Function after oral oncological intervention, reconstruction and rehabilitation

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Function after oral oncological intervention, reconstruction and rehabilitation

(with a summary in English)

Functie na oraal oncologische interventie, reconstructie en rehabilitatie

(met een samenvatting in het Nederlands)

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Voor mijn ouders

Contents

1

Introduction

Epidemiology

Oral cancer is a major health problem worldwide. Cancers of the oral cavity accounted for 274,289 new cases in 2002.[1] The incidence rates are about two times higher in men than in women. The incidence of oral cancer is relatively low in most western countries, but there are exceptions. In parts of Asia it is amongst the most prevalent cancers. In India 40% of all cancers are oral cancer,[2] compared to just 1% in the Netherlands, where 919 cases (554 men) were diagnosed with oral cancer in 2008.[3] The Dutch incidence has a peak for persons between 55 and 75 years old.[3,4] Also of note is the reported increase of 30% in the incidence of oral cancer in the Netherlands between 1998 and 2008.[3] This was caused mainly by a rise in the incidence of oral cancer in women, which was in turn related to an increase in their alcohol consumption and smoking habits.[3,5] There are also indications in Western countries of an increased incidence in patients younger than 40.[6,7] In the Netherlands the survival rate is around 60% at five years, taking into account all the stages of cancer at initial diagnosis.[3] The survival rate for oral cancer depends on where it occurs in the oral cavity and the stage of the cancer when it is diagnosed.

There are several types of oral cancers, but squamous cell carcinoma originating in tissues of the mouth is by far the most common and accounts for about 95% of the cases.[8] The tongue is the most commonly affected area, followed by the floor of the mouth.[9] Cancer may also occur on the gingivae and alveolar ridge, the buccal mucosa, the hard and soft palate, the uvula and other regions of the oral cavity. It can have various histologic types: teratoma, adenocarcinoma, lymphoma or melanoma.[10]

Etiology

The process by which oral cancer develops depends on many factors. Etiologic factors in the environment are the direct or indirect cause of changes in oncogenes, that have the potential to cause cancer, or tumour suppressor genes, that protect cells from progressing to cancer.[11] Epidemiological studies have identified several risk factors that predispose a person to oral cancer. About 75% of the cases are associated with smoking and other types of tobacco usage.[12] With smoking, the inhaled smoke and heat irritate the mucous membranes. Chewing tobacco and snuff dipping, i.e. holding tobacco between the cheek and the gum, causes irritation from direct contact with the mucous membranes.[12,13] The use of alcohol also highly increases the

risk of developing oral cancer.[9,12] It is assumed that the risk of oral cancer due to (excessive) alcohol consumption is greater than that due to the use of tobacco.[14,15] Beverages with high levels of ethanol are associated with a greater risk than low-alcoholic beverages.[16,17] Heavy drinking and heavy smoking have a strong synergistic effect on oral cancer risk. It has been demonstrated that combined heavy drinking and smoking increases the risk of developing oral cancer greatly, when compared to heavy smoking or heavy drinking only.[12,16-18]

Another known risk factor and independent factor that can cause oral cancer is infection with human papillomavirus (HPV), particularly HPV type 16.[19,20] HPV16 has been indicated to be the main risk factor in an increasing proportion of people that develop oral cancer, but who do not have the characteristics usually associated with the risk to get oral cancer.[21] This new subpopulation is growing fast and consists of people younger than 55 years that predominantly are white and do not smoke, males slightly outnumbering females.[22]

In Asian cultures a strong risk factor for oral cancer is 'paan', the tradition of chewing betel leaf filled with substances such as areca nut or tobacco.[23-25] Other suggested risk factors include socioeconomic status,[26] occupation (e.g. painters,[27] pressmen,[28] plutonium workers[29]), dentition,[30] and diet.[26,30,31]

Treatment

The main objective of the treatment of oral cancer is to maximize the survival of the patient and to avoid that the cancer reappears in the treated area. In addition it is important to try to preserve the function of the mouth and the quality of life. In the last ten years progress has been made in combining these goals. If the tumour is small enough and surgery likely leads to little functional impairment, it is usually recommended to excise the tumour. Unfortunately, oral cancers are often diagnosed in a late stage. For example, the relative number of patients with a T4-stage, when the tumour is larger than 4 cm and has invaded deeply in adjacent structures, is increasing in the Netherlands.[32] Because the mouth houses vital structures, surgery for larger oral cancers is technically difficult. Reconstructive surgery may be necessary to obtain an acceptable cosmetic and functional result. Bone grafts and microvascular free flaps, such as the radial forearm flap, are used to help rebuild the structures removed during excision of the cancer. In addition to reconstructive surgery, implants can be placed in bone to support a prosthesis such as dentures. Radiotherapy is often used in conjunction with surgery, for example with the aim to destroy cancer cells that the surgery may have missed. Radiotherapy

can also be applied as the definite treatment, particularly if the tumour cannot be surgically removed. Chemotherapy is used in oral cancers in combination with other treatments, such as surgery and radiotherapy. When the patient cannot be cured, chemotherapy can be used as palliative care with the aim to prolong life and alleviate the symptoms. The recent advances in reconstructive surgery, radiotherapy and chemotherapy result in longer survival and less oral impairment after treatment.

Oral function deficits

The presence of oral cancer and its treatment may have profound effects on the health-related quality of life of a patient. This quality of life has been shown to deteriorate during treatment and slowly recover over the following 12 months.[33] Despite progress in the treatment of oral cancers, patients who have undergone interventions, often show impairment or possibly even loss of essential oral functions.[34] Patients may have problems with mastication, swallowing, nutrition, speech, neck and shoulder function, appearance, and the ability to interact socially. Ablative surgery in the mouth results in defects of soft tissues, and possibly also in defects of bone and skin. Ablative surgery can result in disabling alterations of functional components of occlusion, how the teeth come together when closing the jaw, causing impairment of the ability to chew.[35,36] Radiotherapy causes xerostomia, tissue fibrosis, osteoradionecrosis, and may accelerate dental caries.[37] Radiotherapy often mandates the extraction of various teeth and can also cause trismus, which also affects mastication.[38-40] Chewing also depends on the anatomical-functional integrity of activity structures, such as muscles, passive structures and the functioning of salivary glands.[41] Surgical interventions and radiotherapy may influence this anatomical-functional integrity negatively.[38,42-44]

The tongue is vital for the transport and positioning of food between the molars, selecting fragments for further comminution, incorporation of fragments with saliva, posterior transport of the resulting bolus, and its final deposition into the oropharynx.[45,46] The sensory mechanisms of the tongue, that sense the state and position of the food in the mouth, are necessary to accomplish the changes in shape and position of the tongue and floor of the mouth required for mastication and swallowing.[47-49] During the oral stage of swallowing, the tongue presses against the hard and soft palate and sequentially moves in an anterior to posterior direction to propel the bolus to the pharynx.[50,51] Therefore deterioration of these tongue functions, for instance after surgery of the tonsils or the tongue base, may affect the

swallow function.[52,53] Swallowing can also be affected by tissue fibrosis and xerostomia.[54,55] When the tongue fails, caused by an oncological intervention, the mastication process will deteriorate. This has a negative effect on nutrition possibilities for these patients.[56]

The tongue's flexibility, strength and its ability to take on variable shapes are important in articulation for producing consonants and vowels, both lingual and palatal.[57] Different surgical variables, such as type of reconstruction, correspond to the deterioration of postoperative speech capacity.[47,48,58-60] Patients who develop xerostomia after radiotherapy may also have difficulties in speech.[37]

Neck dissection

An adverse prognostic factor in oral cancer is the presence of cervical lymph node metastasis. This often indicates that a neck dissection must be performed. A neck dissection can cause neck and shoulder complaints and may lead to pain, reduced range of motion of the neck and shoulder, loss of sensation and loss of neck and shoulder function.[61-64] It has been demonstrated that more extensive surgery in the neck is associated with more postoperative shoulder morbidity.[62,65-67] Radiotherapy may result in troublesome and uncomfortable fibrosis which may worsen with time, leading to limited neck mobility.[68]

Assessment of function

Function in patients treated for oral oncology has often been determined using quality of life (QoL) questionnaires, such as the European Organization for Research and Treatment of Cancer Quality of Life Questionnarie-Core 30 Head and Neck 35-questions (EORTC QLQ-H&N C30)[69] and the University of Washington Quality of Life (UW-QoL) questionnaire.[70] An increasing number of studies have measured QoL as an end point in the evaluation of the impact of the disease and of its treatment on the patients' daily life. The above-mentioned questionnaires measure self-perceived function. The outcomes are therefore the patients' experiences and provides the patients' subjective impression of daily function.

Objective information, obtained from measurements of function, may be different from personal experiences, however. The outcomes of objective measurements can complement data of questionnaires in patients with oral cancer. Objective measurements may provide new information about the severity of the affected function and may help in the further

development of rehabilitation strategies for these patients. Therefore, in this research objectively-measured function is evaluated in addition to self-perceived function.

Aim and scope of the thesis

The overall aim of this thesis was to better understand the deterioration and recovery of function of patients with oral cancer following oncological intervention, reconstruction and rehabilitation. This better understanding may lead to better treatment strategies. For this, we investigated the effects of oral oncological intervention, reconstruction and rehabilitation on the function of the mouth, neck and shoulders. Several aspects of (oral) function were measured in patients treated for malignancies in the mouth in a 1-year period before and after intervention. In addition, self-assessed (oral) function was determined from questionnaires. These investigations involved the following topics:

1. To retrospectively determine self-perceived oral function in patients with oral cancer at different stages of treatment in order to obtain insight into deficits of oral function that relate to tumour location in the oral cavity (chapter 2).
2. To develop a satisfactory mastication test with a material that forms a bolus and is soft enough to be chewed by persons with compromised masticatory performance (chapter 3).
3. To investigate whether the mixing of colours after chewing two-colour wax tablets can be assessed equally well using digital image processing and visual assessment by observers (chapter 4).
4. To determine the effect of 'oral oncological surgery only' and 'oral oncological surgery combined with radiotherapy' on objective, mastication-related measures (i.e. dental state, maximum bite force and masticatory performance) in patients with malignancies in the tongue and/or floor of mouth at various moments before and after surgery and radiotherapy and to compare these outcomes with those of healthy controls (chapter 5).
5. To determine the effect of surgery with or without radiotherapy on tongue function (i.e. tongue sensory function, tongue mobility, and maximum tongue force) in patients with malignancies in the tongue and/or floor of mouth in comparison to healthy controls at various moments before and after surgery and radiotherapy (chapter 6).

6. To determine neck and shoulder function (i.e. range of motion of the maximal active lateral flexion of the neck, forward flexion of the shoulder, abduction of the shoulder, and self-perceived neck and shoulder function) in patients with malignancies in the oral cavity treated with and without neck dissection at various moments before and after oral oncological intervention and to compare these outcomes with those of healthy controls (chapter 7).

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2

Oral function after oncological intervention in the oral cavity: a retrospective study

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Abstract

Purpose: To assess self-perceived oral function of patients with oral cavity cancer at different stages of treatment, i.e., before oncological intervention, 5 weeks after intervention, and 5 years after intervention.

Patients and Methods: A cohort of 158 patients with malignancy in the oral cavity treated by surgery in 1999 or 2000 was included. From this cohort we interviewed 69 patients by telephone in 2005 and collected data on dental status, disorders of chewing and swallowing, xerostomia, preference of food consistency, tube nutrition, weight loss, and speech for different stages of treatment.

Results: For patients treated in the maxilla region we observed a significant ($p < 0.05$) recovery of perceived chewing ability after 5 years to the level experienced before oncological intervention. Patients treated in the mandible region reported a deteriorated dental state, chewing ability, lip competence, and xerostomia after 5 years. Patients treated in the tongue and mouth-floor region experienced deterioration for dental state, chewing ability, and xerostomia after 5 years as compared with the level before the oncological intervention.

Conclusions: Our telephone interview on oral function provided supplementary information on how patients experienced their problems with oral function during various phases of oncological treatment. A retrospective interview may thus help to add information to incomplete retrospective data.

Introduction

Treatment of oral cancer is primarily aimed at maximizing survival and locoregional control while trying to preserve normal oral function and quality of life. The previous decade's progress in a combination of reconstructive surgery, radiotherapy, and chemotherapy has made it possible to improve this survival and reduce oral functional deficits after treatment.[1] Despite of this progress patients still have diminished or lost essential oral functions.[2] Surgery in the mouth results in defects of soft tissues and possibly in defects of bone and skin. Radiotherapy causes xerostomia, tissue fibrosis, osteoradionecrosis, and may accelerate dental caries.[3] As a consequence of these interventions patients may have problems with mastication, swallowing, nutrition, speech, appearance, and the ability to interact socially. The impairment of mastication caused by disabling alterations of functional components of occlusion can be a result of surgery.[4,5] Radiotherapy often mandates the extraction of various teeth and causes xerostomia and trismus, which also affect mastication.[6-8] Deterioration of swallowing may be caused by surgery of the tonsils or the tongue base,[9,10] but also by tissue fibrosis and xerostomia.[11,12] This has a negative effect on nutrition possibilities for these patients.[13] Speech may also be impaired after oncological treatment of oral cancer. Different surgical variables correspond to the deterioration of postoperative speech capacity.[14-16] Patients who develop xerostomia after radiotherapy also may have difficulties in speech.[3] Presence and treatment of oral cancer may have profound effects on the health-related quality of life of a patient. Health-related quality of life was found to deteriorate during treatment and slowly recover during the subsequent 12 months.[17]

Assessment of the impact of oral cancer encompasses more than survival and extends beyond functioning to include patient well-being. Little is known about how patients with oral cancer retrospectively experienced their oral function during the treatment period. Clinical, physical, and socio-demographic factors are not wholly responsible for variation in health-related quality of life in head and neck oncology.[18,19] The objective of this retrospective cohort study was to assess self- perceived oral function of patients with oral cancer at different stages of treatment to obtain insight in deficits of oral function difficulties in relation to tumour location in the oral cavity. Patients were grouped according to the location of the tumour, 1) maxilla, 2) cheek/mandible, and 3) tongue/floor of the mouth. We interviewed patients by telephone and collected data on dentition, disorders of chewing and swallowing, xerostomia, preference of food consistency, tube nutrition, weight loss, and speech. During

the interview, the patients first answered the questions for the current situation (thus about 5 years after oncological intervention). After that, the patients answered the questions from memory for 2 time periods: just before oncological intervention, and 4 to 6 weeks after surgery/radiotherapy.

Patients and Methods

Medical data were retrospectively collected from medical files for 158 consecutive patients who had a surgical intervention for oral malignancy at University Medical Center Utrecht (Utrecht, The Netherlands) in 1999 or 2000. In 2005, we interviewed 69 (43%) of these patients by telephone about their oral function. At that time 69 patients (43%) of the 1999/2000 cohort had died, and 22 patients (14%) did not participate in this study: 10 patients could not be contacted, 3 patients were not able to participate, and 7 patients did not want to participate. The patients who participated in the interview were divided into 3 groups based on tumour location: group 1, maxilla, soft/hard palate, maxillary tuber, and superior alveolar process (n = 9); group 2, cheek, retromolar trigone, and inferior alveolar process (n = 18); group 3, tongue and floor of the mouth (n = 42).

