Integration of Periorbital Titanium Implants in Irradiated Bone: Case Report and Histologic Evaluation

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Extraoral implants are used increasingly frequently in the wake of ablative tumor surgery and adjuvant radiation or chemotherapy for craniofacial rehabilitation with facial prostheses and epitheses. However, high rates of nonintegration and implant loss have been reported for extraoral implants, especially for those in the periorbital region following irradiation. This case report and corresponding histologic evaluation describe the osseointegration pattern in irradiated periorbital bone, based on the example of 3 retrieved, clinically integrated, stable titanium screw implants.
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Key words: bone-titanium interface, extraoral implants, facial prostheses, irradiated bone, osseointegration

Radical surgical treatment of malignant tumors often results in major defects in both bone and soft tissue. In the rehabilitation of these patients, titanium implants may provide retention for facial prostheses and epitheses and permit control and inspection of the defect site in oncologic follow-up. Furthermore, implant-supported facial prostheses can provide a very satisfying and esthetic outcome for the patient.[1] Allergies induced by adhesives used for the retention of conventional prostheses or stabilization with eyeglasses can be avoided by the use of extraoral implants.[2,3]

It is currently possible to use implant-supported facial prostheses for the replacement of eyes including periorbital tissues, nasal structures, and ears including bone-anchored hearing aids.[4,5] For social and psychologic reasons, rehabilitation may even become advantageous for patients in whom the tumor cannot be removed completely.[4]

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Radiotherapy is frequently used as an adjunct to surgical treatment.[6] It can affect the success rate of implant integration, and failure may also lead to osteoradionecrosis if the implant leads to infection of the irradiated bone. Although the bone healing capacity following implant placement appears to depend on the time interval after radiation,[7] the low number of cases reported so far makes it difficult to verify any correlation between radiation dosage and implant integration.[8] Higher numbers of cases are available only for intraoral implants in the irradiated jaw. For example, in a study of 1,273 retrieved implants, Quirynen et al[9] reported the success rate of implants in irradiated bone to be far below the 95.2% recorded in nonirradiated bone. For extraoral implants, Jacobsson et al[10] found a 62.7% success rate in the irradiated orbital region. The American-Swedish multicenter study of Parel and Tjellström[4] also reported that periorbital implants in irradiated bone have a higher loss rate than those in the mastoid or perinasal bone. Only 21 of 37 implants showed primary osseointegration, and another 13 were lost after 1 year in the American study group. The loss rate reported for the larger collective of the comparative Swedish group was even higher.[4] Only 1 of 28 orbital implants was lost in a Canadian multicenter study reported by Wolfaardt et al in

1993.[11] The results presented should be interpreted only as trends because of the minimal number of operative sites.

The integration of titanium implants in nonirradiated bone has been well investigated concerning its histologic aspects. Whereas the primary formation of osseous lamellae has been seen at direct contact points between the implant surface and bone, regions with a greater distance have been initially characterized by the formation of fibrous bone, which is converted into lamellar bone within 2 months.[12] However, the immediate biologic environment is separated from the titanium by an oxide layer.[13] With transmission electronic microscopy, the titanium has been shown to be bordered by a 20-nm-thick layer of proteoglycans.[14] In contrast to light microscopy, which indicated a 56 to 85% rate of bone-implant contact for screw implants,[15] transmission electron microscopy revealed nonosseous, extracellular material with connective tissue fibers between the bone cells and the titanium oxide.[16]

