Summary
Surgical treatment of malignancies in the head and neck region often results in an altered anatomical situation, which may cause severe disturbances in, e.g., oral functioning and quality of life. For example, the defects resulting from tumour surgery, either primary closed or reconstructed with free, transposition or vascularised flaps, often result in impairment of speech, chewing (mastication), swallowing and aesthetics. This adverse oral condition often further deteriorates after postsurgical radiotherapy, due to radiation-induced oral sequelae like reduction of salivary secretion, increased sensitivity of the oral mucosa to oral infections and a decreased load bearing capacity for dentures. Therefore, from a prosthodontic point of view, the possibilities for oral rehabilitation of head and neck cancer patients are seriously at risk.

Until recently neither reconstructive surgery nor conventional prosthodontic techniques were capable of successfully addressing the aforementioned problems. Currently, a proper choice of reconstruction techniques in combination with prosthodontic rehabilitation with implant supported or retained prostheses is generally thought to be of some benefit in the oral and maxillofacial rehabilitation of these patients. Based on this assumption, the use of implants has been advocated with increasing frequency for prosthetic support in patients who have been treated for malignancies in the head and neck region. In order to provide better evidence for this approach, the PhD research project described in this thesis was performed with the intent to gain insight into the effects of maxillofacial rehabilitation in head and neck cancer patients using implant-retained prostheses. This research considers the patient’s rehabilitation in regards to treatment planning, implant survival, treatment outcome and quality of life. The outcomes of this research project could provide a sound basis for identifying the preferred oral rehabilitation treatment approach(es).

Chapter 2 includes both a rationale for treatment planning and a literature review of the outcomes associated with the use of implants for oral rehabilitation of the edentulous mandible in patients treated for a malignancy in the lower region of the oral cavity. Surgical interventions after radiotherapy are preferably avoided because of compromised healing. This compromised healing increases the risk of radionecrosis of soft tissues and bone, and the loss of implants. If surgical treatment after radiotherapy is necessary then measures to prevent implant loss and development of radionecrosis have to be considered, e.g., antibiotic prophylaxis and/or pre-treatment with hyperbaric oxygen (HBO). Problems related to compromised healing after radiotherapy in cases where postoperative radiotherapy is scheduled or possibly will be applied, might be avoided by inserting implants during ablative surgery into consideration. This approach requires a thorough
presurgical examination and multidisciplinary consultation (oncologists, dentists, radiotherapists) to determine the best overall treatment plan. Additionally, the primary curative intent of the oncological treatment and the prognosis for later prosthodontic rehabilitation have to be considered. The literature review illustrated that there are still shortcomings in scientific evidence about the timing of implant insertion with regard to radiotherapy and about the indications and potential benefits of preventive HBO therapy (prevention of radionecrosis, reduction of loss of implants). Future research should address these issues.

Currently, there is a strong tendency towards implant insertion during ablative surgery in order to prevent surgery in irradiated tissue and to reduce the time required for final functional rehabilitation of the head and neck cancer patient after tumour surgery. Implant placement during ablative surgery is in doubt in cases where there is a loss of continuity of the mandible, even if the continuity of the mandible is restored with a bone transplant. In the latter cases, it is as a rule better to refrain from implant placement during ablative surgery if proper positioning is in doubt.