Telephone interview

Sixty-nine patients were interviewed by telephone about their oral function. The interviewer had no knowledge of clinical information of the patients. The questions of the telephone interview were based on clinical experience and published reports.[2,20-24] The following 11 items were addressed: dentition, chewing, pain during chewing, drooling, xerostomia, weight loss, tube nutrition, swallow complaints, choke, pain during swallowing, and speech (Appendix 1). The patients answered the 11 questions from memory for the following 3 time periods: before oncological intervention, 4 to 6 weeks after oncological intervention, and current (i.e. about 5 years after oncological intervention).

Statistical analyses

The presentation of results is primarily descriptive with percentages and means. Baseline variables were tested for group differences by χ^2 test. Oral function items were analyzed by McNemar test (nominal items) and by a Wilcoxon signed-ranks test (ordinal items). These tests were used to determine whether the changes in time to the physiological dependent

variables were statistically significant. A *p*-value less than 0.05 was considered statistically significant. All analyses were performed with SPSS 15.0 (SPSS, Inc, Chicago, IL).

Results

Sixty nine patients with oral cancer were included in this study, 39 men and 30 women aged 67 ± 11 years (mean ± SD). Characteristics of patients, diagnosis, and treatment are listed for the total group and for the 3 subgroups based on tumour location (Table 1). χ^2 tests revealed that patient numbers were significantly different among the 3 groups with respect to tumour stage, radiotherapy, and type of reconstruction (Table 1). The percentage of patients with T3 and T4 tumours (7%) was smallest in group 3 (tongue, floor of mouth). Radiotherapy was given in 44%, 56%, and 24% of the patients in group 1, 2, and 3, respectively.

Table 2 presents the results of the telephone interview for the 3 groups. We performed separate tests for each group to avoid a possible influence on the results of the significant differences in composition of patients in the 3 groups. In group 1 (maxilla, soft/hard palate, maxillary tuber, and superior alveolar process) we observed a significant decrease in the perceived chewing ability and a significant loss of weight 5 weeks after oncological intervention (Table 2). Chewing ability recovered in the subsequent 5 years to the level before oncological intervention. The patients in group 2 (cheek, retro molar trigone, and inferior alveolar process) reported significant deterioration of their chewing ability and lip competence at 5 weeks after oncological intervention (Table 2). Furthermore, a significant increase of xerostomia and tube nutrition occurred. From 5 weeks and to 5 years after intervention a recovery of chewing ability was reported. Furthermore, the patients gained weight during this period. After 5 years the patients in group 2 had a deteriorated dental state, chewing ability, and lip competence compared with the moment just before oncological intervention. Also, significantly more xerostomia complaints were reported. Significant deterioration of all items of the telephone interview, except for pain during swallowing, was reported by the patients of group 3 (tongue, floor of the mouth) 5 weeks after oncological intervention (Table 2). From 5 weeks to 5 years after surgery the patients of group 3 reported a significant recovery for chewing ability, weight, and speech, and a significant decrease of pain during chewing and tube nutrition. After 5 years the patients of group 3 reported a deteriorated dental state and chewing ability, and an increase in xerostomia complaints compared with the period just before oncological intervention.

Table 1. Baseline variables for the total population and 3 anatomy groups

	Total	Group 1*	Group 2*	Group 3*	*p*-value
	n = 69	n = 9	n = 18	n = 42	χ^2 Test†
Age, y					
< 55	7 (10%)	2 (22%)	2 (11%)	3 (7%)	
55-74	44 (64%)	6 (67%)	8 (44%)	30 (71%)	0.160
≥ 75	18 (26%)	1 (11%)	8 (44%)	9 (21%)	
Gender					
Male	39 (57%)	6 (67%)	10 (56%)	23 (55%)	0.804
Female	30 (43%)	3 (33%)	8 (44%)	19 (45%)	
T stage					
T1	37 (54%)	6 (67%)	6 (33%)	25 (60%)	
T2	18 (26%)	-	4 (22%)	14 (33%)	0.014‡
T3	1 (1%)	-	1 (6%)	-	
T4	13 (19%)	3 (33%)	7 (39%)	3 (7%)	
N stage					
N0	54 (78%)	7 (78%)	17 (94%)	30 (71%)	
N1	10 (15%)	1 (11%)	-	8 (19%)	0.366
N2	5 (7%)	1 (11%)	1 (6%)	4 (10%)	
N3	-	-	-	-	
Radiotherapy					
No	45 (65%)	5 (56%)	8 (44%)	32 (76%)	0.049‡
Yes	24 (35%)	4 (44%)	10 (56%)	10 (24%)	
Type of Reconstruction					
Primary closure	31 (45%)	1 (11%)	9 (50%)	21 (50%)	
Local flap	24 (35%)	7 (78%)	3 (17%)	14 (33%)	0.007‡
Myocutaneous or free flap	11 (16%)	1 (11%)	3 (17%)	7 (17%)	
Bone graft/flap	3 (4%)	-	3 (17%)	-	
Type of Neck Dissection					
None	17 (25%)	6 (67%)	3 (17%)	8 (19%)	
Unilateral					
Level III – IV / Level V	34 (49%)	2 (22%)	10 (56%)	22 (52%)	
Modified radical	4 (6%)	1 (11%)	-	3 (7%)	0.067
Bilateral					
Both level III – IV / Level V	12 (17%)	-	5 (28%)	7 (17%)	
Level III – IV / Level V and modified radical	2 (3%)	-	-	2 (5%)	

*Group 1: maxilla, soft/hard palate, maxillary tuber, and superior alveolar process; Group 2: cheek, retromolar trigone, and inferior alveolar process; Group 3: tongue and floor of the mouth. †Differences in numbers among the 3 groups were tested with a χ^2 test. ‡$p < 0.05$.

Table 2. Results of the telephone interview for the 3 groups*

Items telephone interview	test [a]	0	5 wks	5 yrs	0 – 5 wks†	*p*-value	5 wks – 5 yrs‡	*p*-value	0 – 5 yrs§	*p*-value
Group 1 (N = 9)										
Dental state	A	0.67	0.89	0.89		0.500		1.000		0.500
Chewing (fluid/soft/hard)	B	0.11	1.25	0.67	↓	0.024‖	↑	0.025‖		0.059
Pain during chewing	A	0.11	0.14	0.00		1.000		1.000		1.000
Drooling	A	0.00	0.11	0.22		1.000		1.000		0.500
Xerostomia	B	0.00	0.56	0.56		0.102		1.000		0.102
Loss of weight	A	0.00	0.67	0.11	↓	0.031‖		0.063		1.000
Tube nutrition	A	0.00	0.33	0.00		0.250		0.250		1.000
Swallowing	A	0.00	0.22	0.22		0.500		1.000		0.500
Choking	A	0.00	0.22	0.11		0.500		1.000		1.000
Pain during swallowing	A	0.00	0.22	0.00		0.500		0.500		1.000
Speech	B	0.00	0.56	0.00		0.180		0.180		1.000
Group 2 (N = 18)										
Dental state	A	0.65	0.83	1.00		0.250		0.250	↓	0.031‖
Chewing (fluid/soft/hard)	B	0.06	1.06	0.41	↓	0.001#	↑	0.013‖	↓	0.014‖
Pain during chewing	A	0.11	0.61	0.00		0.250		0.125		0.500
Drooling	A	0.00	0.25	0.50	↓	0.001#		0.687	↓	0.004¶
Xerostomia	B	0.00	0.39	0.44	↓	0.034‖		0.564	↓	0.020‖
Loss of weight	A	0.17	0.47	0.00		0.125	↑	0.008¶		0.250
Tube nutrition	A	0.00	0.61	0.06	↓	0.001#	↑	0.002¶		1.000
Swallowing	A	0.00	0.17	0.11		0.250		1.000		0.500
Choking	A	0.00	0.11	0.11		0.500		1.000		0.500
Pain during swallowing	A	0.06	0.06	0.00		1.000		1.000		1.000
Speech	B	0.00	0.44	0.00		0.102		0.102		1.000
Group 3 (N = 42)										
Dental state	A	0.52	0.71	0.81	↓	0.021‖		0.125	↓	0.000#
Chewing (fluid/soft/hard)	B	0.02	0.88	0.40	↓	0.0003#	↑	0.000#	↓	0.001#
Pain during chewing	A	0.07	0.31	0.12	↓	0.022‖	↑	0.039‖		0.687
Drooling	A	0.02	0.21	0.10	↓	0.021‖		0.180		0.375
Xerostomia	B	0.05	0.35	0.48	↓	0.005¶		0.132	↓	0.000#
Loss of weight	A	0.12	0.38	0.12	↓	0.027‖	↑	0.013‖		1.000
Tube nutrition	A	0.00	0.24	0.05	↓	0.002¶	↑	0.008¶		0.500
Swallowing	A	0.00	0.17	0.07	↓	0.016‖		0.219		0.250
Choking	A	0.00	0.14	0.07	↓	0.031‖		0.375		0.250
Pain during swallowing	A	0.07	0.12	0.00		0.687		0.063		0.250
Speech	B	0.00	0.50	0.00	↓	0.008¶	↑	0.008¶		1.000

Abbreviations: ↑ : significant improved function; ↓ : significant worsened function; A: McNemar test; B: Wilcoxon signed-ranks test.

*Group 1, maxilla, hard/soft palate, maxillary tuber, superior alveolar process; Group 2, cheek, retromolar trigone, inferior alveolar process;
Group 3, tongue, floor of the mouth.

†Before surgical intervention until 5 weeks after intervention; ‡Five weeks until 5 years after surgical intervention; §Before surgical intervention until 5 years after intervention.

‖ $p < 0.05$; ¶ $p < 0.01$; # $p < 0.001$.

Discussion

Knowledge of self-perceived oral handicaps of patients with oral cancer is important for clinicians. It provides information on how patients experience their oral abilities after an oncological intervention. The information may be used to predict disability after treatment and to improve the process of care. Five years after oncological intervention the patients answered questions on their oral function from memory for various phases of treatment, before and after oncological intervention. Telephone interviews provided information on how patients coped with oral function during several phases of their illness and recovery.

The composition of the 3 groups of patients, based on tumour location, was significantly different with respect to tumour stage, radiotherapy, and type of reconstruction (Table 1). The differences in composition of the groups will have an important influence on the severity of the disease and on the recovery of the patient. Therefore, we did not test for differences in perceived oral function among the 3 groups.

The patients in group 1 (maxilla, hard/soft palate, maxillary tuber and superior alveolar process) did not report significant deterioration of their oral function 5 years after oncological intervention compared with the situation just before the oncological intervention (Table 2). The patients did report that they experienced more difficulty in chewing food directly after oncological intervention. The chewing problems may also have had a negative effect on their weight (Table 2). However, 5 years after oncological treatment a significant improvement in chewing was reported so the patients no longer experienced chewing to be a problem. It should be noted that the number of patients in group 1 was relatively small (n = 9), so that significant effects were less likely to occur than in the other 2 groups (n = 18 and 42 respectively). Moreover, a relatively high percentage of the patients had T1 stage, which may have caused the relatively positive results of group 1. Thus the outcomes of group 1 should be used with caution. Two patients in group 1 used an obturator.

Five years after oncological intervention the patients in group 2 (cheek, retromolar trigone, and inferior alveolar process) experienced deterioration in several aspects of oral function (dental state, chewing, drooling, and xerostomia) compared with the situation just before oncological intervention (Table 2). They reported comparable problems directly after oncological intervention. Although some improvement was reported in the 5-year period after their treatment, the patients still experienced problems in their oral function.

The patients in group 3 (tongue and floor of mouth) reported from memory that, directly after oncological intervention they experienced problems in nearly all items of the telephone interview. Although in the subsequent 5 years, improvement was reported on several aspects of oral function, they still experienced problems on several aspects of their oral function, dental state, chewing, and xerostomia (Table 2). Patients in group 3 thus had more complaints about oral function than patients in the other 2 groups, notwithstanding on average fewer extended tumours, less reconstruction, and less radiotherapy.

Deterioration of dentition was reported by the patients in group 2 and 3. Because of the deteriorated dental status the patients experienced chewing problems. It has been shown in various studies that dental status has a significant effect on masticatory performance.[5,25] Chewing is also dependent on the anatomical-functional integrity of activity structures, such as muscles, passive structures, and the functioning of salivary glands.[26] The tongue has an important role in forming the bolus during the chewing cycle;[27] when the tongue fails, caused by an oncological intervention, the mastication process will deteriorate. Surgical interventions and radiotherapy may have influenced this anatomical-functional integrity negatively.[6,28-30] Xerostomia may be caused by radiation therapy, but also by surgical intervention; submandibular and sublingual glands may be damaged or removed by surgical intervention. Secundary effects of xerostomia cause a difficulty in mastication. Mixing food with saliva during mastication is needed to gather up particles to form a bolus.[7,31] The patients in group 2 experienced comparable deterioration of their oral function as patients in group 3 except for drooling. Drooling is a typical complaint after surgical intervention and reconstruction in the mandibular area; nerves, muscles, and bone positions may be damaged, changed, or removed. The anatomical-functional integrity of lip competence is more likely deteriorated in group 2. In group 2, 3 patients received a bone graft/ flap as reconstruction, which may have hampered oral function more severely. Inability to seal lips and lip dysfunction may also affect masticatory function.[32] We may conclude that patients in groups 2 and 3 experienced their oncological intervention as more severe than the patients in group 1.

It should be noted that the 69 participating patients in this study are a selective group. They are 5-year survivors from a group of 160 patients who had surgical intervention in 1999 and 2000. The clinical data of the deceased patients showed that these patients had significantly larger tumours and, possibly related, significant more radiation therapy. Therefore, a selection

bias played an important role in this study,[33] which may have influenced the results on self-perceived oral function in a positive direction.

Retrospective clinical data are often incomplete. A retrospective questionnaire may help to add information. In this study we obtained information on how oral function was perceived during several phases of illness. Unfortunately, retrospective assessments appear to provide information that is different from prospective data. The retrospective results are more sensitive to change and are more highly correlated with patient satisfaction at that moment.[34] When asking our patients to recall their retrospective data, they have to use their retrospective memory. This retrospective memory may have influenced the outcomes of this study by consistency bias.[35] Consistency bias means that we often reconstruct the past to make it more compatible with our current attitudes and behaviour. In this study, consistency bias may have caused a systematic error resulting from imperfect recall. In epidemiological terms this is called *recall bias*.[36] Recall bias may have caused a shift in the responses on perceived oral function. This response shift is the result of informative shifts in a patient's internal standards, values, and priorities in addition to changes in actual health state.[37] The memorized results on perceived oral function just before and after oncological intervention may thus be different from the originally perceived oral function during that period. However, the reliability of memorized results significantly increased when subjects were given memory aids compared with subjects not given such aids.[38] In our study the oncological intervention can be considered as such a memory aid.

