Histology of Retrieved Immediately and Early Loaded Oxidized Implants: Light Microscopic Observations after 5 to 9 Months of Loading in the Posterior Mandible

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ABSTRACT

Background: An increased number of publications report that one-stage surgery and immediate/early loading of dental implants may be a feasible approach for prosthetic reconstruction of the edentate patient. However, little is known about the histologic response to implants subjected to immediate/early loading in patients.

Purpose: The aim of the present study was to histologically evaluate oxidized titanium implants subjected to loading immediately following surgery or after 2 months of healing and removed after 5 to 9 months loading.

Materials and Methods: Five patients participated in the study; each had consulted for implant treatment in the posterior mandible and subsequently volunteered to have extra implants inserted for the purpose of histologic research. Nine oxidized titanium implants (Brånemark System® TiUnite™, Nobel Biocare AB, Gothenburg, Sweden) were retrieved after 5 to 9 months in function. Two implants had been loaded the same day, whereas seven implants were loaded after 2 months of healing. Resonance frequency analysis was performed at retrieval on seven implants. Ground sections were prepared for histology and analyzed using light microscopic morphometry.

Results: Seven and 8.5 mm implants were placed, predominantly in quality 3 and 4 bone. Four implants were straight (Mk III), and five were tapered (Mk IV). All implants were clinically stable at retrieval and showed ISQ values of 65 to 79 with a mean of 71.4 ± 4.4. Eight of the implants were able to be used for histology. A gross histologic examination showed an undisturbed healing of soft and bone tissues with no apparent differences between response to immediately and early loaded implants. Lamellar bone surrounded the implants, and remodeling was evident and more marked near the implant surface. A condensation of bone toward the implant surface was seen; this resulted in a lamina dura–like structure in trabecular bone. Thin rims of newly formed bone were often seen following the contour of the implant surface. The morphometric measurements showed a mean bone-to-implant contact value of 84.2 ± 10.5% and a mean bone area value of 79.1 ± 6.8%. The two immediately loaded implants showed bone-to-implant contact and bone area values of 92.9 ± 0.1% and 84.9 ± 0.9%, respectively. The corresponding values for the six early loaded implants were 81.4 ± 10.6% and 77.1 ± 6.8%, respectively.

Conclusions: The present study demonstrated that oxidized implants subjected to immediate or early loading do integrate with soft and bone tissues in the posterior mandible.

KEY WORDS: dental implants, early loading, histology, immediate loading, oxidized surface

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An increasing number of publications and reports from scientific meetings illustrate that one-stage surgery and immediate/early loading of dental implants ad modum Brånemark can be used successfully in many indications.[1–5] These findings challenge the early treatment protocols, which were based on the conception that an implant had to be integrated in bone prior to loading.[6] More recent clinical findings demonstrate that implants can heal under the influence of occlusal and nonocclusal loading and maintain stability over time, at least in dense bone qualities and as evaluated with clinical and radiographic examinations. The clinical experiences have also indicated that immediate/early loading in soft bone qualities, of single-tooth replacements, and of implants placed in fresh extraction sockets may result in increased failures than with implants placed in dense bone, splinted implants, and implants placed in healed bone.[5,7–10] Most of the studies referred to have used machined screw implants, and it is possible that surface modification can facilitate implant healing and improve the clinical outcome. Anodic oxidation is one technique of surface modification that results in growth of the implant surface oxide to a thickness of about 1 to 10 µm and a porous surface structure.[11] Experimental studies have demonstrated higher bone-to-implant contact values and removal torque values for oxidized implants compared with those for machined implants, indicating a rapid development of a strong bone-implant fixation for the oxidized implants.[12–14] Indeed, the present authors found some differences in a recent evaluation of machined and oxidized titanium implants when used for immediate loading in the posterior mandible of 44 patients.[15] More machined implants failed than did oxidized implants (14.4% versus 4.5%). Losses of machined implants occurred predominantly in quality 4 bone and in smokers, a pattern that was not observed for the oxidized implants. Similar differences in survival rates have been reported in two studies by Glauser and colleagues.[16,17] Thus, these studies indicate that the use of oxidized implants may improve the outcome in challenging situations. Although experimental studies and case reports have been published,[18–22] little is known about the quality of the tissue-implant interface of oxidized implants subjected to immediate/early loading in patients.

This investigation was undertaken to evaluate histologically the tissue response to oxidized implants subjected to loading immediately after surgery or after 2 months of nonsubmerged healing and retrieved after 5 to 9 months of loading.