A mandibulotomy can be necessary to approach a tumour in the oral cavity or oropharynx. The aim of the study, described in Chapter 3, was to develop and prospectively evaluate a technique that enables the simultaneous performance of a mandibulotomy and implant insertion in the same area. As successful post surgery prosthodontic rehabilitation of oral and oropharyngeal tumours needs to start in time with treatment planning in the pre-ablative stage, it is important to consider whether implants might be beneficial in the given situation, particularly when radiotherapy is or might be indicated. The developed technique composed of pilot drilling of the implants before performing the mandibulotomy. After tumour resection, reconstruction and restoration of the continuity of the mandible, the final drilling and insertion of the implants is completed. Subsequently, all patients received radiation therapy within 6 weeks after surgery. Implant retained mandibular overdentures were fabricated 6 months after irradiation. Furthermore, a standardised clinical and radiographic evaluation was performed at regular intervals of time. No complications with respect to the combination of implant insertion and mandibulotomy were observed, either during and post surgery. In addition, no adverse mucosal reactions were observed during the course of radiotherapy, no cases of osteoradionecrosis developed and no implants were lost. Clinical and radiographic evaluation revealed healthy peri-implant parameters. From this study it was concluded that, when following the technique described, a mandibulotomy can be safely combined with the insertion of implants in the ventral part of the edentulous mandible.
Chapter 4 presents the results of an assessment of the quality of life related to oral functioning in edentulous head and neck cancer patients following oncology treatment of malignancies in the lower region of the oral cavity with a combination of surgery and radiotherapy. In order to measure the effects of implant therapy on quality of life and functional outcome there was also a requirement to understand the oral status of patients who were not being treated with implant-retained mandibular overdentures. The study was also aimed at obtaining insights into the instruments that might be useful to measure quality of life and effects of oral rehabilitation in head and neck cancer patients. Patients treated between 1990 and 2000 with surgery and radiotherapy for a squamous cell carcinoma in the oral cavity and who were edentulous in the mandible and had been treated with a conventional, non-implant retained denture, received an invitation for a clinical check-up. The check-up included a standardised anamnesis, a clinical assessment and questionnaires regarding oral functioning and quality of life. In total 67 out of the 84 patients who met the criteria were willing to participate in this study. The mean irradiation dosage that these patients had received in the oral region was 61.8±5.4 Gy. The results showed that many patients were not very satisfied with their prostheses. Furthermore, half of the patients (N=33) wore their mandibular prostheses at most only a few hours a day. It was concluded from the clinical assessment that two thirds of the patients (N=44) could possibly benefit from an implant-retained mandibular denture. Analyses of the questionnaires revealed no significant associations between functional assessments, quality of life and parameters like size of the primary tumor, location of the primary tumor and different treatment regimes. Despite being treated for cancer, the patients reported a relatively good general quality of life. Moreover, many oral complaints were related to radiation sequelae rather than to the problems the patients had experienced with the conventional dentures per se. It was concluded that sequelae resulting from radiotherapy probably dominate oral functioning and quality of life after oncology treatment. As in two thirds of the patients improvement of oral functioning and the aspects of quality of life related to oral functioning was expected from making an implant-retained mandibular denture, it was decided to perform a prospective trial assessing the effects of implant-retained mandibular overdentures on oral functioning and quality of life in this category of patients (chapter 5).

The aim of the study described in Chapter 5 was to prospectively evaluate the treatment outcome (condition of peri-implant tissues, implant survival, oral functioning) and the impact on quality of life of prosthodontic rehabilitation with implant-retained mandibular overdentures in head-neck cancer patients. As implant surgery at
irradiated sites carries the significant risk of the development of soft and hard tissue necrosis, and the loss of implants, for this study it was thought to be reasonable to place implants prior to post-operative radiotherapy, preferably simultaneously with ablative surgery. The treatment outcome of prosthodontic rehabilitation with implant-retained mandibular overdentures was also related to the treatment outcome of prosthodontic rehabilitation with conventional dentures as described in chapter 4. Therefore, in the studies described in these two chapters the same instruments for measuring quality of life and the effects of oral rehabilitation were applied. The treatment outcome and the impact on quality of life of implant-retained lower dentures in the first year of functioning after oncology treatment were evaluated in 50 head neck cancer patients by using the standardized questionnaires and clinical assessment evaluated in chapter 4. All patients received four implants during ablative tumor surgery. About two-thirds of the patients needed radiotherapy post-surgery (mean cumulative dose at implant site was 61.1±5.3 Gy). Both in irradiated and non-irradiated bone two implants were lost resulting in comparable implant survival rates of 97.4% and 96.9%, respectively. Peri-implant tissues all had a healthy appearance. No cases of osteoradionecrosis occurred. All patients functioned well with their implant-retained lower dentures and the quality of life related to oral functioning improved.

Major functional improvement was observed in non-radiated patients. In the radiated patients, a slighter, but still significant, improvement in the functional items not related to the oral sequelae of radiotherapy was observed. In concordance with the quality of life assessments, denture satisfaction improved and this improvement tended to be higher in non-irradiated than in irradiated patients. It was concluded that implant-retained lower dentures can substantially improve the quality of life related to oral functioning and denture satisfaction in head-neck cancer patients. The potential effect on oral functioning and quality of life with implant-retained mandibular overdentures is expected to be larger in non-irradiated than in irradiated cancer patients.

