose variations showed an apparent dependence on the incidence of the photon beams. It is particularly relevant that irradiation directed along the screw axis was associated with a very small increase in dose for either ^{60}Co or 6-MV photons, because this situation reflects the main photon beam incidences used in the radiotherapy of head and neck cancers. Opposed lateral photon fields are most commonly used for at least the major part of treatment and, generally, their incidences are parallel to the axes of the screws.

When using beams perpendicular to the screw axis, over- and underdosages were noted, consistent with the results of other investigators using solid titanium plates (3, 16), but with markedly less dose variation (with a maximum of 10%) in the present study. When the cumulative dose resulting from irradiation of both opposite laterals was taken into account, no significant dose variation resulted, because the underdosage (due to the metal absorption) compensated totally or partially for the overdosage (due to backscatter). This finding was also reported by Ryu et al. (20). Nonetheless, in many cases, the boost dose to the tumor bed is delivered by unopposed photon beams, for which no overdosage compensation can be expected. However, the boost accounts for a small fraction of the total dose, and even an overdosage of 10–15% would probably be clinically insignificant.

In the setting of postoperative irradiation involving mandibular reconstructions using the THORP system, the present study thus suggests that only a marginally significant dose variation should be expected surrounding the THORP screws and, consequently, that failures of osseointegration of the prosthesis are unlikely to be explained by an overdosage at the bone/titanium interface. This conclusion is supported by the experimental findings of Rosengren et al. (19), who demonstrated similar colony-forming capacity after irradiation of cells grown on titanium and those grown on plastic control supports. However, these results cannot exclude a decrease in the radiation tolerance of bones with integrity that had been altered by surgical procedures, thus possibly leading to osteonecrosis at doses below the accepted tolerance limits. Moreover, as suggested by an in vivo study (14), it cannot be excluded that radiation at the usual prescribed doses might decrease the rate of bone formation at the screw/bone interface.

For the time being, clinical observations fail to provide a clear explanation for the phenomenon of osseointegration failure. Indeed, results reported in the literature are conflicting because some investigators found implant failure to be unrelated to postoperative irradiation (6, 13), and others found radiotherapy to be a detrimental factor (10, 20), but without evidence of dose-dependence (20). Thus, recommendations concerning the use of titanium reconstruction in patients destined to receive radiotherapy remain controversial (10, 11, 17, 20, 23), and only well-designed prospective studies are likely to shed further light on this problem in the future.

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