We may conclude that 5 years after oncological intervention patients treated for malignancies in the maxilla, soft/hard palate, maxillary tuber, and superior alveolar process (group 1) reported no significant change in oral function compared with the situation before oncological intervention. Patients treated for malignancies in the cheek, retromolar trigone, inferior alveolar process (group 2) and tongue, floor of mouth (group 3) still experienced problems with chewing and xerostomia after 5 years. In addition patients in group 2 reported problems with lip competence. Our telephone interview on oral function provided supplementary information on how patients experienced their problems with oral function during various phases of oncological treatment.

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Appendix 1

1. Dental state

☐ Normal dentition
☐ Not normal dentition
☐ Unknown

2. Chewing

☐ Hard food (e.g., carrots, peanuts, meat)
☐ Soft food (e.g., cake, bread, paste, minced meat)
☐ Fluid food (e.g., apple-sauce, pap)
☐ Unknown
☐ Not applicable

3. Pain during chewing

☐ No pain
☐ Pain
☐ Unknown
☐ Not applicable

4. Drooling

☐ No drooling
☐ drooling
☐ Unknown
☐ Not applicable

5. Xerostomia

☐ Normal amount of saliva
☐ Less saliva
☐ No saliva
☐ Unknown

6. Weightloss

☐ No loss of weight
☐ Loss of weight
☐ Unknown

7. Tube nutrition

☐ No
☐ Yes
☐ Unknown

8. Swallow complaints

☐ No
☐ Yes
☐ Unknown
☐ Not applicable

9. Choking

☐ No
☐ Yes
☐ Unknown
☐ Not applicable

10. Pain during swallowing

☐ No
☐ Yes
☐ Unknown
☐ Not applicable

11. Speech

☐ Normal intelligibility
☐ Intelligible by telephone
☐ Intelligible for nearest family only
☐ No intelligibility
☐ Unknown
☐ Not applicable

3

Mixing ability test compared to a comminution test in persons with normal and compromised masticatory performance

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Abstract

A mastication test was needed with a material that forms a bolus and is soft enough to be chewed by persons with compromised oral function, in particular patients confronted with oral cancer. We therefore developed a wax-mixing ability test and compared it with a comminution test using Optocal as test food. We hypothesized that the mixing ability test would be better at differentiating between groups of persons with compromised masticatory performance than the comminution test. Sixty healthy subjects were recruited in three groups of 20, matched for age and gender: a group with natural dentition; a group with full dentures; and a group with maxillary denture and implant-supported mandibular overdenture. The mixing ability test was found to discriminate better between the two full-denture groups than the comminution test.

Introduction

Mastication plays an important role in the lives of humans. In the oral cavity, food is subjected to several mechanical and chemical processes. It is fractured by the teeth, diluted and broken down by saliva, formed into a bolus, and finally swallowed. People confronted with oral cancer run a high risk of experiencing deteriorated masticatory performance. This deterioration may be caused by the tumour itself, but may also be induced by the oncological intervention (i.e. surgery and radiotherapy). Mutilating surgery may have an enormous effect on the masticatory system. Surgery in the mouth results in defects of soft tissues and possibly also in defects of bone, skin, and dentition. The disabling alterations in the functional components of occlusion may lead to severly impaired mastication.[1,2] Although head and neck oncology surgeons try to reduce functional deterioration by reconstructive surgery,[3,4] patients still report deterioration in masticatory performance 5 yr after oncological intervention (i.e. surgery and radiotherapy) in the oral cavity (unpublished findings, C.M. Speksnijder). Radiotherapy may lead to xerostomia, tissue fibrosis (resulting in trismus), osteoradionecrosis, and accelerated dental caries,[5] which often results in the extraction of several teeth. All of these conditions have a negative effect on the masticatory performance in patients with oral cancer.[6-9] Therefore, it is important to evaluate masticatory performance, so that it becomes possible to determine how oncological intervention (i.e. surgery and radiotherapy) in the mouth influences oral function.

In the majority of the studies on chewing performance, the degree of breakdown of natural or artificial food has been determined by sieving the comminuted food.[10-15] Sieving of fragmented food particles has proven to be a reliable way of quantifying masticatory performance. However, subjects with a compromised oral function were not always able to fragment the test food, because their maximum bite force was lower than the force needed to break the test food particles (Optosil). To overcome this problem, artificial test food (Optosil) was degraded by adding other ingredients (Optocal), so that the test food could be more easily fragmented.[16] However, even then, not all subjects were able to adequately comminute the degraded test food adequately, as demonstrated, for instance, in a study carried out by van Kampen et al.,[17] in which six out of the 18 denture wearers performed so badly that the median particle size of the test food was still larger than 5.0 mm after 15 chewing strokes (as shown in Figure 1 of van Kampen's publication). Thus, the test food was comminuted only minimally. Furthermore, fragmented Optosil particles do not form a coherent bolus, which

makes the test food unsuitable for patients with a mutilated oral cavity (which may occur after, for instance, maxillectomy). In other words, food comminution tests are inappropriate for use in evaluation of the masticatory performance of patients treated for oral cancer.

Another method to determine masticatory performance, which is now widely used, evaluates the ability to mix and knead a food bolus. Two-coloured chewing gum[18-20] and paraffin wax[21-23] have been used as materials to quantify of masticatory performance. The degree of mixing of the two colours was determined by optical methods[19,21] or visual inspection.[18] A validity and reliability study showed that chewing on two-coloured paraffin wax is a reliable alternative to comminution tests.[24] For patients with compromised oral conditions, such as patients with oral cancer, a two-colour chewing gum or paraffin wax mixing test could be a good alternative for food comminution tests: the test food is soft and forms a bolus that can easily be chewed on.[22]

Maximum voluntary bite force is an important variable for using to assess the functional state of the masticatory system. It explains over 60% of the variance in masticatory performance.[8,25] Bite force and chewing efficiency are reduced when natural teeth have been replaced by complete dentures[12,26,27] or implant-retained overdentures.[17,28,29]

The objective of this study was to develop a mastication test with a material that forms a bolus and is soft enough to be chewed by persons with compromised masticatory performance. The results on masticatory performance were compared to the results obtained with a commonly used chewing test, the Optocal comminution test. Three groups participated in the study: subjects with a full natural dentition; subjects with complete dentures; and subjects with complete dentures with mandibular implants. We hypothesized that the mixing ability test would be better than the comminution test at detecting differences in masticatory performance between the two groups of persons with compromised masticatory performance (denture wearers with and without mandibular implants).

Materials and Methods

Subjects

We recruited 60 healthy people in three groups of 20 subjects matched for age and gender: a group with natural dentition; a group with maxillary dentures and implant-supported mandibular overdentures; and a full denture group (Table 1). The experimental protocol was approved by the Ethics Committee of University Medical Center Utrecht. All subjects

received a written explanation of the study, and informed consent was obtained from each subject before the start of the study.

Table 1. Characteristics of subjects in the natural dentition group (A), the maxillary denture and implant-supported mandibular overdenture group (B), and full denture group (C)

	Gender				
Group	Men	Women	Age*	Lifetime of Implants*	Lifetime of Dentures*
A	10	10	58.2 (4.4)		
B	11	9	62.2 (7.3)	2.5 (0.6)	2.2 (0.7)
C	10	10	60.5 (9.0)		1.7 (1.2)

* Data are presented as mean years (standard deviation)

Mixing ability test

The mixing ability test measures how well a subject mixes a tablet, which consists of a red and a blue wax layer, by chewing on it. The chewed wax is flattened and photographed from both sides. The spread of the colour intensities in the combined image of both sides is the measure of mixing. If the wax tablet has not been chewed, one side is red and the other blue, and the spread of the intensities of both colours is maximal. Chewing the tablet mixes the colours, intermediate intensities appear and the spreads of the intensities decrease. Each subject chewed four sequences on a wax tablet, with respectively 5, 10, 15, and 20 chewing strokes. The wax tablets were offered to the subjects at room temperature (20˚C).

The tablet

The tablet (Figure 1) has a diameter of 20 mm and consists of two 3 mm layers of red and blue wax (Plasticine modelling wax, non-toxic DIN EN-71, art. nos. crimson 52801 and blue 52809, Stockmar, Kalten Kirchen, Germany). This wax is a soft material that forms a compact bolus during chewing.

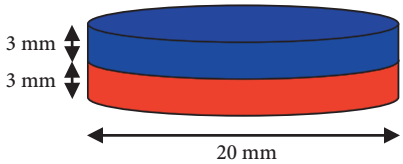


Figure 1. Wax tablet.

Flattening of the chewed tablet

After being chewed, the wax was flattened to avoid shadows in the image by the oblique illumination of the scanner's lamp. Then the wax was rinsed, brought to a temperature of 28°C and placed between two 8 x 8 cm sheets of stiff, clear foil (antistatic polyester montage foil, 0.18 mm). This sandwich of foil and wax was placed between two 3.4 cm thick brass plates and pressed to a thickness of 2.0 mm using a hydraulic hand press at 50 bar.

Scanning the flattened wax

The wax flattened between the foil was photographed using a high-quality scanner (Epson® V750, Long Beach, CA, USA). An opaque cover on the glass plate prevented light from outside reaching the wax. The cover had an 11 x 11 cm hole in which the wax was placed. A square 13 x 13 cm lid was placed over the hole. The inside of the lid was a uniform green background positioned 2.8 cm over the wax. The distance gave a better contrast between the wax and its shadow on the background than if the lid was placed directly on the wax. An area of about 8 x 8 cm with the wax in the middle, was scanned at 600 dpi (dots per inch) and the raw output of the charge-coupled device (CCD) was stored as a 16-bit TIFF file. Subsequently, the other side of the wax was photographed.

Segmentation of the wax image

The images of the wax were processed with Adobe Photoshop, CS3 extended (Adobe, San Jose, CA, USA). The wax was fairly dark with intensities well below 20% of the red, green, and blue ranges. Therefore, the images were brightened by a factor 5. Because the wax is red and blue only, its image in the green channel is a dark blob on a brighter background. Occasional bright patches in the wax indicated where it had not been in contact with the montage foil as a result of inclusion of air during flattening. Using the Magic Wand tool, applied at a dark spot in the centre of the wax image, this was isolated from the entire image, leaving out the air bubbles. The Magic Wand settings were: tolerance 15, no anti-alias, contiguous. The intensity distributions of the red and blue channels were exported as 8-bit histograms. The histograms of both sides of the wax were added to obtain the red and blue intensity distributions of the combined image of both sides of the flattened wax. These histograms were analyzed to obtain a measure for the mixing of the wax: the mixing index.

Comminution test

The outcomes of the mixing ability test were compared with those obtained using a standardized artificial test food called Optocal Plus, which is based on the silicone component Optosil PlusR (version 1997; Bayer Dental, Leverkusen, Germany). Optocal Plus portions of 17 cubes (edge size 5.6 mm), which corresponds to approximately 3 cm^3, were offered to the subjects. Each subject was instructed to chew Optocal PlusR in a normal manner. After 15 chewing strokes, the subject was told to spit out the particles. Mouths and dentures were rinsed with water and the rinsings were added to the expectorated particles. Collected particles were dried for 24 h. Then, the particles were sieved for 20 min on a stack of up to 10 sieves, with square apertures decreasing from 5.6 to 0.5 mm and a bottom plate (Laboratory Sieving machine AS 200 control; F. Kurt Retsch, Haan, Germany). From the weights of the particles left on the sieves the median particle size (X_{50}) was determined, which is the theoretical sieve aperture through which 50% of the weight would pass.[30]

Mechanical testing of Optocal and wax tablets

Mechanical testing of Optocal and wax tablets was performed using a texture analyzer (TA-XT Plus; Stable Micro Systems, Surrey, UK). The materials were placed on a flat table and were crushed (Optocal) or cut (wax tablet) using a wedge (30˚ cutting angle) with a compression speed of 40 mm s^{-1}. We determined the force needed to crush or cut the materials. Five samples of Optocal cubes and twenty samples of wax tablets were measured. The wax tablets were measured in batches of five at 20, 25, 30, and 35˚C.

Maximum bite force

Maximum vertical interocclusal bite forces were measured using a bite force transducer. The device consists of one (unilateral) strain gauge mounted on a mouthpiece. The strain gauge element was placed between the lower first molar to measure the interocclusal forces. The strain gauge has a surface area of 100 mm^2 and a vertical height of 2.8 mm.[26] The bite force experiments consisted of four tasks: clenching, as hard as possible, twice on the right side of the jaw and twice on the left side of the jaw. The highest bite force of the right side and the highest bite force the left side were the maximum bite forces used in this study.

Statistical procedures

Analysis of variance (ANOVA) was applied to test the null hypothesis that there would be no statistical difference between the three groups in the outcomes of the comminution test (15 chewing strokes on Optocal) and the mixing ability tests (5, 10, 15, and 20 chewing strokes on a wax tablet). Subsequently, *post hoc* tests (least significant difference multiple comparison tests) were used for pairwise comparisons of the groups. We calculated Pearson correlations between maximum bite force and the chewing efficiency values (outcomes of Optocal and 5, 10, 15, and 20 chewing strokes on a wax tablet). A *p*-value less than 0.05 was considered statistically significant. All analyses were performed with SPSS 15.0 software (SPSS, Chicago, IL, USA).

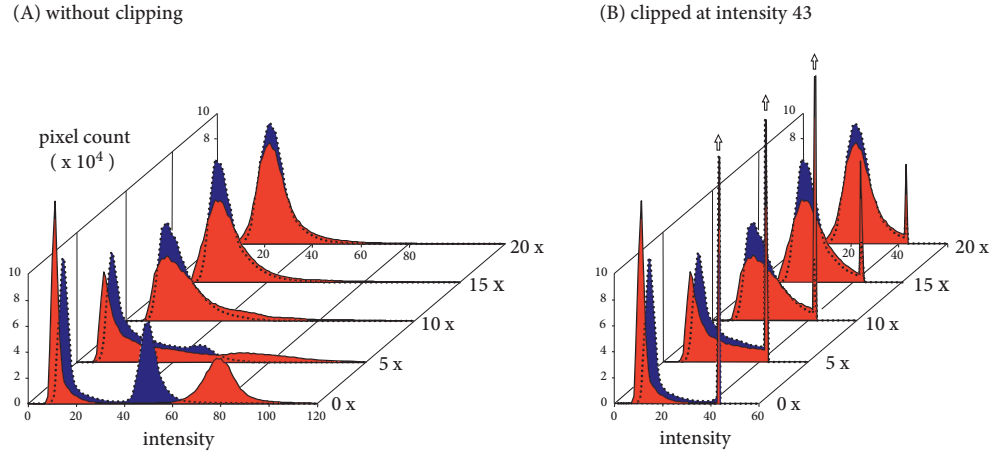


Figure 2. (A) Intensity distributions of red and blue light in the wax image after 0, 5, 10, 15, and 20 chewing strokes carried out by a dentate subject. (B) After reducing intensities exceeding 43 to 43.