In spite of the rather detailed knowledge concerning the integration of implants in nonirradiated bone, only a few histologic studies, especially in the mandible, are available with respect to the integration of implants in irradiated bone. Basically, radiotherapy changes the balance of physiologic bone resorption and regeneration, with osteoblasts and osteocytes reacting more sensitively than osteoclasts.[17] The consequent predominance of osteoclasts results in increased bone resorption, while regeneration is limited by a defect in the osteoprogenitor cells.[18] This results in bone of inferior quality, which shows empty lacunae and is replaced by connective tissue on a large scale.[19] The blood vessels undergo changes 4 to 6 weeks after radiation. Whereas the lumen grow smaller, the vessel walls thicken. Vacuoles form within the endothelial cells, and muscular atrophy occurs in the media. There is an overall increase in the number of peripheral, periosteal arteries and veins.[20] With regard to the integration of implants in irradiated bone, Jacobsson et al[8] found direct contact to bone in their histologic investigation of clinically stable extraoral implants. However, they neither published data on pathologic, radiation-induced changes in bone cells and vessels, nor did they quote the percentage of osseointegrated implant surface. The connective tissue components of the skin were reported to contact the implant surface without irritation, and mononuclear cells collected around the peripheral vessels. Tolman and Taylor[21] in 1996 held the low vascularity of the dense, thin orbital bone responsible for the higher rate of implant loss, since radiation had a more destructive effect on this site.

In this context, the histologic examination of 3 clinically stable titanium screw implants (extraoral Brånemark implants, Nobel Biocare AB, Göteborg, Sweden) was designed to provide detailed information on the mode of osseointegration in irradiated periorbital bone and to shed light on the possible causes for the high rate of implant loss in this region after radiation therapy.

Materials and Methods

Case Report. A 41-year-old female underwent surgery for removal of a low-differentiated carcinoma in the left ethmoidal sinuses ($pT_2N_0G_3$). This was followed by postoperative radiation therapy up to a level of 50 Gy. A recurrence of the tumor took place 3 years later, necessitating radical resection, including the left orbit, maxilla, and ethmoidal cells with corresponding skull base. Immediately before surgery, the patient underwent adjuvant chemotherapy with 3 cycles of a regimen of carboplatinum and 5-fluoruracil.

After another 3 years, the patient was referred to our department for the first time because of another tumor recurrence at the supraorbital rim. The local tumor resection demonstrated tumor-free margins in the pathohistologic evaluation. To enable the social reintegration of the patient,[17] the placement of implants 1 cm distant to the resection margins was deemed justifiable. Therefore, 4 titanium screw implants were placed to provide prosthetic rehabilitation; 3 were placed in the supraorbital rim (1 × 3 mm and 2 × 4 mm length) and 1 was placed in the transition to the infraorbital rim (4 mm). The wound was closed with monofilament sutures, using the double-layer technique, and clindamycin was given postoperatively for 1 week in 300-mg doses 4 times daily. Wound-healing was uneventful.

As recommended by Lundgren et al,[22] 4-mm abutments were connected to the implants after a period of 4 months. Another 4 weeks later, an indurated swelling was noted around the lateral supraorbital implant, where the presence of carcinoma was again confirmed by biopsy. Therefore, another radical resection was performed, which included an en bloc removal of the 3 supraorbital implants together with the supraorbital rim, the orbital roof, and the adjacent skull base. Pathohistologic examination indicated the complete removal of the tumor, since all resection margins were free of carcinoma. Later, further histologic

Fig 1 Operation specimen with the 2 lateral implants at the supraorbital rim 5 months after placement. The rough, brown surface of the dermis between the implants shows no signs of inflammation.

Fig 2 Histologic overview of the implant adjacent to soft and hard tissue. The implant is surrounded by compact bone, showing focal and plane direct bone contact. In only the marginal part of the sulcular epithelium can some adnexal structures be shown (original magnification ×2.5).

examination was performed with respect to the questions related to implant integration, as mentioned previously.

Histologic Techniques. The implants surrounded by hard and soft tissue were fixed by immersion in buffered formalin and dehydrated in an ascending series of ethanols. After infiltration and polymerization of the specimens in Technovit 7200 VLC (Kulzer, Friedrichsdorf, Germany), preparation of the ground sections was performed by the cutting-grinding technique.[23,24] All slices were stained with toluidine blue and examined and documented by a Zeiss Axiophot (Carl Zeiss, Jena, Germany).

Results

Macroscopic Examination. All 3 implants were in direct contact with the dermis, without any signs of inflammation. The skin between the 2 lateral implants had a rough, brown surface (Fig 1).

