Chapter 6

General discussion

Implant insertion in head and neck cancer patients

Oral cancer patients

Primary mandibular implant insertion in edentulous patients has become a standard treatment in our institute in patients with a malignancy of the lower oral cavity in whom is foreseen that they can benefit from implant-retained prostheses.

From chapter 2 we learned that implant survival is high, although still lower in irradiated patients compared with non-irradiated patients (91.5% compared with 99.5%). This is not surprising as, amongst others, radiotherapy may result in progressive fibrosis of blood vessels and soft tissues, in xerostomia, in a reduced bone-healing capacity, and may even sometimes lead to osteoradionecrosis. Because of the cumulative effects of radiation on vascularisation and cellularity of bone, the regenerative capacity of these tissues is limited, which may exert a negative impact on subsequent implant osseointegration. These concerns are in line with the reported survival rates of implants inserted in irradiated patients, which vary largely, but are usually lower than survival rates of implants inserted in non-irradiated patients (Colella et al. 2007, Ihde et al. 2009, Javed et al. 2010, Chrcanovic et al. 2014). So far, no difference in implant survival in implants inserted pre-radiotherapy and implants inserted post-radiotherapy has been reported, but the reported number of implants inserted pre-radiotherapy is still low (Colella et al. 2007, Barber et al. 2011, Chrcanovic et al. 2014). A concern mentioned of implants inserted pre-radiotherapy is the backscattering that occurs from the metal of the implants in the radiation beam. This backscattering can result in an increased radiation dose in the surrounding bone in front of and next to implants of 10-21% (Ozen et al. 2005, Friedrich et al. 2010). Also shielding of the radiation beam by the implants within the radiation beam, which may result in a lower cumulative radiation dose to the tumour, is mentioned as an unwanted effect. Both side effects can be reduced by multi-beam radiotherapy strategies nowadays. Osteoradionecrosis linked to implant loss was observed in 5% of irradiated patients in our study (chapter 2).

When implants are inserted during ablative surgery, the number of prosthetically rehabilitated patients is much higher than when the need for implant-retained prosthetics is only established after oncologic therapy (Kwakman et al. 1997, Schoen et al. 2007a, Mizbah et al. 2013). Thus, many patients will benefit from their implant-retained prosthesis at an early stage. Although the number of rehabilitated patients is high with primary inserted mandibular implants, a concern of inserting implants during the ablative surgery is loss of resources. Our study (chapter 2) revealed that 16-17% of the patients with primary mandibular implants were not rehabilitated with an implant-retained prosthesis after completion of their oncologic treatment. The main reason for this was that the patient deceased or that recurrent disease occurred before prosthetic rehabilitation was started or could be finished. Although this seems to be an economic disadvantage, it has to be recalled that if implant insertion is postponed until after the oncologic treatment is completed, patients are often psychologically and physically weakened by the therapy. As

a result many of them postpone or even cancel their prosthetic rehabilitation, despite the expected significant improvement of oral functioning with implant-retained prosthetics (Kwakman et al. 1997, Schoen et al. 2007b, Mizbah et al. 2013). Therefore, a large percentage of patients and even patients with a worse general prognosis can benefit for some time from the early improvements in aesthetics and oral function when implants are inserted during ablative surgery.
It has to be mentioned that, although no patients could be identified who were less likely to benefit from primary implant insertion (chapter 2), there is a hazard of incorporation bias regarding the very favourable results we reported in our study. The patients included in our study were in fact a selection of oral cancer patients. All patients were edentulous, had tumours in the lower oral cavity and all implants were inserted in native mandibular bone. So, do primary mandibular implants in oral cancer patients improve oral functioning and quality of life? In healthy patients, implant-retained prostheses improve oral function and chewing ability, both subjectively and objectively (Boerrigter et al. 1995, Stellingsma et al. 2005, Meijer et al. 2009). The results of our studies show that a large number of oral cancer patients is rehabilitated with implant-retained prostheses, when the implants are installed during ablative surgery. However, as expected, the beneficial effects are lower than usually observed in healthy subjects (chapter 2). Amongst others the improvement in chewing ability is not as high as in healthy subjects (Stellingsma et al. 2005). Whether general quality of life improves as a result of implant-retained prostheses could not be shown in our study (Chapter 2). Other factors, such as concurrent comorbidity both as a result of the oncological treatment and other, were shown to be far more important determining patients' quality of life.