MATERIALS AND METHODS

Patient Selection

Five patients, three females and two males 43 to 56 years in age participated in the study. They had all consulted for implant treatment in the posterior mandible. The treatment plan included placement of implants and immediate loading with a provisional bridge on the same day or after a healing period of 2 months. The patients volunteered to have extra implants inserted, to be retrieved later for histologic examination. An informed consent form according to the Helsinki declaration was signed by the patients. It stated that the patient could withdraw from the study at any time point without consequences for the treatment.

Titanium screw implants (Brånemark System® TiUnite™, Nobel Biocare AB, Gothenburg, Sweden) destined to be removed were placed in second and third molar regions and were 7 to 8.5 mm long (Table 1). Straight (Mk III, 3.75 mm in diameter) and tapered

TABLE 1 Characteristics of Implants and Sites

Patient	Specimen No.	Tooth Position	Bone Quality*	Implant Type	Insertion Torque (Ncm)	Duration of Healing (mo)	Duration of Loading (mo)
1	1	46	3	Mk III 8.5 mm	40	0	9
	2	48	3/4	Mk IV 8.5 mm	< 50	0	9
2	3	47	2/3	Mk III 7 mm	40	2	7
	4	48	2	Mk IV 7 mm	50	2	7
3†	5	38	3	Mk IV 7 mm	40	2	7
	6	36	2/3	Mk IV 7 mm	50	2	7
4	7	48	3/4	Mk IV 7 mm	30	2	7
5	8	38	4	Mk III 7 mm	30	2	5
	9	35	3/4	Mk III 7 mm	50	2	5

*According to Lekholm and Zarb's classification.
†Patient is a smoker.

(Mk IV, 4 mm in diameter) implants were used (see Table 1). Bone quantity and quality and insertion torque were registered for these implants (see Table 1). In one patient temporary abutments were placed and a prefabricated provisional acrylic bridge was delivered the same day. In four patients healing abutments were placed and provisional bridges were connected after 2 months of healing (Figure 1). The bridges were in full contact in centric occlusion but adjusted to avoid contacts in lateral movements. The patients attended checkups weekly during the first month and monthly thereafter to the final evaluation.

Biopsy Retrieval and Histology

The implants were retrieved 7 to 9 months after their placement (see Table 1). Two implants had been immediately loaded for 9 months, and seven implants had been loaded for 5 to 7 months after 2 months of initial healing (see Table 1). At the day of retrieval, the bridges were removed and resonance frequency analysis (RFA) (Osstell®, Integration Diagnostics AB, Sävedalen, Sweden) was performed on seven implants in four patients to measure implant stability. The stability was measured in implant stability quotient (ISQ) units from 1 to 100. Healing abutments were attached to the selected implants, and a trephine was used to remove the implant with surrounding soft and bone tissues. The biopsies were fixed by immersion in 4% buffered formaldehyde.

The specimens were then dehydrated in a series of alcohol baths and finally embedded in light curing resin. Ground sections were prepared with sawing and grinding (Exakt Apparatebau, Norderstedt, Germany). One central section was taken from each sample, ground to a final thickness of about 10 μm, and stained with toluidine blue O and pyronin G.

The slides were viewed and photographed in a Leitz Orthoplan microscope equipped with a Microvid unit, Esselte-Leitz, Stuttgart, Germany, for morphometric measurements. A gross anatomic description was recorded. Morphometric measurements were performed in threads situated in bone tissue. The degree of bone-to-implant contact and the implant thread area occupied by bone were measured for each implant. A mean number was calculated for each parameter and implant.