Chapter 6 offers a prospective assessment of the effect of HBO therapy on the outcomes of treatment (condition of peri-implant tissues, implant survival, oral functioning and quality of life) of prosthodontic rehabilitation with implant-retained mandibular overdentures in irradiated head and neck cancer patients. The assessment was carried out at both 6 weeks and 1 year after placement of new dentures. This study was performed, because there was no consensus or sound evidence in the literature concerning the benefits of HBO in improving osseointegration of dental implants in mandibles, in reducing loss of implants and in minimising the risk on development of osteoradionecrosis in patients who have
been treated with radiotherapy following cancer treatment (see chapter 2). The treatment outcome of the effect of HBO therapy was assessed in a randomized controlled clinical trial in a group of 26 head and neck cancer patients who were subjected to radiotherapy after tumor surgery. Standardized questionnaires were completed and clinical and radiographic assessments were performed. After randomization, endosseous Brånemark implants were placed in the anterior part of the mandible either under antibiotic prophylaxis (13 patients) or under antibiotic prophylaxis in combination with pre and post surgery HBO treatment (13 patients). In the HBO and non-HBO group, respectively, 8 (implant survival 85.2%) and 3 (implant survival 93.9%) implants were lost. Peri-implant tissues had a healthy appearance in both groups. Osteoradionecrosis developed in one patient in the HBO group. All patients functioned well with their implant-retained mandibular overdentures. The quality of life related to oral functioning and denture satisfaction were improved to a comparable extent in the HBO and non-HBO groups. In agreement with the results described in chapter 5, this study also showed that implant-retained mandibular overdentures can improve the quality of life related to oral functioning and denture satisfaction in head and neck cancer patients. Remarkably, adjuvant hyperbaric oxygen therapy could not be shown to enhance implant survival in irradiated mandibular jaw bone.

Endosseous implants are not only used in the oral rehabilitation of patients, but percutaneously placed endosseous implants have also acquired an important place in the prosthetic rehabilitation of patients with craniofacial defects. The aim of the retrospective study described in Chapter 7 was to evaluate the clinical outcome of the use of endosseous implants in the orbital and auricular region and to assess the satisfaction of patients with implant retained craniofacial prostheses after tumor surgery. The clinical outcome and patient satisfaction of implant-retained craniofacial prostheses in the auricular and orbital region were evaluated in a group of 26 patients with facial defects after tumor surgery using standardized questionnaires and clinical assessment. Twelve patients (N=31 implants) received the implants during ablative tumor surgery, from which 7 patients (N=20 implants) were treated with radiation therapy post-surgery (mean 65 Gy). Fourteen patients (N=44 implants) received the implants after the tumor surgery, from which 5 patients (N=21 implants) were irradiated after ablative surgery (mean 54.4 Gy), but before implant placement. No implants were lost in non-irradiated patients (implant survival 100%), while five implants were lost in the irradiated group (implant survival 87.8%). The peri-implant tissues had a healthy appearance and no cases of osteoradionecrosis occurred. When compared to patients treated with conventional adhesive
Thus, based on the very promising treatment outcomes of implant-retained prostheses in the rehabilitation of oral and craniofacial defects, the use of implants should be considered for all edentulous patients or patients with a deformity of the craniofacial skeleton. Moreover, such rehabilitation should be considered an integral part of the care for the head and neck oncology patient. To achieve the best results, maxillofacial prosthodontists and implant surgeons should be members of the multidisciplinary head and neck oncology team, and they should be involved in treatment planning. Implant insertion has to be considered already during ablative surgery in order to prevent additional surgery in irradiated tissue and to reduce the time required for functional rehabilitation of the head and neck cancer patient. During ablative surgery insertion of implants can even be considered in more complex surgical cases as it was shown that a mandibulotomy was not a contraindication for insertion of implants during ablative surgery. From a prosthetic point of view, the only reason for not inserting implants during ablative surgery are in the cases where proper positioning of the implants can not be assured, a condition that, e.g., can occur in cases in which the continuity of the mandible is restored with a bone transplant.

In the general discussion (Chapter 8) the results of the previous chapters are placed in a broader context. Based on results of the various studies described in this thesis it was concluded that the use of implant-retained mandibular overdentures and craniofacial prostheses has resulted in great achievements in the rehabilitation of head and neck cancer patients. Although the sequelae resulting from radiotherapy dominated oral functioning and overall quality of life after oncology treatment, implant-retained mandibular overdentures were shown to substantially improve the quality of life related to oral functioning and denture satisfaction in head and neck cancer patients. Similar beneficial effects on satisfaction and quality of life were observed in implant-based rehabilitation of craniofacial defects. It was also concluded that there is still a need for developing more specific questionnaires that can better refine the impact of oral rehabilitation on quality of life.