Introduction

Head and neck cancer can be treated with different modalities, including surgery, radiotherapy, and chemotherapy. During and after treatment, patients can suffer from side-effects such as mucositis and xerostomia. Head and neck cancer patients also frequently suffer from trismus: a limited ability to open the mouth. The cancer treatment and its side-effects can impede mandibular function. Mandibular function includes speaking, eating, laughing, yawning, and social activities. Side-effects and impairment of mandibular function can be a burden for patients and can impede on quality of life (QoL).

A mouth opening of 35 mm or less is a commonly used cut-off point for trismus. Large differences in prevalence and incidence of trismus in head and neck cancer patients have been reported: between the 5 and 42%. Trismus can be caused by the tumor itself (invasion in the masticatory muscles and temporomandibular joint, or their surrounded tissues) or by the treatment of it (scar formation and fibrosis as a result of surgery and radiotherapy).

A decrease in mouth opening of head and neck cancer patients cannot always be prevented by exercise therapy. When trismus is present, generally a limited increase in mouth opening can be achieved. There is no standard treatment for trismus; many different types of exercise therapy have been described in literature and are clinically applied.

Studies in this thesis

In Chapter 2, the oral symptoms of 89 patients treated for oral or oropharyngeal cancer were assessed. Additionally, it was assessed how these patients rank the burden of oral symptoms and how the tumor, the treatment, and the oral symptoms impacts on functional outcome. The Mandibular Function Impairment Questionnaire (MFIQ) was used to assess functional outcome. Lack of saliva was not only the most frequently reported oral symptom, but also the most burdensome. The second and third most frequently reported oral symptoms were a restricted mouth opening and restricted tongue mobility, respectively. For irradiated and non-irradiated patients, different risk factors for impairment of mandibular function were found. However, in all patients, MFIQ scores were strongly influenced by an inability to wear a dental prosthesis.

In Chapter 3.1, the course of mouth opening of 641 patients up to 48 months post-radiotherapy for head and neck cancer was analyzed, risk factors predicting decrease in mouth opening were assessed, and a multivariate prediction model for change in mouth opening was developed. Mouth opening was measured prior to radiotherapy (baseline) and at 6, 12, 18, 24, 36, and 48 months post-radiotherapy. Mean mouth opening at baseline was 38.7 mm (SD 10.8). The smallest mean mouth opening found at 6 months post-radiotherapy, namely 36.7 mm (SD 10.0). Overall, mouth opening decreased the first 6 months post-radiotherapy and gradually recovered up to 48 months post-radiotherapy. Mouth opening was predicted by the sex and age of the patient, the location and classification of the tumor, baseline mouth opening, the irradiation dose, and the time since radiotherapy. The model can be used to predict mouth opening. In Chapter 3.2, the incidence of trismus at various time points and risk factors for the development of trismus
post-radiotherapy in head and neck cancer patients were assessed. The same patient population and measurements of mouth opening as in Chapter 3.1 were analyzed. Over a total period of 48 months post-radiotherapy, the incidence of trismus was 3.6 per 10 person years at risk. Six months post-radiotherapy, 28.1% of the patients without trismus prior to radiotherapy developed trismus. Tumor location and overall treatment time of radiotherapy were risk factors for developing trismus the first 6 months post-radiotherapy. Mouth opening at any time point was a significant predictor for developing trismus at all subsequent time points. Therefore, regular measurements of mouth opening are needed to predict trismus. High-risk patients, identified by the presence of risk factors for trismus, can be offered preventive measures.