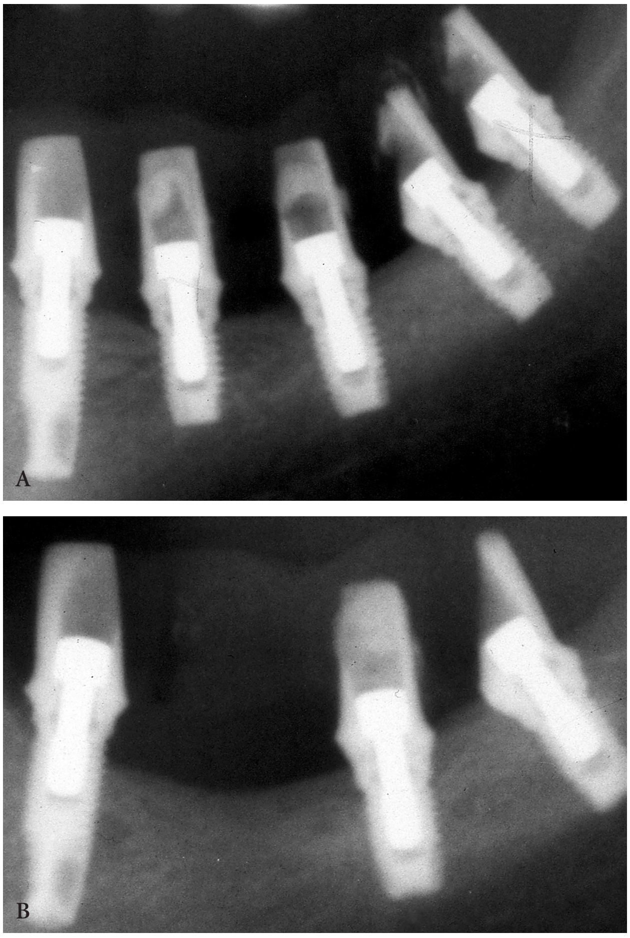

Figure 1 *A,* Radiograph of patient 5 showing five implants loaded after 2 months of healing in the posterior mandible. *Arrows* point to implants to be removed. *B,* Radiograph after retrieval of two implants.

Statistics

The Spearman correlation test was used to find possible correlations between morphometric parameters and ISQ measurements at implant retrieval. A statistically significant correlation was considered if $p < .05$.

RESULTS

All nine implants were successfully retrieved. One implant could not be used because of mishaps during the histologic processing. The remaining eight implants were surrounded by soft and bone tissues in the ground sections. Four straight and four tapered implants were analyzed. The retrieval process had caused some tearing of the tissues in the peripheral parts of the specimens. The bone was sometimes separated from the implant surface. This was interpreted as an artefact owing to shrinking of the tissues and/or a result of manipulation during retrieval and histologic processing because the bone was congruent with the implant surface in most such areas.

Gross Anatomy

The periimplant mucosa contained a keratinized oral epithelium that was continuous with a junctional epithelium facing the abutment surface (Figure 2). The junctional epithelium seemed to terminate near the implant-abutment junction. The subepithelial connective tissue comprised collagen fibers, vessels, and numerous cells. The number of inflammatory cells varied between specimens from moderate to extensive. Collagen fibers ran parallel near the abutment surface and in random directions in deeper portions of the soft tissue. The soft tissue–marginal bone interface showed signs of both resorption and bone formation, indicative of active remodeling in this region. The marginal bone level was situated just below the implant head or at the first thread in five implants, and in three specimens the marginal bone level was below the first thread.

Mature lamellar bone was observed in the specimens. Seven of the implants were surrounded by trabecular and cortical bone (Figures 2A and 3–5). One immediately loaded implant was surrounded by cortical bone only (Figure 6). The implant surfaces were in contact with dense periimplant bone in the first 4 to 5 mm and were almost totally covered with bone. Remodeling was evident and appeared more active near the implant surfaces (Figures 7 and 8). This was seen as formation of secondary osteons or resorption and bone formation at the surface of bone trabeculae. In trabecular bone it was evident that bone formation had resulted in compaction of bone toward the implant surface, which appeared as a lamina dura–like structure normally seen around teeth (Figures 9 and 10). In deeper portions thin rims of bone lined with osteoblast and osteoid seams were often observed to follow the contour of the implant surfaces (Figures 11 and 12). Osteoblasts were seen to form osteoid at the implant surface and toward the marrow tissue (Figure 13). Nonmineralized areas were occupied by marrow tissue, that is, loose connective tissue rich in hemopoietic cells, vessels/sinusoids, and fat cells. In areas of no bone con-