Results

Figure 2A shows how chewing reduces the spread of the intensities of red and blue light in the wax image. One tablet was not chewed and four were chewed with 5, 10, 15 and 20 strokes, respectively, by a dentate chewer. On the unchewed tablet, which has a red and a blue side, both light distributions show a peak at high intensities (red 80, blue 50) and a peak at low intensities (red 11, blue 15). After mixing the wax with five chewing strokes, the high-intensity peaks have largely disappeared, whereas the intermediate regions rose and fused

with the low-intensity peaks. Chewing for longer made the distributions unimodal and the tails with high intensities continued to shorten. After twenty strokes, the distributions were nearly symmetrical with the maximum at about 22. These results showed that mixing the wax by chewing not only removes high light intensities from the wax image, but also makes the image darker, in general.

Table 2. Pearson correlations among the comminution test, the mixing ability test, and maximum bite force for all 60 subjects

	Optocal	*p*-value	Wax 5x	*p*-value	Wax 10x	*p*-value	Wax 15x	*p*-value	Wax 20x	*p*-value
Wax 5x	0.52	0.000	-	-						
Wax 10x	0.57	0.000	0.67	0.000	-	-				
Wax 15x	0.66	0.000	0.64	0.000	0.76	0.000	-	-		
Wax 20x	0.60	0.000	0.62	0.000	0.79	0.000	0.86	0.000	-	-
Maximum bite force	-0.73	0.000	-0.41	0.001	-0.41	0.001	-0.54	0.000	-0.50	0.000

First of all, we looked at the sum of the standard deviations (SDs) of the red and blue light distributions as mixing index. The highest correlation was found to occur between the tests with 15 and 20 chewing strokes ($r = 0.71$, $p < 0.001$); the test with five chewing strokes showed no significant correlation with the wax-mixing tests that had more strokes. However, we found that attenuating high intensities with respect to low intensities, before computing the SDs, improved the correlations between all the tests. We tried a series of tonal curves that lower high intensities. The mixing indices described here were obtained after clipping at intensity 43, (i.e. reducing to 43 all the intensities of red and blue light that are higher than 43) (Figure 2B). This increased the correlation between the tests with 15 and 20 chewing strokes from $r = 0.71$ to 0.86, ($p < 0.001$), and the results with five chewing strokes became significantly correlated with the other wax-mixing tests (Table 2).

Figure 3 shows the mean mixing index of the three subject groups as a function of the number of chewing strokes. The decrease in mixing index showed that more chewing strokes led to better mixing of the wax. The lower line shows that dentate subjects mixed the red and blue wax layers better than the denture wearers. Furthermore, when the wax was chewed 15 or 20 times, the mixing ability test was able to discriminate between the chewing performances of the two denture-wearer groups.

Table 3. Masticatory performance by wax mixing and Optocal test and maximum bite force for the three groups of subjects.

	Group A†	Group B†	Group C†	F-value‡	*p*-value‡	*p*-value A-B§	*p*-value A-C§	*p*-value B-C§
Wax 5x	24.3 (1.9)	25.3 (2.0)	27.0 (2.4)	8.2	0.000***	0.140	0.000***	0.015*
Wax 10x	20.4 (2.9)	22.7 (2.4)	24.1 (3.1)	9.0	0.000***	0.014*	0.000***	0.101
Wax 15x	18.3 (2.0)	20.4 (2.3)	22.2 (3.4)	11.0	0.000***	0.015*	0.000***	0.033*
Wax 20x	15.8 (2.0)	18.5 (3.1)	21.2 (3.6)	16.3	0.000***	0.006**	0.000***	0.006**
Optocal (mm)	3.3 (0.7)	5.0 (1.0)	5.3 (0.7)	35.2	0.000***	0.000***	0.000***	0.217
Maximum bite force (N)	439 (177)	141 (54)	89 (73)	54.1	0.000***	0.000***	0.000***	0.161

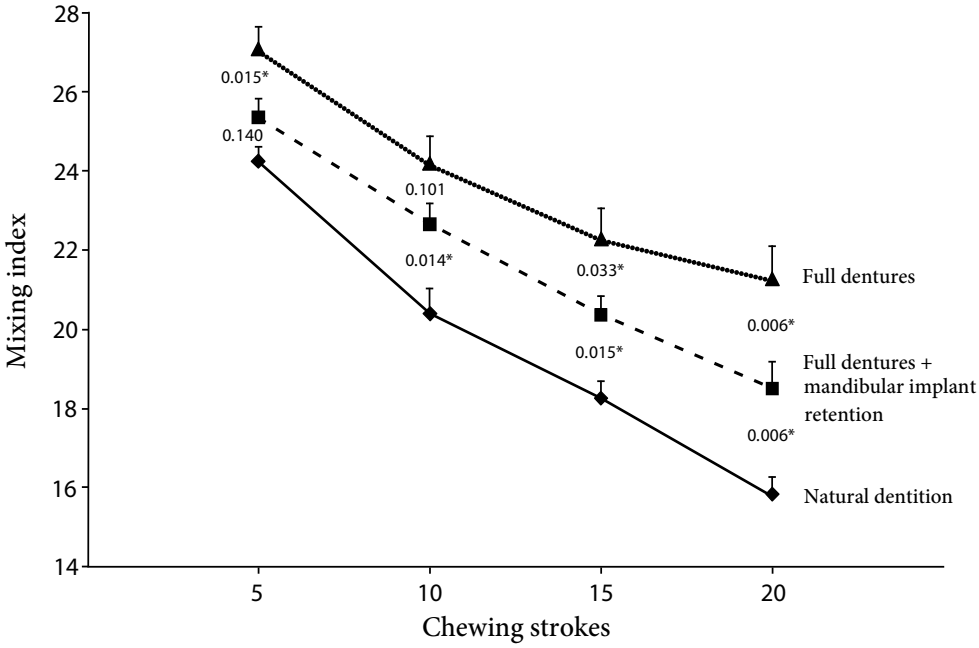
Group A: natural dentition.
Group B: maxillary denture and implant-supported mandibular overdenture.
Group C: full denture.
† Data are presented as mean (standard deviation)
‡ F- and *P*-values of between-subjects effects, determined using analysis of variance (ANOVA)
§ *P*-values of post hoc pair wise group comparisons, determined using ANOVA
*: $p < 0.05$; ** $p < 0.01$; ***: $p < 0.001$

Table 3 presents the averaged results of the wax-mixing tests, the Optocal comminution test and the bite force measurements for the three subject groups. Differences between the three groups were larger for the comminution test than for the wax-mixing test, which can be seen from the F-values in Table 3. The comminution test shows significantly better masticatory performance in dentate subjects than in denture wearers with and without mandibular implant retention. However, the comminution test revealed no significant differences between the groups of denture wearers. By contrast, the mixing ability test demonstrated significant differences between the two denture groups after 15 and 20 chewing strokes. In general, the maximum bite force was significantly higher in the dentate subjects than in the two groups of denture wearers. No significant difference in bite force was observed between the two groups of denture-wearers.

The results of the wax-mixing ability tests were significantly correlated with the Optocal comminution test (Table 2). Furthermore, maximum bite force had a significant influence on the chewing performance, as measured using the comminution as well as the mixing ability test. The negative sign of the correlation indicates that better chewing performance, and thus smaller median particle size or mixing index, was observed for subjects with a higher maximum bite force.

Mean (SD) objective hardness scores of the wax tablet were 99.7 (± 3.3), 82.8 (± 3.6), 64.6 (± 2.2), and 47.8 N (± 1.9) for 20, 25, 30, and 35˚C, respectively. The hardness score of an Optocal cube was 53.6 N (± 3.9).

Figure 3. Mean (standard error of the mean) results of the mixing ability test for various numbers of chewing strokes for the three groups of subjects.



The *p*-values by were obtained by analysis of variance (ANOVA); *: $p < 0.05$ (see Table 3)

Discussion

The results of our chewing tests indicated that the mixing ability test is capable of discriminating the masticatory performance between different groups of subjects with compromised oral function. The results of the mixing ability test indicate that denture wearers with implant support have a significantly better masticatory performance than the full denture wearers according to the mixing ability test. No significant difference in chewing performance between the two denture groups was detected from the results of the comminution test.

Both groups of denture wearers were barely able to comminute the Optocal cubes. The median particle size of Optocal, after 15 chewing strokes, was 5.0 mm for the denture wearers with implant retention and 5.3 mm for those without implant retention. Thus, after chewing,

the Optocal particles were, on average, only slightly smaller than the Optocal cubes before chewing (5.6 mm). Apparently the task of fragmenting the Optocal cubes was too difficult for both groups of denture wearers. The force needed to fragment one cube of Optocal is 53 N. The maximum bite force of full denture wearers with and without implant retention is, on average 141 and 89 N respectively. Thus, with maximum effort denture wearers are able to fragment only two or three Optocal particles at a time. When more particles are present between the opposing teeth no fragmentation will occur. Precise manipulation of a large number of Optocal particles has proved to be difficult for denture wearers.[16] Particles may end up under the mandibular prosthesis, thus preventing further chewing. Previous studies have shown a better discrimination of median particle sizes between full denture wearers with and without mandibular implant support after more than 15 chewing strokes.[15,31] Thus, if patients had chewed longer on the Optocal particles, we might have detected larger differences in median particle sizes between our two denture wearer groups. However, chewing for longer has the disadvantage that median particle sizes of dentate subjects reach a lower limit of about 1 mm and no longer decrease upon further chewing.[15] Therefore, the number of chewing strokes should not be too high. In a recent study we determined masticatory performance before and after implant treatment.[17] In that study, patients chewed 15 and 30 chewing strokes on Optocal. The study showed that 15 chewing strokes was an adequate number. Based on this finding, we chose for 15 chewing strokes as an optimal compromise for the three groups of subjects. In contrast with denture wearers, dentate subjects were able to comminute Optocal with ease. After 15 chewing strokes, the median particle size had been reduced to nearly half its original size. Thus, for subjects with a normal masticatory performance, the comminution test is an easy and reliable way of determining the ability to fragment a food.

In the mixing ability test, when subjects chewed at least 15 times on the wax tablet, significant differences in masticatory performance were observed between all three groups. As seen from the results shown in Figure 3, the wax mixing index decreases as a function of the number of chewing strokes for all three groups, which indicates that the two colours of the wax become mixed more thoroughly. A clear and significant difference was observed between the two groups of denture wearers. Implant retention of the denture had a significant, positive effect on the ability to mix the two colours. Thus, in contrast to the comminution test, the mixing ability test is a suitable test for measuring differences in masticatory performance for groups of subjects with compromised oral function. Our results confirm previous

studies in which the mixing ability test was reported to be capable of detecting changes in masticatory function.[24,32] However, it should be noted that the overall discrimination among the three groups of subjects, indicated by the F-values of the ANOVA test, was better for the comminution test than for the mixing ability test (Table 3). Using a softer test food that can be more easily fragmented may lead to a better discrimination of masticatory performance among groups with compromised masticatory performance.

Denture wearers were able to deform and mix the two colours of the wax tablet, even though they have relatively low masticatory forces. The force needed to deform the wax tablet decreases from 99.7 N at 20˚C to 47.8 N at 35˚C. Thus, at the start of the chewing process when the wax is at room temperature subjects needed up to 100 N to mix the two colours of the wax. After a few chewing strokes, less force is needed because the wax bolus warms up in the mouth. Thus, the hardness of the wax tablet is well below the maximum bite force of the denture wearers, so they will be able to knead the wax. Offering wax tablets at a higher temperature may be useful when studying mixing ability in groups of patients with severely compromised masticatory performance. At higher temperatures, the wax tablets will be softer and easier to mix. Salleh et al.[22] found comparable forces required to deform the wax in their mixing ability test: 32.6 N at 37˚C.

In comminution tests the food is fragmented and after some chewing strokes large numbers of food particles will be present. Manipulation of the food particles may be a problem for patients with compromised oral function caused by, for example, dental status,[16] muscle disease,[33] or oncological intervention.[4] In some studies this problem was solved by putting the test food in a finger cot, to keep the fragmented particles together.[33,34] The mixing ability test has the advantage that the wax forms one bolus. Therefore, manipulation of the food is relatively easy, which makes the test food more suitable for subjects with compromised oral function. Occasionally, denture wearers complained about a wax bolus sticking to the denture, but this was not a major problem. The mixing ability test was also found to be suitable for measuring differences in masticatory performance of subjects with normal oral function.

Significant correlations, of between 0.52 and 0.66, were observed between the comminution test and the colour mixing tests. Comparable results were recently reported.[23] The internal correlations among the results of the mixing test after the various numbers of chewing strokes were higher (between 0.62 and 0.86). The highest correlation, 0.86, was observed after

15 and 20 chewing strokes. Thus, the mixing test becomes more reproducible after at least 15 chewing strokes. This concurs with the results shown in Figure 3. The best discrimination among the three groups of subjects was observed after chewing 20 times on the wax tablets. The correlation between the maximum bite force and the comminution test was higher than the correlation between maximum bite force and mixing index (Table 2). This difference in correlation may be explained by the fact that the comminution test requires higher bite forces than the mixing ability test.

Based on the results of this research, we expect that the mixing ability test will be useful for evaluating masticatory performance of patients with oral cancer. The two-colour wax is easy to chew and forms one bolus. We therefore conclude that the mixing ability test is more suitable for, and discriminates better between, persons with compromised masticatory performance than the comminution test.

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4

Digital image processing versus visual assessment of chewed two-colour wax in mixing ability tests

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Abstract

Two-coloured chewing gum and wax have been widely used as test foods to evaluate the ability to mix and knead a food bolus. The mixing of the colours has been assessed by computer analysis or by visual inspection. Reports contradict each other about whether computer analysis and visual assessment could equally well discriminate between the masticatory performances of groups of participants with different dental status. This study compares the results of computer analysis of digital images of chewed two-colour wax with the results of visual assessment of these images. Sixty healthy subjects participated and chewed on red-blue wax for 5, 10, 15 and 20 chewing strokes. The subjects were divided in three groups of 20, matched for age and gender, according to their dental status: natural dentition, full dentures and maxillary denture plus implant-supported mandibular overdenture. Mixing of the chewed wax was determined by computer analysis of images of the wax and by visual assessment of the images by five examiners. Both the computer method and the observers were able to distinguish the group with natural dentition from the denture wearer groups. However, computer analysis discriminated the mixing abilities of the two denture groups much better than the observers.

