Chapter 8

Summary
Pre-treatment dental screening of, amongst others, head and neck cancer (HNC) patients and hematology patients aims to identify and eliminate oral foci of infection to prevent oral sequelae during or post-treatment. The efficacy of dental screening is yet not evidence based, it is even set whether it is effective at all, particularly in chemotherapy patients. While radiotherapy to the head and neck region is accompanied by a life-long risk of developing severe oral sequelae related to irreversible radiation injury to hard and soft tissues, the changes induced in these tissues by chemotherapy are mostly reversible. Thus, what is considered an oral focus of infection needing treatment might differ between patients scheduled for radiotherapy or chemotherapy as, when the effects of oncologic treatment are reversible, the risk of developing complications related to oral foci of infection is probably not higher than in healthy subjects. Moreover, the recent introduction of intensity modulated radiation therapy (IMRT) has changed the dose distribution in soft and hard tissues within the radiation portal and thus might be accompanied by another risk profile on radiation sequelae than conventional radiotherapy.

The general aim of this thesis was to assess the efficacy of pre-treatment dental screening in HNC patients subjected to radiotherapy and in hematology patients subjected to intensive chemotherapy regarding complications during treatment and follow-up.

A systematic review was performed to analyze the available evidence on the efficacy of pre-radiation elimination of oral foci of infection in preventing oral sequelae (Chapter 2). A literature search was conducted (MEDLINE/EMBASE) for papers published up to May 2014. Papers on HNC patients subjected to pre-radiation dental screening, (chemo)radiation and oral follow-up were included. Of the 1770 identified papers, 20 studies fulfilled the inclusion criteria of which 17 were retrospective. A great heterogeneity in patient groups, dental screening techniques, definitions of oral foci of infection and techniques for eliminating foci was found. Most papers lacked essential details on how dental screening was performed and a clear definition of an oral focus of infection. The evidence for efficacy of elimination of oral foci of infection to prevent post-radiotherapy oral sequelae was inconclusive. Consequently, the efficacy of pre-radiation elimination of oral foci of infection remains unclear. No conclusions could be drawn about a definition of an oral focus of infection and whether pre-radiation elimination of these foci should be mandatory.

In Chapter 3, a retrospective study is described in which an inventory was made of oral foci detected during pre-radiation dental screening and follow-up of those patients in order to assess risk factors for developing oral sequelae after radiotherapy. Charts of 185 consecutive HNC patients, subjected to a pre-radiation dental screening between January 2004 and December 2008, were reviewed. Eighty (partially) dentate patients scheduled for curative head and neck radiotherapy met the inclusion criteria. Oral foci were found in 76% of patients, predominantly periodontal disease. Osteoradionecrosis (ORN) had developed in 9 out of 80 patients (11%). Overall, patients presenting with periodontal pockets ≥6 mm at dental screening had an increased risk of developing ORN compared to the total group of patients. Patients in whom periodontal disease treatment was composed of initial periodontal instead of removal of the affected teeth, the risk of developing ORN was even higher. A worse periodontal condition at dental screening and initial periodontal therapy to safeguard these patients to develop severe oral sequelae after radiotherapy were shown to be major risk factors of developing ORN.

It is not yet known how changed treatment modalities for HNC affect the composition of the oral flora. In Chapter 4 a prospective study is described that assessed the effects of a variety of treatments for HNC on the oral microflora. This study was composed of 82 patients, diagnosed with a primary oral or oropharynx carcinoma, seen for a pre-treatment dental screening between May 2011 and May 2013. Patients were grouped by oncologic treatment; surgery (SURG; n=29), IMRT (IMRT; n=26) or IMRT combined with chemotherapy (CHIMRT; n=27). Dental screening data, demographic data, subgingival biofilm samples, oral lavages and whole saliva samples were obtained to microbiologically analyze the effects of cancer treatments (1 year follow-up). In the IMRT- and CHIMRT-group increased prevalence of enteric rods, staphylococci and Candida species was observed. In these groups, elimination of oral foci decreased the frequency of detection of pathogens such as P. gingivalis, T. forsythia and S. mutans. In the SURG group, the increase of opportunistic pathogens was not seen. The prevalence of periodontal bacterial species in SURG patients tended to decrease at 6 and 12 months, but was only statistically significant for T. forsythia. Thus, different treatments in HNC patients resulted in different changes in the oral microflora. Opportunistic pathogens such as staphylococci, enteric rods and Candida species tended to increase in prevalence after IMRT with or without chemotherapy, but not after surgical intervention.

The prospective study described in Chapter 5 assessed the efficacy of pre-radiation dental screening and elimination of oral foci of infection to reduce post-IMRT oral sequelae. All consecutive dentate patients >18 years, diagnosed with a primary oral or oropharynx carcinoma, seen for pre-treatment dental screening between May 2011 and May 2013, were included and followed for 2 years. Patients were subjected to IMRT or IMRT with chemotherapy (CHIMRT). Dental screening data, demographic data and data on oral sequelae during follow-up were recorded. Oral foci were found in 44/56 (79%) patients and consisted predominantly of periodontal breakdown. Bone healing problems after radiotherapy occurred more often in patients with periodontal pockets ≥6 mm at baseline (p<0.05). Osteoradionecrosis developed in 4/56 patients (7%) during follow-up. It was concluded that patients with periodontal disease before radiotherapy are prone to develop bone healing problems after IMRT/CHIMRT.
The prospective study described in Chapter 6 assessed the effect of leaving chronic oral foci of infection untreated on the development of infectious complications in intensively treated hematological patients. Included were 28 intensively treated leukemic patients and 35 patients undergoing high-dose chemotherapy and autologous stem cell transplantation (ASCT), between September 2012 and May 2014. Acute oral foci of infection (tooth related or oral mucosa related pain, percussion or palpation tenderness of oral structures, fever related to oral pathology, swelling of oral tissues and/or tooth related purulent drainage) were removed before chemotherapy or ASCT, while chronic oral foci (focus had not exacerbated and was asymptomatic during the previous 3 months) were left untreated. Acute oral foci of infection were found in 2 leukemic (7%) and 2 ASCT-patients (6%), chronic oral foci of infection in 24 leukemic (86%) and 22 ASCT-patients (63%). Positive blood cultures with microorganisms potentially originating from the oral cavity occurred in 7 patients during treatment, but were uneventful on development of infectious complications. The results of this prospective study support the hypothesis that chronic oral foci of infection can be left untreated as this does not increase infectious complications during intensive chemotherapy.

In chapter 7 the various outcomes of the studies described in the previous chapters were placed in a broader perspective. The main conclusions of the research described in this thesis are that the assessed dental screening protocol was equally effective in patients treated with conventional radiotherapy, IMRT or IMRT combined with chemotherapy (CHIMRT) as the post-radiotherapy oral and dental morbidity was comparable. Not all oral sequelae can be prevented, however, and thus the need for further research remains. Also, HNC patients with periodontal disease before radiotherapy were shown to be prone to develop bone healing problems after radiotherapy.

In hematology patients, it was shown that chronic oral foci of infection can be left untreated as leaving these foci untreated does not increase infectious complications during intensive chemotherapy.