In Chapter 4.1, studies regarding exercise therapy interventions for trismus secondary to head and neck cancer were systematically reviewed. The quality of the included studies found was assessed and the results were summarized. Of the 211 found studies, 20 could be included. The included studies had a large variation in research methodology, stretching techniques, duration of stretch, and repetition of exercises. The overall quality was moderate. In 5 out of the 8 preventive studies, a reduction in mouth opening was not prevented. In 4 therapeutic case-studies, mouth opening increased between 17 and 24 mm. In 8 other therapeutic studies, mouth opening changed between -1.9 and 13.6 mm. Better results were found if the exercise therapy started early and in compliant patients. No exercise therapy was clearly superior. Clinical guidelines could not be given based on this systematic review. In Chapter 4.2, the effects of TheraBite® Jaw Motion Rehabilitation System™ (TheraBite) exercises on mouth opening in 69 head and neck cancer patients of 2 university medical centers (University Medical Center Groningen and Radboud University Medical Center) was evaluated. Additionally, factors influencing this effect were analyzed. An increase of 5 mm or more was studied, which corresponds with the smallest detectable difference. Baseline mouth opening was 22.0 mm (SD 6.4), the mean increase was 5.4 mm (SD 5.7). Chemotherapy, the medical center, and the time from oncological treatment to start TheraBite exercises were significantly associated with an increase in mouth opening. The odds of an increase in mouth opening of 5 mm or more reduced when the time from oncological treatment to start TheraBite exercises lengthened. In Chapter 4.3, the effects of Dynasplint Trismus System® (DTS) exercises on changes in mouth opening, pain, mandibular function, QoL, and symptomatology of 18 consecutive head and neck cancer patients were determined. Additionally, user-satisfaction, experiences, comfort, and compliance of these exercises were analyzed. Baseline mouth opening was 22.6 mm (SD 7.6), the mean increase was 7.1 mm (SD 4.7) (significant). About one-third of the gained increase was lost in the follow up period of 14 weeks. The perceived difficulty of opening the mouth improved significantly. No other significant effects were found. Patients’ perception was diverse. However, in general, patients were satisfied about the DTS exercises.

Future perspectives
Risk factors for trismus in head and neck cancer patients that were identified in this thesis should, where possible, be eliminated or positively influenced to prevent trismus.
High-risk patients should be identified by the presence of risk factors for trismus. Of these patients, regular measurements of mouth opening should take place during and after the treatment of head and neck cancer. Attention should be paid to the development of a preventive rehabilitation program for those patients with a high risk of developing trismus or for patients with a decrease in mouth opening. Since exercise therapy is burdensome, expensive, and cannot always prevent trismus, it should not routinely be advised to every patient. The prevention of trismus should be added or integrated in the supportive care program for head and neck cancer patients; like the prevention of malnutrition, the support of oral hygiene including fluoride prophylaxis, and exercises to prevent arm and shoulder problems after a neck dissection.

For patients who developed trismus, the search for the most effective exercise therapy to treat trismus should be continued. The effects of exercises with a TheraBite and a DTS should be compared in randomized controlled trial.

For reaching the most optimal results, the exercise therapy should be initiated as early as possible and therapists should stimulate patients’ compliance. Patients should be informed that sometimes, a reduction of further decrease in mouth opening is the best feasible result.

Conclusions
After treatment of head and neck cancer, many patients suffer from side-effects, including trismus. In this thesis, the identified risk factors for trismus are: higher age, female sex, several locations of the tumor (oral cavity, oropharynx or nasopharynx, nasal cavity, maxillary sinus, salivary glands, and ear), T4 tumors, irradiation dose, smaller mouth opening prior or during radiotherapy, and more time since radiotherapy. Of patients treated with radiotherapy, mouth opening can be predicted by means of the prediction models. Additionally, trismus can be predicted for different time points post-radiotherapy. Despite the identification of risk factors for trismus, it is not realistic to prevent trismus since most of these risk factors cannot be modified. Therefore, preservation of mouth opening in head and neck cancer patients, especially after radiotherapy, is difficult.

In this thesis, no exercise technique was found clearly superior and the results varied considerably. As a result of exercise therapy, less decrease (in case of preventive exercises) or a larger increase in mouth opening (in case of therapeutic exercises) can be expected in compliant patients and when exercise therapy initiated early. Despite positive results of exercise therapy in general, trismus secondary to head neck cancer cannot always be prevented or treated.