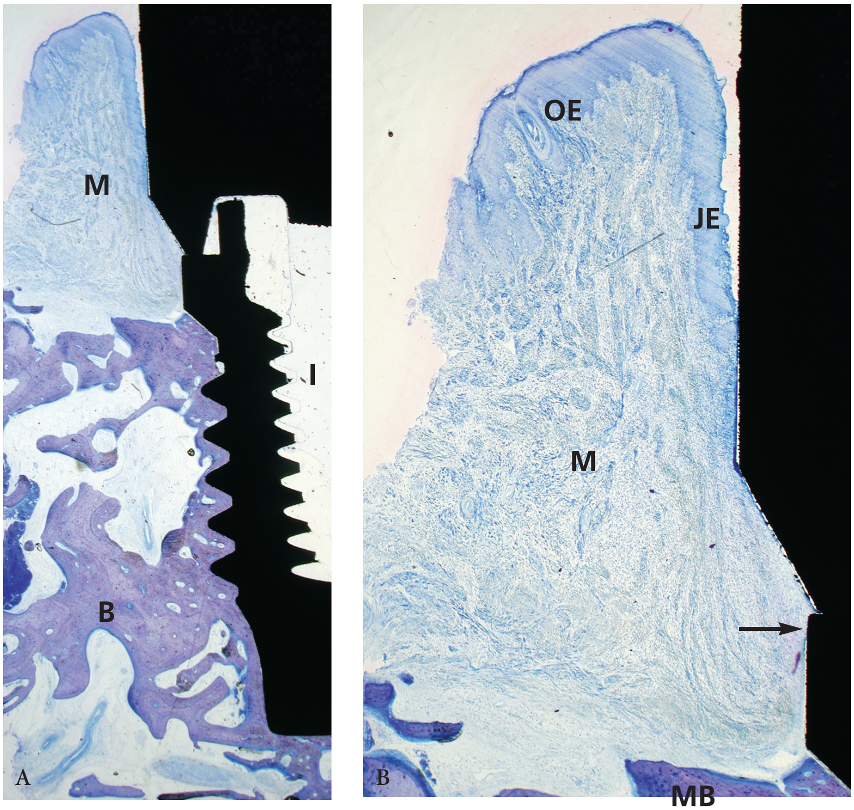

Figure 2 *A,* Light micrograph showing overview of an implant loaded for 5 months after initial healing of 2 months. Periimplant mucosa (*M*) and bone tissue (*B*) are present. Distance between two threads = 0.6 mm. (× 10 original magnification, stained with toluidine blue and pyronin G). *B,* Close-up view of periimplant mucosa. *A* = abutment; *JE* = junctional epithelium; *MB* = marginal bone; *OE* = oral epithelium; *arrow* = apical termination of junctional epithelium; *bar* = 0.5 mm (× 16 original magnification; stained with toluidine blue and pyronin G).

Figure 3 Overview of an early loaded tapered implant. *Arrows* = marginal bone level; distance between two threads = 0.6 mm (× 16 original magnification; stained with toluidine blue and pyronin G).

Figure 5 Overview of an immediately loaded straight implant. *Arrows* = marginal bone level; distance between two threads = 0.6 mm (× 16 original magnification; stained with toluidine blue and pyronin G).

Figure 4 Overview of an early loaded straight implant. *Arrows* = marginal bone level; distance between two threads = 0.6 mm (× 16 original magnification; stained with toluidine blue and pyronin G).

Figure 6 Overview of an immediately loaded tapered implant. *Arrows* = marginal bone level; distance between two threads = 0.6 mm (× 16 original magnification; stained with toluidine blue and pyronin G).

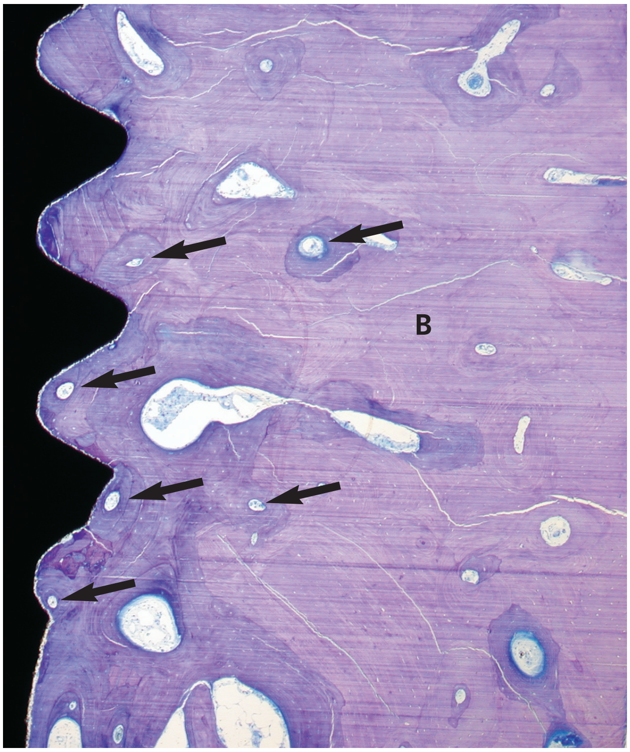

Figure 7 Detail of Figure 6 showing remodeling of cortical bone (*B*) at the implant (*I*) interface. *Arrows* point to some areas of remodeling; distance between two threads = 0.6 mm (× 40 original magnification; stained with toluidine blue and pyronin G).