Introduction

During chewing, food is reduced in size, while saliva moistens the food and binds the masticated food into a bolus that can be easily swallowed. Masticatory performance has often been measured by determining an individual's capacity to grind or pulverize a test food after a fixed number of chewing cycles.[1] The degree of breakdown of a food was determined by sieving the comminuted food. Another method to determine masticatory performance, which is now widely used, evaluates the ability to mix and knead a food bolus. Two-coloured chewing gum[2-6] and paraffin wax[7-14] have been used as test foods for the quantification of masticatory performance. Validity and reliability studies have shown that mixing ability tests are a reliable alternative to comminution tests.[11,12] The degree of mixing of the two colours has been determined by computer analysis of digital images of the chewed wax,[3,7,12] by visual inspection[2] or by both.[3,4] Digital images of both sides of the chewed bolus were captured using a digital camera[3,7] or a flatbed scanner.[4,12] Before scanning the chewed bolus samples must be flattened to avoid shadows in the image by the oblique illumination of the scanner's lamp. Flattening of the chewed bolus did not have a significant effect on the degree of colour mixing as determined from image analysis, but it did increase the accuracy of subjective evaluation.[3] Computer analysis can determine various parameters from the digital images, such as areas of unmixed colours,[4,7] size of separate colour areas (spatial frequency analysis),[3] maximum length and width of chewed bolus,[7] and intensity distributions of colours.[12] These variables or a combination of variables were used as a measure for the mixing of the wax. Visual assessment was done by visual inspection of both sides of the chewed bolus and scoring the degree of mixing into categories according to reference examples[2,4] or by ranking a set of samples.[3] Visual assessment of two-colour chewing gum (ten healthy fully dentate subjects) was reported to have similar accuracy as image processing of the chewed gum.[3] However, contradicting results were reported in a later study on two-colour chewing gum (twenty healthy fully dentate subjects): visual assessment appeared to be less reliable than digital image processing, but it might still be useful in screening for chewing deficiencies in a clinical setting.[4] In that study all chewed samples were assessed by two independent operators, both as 'chewed bolus' and as flattened 1 mm thick 'wafers'. Subjective assessment proved less accurate for 'bolus' than for 'wafer'. Although substantial agreement was observed between examiners, it was not clear from this study whether digital image processing and visual assessment could equally well discriminate between the masticatory performances of

groups of participants with different dental status.

The objective of this study was to compare the results of computer analysis of digital images of chewed two-colour wax with the results of visual assessment of these images. In a previous study two-colour wax was chewed by participants of three dentition groups: subjects with a full natural dentition; subjects with complete dentures with mandibular-implant support; and subjects with complete dentures.[12] The digitized images of the chewed wax were processed and a measure for the mixing of the wax was determined from the intensity distributions of the mixed colours. In this study the degree of colour mixing of the same digital images was rated into categories by five examiners according to reference samples. We hypothesized that computer analysis and visual assessment of the digital images of chewed two-colour wax would discriminate equally well between the three dentition groups.

Materials and Methods

Subjects

Tablets of two-coloured wax were chewed by 60 healthy participants divided in three groups of 20 subjects (matched for age and gender) based on their dentition: natural dentition, maxillary dentures plus implant supported mandibular overdentures, and full dentures. The experimental protocol was approved by the Ethics Committee of University Medical Center Utrecht. All subjects received a written explanation of the study, and informed consent was obtained from each subject before the start of the study.

Mixing ability test

The mixing ability test measures how well a participant mixes a tablet (diameter 20 mm), which consists of a red and a blue wax layer (3 mm each), by chewing on it. The spread of the colour intensities in the combined image of both sides is the measure of mixing. If the wax tablet has not been chewed, one side is red and the other blue, and the spread of the intensities of both colours is maximal. Chewing the tablet mixes the colours, intermediate intensities appear and the spreads of the intensities decrease. Each participant chewed four sequences on a wax tablet, with, respectively 5, 10, 15, and 20 chewing strokes. The degree to which the colours were mixed, was determined by an optical method, which has been described in detail in a previous article, so only a short outline is given here.[12] The chewed wax was rinsed, brought to a temperature of 28°C and placed between two sheets of stiff and clear

foil. The sandwich of foil and wax was pressed between two thick brass plates and pressed to a thickness of 2.0 mm. Then, both sides of the wax were optically scanned using a high-quality scanner (Epson® V750, Long Beach, CA, USA). The images of the wax were processed using Adobe Photoshop, CS3 extended (Adobe, San Jose, CA, USA). Because the wax is red and blue only, its image in the green channel is a dark blob on a brighter background. Occasional bright patches in the wax indicated where it had not been in contact with the foil as a result of inclusion of air during flattening. Using the Magic Wand tool, applied at a dark spot in the centre of the wax image, this was isolated from the entire image, leaving out the air bubbles. The exclusion of air bubbles can be seen as "holes" in the example wax images shown in Figure 1. The intensity distributions of the red and blue channels were exported as histograms. The histograms of both sides of the wax were added to obtain the red and blue intensity distributions of the combined image of both sides of the flattened wax. These histograms were analyzed to obtain a measure for the mixing of the wax: the mixing index.

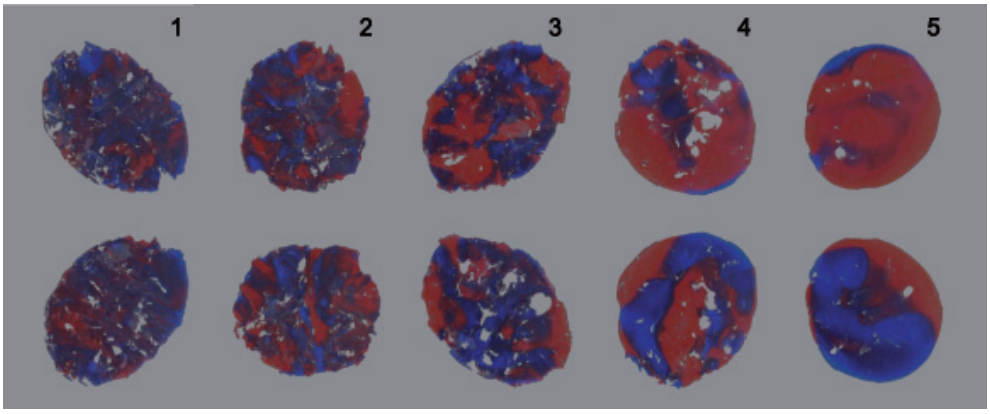

Figure 1. Examples of digitized images of chewed and flattened two-colour wax. The examiners rated the images according to these examples; 1: very well mixed, only very small areas of red and blue visible plus intermediate colour (purple); 2: well mixed, only small areas of red and blue and some intermediate colour; 3: intermediately mixed, red and blue ares clearly visible; 4: badly mixed, 3 to 5 separate red and blue areas visible; 5: very badly mixed, 1 or 2 separate red and blue areas visible.

Statistical procedures

Intra- and inter-observer agreement among the scores of the examiners was measured with Cohen's kappa. Normality of the mixing index and average observer ratings were tested with the one-sample Kolmogorov-Smirnov test. Furthermore, we calculated Pearson correlations between the mixing index and average observer scores. Repeated measures analysis of variance

(ANOVA) was used to determine the overall influence of the within-subject factor number of chewing strokes (5, 10, 15 or 20) and the between-subject factor participants group (natural, implants, full denture) on the outcomes of the mixing index (computer) and of the average observer scores. Subsequently, *post hoc* tests (least significant difference multiple comparison tests) were used for pair wise comparisons of the groups. Furthermore, we used separate one-way ANOVA's to determine the influence of the between-subject factor participants group on the outcomes of the mixing index and of the average observer scores after a fixed number of chewing strokes (5, 10, 15 or 20). A p-value less than 0.05 was considered statistically significant. All analyses were performed with SPSS 15.0 software (SPSS, Inc., Chicago, IL, USA).

Visual assessment

The 240 images of chewed wax (60 participants and 4 chewing sequences: 5, 10, 15 and 20 chewing strokes) were randomized and then rated by five examiners at separate occasions. The wax images were shown on a computer screen and the examiner could proceed at their own pace while scoring the images. At least 1 month later the examiners rated the wax images for the second time. The examiners rated the images of the chewed wax in five categories: 1: very well mixed, only very small areas of red and blue visible plus intermediate colour (purple); 2: well mixed, only small areas of red and blue and some intermediate colour; 3: intermediately mixed, red and blue are clearly visible; 4: badly mixed, 3 to 5 separate red and blue areas visible; 5: very badly mixed, 1 or 2 separate red and blue areas visible. The rating was performed based on the examples given in Figure 1.

Results

The agreement in observer scores of the first and second rating session for all 240 images varied between $\kappa = 0.70$ and $\kappa = 0.78$ ($p < 0.001$; substantial agreement) for the 5 examiners. Slightly smaller Cohen's kappa's, but still highly significant agreement scores, were observed among the 5 examiners, $0.55 < \kappa < 0.65$ ($p < 0.001$; moderate to substantial agreement). Average mixing scores were calculated for the 5 observers and 2 replicate measurements. One-sample Kolmogorov-Smirnov tests showed that both the average observer scores and the mixing index obtained from the computer analysis were normally distributed. Figure 2 shows the average observer scores as a function of the mixing index obtained from the computer analysis for all 240 images.

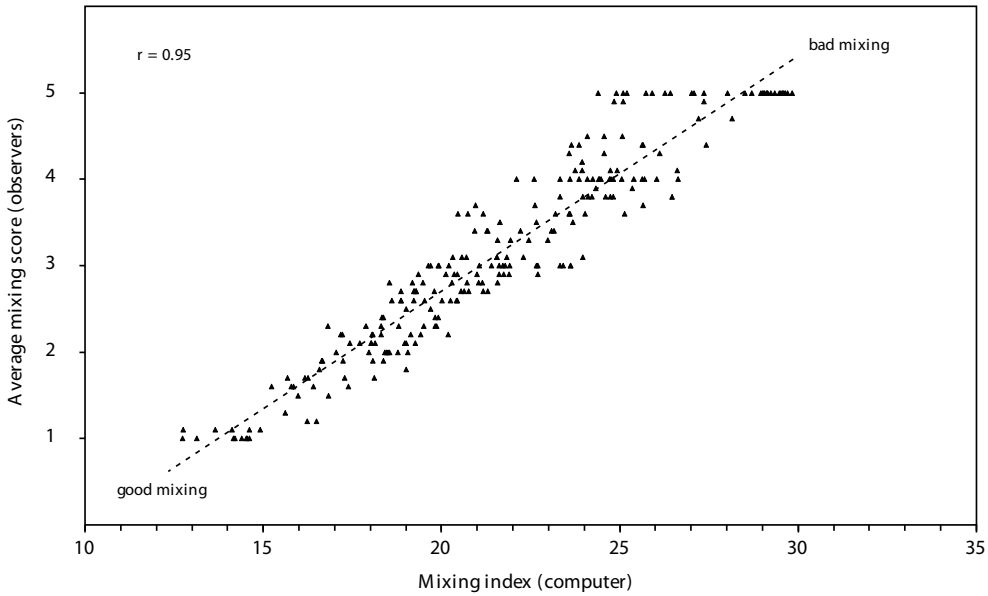

Figure 2. Average observer scores as a function of the mixing index obtained from the computer analysis for all 240 images. The correlation between the two variables was highly significant (r = 0.95, $p < 0.001$). At the lower left corner the data points represent the results of the images of very well mixed wax and at the upper right corner of very badly mixed wax.

The correlation between the two variables was highly significant (r = 0.95, $p < 0.001$). At the lower-left corner of Figure 2 the data points represent the results of the images of well mixed wax and at the upper-right corner of badly mixed wax. Clusters of data points are visible at integer numbers of the mixing score assessed by the observers, especially at the values 4 and 5 (bad mixing). Figure 3 shows measures of the masticatory performance of the three groups of participants as a function of the number of chewing strokes. In the upper figure (a) the mixing index as determined from the computer analysis is shown, whereas in the lower picture (b) the results obtained from the visual assessment of the 5 examiners is depicted. Both pictures show that more chewing strokes lead to better mixing of the wax (lower values of mixing index and mixing score; $p < 0.001$). The line representing the dentate participants is lowest in both figures, which means that both methods indicate a better mixing ability for these subjects than for the two groups of denture wearers. *P*-values indicating statistical differences at various numbers of chewing strokes are given in Figure 3. Furthermore, the computer method was able to discriminate between the chewing performances of the two denture-wearer groups, when the wax was chewed 5, 15 or 20 times (upper figure), whereas

the visual assessment method could only discriminate the results of the two denture wearer groups after 20 chewing strokes (lower figure). Repeated measures analysis results, indicating possible statistical differences between the groups based on 5, 10, 15 and 20 chewing strokes, are given at the right side in the two figures. From these *p*-values it can be seen that examiners could not discriminate between the two denture groups ($p = 0.273$).

Discussion

Computer analysis of digital images of chewed two-colour wax discriminated between the mixing abilities of all three groups of participants. Visual assessment of the images discriminated between the results of the group with natural dentition and the two denture-wearer groups. However, the visual examiners could not distinguish between the mixing abilities of the complete-denture wearers and the denture wearers with mandibular implant-supported overdentures.

Intra-examiner agreement was high for all examiners, which indicates that the examiners were able to rate the images in a consistent way. Inter-examiner agreement was also high, which means that examiners rated the images in a comparable way. High intra- and inter-examiner agreement was also reported for the rating of chewed and flattened two-colour chewing gum.[4] This agreement indicates that examiners are able to score the digital images in a predictable and consistent way, but gives no information on how well the examiners perform the test in comparison with image processing.

Figure 2 gives a detailed picture of the relationship between the averaged examiner scores and the computer analysis results for the 240 digital images. The results of the badly mixed wax are depicted in the upper-right corner. Thirty-one images were unanimously given the maximum score of 5 (very badly mixed) by the examiners, whereas the computer index showed a large variation for these images, the index ranging from 24.4 up to 29.8 (cluster of data points at horizontal line). Apparently, the computer program detected differences in the images, whereas all observers gave these images the maximum score. Comparable results were seen for observer scores of 4 (badly mixed; 19 points) and 3 (intermediately mixed; 17 points). Less clustering of observer scores was seen in the lower left corner for scores 2 (well mixed) and 1 (very well mixed).