Patients with nasal defects after total rhinectomy

Implant-retained nasal prostheses have been shown to be a very valid option for rehabilitation of a patient after total rhinectomy (chapter 4). In line with intraoral implant insertion in oral cancer patients, timing of implant insertion in the nasal floor, either during the ablative tumour surgery or at a second stage, is still subject of discussion. Studies report that implants inserted in irradiated nasal bone are accompanied by a lower survival rate (Roumanas et al. 1994, Nishimura et al. 1996, Roumanas et al. 2002) compared with implants inserted in non-irradiated nasal bone. In addition, Dings et al. (2011) reported an improved success rate for implants inserted during the ablative surgery. In our study we noticed no difference in implant survival in irradiated patients and non-irradiated patients. Also we did not see a difference in implant survival between primary inserted implants and implants inserted in a second procedure. The good quality of bone in the nasal floor, and the fact that intraoral implants were used, might have contributed to the high survival rate in our study. Since inserting implants during ablative surgery saves a considerable amount of time for patients in being rehabilitated with an implant-retained prosthesis and our favourable results, we recommend this approach for patients needing total rhinectomy too.

Implant insertion in patients with Sjögren's syndrome

To the best of our knowledge, in chapter 5 the first study on the prevalence and treatment outcome of dental implants in a large cohort of well-classified patients with Sjögren's syndrome compared with matched healthy controls is described. Apparently, there is a large demand for the use of implants in Sjögren's patients, but not much is known whether this treatment is successful or not. This large demand can be explained by the hazard of early loss of teeth in because of the hostile oral environment for preserving the patients' teeth. Also Sjögren's patients often report difficulty wearing (partial) dentures because of the dry, sensitive oral mucosa. Moreover, to our experience, Sjögren's patients have a rather high dental awareness and might thus be more demanding regarding optimal dental care including insertion of dental implants to solve dental problems.

While implant survival in Sjögren's patients is comparable to that in healthy subjects, as shown in chapter 5, Sjögren's patients had more signs of soft tissue infection compared with healthy controls. Care must be taken in interpreting these results, however. The matched healthy controls were obtained from previous well-designed, prospective randomized trials, with long follow-ups. In our group of Sjögren's patients, the implants had been inserted in routine dental care settings by several dentists and oral and maxillofacial surgeons reflecting common dental care in the Netherlands. As a result, not all Sjögren's patients had been subjected to strict, standardized follow-up and oral hygiene measures as usual in the well controlled clinical studies we performed. Furthermore, salivary secretion is reduced in Sjögren's patients and as a result the related self-clearance of the oral tissues is reduced too. Debris will collect and remain on the implant surfaces more quickly in Sjögren's subjects than in healthy controls. As a result the marginal peri-implant tissue is thought to be more prone to continuous inflammatory insults than the peri-implant tissue in healthy controls. This continuous attack has probably resulted in more gingival swelling, bleeding and increased pocket probing depths in Sjögren's patients.

As we only had access to pre- and post-implant insertion radiographs in a subset of our Sjögren's patients, no firm conclusions can be drawn on the observed level of bone loss around the implants and thus peri-implantitis. However, it seems that there is no difference in peri-implantitis in our study between Sjögren's patients and healthy controls. Probably, the patients clean their implants well: as a result the chronic irritation of the peri-implant mucosa is mild due to the fact that the rapid accumulation of debris around implants due to the reduced oral self-cleansing is compensated by the frequent proper cleansing of the implants by the patients themselves.

Oral functioning is impaired in patients with Sjögren's syndrome and continues to be impaired in patients with implant-retained prosthetics. The findings of the oral functioning questionnaires in our study were consistent with the results from previous studies in Sjögren's patients (Fox et al. 2008, Stewart et al. 2008, Enger et al. 2011, Lopez-Jornet et al. 2008). Sjögren's patients with implant-retained prosthetics still reported difficulty chewing tough and hard food, although there was a large variety in results. These problems

could be due to the sicca component that is present in Sjögren's patients, as shown by the direct correlation between severity of reported oral dryness (ESSPRI dryness) and chewing ability. This could also explain why Sjögren's patients were less satisfied with their implant-retained prosthetics than healthy subjects.