Microscopic Examination. The epidermis was in contact with the abutment. A sulcus existed around the entire surface and contained horn lamellae and inflammatory cells, as well as bacteria (Fig 2). The sulcular epithelium contained regressively changed hair follicles and sebaceous glands in the upper part. No adnexal structures of the skin were seen in the lower ⅔ of the lining epithelium. The most apical epithelial cells were located in the interface region between the abutment and the implant. The adjacent connective tissue was infiltrated by plasma cells, lymphocytes, single polymorphous leukocytes, and macrophages. Only the loose connective tissue of the lower ⅔ contained sinusoidal vessels. There were no differences between the epithelial attachment and the inflammatory reaction of the peri-implant soft tissue of all 3 implants.

The implants were situated within compact bone that showed ongoing signs of remodeling (Fig 3). The bone surfaces of the Haversian canals consisted of newly formed bone of different age. Most were lined by osteoid and osteoblasts. All 3 implants were surrounded by compact bone, with variable amounts directly contacting the implant surface. The threads showed changing focal and plane bone contact zones (Fig 4). Bone formation with osteoid directed to the implant was still occurring. Bone-free implant surfaces were in contact with macrophages. The adjacent loose connective tissue contained sinusoidal vessels filled with erythrocytes. The bone around the implants was lamellar, with only small areas of woven bone. Concerning bone resorption, no difference was seen in bone deposition and fibrosis with respect to the implant location. The morphometrically determined amount of direct bone-to-implant contact ranged from 30% to 70%.

Fig 3 All 3 implants are surrounded by compact bone, in variable amounts of direct contact with the implant surface. The threads show changing focal and plane bone contact zones. Bone formation with osteoid directed toward the implant is still occurring. Bone-free implant surfaces are in contact with macrophages. The adjacent loose connective tissue contains sinusoidal vessels filled with erythrocytes (original magnification ×10).

Fig 4 Bone in direct contact with the implant. The bone around the implants is lamellar, with small areas of woven bone. The surfaces of the Haversian canals consist of newly formed bone; most of them are lined by osteoid and osteoblasts. The morphometrically defined amount of direct bone-to-implant-contact ranges from 30% to 70% (original magnification ×20).

Discussion

The histologic examination demonstrated the mode of osseointegration of 3 clinically stable implants in bone that had received a radiation dose of 50 Gy 6 years prior to surgery. The amount of direct bone-to-implant contact is comparable to implants in nonirradiated bone.[25,26] Although radiation damage in the bone tissue can clearly be observed, in contrast to other investigations,[8] bone healing around the implants cannot be interpreted as being reduced as far as the amount of bone-to-implant contact is concerned.

The osseointegration mode may be influenced by the long period of time between radiation and surgery. Experimental studies indicate that shortly after radiation, a 70.9% reduction of osteogenesis occurs. Recovery of bone healing capacity may be explained by an impairment of cell reproduction.[27] A long-term observation period seems to be indicated before implants can be placed in irradiated bone.

With regard to the epithelial attachment at the abutment, our observations are similar to those of Jacobsson and coworkers,[8] who also found mononuclear cells in the upper part of the dermis only. The connective tissue adjacent to the implants represents scar tissue without adnexal structures; only the loose connective tissue of the lower ⅔ contains sinusoidal vessels. The protection against microorganisms in the upper part appears to be restricted to the epithelium alone.

Summary

This investigation may be the first quantitative evaluation of direct bone-to-implant contact in irradiated bone. The long period of time may be responsible for the high survival rate, both clinically and histologically. Furthermore, the radiation dose of 50 Gy did not reach an extraordinary level, although radiotherapy was combined with chemotherapy in the course of the disease. In this case, the influence of chemotherapy, since it was performed 3 years prior to implant placement, may be ignored. Further clinical and histologic reports on cases of retrieved implants in irradiated extraoral tissues may demonstrate how radiation dose and course of time are related to one another in determining overall survival rate. Electron microscopic studies and animal experiments may also provide further details in that respect.

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