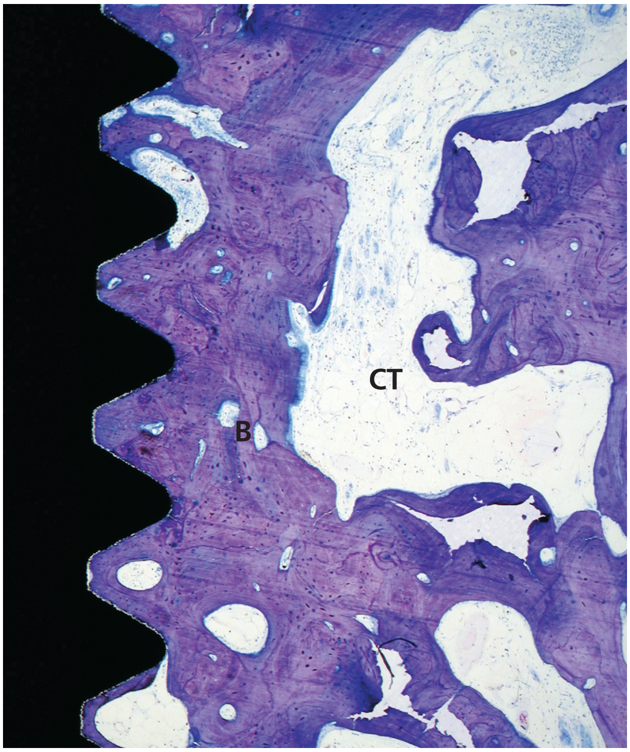

Figure 9 Image of bone (*B*) condensation toward the surface of an immediately loaded straight implant (*I*). CT = connective tissue; distance between two threads = 0.6 mm (× 40 original magnification; stained with toluidine blue and pyronin G).

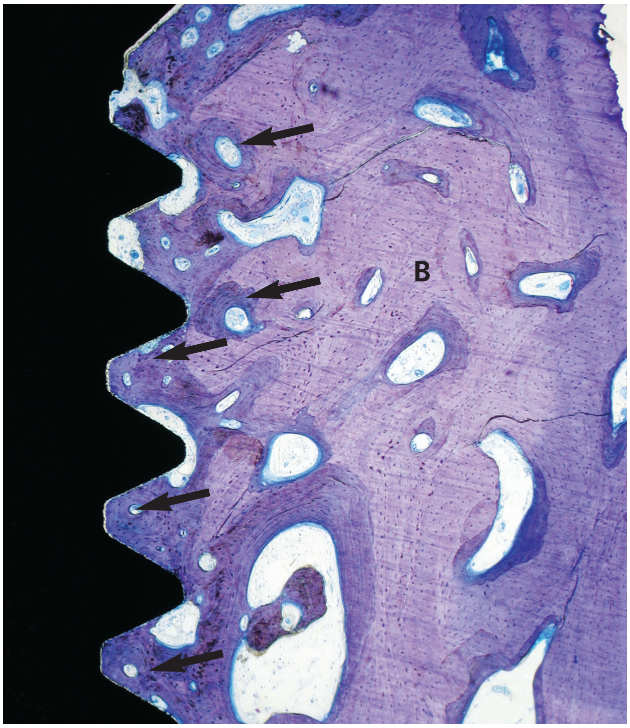

Figure 8 Detail of an early loaded straight implant showing active remodeling of the bone (*B*) adjacent to the implant (*I*) surface. *Arrows* point to some areas of active remodeling; distance between two threads = 0.6 mm (× 40 original magnification; stained with toluidine blue and pyronin G).

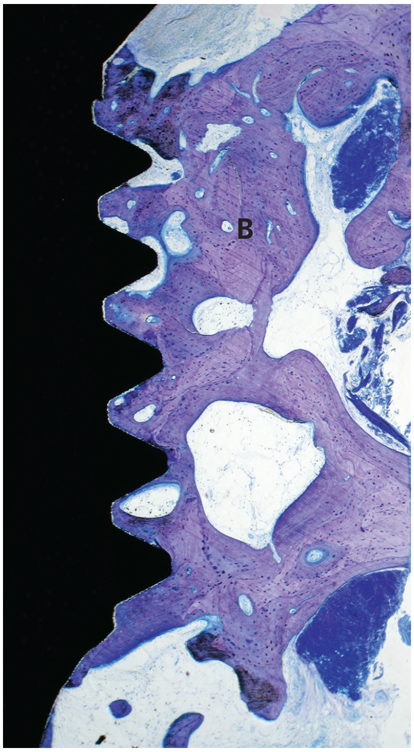

Figure 10 Image showing condensation of trabecular bone (*B*) toward an early loaded tapered implant (*I*). Distance between two threads = 0.6 mm (× 40 original magnification; stained with toluidine blue and pyronin G).