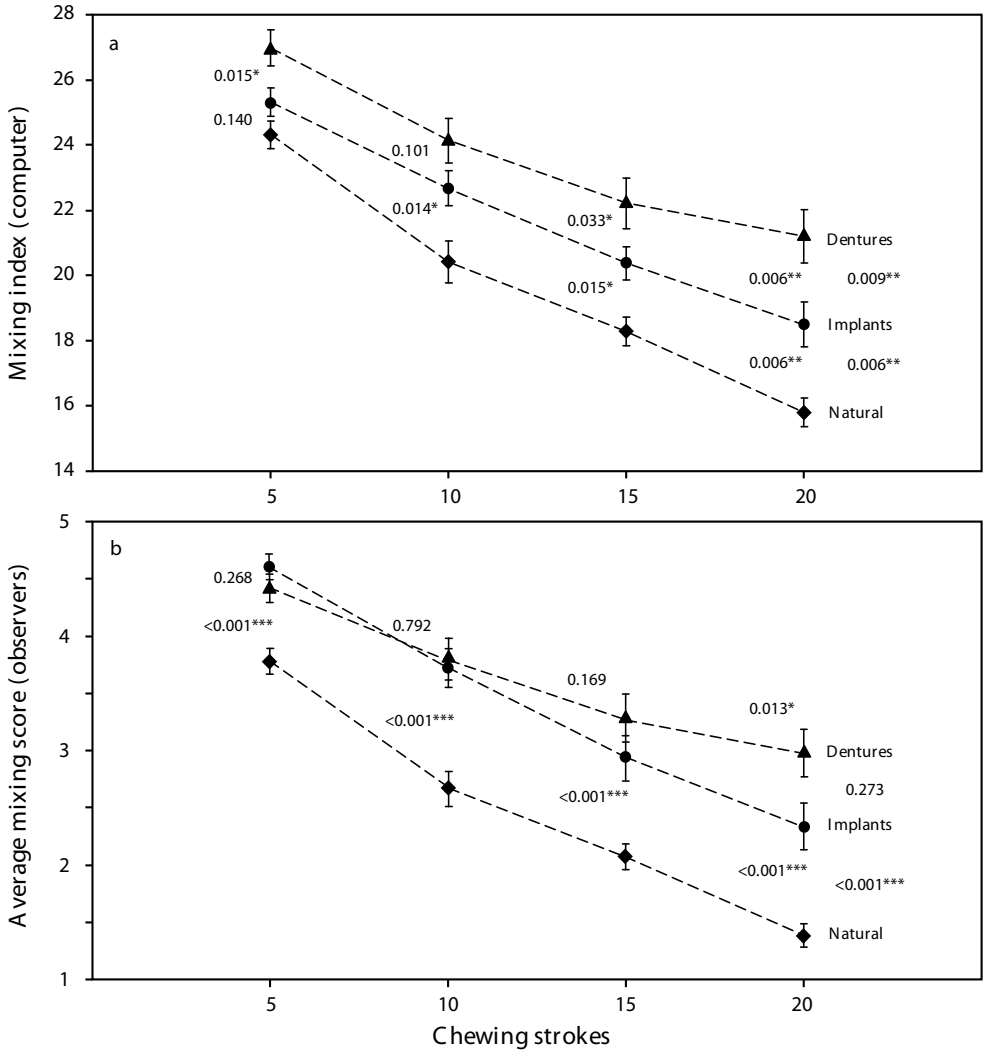

Figure 3. Mean (standard error of the mean) results of the mixing index (computer analysis; upper figure) and mixing score (average of 5 examiners and 2 replicate assessments; lower figure) as a function of the number of chewing strokes for the three groups of participants. More chewing strokes lead to significant better mixing of wax for both methods ($p < 0.001$). The computer method could discriminate between the mixing ability of the two denture groups ($p = 0.009$; repeated measures ANOVA), whereas examiners were unable to detect a significant difference ($p = 0.273$). The values near data points represent possible statistical differences (p-values) obtained from separate one-way ANOVA tests. The line representing the dentate participants is lowest in both figures, which indicates a better mixing ability for these subjects than for the two groups of denture wearers.

Measures of mixing ability of the three groups of participants are plotted as a function of the number of chewing strokes (Figure 3).

The figure clearly illustrates that computer analysis of the digital images could very well discriminate the mixing abilities of the full denture wearers (upper line) and the full denture wearers with mandibular implant support. In contrast, the observers were not able to distinguish the mixing ability results after 5, 10 and 15 chewing strokes; the lines representing the results of the two denture wearer groups coincide. Only after 20 chewing strokes a significant difference between all three groups could be detected by the observers. On the other hand, observers were good in detecting differences in mixing ability between the participants with a full natural dentition and participants with mandibular implant supported dentures ($p < 0.001$).

To understand the differences in the results of the computer analysis and visual assessment by the observers, we performed a detailed inspection of the digital images, especially those where the differences were large. We noticed that chewing the wax results in two ways of mixing the red and blue colours. The red and blue wax can be pressed together and fuse into a darkish purple tint, and the wax can be cut up and rejoined resulting in intermingled patches of red and blue. Fusion of the colours decreases the spread in intensities of red and blue and therefore the mixing index. When the wax is cut up and rejoined, fusion of the colours also occurs, along the boundaries between red and blue patches, and the appearance of the wax changes considerably.

Denture wearers often could not cut up the wax or just little, particularly with a limited number of chewing strokes. Instead they pressed, to a greater or lesser degree, the red and blue sides of the tablet together between the teeth. This could result in fused, purplish areas on both sides of the wax, although the images of the two sides remained generally red and blue respectively. The observers rated these images as badly mixed and are not able to discriminate between the two denture-wearer groups. The computer analysis, however, picked up the difference in colour fusion between the two denture-wearer groups, even after just five or ten chewing strokes. With more chewing strokes the denture wearers produced more heterogeneously coloured images of the two sides of the wax, particularly the group with mandibular-implant supported overdentures. Eventually, judging from images of wax that has been chewed with 20 strokes, the observers scored the wax mixing by the group with mandibular-implant support better than the full dentures group without implants.

The subjects with a natural dentition were always able to cut up the wax, even after just five chewing strokes, in all cases except one. The observers rated the intermingling of red and blue patches as a better chewing result than that of the denture wearers. Likewise, the computer analysis resulted in lower (better) mixing indices due to the colour fusion between the red and blue patches.

This study indicates that observers have difficulty assessing wax mixing that results from fusion of red and blue wax into purple-coloured wax. Instead, they appear to rate the heterogeneity of the wax image, the extent to which red and blue areas are intermingled. With participants with compromised oral function, such as denture wearers, a limited number of chewing strokes results in wax images with too little heterogeneity for the observers to be able to distinguish between different groups of these participants. Therefore, if wax-mixing is to be assessed by visual examination, it is recommended that participants chew the wax 20 times. Figure 3 shows that both the computer analysis and observer assessment improve when the number of chewing strokes increases, as the results of the three groups of participants become better separated. Beyond 20 chewing strokes it is not known, however, until what number of strokes the curves of the three groups keep diverging.

The computer analysis used in this study does not use spatial information about the wax images. The observers, however, do and although they have difficulty assessing wax-mixing in badly chewed wax tablets, they still are able to discriminate between participants with and without impaired oral function. The digital processing technique may improve when information about the spatial heterogeneity of the wax image, for example like the frequency analysis described by Prinz,[3] were added to the analysis of the variation in light intensities in the wax image.

Acknowledgements

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5

Mastication in patients treated for malignancies in tongue and/or floor of mouth: a 1-year prospective study

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Abstract

Background: People confronted with oral cancer run a high risk of deteriorated masticatory performance. Reduced masticatory function may affect quality of life and food choice. An altered food choice may result in lower intakes for key nutrients and weight loss.

Methods: Dental state, bite force, and masticatory performance were determined in a group of 45 patients with squamous cell carcinoma of tongue and/or floor of mouth. Measurements were performed before surgery and at various moments after surgery and/or radiotherapy.

Results: Surgical intervention had a large negative impact on oral function. Radiotherapy further worsened oral function. Also, the recovery of oral function 1 year after surgery was less prominent for the surgery-radiotherapy group than for the surgery group.

Conclusion: Objective determination of oral function 1 year after surgery showed that patients treated for malignancies in tongue and/or floor of mouth had significantly deteriorated masticatory performance, bite force, and dental state.

Introduction

People confronted with oral cancer run a high risk of deteriorated masticatory performance. This deterioration may be caused by the tumour itself, but it may also be induced by the treatment prescribed. The treatment of oral cancer is primarily focused on maximizing survival and loco-regional control while trying to preserve or restore "normal" oral function and quality of life. Progress in (reconstructive) surgery and radiotherapy has made it possible to improve survival and reduce oral functional deficits.[1] Despite this progress patients still have diminished or lost essential oral functions.[2] Surgery in the tongue and/or floor of mouth results in defects of soft tissues, dentition, and sometimes bone of the mandible, which may lead to impairment of mastication.[3] Although head and neck surgeons try to restore oral function by reconstructive surgery, patients still report deterioration in dentition and mastication 5 years after oncological intervention in the oral cavity.[4] Radiotherapy may lead to tissue fibrosis, osteoradionecrosis, and accelerated dental caries, which often results in the preventive extraction of several teeth during surgery.[5] All these conditions have a negative effect on the quality of mastication in patients receiving oral oncology.

Oral function in patients treated for oral oncology has often been determined from quality of life (QoL) questionnaires, such as the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Head and Neck 35-questions (EORTC QLQ-H&N C30) and the University of Washington Quality of Life (UW-QoL) questionnaire. An increasing number of studies have measured QoL as an end point in the evaluation of the impact of the disease and its treatment on the patient's daily life. The above mentioned questionnaires measure self-assessed oral function. The outcomes are based on experiences of a patient, and thus the questionnaire gives the patient's subjective impression of daily oral function. However, objective information obtained from measurements of oral function may be different from personal experiences. The outcomes of objective measurements will complement the knowledge of oral function in patients receiving oral oncology and may help in further development of rehabilitation of these patients. It will supply new information about the severity of the affected oral function. Therefore, it is important to evaluate oral function objectively, so that the degree of deterioration of oral function as a result of the oral oncological intervention can be quantified.

An optimal dental state is a prerequisite for an adequate masticatory performance.[6] Furthermore, maximum voluntary bite force is an important variable for assessing the

functional state of the masticatory system. It is reduced, for example, when natural teeth have been replaced by complete dentures[7] or implant-retained overdentures.[8] Bite force explains over 60% of the variance in masticatory performance in healthy persons.[9] Another objective indicator is a test in which the subject chews on a wax tablet, mixing 2 layers of different coloured wax in the tablet. To measure masticatory performance, this wax-mixing ability test has been shown to be particularly well suited for patients with compromised oral function.[10]
The purpose of this prospective cohort study was to examine the effect of "oral oncological surgery only" and "oral oncological surgery combined with radiotherapy" on objective, mastication related measures (i.e., dental state, maximum bite force, and masticatory performance) in patients with malignancies in the tongue and/or floor of mouth. Measurements were performed 4 weeks before surgery, shortly after surgery (4-6 weeks), shortly after radiotherapy (4-6 weeks), half a year, and 1 year after surgery. We analyzed whether tumor size, tumour location, and surgical intervention were related to changes in dentition, maximum bite force, and masticatory performance due to surgical intervention. Furthermore, we determined relationships between the changes in dental state, maximum bite force, and masticatory performance. Finally, we compared the outcomes of the included patients with outcomes of healthy controls.
Our hypothesis was that oral oncological treatment significantly deteriorates dental state, maximum bite force, and masticatory performance. Furthermore, we hypothesized that treatment of surgery and radiotherapy, as opposed to surgery only, has significantly more negative influence on dental state, maximum bite force, and masticatory performance.

Materials and Methods

Subjects

In the period from January 2007 to January 2008, a group of 45 patients with a diagnosed malignancy in the tongue and/or floor of mouth and a group of 60 healthy controls matched for age was recruited for this study. The group of healthy controls consisted of 3 subgroups of 20 subjects: a group with natural dentition (Group A), a group with maxillary dentures and implant-supported mandibular overdentures (Group B), and a full denture group (Group C). More details of the control group were published recently.[10] The experimental protocol was approved by the Ethics Committee of University Medical Center Utrecht and Radboud

University Nijmegen Medical Centre. All subjects received a written explanation of the study and informed consent was obtained from each subject before the start of the study.

Patients were eligible for this study if they had a primary malignant tumour in the tongue and/or floor of the mouth treated by surgery (with or without radiotherapy). Pretherapy oral screening and dental management was done in all patients before surgery. Postoperative radiotherapy was given within 6 weeks after surgery when indicated according to the treatment guidelines of the National Cooperative Head and Neck Oncology Group based on the histology of the resection specimen. Exclusion criteria were previous or synchronous malignancies, cognitive impairment, and inability to understand Dutch. Tumour stage, resection site, and reconstruction were collected from medical records. Patient characteristics are summarized in Table 1.

Table 1. Characteristics of the surgery group and the surgery-radiotherapy group.

	Surgery (N=23)	Surgery & Radiotherapy (N=22)	p-value
Pathalogical Tumour stage (pT)			
T1	18	5	
T2	5	9	0.001**
T3	0	4	
T4	0	4	
Resection site			
Tongue	17	10	
Floor of mouth	4	5	
Floor of mouth & Slice mandible	2	4	0.233
Tongue & Floor of mouth	0	2	
Tongue & Floor of mouth & Slice mandible	0	1	
Reconstruction			
Primary closure	17	5	
Local flap	1	0	0.001**
Myocutaneous or free flap	5	17	
Bone graft/flap	0	0	

* $p < 0.01$.

Note: Possible differences in number of patients in the 2 groups were tested by chi-square tests.

Measurements

Patients with a malignant tumour were measured maximal 4 weeks before surgery, shortly after surgery (4-6 weeks), shortly after radiotherapy (4-6 weeks), at half a year, and 1 year after surgery. Healthy persons were measured once. We determined the following variables: dental state, maximum bite force, and mixing ability.

Dental state

The dentitions of the upper jaw and the lower jaw were each scored on an ordinal scale, as shown in Table 2. The sum of the dentition scores of the upper jaw and lower jaw was used as an outcome measure of the dental state.

Maximum bite force

Maximum vertical interocclusal bite forces were measured using a bite force transducer. The device consists of 1 (unilateral) strain gauge mounted on a mouthpiece. The strain gauge element was placed between the first molars to measure interocclusal forces. The strain gauge has a surface area of 100 mm^2 and a vertical height of 2.8 mm.[7] The bite force experiments consisted of clenching teeth as hard as possible twice on the right side of the jaw and twice on the left side of the jaw. The presented outcome measure is the mean of the highest bite force of the left side and the highest bite force of the right side.