Conclusions and suggestions for future research

Based on the studies described in the previous chapters and discussion, implants can be of great help in the prosthetic rehabilitation of patients with a compromised intraoral condition or a nasal defect. In this respect, the role of the (maxillofacial) prosthodontist is of crucial importance. Treatment planning should take place in a multi-disciplinary setting as well as that prosthodontists should be involved in the full trajectory of treatment planning as they are involved in all stages of care and aftercare.
For edentulous patients with a malignancy in the lower oral cavity, inserting at least 2 mandibular implants during ablative surgery contributes to an early and reliable rehabilitation of oral function, irrespective of radiotherapy, location and size of the tumour and the type of reconstruction. Thus, involvement of maxillofacial prosthodontists should routinely be incorporated in the process of surgical planning in order to judge whether and which implant-based prosthetics is feasible for a particular patient. The latter, however, does not imply that all patients will end with a functional prosthesis. Although, when inserting primary mandibular implants, most patients will end with a functional implant-based prosthetic solution, still not all patients will benefit from the implants.
As mentioned before, the main reason of not using the implants was that the patient deceased or that recurrent disease occurred before prosthetic rehabilitation was started or could be finished. Soft tissue problems resulting from ablative tumour surgery were a second reason, making a proper functioning prosthesis difficult or even impossible as no functional suprastructure and/or overdenture could be made on the implants. Soft tissue problems mainly occurred in patients in whom the primary tumour was in the same area in which the implants were inserted. When indicating primary insertion of implants in these patients, specific attention must be paid whether it is feasible to get a peri-implant mucosal condition that allows for proper attached mucosa around the implants and a proper buccal and/or lingual vestibule to accommodate an overdenture (neutral zone).
While primary insertion of implants should be considered the standard treatment in the edentulous mandible, primary implant insertion can be considered for the maxilla, and in areas in which the mandible or maxilla is reconstructed with, e.g., a fibula, at time of tumour surgery too. Whether this approach is as feasible as in the mandible has to be proven in the future. Latter two treatments are in need of a very meticulous implant planning. To facilitate implant planning in (to be) reconstructed mandibular and maxillary defects, methods for 3D computerized planning of both the surgical reconstruction and the most ideal position of the implants are currently developed. The first results using 3D technology in secondary reconstructions are promising (Schepers et al. 2013)

Other patients that potentially might benefit from primary implant insertion are pre-edentulous patients. Oral cancer patients require dental evaluations as part of their oncological work-up. A common result is that teeth have to be removed due to periodontal infection, periapical infection and/or profound caries. One might consider providing pre-edentulous patients with primary implants so that also these patients, as now is common in our clinic for longstanding edentulous patients, might benefit from an early implant-retained prosthesis. However, it seems advisable to limit primary implant insertion to pre-edentulous patients with just remaining teeth in the mandible and no active periodontal disease as periodontal disease is accompanied by high implant loss in healthy subjects and a high risk of developing osteoradionecrosis (Schuurhuis et al. 2011).
In our study second stage implants were used for primary implant insertion. Another possibility is to insert single stage implants in oral cancer patients, or to insert two-stage implants as single stage implants. With this, the time between implant insertion and completion of prosthetic rehabilitation could be shortened further and no second procedure is needed to use the implants for prosthetic rehabilitation.
In patients with nasal defects resulting from total rhinectomy prosthetic rehabilitation with implant-retained nasal prostheses is accompanied by a favourable treatment outcome, with minor need for surgical aftercare. Prosthetic aftercare is limited to the remake of implant-retained nasal prostheses because the limited average life span of these prostheses. A remake, however, is relatively simple and fast using the existing mould of that patient for a new nasal prosthesis.
In patients with Sjögren's syndrome, insertion of implants is a good treatment option, considering the reasonably good peri-implant health, limited prevalence of peri-implantitis, high implant survival and high patients' satisfaction. In our study implant therapy in patients with Sjögren's syndrome was assessed retrospectively. Prospective assessment of implants in patients with Sjögren's syndrome and healthy controls should be performed to rate the true value of implant-based prosthetics, focussing on implant survival, prevalence peri-implant mucositis and peri-implantitis, oral function and patients' satisfaction.

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