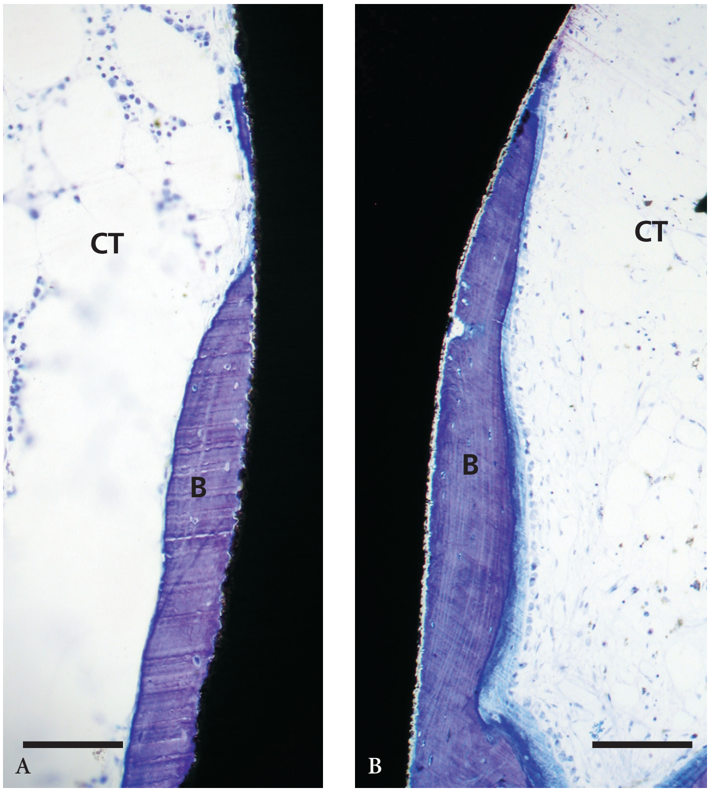

Figure 11 *A* and *B*, Two examples of thin rims of bone (*B*) following the contour of the implant surface (*I*). *CT* = connective tissue; *bar* = 50 μm (× 100 original magnification; stained with toluidine blue and pyronin G).

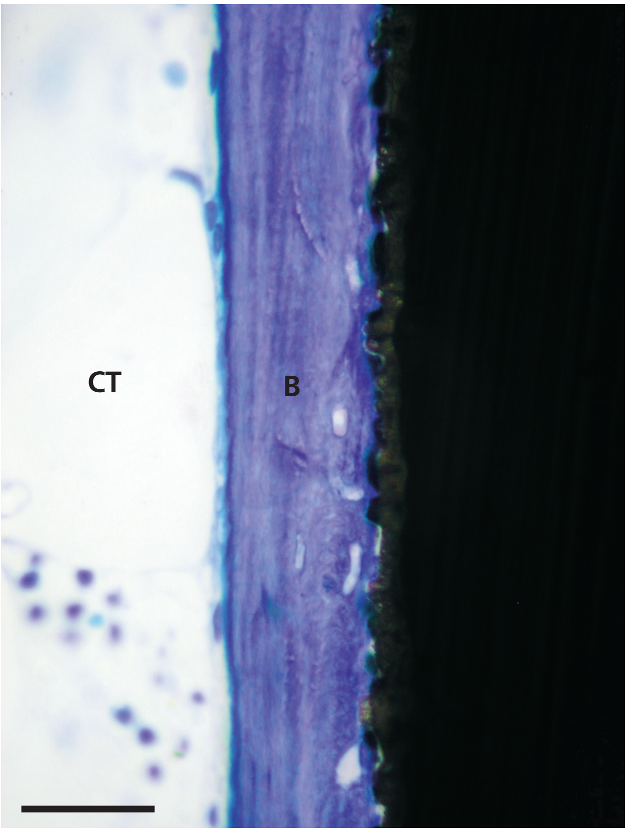

Figure 12 Image of intimate contact between a thin rim of lamellar bone (*B*) and the oxide (*) of an implant (*I*). *CT* = connective tissue; *bar* = 25 μm (× 250 original magnification; stained with toluidine blue and pyronin G).

tact, loose connective tissue was present, and sometimes macrophages and multinuclear cells could be distinguished near or at the surface.

There were no apparent differences between straight or tapered implants in any respect, nor were there any differences seen for immediately (n = 2) and early (n = 6) loaded implants.

Morphometry

The morphometric measurements showed a mean bone-to-implant contact of 84.2 ± 10.5% (Table 2) for all implants and 92.9 ± 0.1% and 81.4 ± 10.6% for immediately and early loaded implants, respectively (Table 3). Straight implants had 82.2 ± 11.0% and tapered implants had 86.4 ± 11.1% of bone-to-implant contact (see Table 3).

The mean bone fill of implant threads was 79.1 ± 6.8% for all implants (see Table 2) and 84.9 ± 0.9% and 77.1 ± 6.8% for immediately and early loaded implants, respectively (see Table 3). Straight implants showed 78.1 ± 6.8% and tapered implants showed 80.1 ± 7.7% of bone fill in the threads (see Table 3).