Mixing ability

Masticatory performance was measured with the mixing ability test. The test measures how well a subject mixes a tablet that consists of a red and a blue wax layer by chewing on it. The tablet has a diameter of 20 mm and consists of two 3 mm layers of red and blue wax. The chewed wax is flattened and photographed from both sides. The spread of the colour intensities in the combined image of both sides is the measure of mixing. If the wax tablet has not been chewed, 1 side is red and the other blue, and the spread of the intensities of both colours is maximal. Chewing the tablet mixes the colours, intermediate intensities appear, and the spreads of the intensities decrease. Each subject made 20 chewing strokes on a wax tablet. The wax tablets were offered at room temperature (20˚C). A detailed description of the mixing ability test was recently published.[10]

Statistical analyses

The presentation of results is primarily descriptive with means, SD, and SEMs. Characteristics of the patients of the surgery group and the surgery-radiotherapy group before intervention were compared by a Chi-square test. In each treatment group (i.e., the surgery group and the surgery-radiotherapy group), changes in time of dental state, maximum bite force, and mixing ability were analyzed by repeated measures analysis of variance (ANOVA) for continuous data and by a Friedman test for ordinal data. Repeated measures ANOVA and the Friedman test determine possible differences among all measurement moments. Therefore, these tests are susceptible for missing data, due to patients who died, stopped, or missed a measurement. To avoid this disadvantage, we also performed paired *t*-tests (continuous data) and Wilcoxon signed rank tests (ordinal data) to test differences between 2 measurement moments only. Differences among the surgery group, the surgery-radiotherapy group, and the healthy controls (3 groups) were analyzed by unpaired *t*-tests (continuous data) and Mann-Whitney U-test (ordinal data). One-way ANOVA was used to find possible significant explanatory factors for the change among outcomes of dental state, maximum bite force, and mixing ability before and shortly after surgery for all subjects. The Pearson (continuous data) and Spearman (ordinal data) correlations were used to analyze relationships among dentition, maximum bite force, and mixing ability before and shortly after surgery. A *p*-value less than 0.05 was considered statistically significant. All analyses were performed with SPSS 15.0 software (SPSS, Chicago, IL).

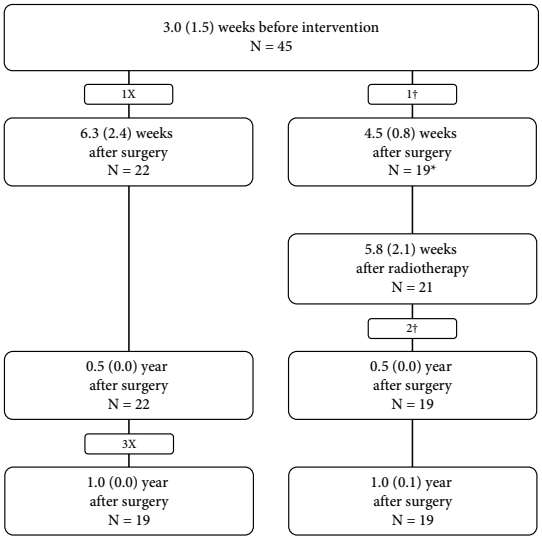
Results

Forty-five patients with a squamous cell carcinoma of tongue and/or floor of mouth, were included in this study. Twenty-three patients were treated by surgery only, 9 women and 14 men aged 63.9 ± 14.0 years (mean ± SD). Twenty-two patients were treated by surgery and radiotherapy, 6 women and 16 men aged 61.8 ± 10.0 years. Characteristics of pathological tumour stage[11] and surgical intervention are listed for both groups in Table 1. Chi-square tests revealed that patient numbers were significantly different for both intervention groups with respect to pathological tumour stage and type of reconstruction (Table 1). Before intervention dental state, maximum bite force, and mixing ability were not significantly different between the surgery group and the surgery-radiotherapy group.

A flow-chart of the measurements is depicted in Figure 1. Four patients stopped participation,

and 3 patients died within a year after surgery. One year after surgery, each group consisted of 19 patients. Two patients were not measured between surgery and the start of radiotherapy because of time constraints. Furthermore, 2 patients of the surgery group had an additional resection within a month after surgery. In the surgery-radiotherapy group, 1 patient had a reconstructive procedure between half a year and 1 year after surgery because of extensive radionecrosis.

Figure 1. Flowchart of measurement moments in mean (SD).



X, patient(s) stopped to participating; †, patient(s) died; *, 2 missing measurements.

Dental state

Characteristics of upper and lower jaw dental state are listed for both treatment groups in Table 2. The dental state outcome measure showed a significant (p = 0.000) change in dental state in the surgery-radiotherapy group over the 1-year period (Figure 2). No such change was found for the surgery group, although shortly after surgery the dental state had deteriorated significantly in this group (p = 0.027) as compared to the outcomes before surgery. The dental state of the surgery-radiotherapy group also deteriorated significantly (p = 0.001) in that period. Between half a year and 1 year after surgery, dentition improved significantly (p = 0.048) for the surgery-radiotherapy group.

Patients in the surgery-radiotherapy group had a significantly worse dental state than the

surgery group, measured shortly after surgery (p = 0.027) and half a year after surgery (p = 0.037). All patients had a significantly worse dental state than healthy controls with natural dentition (group A; $p < 0.001$) at all measurement moments (Table 3). Patients in the surgery group had a significantly better dental state than healthy controls with maxillary dentures and implant supported mandibular overdentures (group B; $p < 0.05$) and healthy controls with full dentures (group C; $p = 0.000$), when measured before surgery and 1 year after. Half a year after surgery, the surgery group had a significantly better dentition index than healthy controls with full dentures (group C; $p = 0.006$). Before treatment, patients in the surgery-radiotherapy group had a significantly better dentition index than healthy controls with full dentures (group C; $p = 0.011$). Shortly after surgery and shortly after radiotherapy, the surgery-radiotherapy group showed a worse dental state than healthy controls with maxillary dentures and implant-supported mandibular overdentures (group B; $p < 0.05$).

Table 2. Frequency of dental outcomes at all measurement moments.

	Surgery group (n = 23) by dental state					Surgery-radiotherapy group (n = 22) by dental state				
	0	1	2	3	4	0	1	2	3	4
Upper jaw										
Before Intervention	0	3	0	19	1	0	2	0	18	2
Shortly after surgery	0	3	0	18	1	0	1	0	11	7
Shortly after radiotherapy	-	-	-	-	-	0	3	0	10	7
Half a year after surgery	0	3	0	18	1	0	3	0	11	5
One year after surgery	0	3	0	15	1	0	4	1	11	3
Lower jaw										
Before Intervention	0	7	2	11	3	0	4	1	15	2
Shortly after surgery	0	7	0	8	7	0	3	0	2	12
Shortly after radiotherapy	-	-	-	-	-	0	4	0	2	14
Half a year after surgery	0	7	2	8	5	0	5	0	3	11
One year after surgery	0	8	2	7	2	0	3	5	5	6

Dental state: 0, edentate; 1, full denture; 2, full denture + implant retention; 3, partially dentate; 4, dentate.

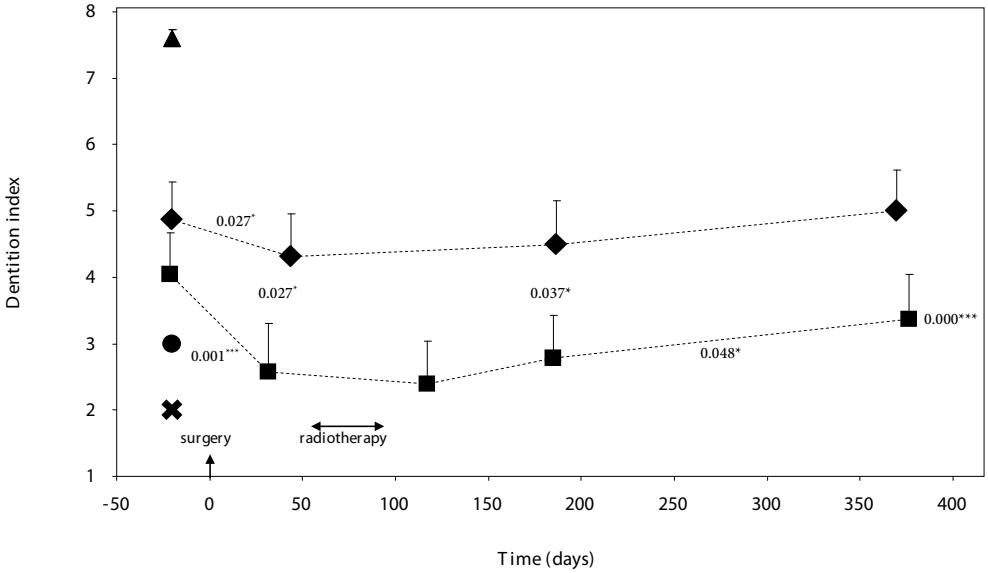


Figure 2. Mean (SEM) dentition index for 2 intervention groups and 3 groups of healthy controls. The *p*-values by Friedman Test, Mann-Whitney U Test, and the Wilcoxon rank test. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Patient groups: ◆ Surgery group (before treatment, shortly after surgery, half a year after surgery, and 1 year after surgery); ▪ Surgery-radiotherapy group (before treatment, shortly after surgery, shortly after radiotherapy, half a year after, and 1 year after surgery). Healthy Controls: ▲ Natural dentition; • Maxillary denture and implant-supported mandibular overdenture; X Full denture. The lines are for visual aid only.

Maximum Bite Force

Maximum bite force showed a significant longitudinal change ($p = 0.049$) for the surgery-radiotherapy group (Figure 3). The bite force of these patients had decreased significantly ($p = 0.002$) shortly after surgery. However, a significant recovery of bite force ($p = 0.011$) was observed between the situation shortly after radiotherapy and half a year after surgery. No significant differences were observed between the surgery group and the surgery-radiotherapy group.

All patients showed significantly less maximum bite force than healthy controls with natural dentition (group A; $p < 0.001$) at all measurement moments (Table 3). Before and half a year after surgery, the surgery group had a significantly larger maximum bite force than healthy controls with full dentures (group C; $p < 0.05$). Before treatment, the surgery-radiotherapy group had a significantly larger maximum bite force than healthy controls with full dentures (group C; $p = 0.015$). However, after surgery, the maximum bite force of the surgery-radiotherapy group decreased to the level of healthy controls with full dentures.

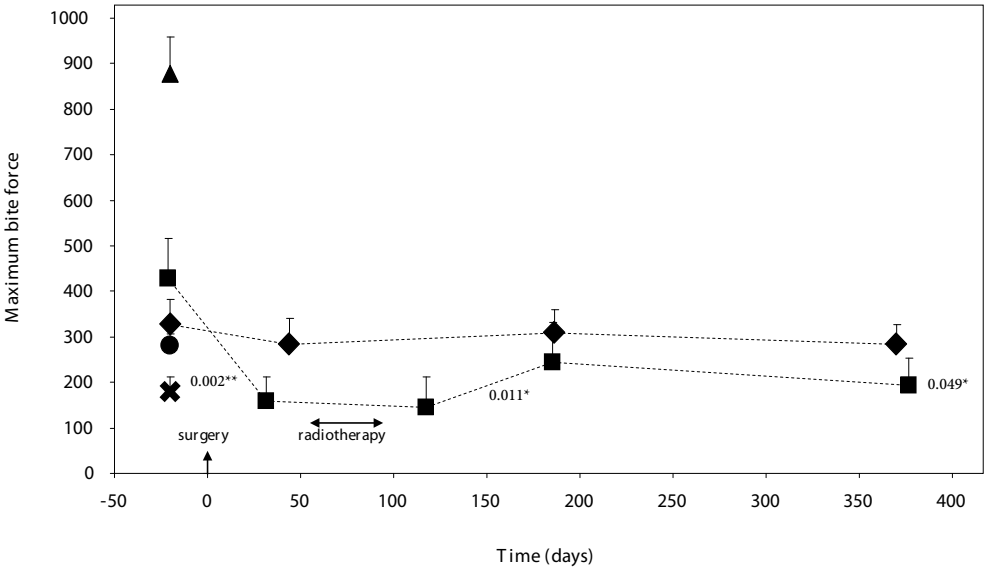


Figure 3. Mean (SEM) of maximum bite force. The *p*-values were reached by repeated measurement analysis of variance (ANOVA), paired *t*-test, and independent *t*-test. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Patient groups: ◆ Surgery group (before treatment, shortly after surgery, half a year after surgery, and 1 year after surgery); ▪ Surgery-radiotherapy group (before treatment, shortly after surgery, shortly after radiotherapy, half a year after surgery, and 1 year after surgery). Healthy Controls:▲ Natural dentition; • Maxillary denture and implant-supported mandibular overdenture; **X** Full denture. The lines are for visual aid only.

Mixing Ability

Mixing ability showed a significant longitudinal change ($p = 0.001$) for the surgery-radiotherapy group (Figure 4). The mixing ability of these patients had deteriorated significantly shortly after surgery ($p = 0.000$). Mixing ability in the surgery group had also decreased significantly ($p = 0.001$) shortly after surgery, but improved significantly ($p = 0.045$) between shortly after surgery and half a year after surgery.

The surgery group showed a significantly worse mixing ability than that of the healthy controls with natural dentition (group A; $p = 0.000$) and healthy controls with maxillary dentures and implant supported mandibular overdentures (group B; $p < 0.05$; Table 3). Shortly after surgery, these patients also had a significantly worse mixing ability than the healthy controls with full dentures (group C; $p = 0.011$).

The surgery-radiotherapy group had a worse mixing ability at almost all moments compared to all healthy control groups (group A, group B, group C; $p < 0.01$). Only before therapy these patients showed no significantly different mixing ability than that of the 2 groups of healthy controls with dentures (group B and group C)

Influence of Surgery on Dental State, Bite Force, and Mixing Ability

For all patients, the decrease in maximum bite force observed shortly after surgery was significantly related to the resection site ($p = 0.000$) and type of reconstruction ($p = 0.012$; Table 4). The deterioration due to surgery of all outcome measures was significantly correlated to each other ($p < 0.05$; Table 5). The negative sign of the correlations is caused by the reverse coding of the mixing ability scale, a large value indicates a bad mixing ability.

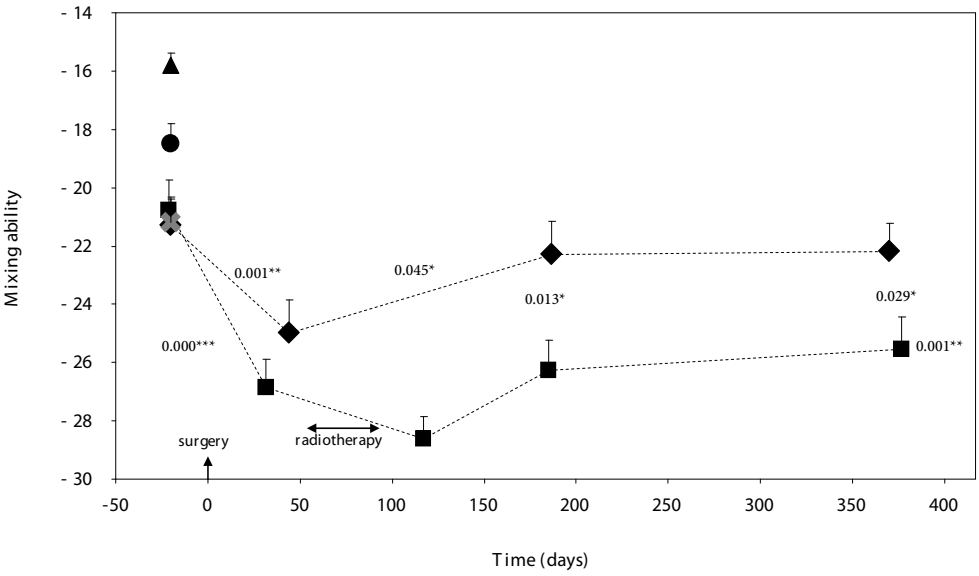


Figure 4. Mean (SEM) of mixing ability test. The *p*-values were reached by repeated measurement analysis of variance (ANOVA), paired *t*-test, and independent *t*-test. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Patient groups: • Surgery group (before treatment, shortly after , half a year after, and 1 year after surgery); ▪ Surgery-radiotherapy group (before treatment, shortly after surgery, shortly after radiotherapy, half a year after, and 1 year after surgery). Healthy Controls: ▲ Natural dentition; ● Maxillary denture and implant-supported mandibular overdenture; **X** Full denture. The lines are for visual aid only. It should be noted that in this figure the values of the mixing ability were multiplied by -1, so that large values of the index (bad mixing) are in the lower part of the figure.