RFA

RFA showed a mean ISQ value of 71.4 ± 4.4 with a range of 65 to 79 (see Table 2). No correlations could be

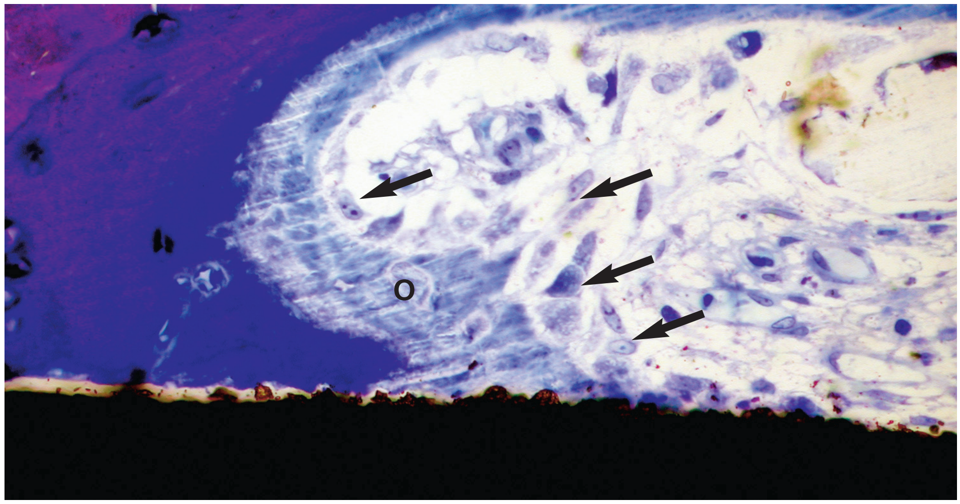

Figure 13 Osteoid (*O*) formation by osteoblasts (*arrows*) at the surface of the bone and implant. *I* = implant; *bar* = 20 µm (× 500 original magnification; stained with toluidine blue and pyronin G).

found between any of the morphometric parameters and ISQ values.

DISCUSSION

The present study evaluated the tissue response to immediately and early loaded oxidized implants after 5 to 9 months of loading in the posterior mandible. The majority of the implant sites in this study were of quality 3 or 4 bone, and the prostheses were in full centric occlusion, which means that the implants had been biomechanically challenged to a high extent. In spite of this, gross histologic examination showed an apparent undisturbed healing in all examined specimens. The implant sites showed signs of active remodeling that was more marked near the implant surface, possibly as a response to loading.

Our results are comparable with the histomorphometric measurements in a previous publication on clinically retrieved two-stage machined Brånemark implants.[23] In that study 30 loaded implants removed on average 7.2 years after surgery showed a mean bone-to-implant contact value of 84.9% and a mean bone area value of 81.8%, similar to the corresponding values of 84.3% and 79.1% from the present study. Our findings are also in line with a previous case report, although examining a different implant surface, in which Testori and colleagues[20] evaluated the bone tissue response to acid-etched implants after 4 months of immediate loading in the mandible and found bone-to-implant contact values of 78% and 85%. Balleri and colleagues[24] placed 45 two-stage machined Brånemark

TABLE 2 Results from Histomorphometry and RFA Measurements

Specimen Number	Bone Contact (%)	Bone Area (%)	ISQ at Retrieval
1	92.8	84.2	—
2	93.0	85.5	—
3	67.1	76.8	74
4	70.8	69.6	72
5	86.1	87.1	71
6	—	—	65
7	95.5	78.0	68
8	82.1	69.7	71
9	86.6	81.6	79
Mean + SD	84.3 + 10.5	79.1 + 6.8	71.4 + 4.4

TABLE 3 Results from Histomorphometry and RFA Measurements for Different Subgroups of the Material

	Bone Contact (%)	Bone Area (%)	ISQ at Retrieval
Immediate loading ($n = 2$)	92.9 + 0.1	84.9 + 0.9	—
Early loading ($n = 6$)	81.4 + 10.6	77.1 + 6.8	71.4 + 4.4
0 + 9 mo ($n = 2$)	92.9 + 0.1	84.9 + 0.9	—
2 + 5 mo ($n = 2$)	84.4 + 3.2	76.6 + 8.4	75.0 + 5.7
2 + 7 mo ($n = 4$)	79.9 + 13.3	77.9 + 7.2	71.3 + 2.5
Straight (Mk III) ($n = 4$)	82.1 + 11.0	78.1 + 6.8	72.3 + 5.9
Tapered (Mk IV) ($n = 4$)	86.4 + 11.1	80.1 + 7.7	69.0 + 3.2

implants in 14 partially edentulous patients and evaluated the implants' stability with RFA measurements after 1 year of loading. They observed a mean ISQ of 72.8 for mandibular implants, which is similar to the mean ISQ value of 71.4 measured in the present study. In comparison with the above-mentioned studies, our results indicate a normal integration of the implants both from a histologic and biomechanical point of view.

It can be speculated that loading within physiologic limits stimulates bone formation as a result of the bone's adaptation to loading, as shown in animal studies. Piatelli and colleagues[19] compared immediately loaded titanium-plasma sprayed implants with unloaded implants in a monkey model. Histology after 9 months showed statistically more bone at the loaded implants. Romanos and colleagues[18] studied sandblasted implants subjected to immediate loading after 3 months of healing. Histomorphometric measurements after 3 months of loading showed no differences in bone-to-implant contact values but more bone within the threads of the immediately loaded implants. In the present study, higher values of bone-to-implant contact and area values were observed for the immediately loaded implants, although specimens were too few for statistical analyses. In a recent case report, Testori and colleagues[21] compared one immediately loaded implant with two submerged acid-etched implants and found more bone at the immediately loaded one (64.2% versus 38.9% for the submerged implants), which also indicated a stimulation effect of loading.

In the present study, healing resulted in a compaction of bone toward the implant surface, and a lamina dura–like structure was observed for implants placed in trabecular bone. This compaction of bone probably has an influence on implant stability because of an increased stiffness of the bone-implant system; this may explain why implants placed in soft bone show an increased stability with time. Friberg and colleagues[25] evaluated the stability of maxillary implants in nine patients from placement to abutment connection and after 1 year of loading using RFA. The bone density was low (ie, quality 3 and 4) and was also characterized by cutting torque measurements at implant placement. They found a correlation between cutting torque and primary implant stability. With time, however, all implants reached a similar degree of stability despite bone density at the start. The RFA values increased to abutment connection, which was performed 8 months after implant placement. A further increase was seen from abutment to 1 year of loading, which indicates that loading may stimulate further bone formation, as discussed above.

The periimplant mucosa had a morphology with features previously described,[26] that is, a keratinized oral epithelium that was continuous with a junctional epithelium at the abutment surface and a connective tissue compartment. No attempts were made to characterize this area morphometrically because evaluation of soft tissue and cellular components is difficult to make in the relatively thick (10 μm) ground section. It seemed that the junctional epithelium terminated just above or below the implant-abutment junction. Because abutments were changed once for the immediately loaded and twice for the early loaded implants, it is possible that the morphology was thus influenced. A previous study in dogs by Abrahamsson and colleagues[27] showed that abutment dis- and reconnections resulted in a more apical termination of the junctional epithelium. Inflammatory cell infiltration was seen in the specimens, probably as a response to bacterial challenge in the region, as previously reported by other authors.[28–30]

The implants used here were modified by anodic oxidation, which results in a polycrystalline thick oxide with a specific microporous roughness structure. Animal experiments have shown a stronger bone response to oxidized implants compared with the response to machined and acid-etched implants. Both higher values of bone-to-implant contact and removal torque have been demonstrated. In a recent study, Ivanoff and colleagues[14] inserted 20 pairs of oxidized and machined microimplants and evaluated the bone response after 3 to 6 months of submerged healing in 20 patients. They found significant differences in the degree of bone-to-implant contact in favor of the oxidized implant, 34% versus 13%. As also observed in the present study, the authors described the formation of thin rims of bone at the surface of the oxidized implant, which was not detected for the machined implants. The question is, however, whether this has any impact on implant stability and the clinical outcome. In a clinical study, Glauser and colleagues[31] compared the stability of oxidized and machined implants subjected to immediate loading in the posterior maxilla during 6 months by means of RFA. The oxidized implants were more stable after 1, 2, and 3 months but not after 6 months. The results indicate that the favorable effect of surface modification is seen during the early healing phase. Recent clinical results point to a better performance of oxidized implants when subjected to immediate/early loading.

The present authors have experienced more failures with machined implants than with oxidized implants when subjected to immediate loading in the posterior mandible (14.4% versus 4.7 % failures).[15] Glauser and colleagues[16,17] reported similar differences when applying immediate loading in all jaw regions, 17.3% and 3% failures for machined and oxidized implants, respectively. However, other authors have demonstrated high survival rates with machined implants when used for immediate/early loading.[1–5,9,10]

CONCLUSION

It is concluded that implant healing can occur around oxidized implants placed in the posterior mandible and subjected to loading immediately following surgery or after 2 months of healing.

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