Table 3. The *p*-values for differences of dentition, maximum bite force, and mixing ability between 3 groups of healthy persons and 2 groups of patients.

	Surgery patients			Surgery & radiotherapy patients		
	HC-A	HC-B	HC-C	HC-A	HC-B	HC-C
Dentition §						
Before intervention	0.001‡	0.018*	0.000‡	0.000‡	0.415	0.011*
Shortly after surgery	0.000‡	0.284	0.101	0.000‡	0.034*	0.065
Shortly after radiotherapy	-	-	-	0.000‡	0.040*	0.142
Half a year after surgery	0.000‡	0.102	0.006†	0.000‡	0.066	0.351
One year after surgery	0.001‡	0.005†	0.000‡	0.000‡	0.748	0.058
Maximum bite force ¶						
Before intervention	0.000‡	0.462	0.028*	0.001‡	0.135	0.015*
Shortly after surgery	0.000‡	0.985	0.143	0.000‡	0.039*	0.758
Shortly after radiotherapy	-	-	-	0.000‡	0.061	0.657
Half a year after surgery	0.000‡	0.636	0.040*	0.000‡	0.674	0.471
One year after surgery	0.000‡	0.981	0.066	0.000‡	0.173	0.827
Mixing ability ¶						
Before intervention	0.000‡	0.027*	0.952	0.000‡	0.082	0.751
Shortly after surgery	0.000‡	0.000‡	0.011*	0.000‡	0.000‡	0.000‡
Shortly after radiotherapy	-	-	-	0.000‡	0.000‡	0.000‡
Half a year after surgery	0.000‡	0.008†	0.448	0.000‡	0.000‡	0.000‡
One year after surgery	0.000‡	0.004†	0.444	0.000‡	0.000‡	0.003‡

Abbreviation: HC, healthy control.
Healthy controls: A: natural dentition. B: maxillary denture and implant-supported mandibular overdenture. C: full denture.
*: $p < 0.05$; †: $p < 0.01$; ‡: $p < 0.001$
§ Mann-Whitney U tests
¶ Independent T tests

Table 4. The influence of tumour stage, resection site, and reconstruction on the change in dentition, maximum bite force, and mixing ability before and shortly after surgery was tested with 1-way analysis of variance (ANOVA). The *p*-values of these tests are listed.

	Tumour stage	Resection Site	Reconstruction
Δ Dentition	0.776	0.409	0.262
Δ Maximum bite force	0.300	0.000†	0.012*
Δ Mixing ability	0.780	0.224	0.217

Δ: Difference of physical outcomes before and shortly after surgery.
* $p < 0.05$.
† $p < 0.001$.

Discussion

Our study demonstrated a decrease in dental state, maximum bite force, and masticatory performance (i.e., mixing ability) in patients treated for malignancies in tongue and floor of mouth region. These physiological outcome measures showed more deterioration in patients treated by surgery and radiotherapy than in patients treated by surgery only. To our knowledge, no other studies reported on masticatory function in patients treated for tongue and floor of mouth malignancies using objective measures for dental state, maximum bite force, and masticatory performance. This study will complement the existing knowledge in QoL obtained by questionnaires. The results of our study are in accordance with the deterioration of masticatory performance reported in a cross sectional study of 2 year survivors using the UW-QoL.[12] That study showed that patients treated by surgery and radiotherapy had significantly lower scores for the item "chewing" than patients treated by surgery only. In a study using a self-questionnaire on chewing and swallowing, using the Functional Intraoral Glasgow Scale, it was reported that radiotherapy is a negative prognostic factor for oral function.[13] These results were obtained on patients treated for oral malignancies between 2 and 6 years after intervention. That same study also reported a significant correlation between resection size and functional outcome, meaning better functional outcome with smaller excisions. Another study using the UW-QoL questionnaire also reported a significant relationship between tumor size and chewing.[14] However, this relationship was only observed preoperatively and not postoperatively.

The average dental status of the patients before surgery did not differ significantly from the average dental status of the healthy controls (Figure 2). However, after surgical intervention, the dental status deteriorated significantly. Similar results were reported previously.[2,15] Surgical defects compromised the occlusal function in these patients. The dental status after surgery and radiation was near the level of full denture wearers. When radiotherapy is part of the treatment, extraction of teeth is often required to prevent subsequent infection from dental caries and radionecroses, resulting from radiation.[16] Oral rehabilitation restored the dental status significantly, but it remained below the level before treatment in the surgery-radiation group. The dental status of the surgery group was restored to pretreatment levels 1 year after surgery.

Table 5. Correlations of changes (before and shortly after surgery) in physiological outcomes.

	Δ Dental State	Δ Maximum bite force
Δ Maximum Bite Force		
R	0.437‡	
p value	0.005†	
Δ Mixing ability		
R	- 0.347‡	- 0.483§
p value	0.026*	0.002†

Δ Difference between outcomes before and shortly after surgery.
*: $p < 0.05$.
†: $p < 0.01$.
§: Spearman correlation.
‡: Pearson correlation.

The average maximum bite force of the patients before treatment was on the level of the healthy controls with implant-supported mandibular dentures (Figure 3). The maximum bite force of the surgery group was not significantly affected by surgery. However, in the surgery-radiotherapy group shortly after surgery, the bite force had temporarily decreased

to a level below that of the healthy full denture wearers. Although some recovery occurred, the bite force of the surgery-radiation group remained well below the presurgical level. The decrease in maximum bite force, observed shortly after surgery in all patients in this study, was significantly related to the resection site and the extent of reconstruction (Table 4). Thus, the resection site will influence the initial decrease in maximum bite force, with larger reconstructions leading to a stronger decrease in maximum bite force.

Masticatory performance, as measured from the mixing index of 2-colored wax, showed a large deterioration as a result of surgery (Figure 4). Before surgery, the masticatory performance of the patients was similar to the performance of healthy denture wearers. After surgery, the masticatory performance decreased dramatically. A further decrease occurred after radiotherapy. The patients of the surgery-radiotherapy group performed significantly worse than the surgery group. An explanation for this difference may be that patients treated for surgery and radiotherapy had overall higher tumour stages and needed more extensive reconstructions (Table 1). As a consequence, the dental state in these patients was more affected than in the patients treated by surgery only (Figure 2). Furthermore, the additional radiotherapy caused a longer intervention period and an extra negative impact on the oral system.[16] Deteriorated masticatory performance after surgical intervention was also demonstrated in a study on patients treated for mandible and maxilla malignancies with implant-supported mandibular supported overdentures.[17]

Changes in dental state, maximum bite force, and mixing ability due to surgical intervention were significantly correlated (Table 5). Thus, a less good dental status will lead to decreases in maximum bite force and masticatory performance (i.e., mixing ability). In healthy persons, the maximum voluntary bite force was reported to explain over 60% of the masticatory performance.[9] Maximum bite force and chewing performance are reduced in healthy persons, when natural teeth have been replaced by complete dentures[7] or implant-retained overdentures.[8] Combining the knowledge of healthy persons and the outcomes of this study, we may conclude that the state of dentition, resection site, and the extent of reconstruction influenced the decrease of maximum bite force shortly after surgery. Furthermore, the decrease of dental index and maximum bite force influenced the decrease of masticatory performance shortly after surgery.

Dental rehabilitation after surgery improves the dental state in the patients. As a result, the maximum bite force and masticatory performance also improved. Similar results were

reported previously.[3,18,19] However, between half a year and 1 year after surgery, no further recovery was observed for maximum bite force and masticatory performance (Figures 3 and 4). Deterioration of masticatory performance may lead to changes in the diet, because some foods become troublesome to eat. The altered food choice may result in lower intakes for key nutrients as iron and fiber.[20] Therefore, research on revalidation interventions, such as orofacial phyiosiotherapy[21] is needed to further improve oral function half a year after oral oncological intervention. The orofacial physiotherapist, specialized in training and optimization of the mobility of the masticatory system, may help to improve masticatory function. Furthermore, tailored nutrition intervention by a dietician aimed to increase the fruit and vegetable intake of the patients can change dietary behaviour positively.[22]

From the results of our study, we may conclude that surgical intervention has a large negative impact on oral function. The deterioration of oral function was significantly larger for patients treated by surgery and radiotherapy as compared to the patients who had surgery only. Also the recovery of oral function was less prominent for the surgery-radiotherapy group than for the surgery group. On average, patients treated by surgery and radiotherapy had larger tumors, more extended resections, and more radiotherapy. Clinicians should be alerted on this patient category to prevent loss of function as much as possible to maintain the patient's QoL.

Half a year after surgery we observed no further improvement in maximum bite force and masticatory performance. Therefore, in addition to dental rehabilitation by the maxillofacial prosthodontist, orofacial physiotherapy may help to restore oral function to an adequate level in patients treated for malignancies in the tongue and floor of mouth.

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6

Tongue function in patients treated for malignancies in tongue and/or floor of mouth: a 1-year prospective study

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Abstract

Progress in (reconstructive) surgery and radiotherapy tends to improve survival and reduces oral functional deficits. Despite the growing sophistication of cancer treatment, patients still report deterioration in tongue function. Sensory function, mobility, and force of the tongue were determined in 45 patients with a carcinoma of tongue and/or floor of mouth. Measurements were performed before surgery, shortly after surgery, shortly after radiotherapy, 6, and 12 months after surgery. Surgery had a negative impact on tongue sensory function and mobility. Post-surgery radiotherapy did not further deteriorate sensory function, mobility, or force of the tongue. Nevertheless, patients of the surgery-radiotherapy group had significantly worse tongue sensory function and mobility than patients of the surgery group, probably caused by more advanced tumour stage and more extensive reconstructions and related scar tissue. The tongue force in patients of both groups significantly increased in the first 6 months after surgery. However, this increase disappeared in the next 6 months. We may conclude that surgery had a significant negative influence on tongue function, especially in the group of patients treated with post-surgical radiotherapy. No further deterioration of tongue function was observed after post-surgical radiotherapy within the first year after surgery.

Introduction

Patients with cancer in the tongue and/or floor of mouth region run a high risk of deteriorated tongue function caused by the tumour itself or induced by treatment. Progress in (reconstructive) surgery and radiotherapy tends to improve survival and reduces oral functional deficits.[1] Despite the growing sophistication of cancer treatment, patients still report deterioration in tongue function.[2] The tongue plays a major role in mastication, deglutition, oral hygiene, and speech. The strength of the tongue, its great flexibility, and ability to take variable shapes are conditioned by the activity of the intrinsic tongue muscles and the extrinsic floor of the mouth muscles, that are complementary to one another.[3] The tongue is vital for the transport and positioning of food between the molars, selecting fragments for further comminution, incorporation of fragments with saliva, posterior transport of the resulting bolus, and its final deposition into the oropharynx.[4,5] During the oral stage of swallowing, the tongue presses against the hard and soft palate and moves sequentially in an anterior to posterior direction to propel the bolus to the pharynx.[6,7] The ability to take variable shapes, flexibility, and strength of the tongue is important in articulation to produce consonants and vowels either lingual or palatal.[3] The sensory mechanisms of the tongue are necessary to accomplish the changes in shape and position of the tongue and floor of the mouth required for mastication, deglutition, and proper articulation.[8-10] Thereby, the perception of the bolus is important for the efficacy of mastication and deglutition. Moreover, the sensory function of lips, tongue, and teeth overlap on the primary somatosensory cortex.[11] Deterioration of peripheral afferent input of the tongue causes a disturbance in the central control of the cortex during mastication, deglutition and articulation.[12] Loss of sensory function in the oral cavity will thus hamper full functional rehabilitation. The aim of this prospective cohort study was to examine and quantify the effect of surgery with or without radiotherapy on tongue function in patients with malignancies in the tongue and/or floor of mouth. We measured tongue sensory function, tongue mobility, and maximum tongue force at various moments before and after surgery and radiotherapy. We determined the influence of tumour size, tumour location, and surgical intervention on the deterioration of tongue function as measured shortly after surgery. Furthermore, we determined relationships among these deteriorations in tongue function. Finally, we compared the outcomes of the oral oncology patients with outcomes of healthy controls. Our hypothesis was that treatment would significantly deteriorate tongue function.

Materials and Methods

Subjects

In the period from January 2007 till January 2008 a group of 45 patients with a primary malignancy in tongue and/or floor of mouth and a group of 60 healthy controls matched for age were recruited for this study. Exclusion criteria were previous or synchronous or recurrent malignancies in the head and neck area, cognitive impairment, and inability to understand Dutch. Patients were treated with curative intend by surgery only (n = 23) or by surgery and radiotherapy (n = 22). In 4 dental practices 60 healthy people matched for age and gender were recruited. More details of the control group were recently published.[13] The protocol was approved by the Ethics Committee of University Medical Center Utrecht and Radboud University Nijmegen Medical Centre. All subjects received a written explanation of the study, and informed consent was obtained from each subject before the start of the study. Postoperative radiotherapy was given within 6 weeks after surgery when indicated according to the treatment guidelines of the Dutch Head and Neck Oncology Group, based on the histology of the resection specimen. Pathological tumour stage (pT),[14] resection site, and reconstruction were collected from medical data. Patient characteristics are summarized in Table 1.

Measurements

Patients were measured maximal 4 weeks before surgery, shortly after surgery (4-6 weeks), shortly after radiotherapy (4-6 weeks), 6, and 12 months after surgery. Healthy persons were measured once. We determined the following variables: thermal sensory function, tactile sensory function, protrusion, lateralization, and maximum force of the tongue.

Sensory function of tongue

Thermal sensory function (thin afferent fibres) and tactile sensory function (thick afferent fibres) were tested by presenting pairs of stimuli: a real stimulus and a sham one. The real and sham stimuli were presented in random order, during two times of attention that were announced by the examiner while the patient kept the eyes closed. After each pair, the patient had to report the order of real and sham stimulation (forced-choice procedure). Three pairs of stimuli were presented. The magnitude of the test stimulus was chosen as the value at which control subjects could just detect this stimulus with nearly zero errors, so that patients

could consistently make the correct choice for uninjured sites. The test sites (right and left) were 10 mm from the tongue tip and 10 mm from the right and left edge of the tongue as good as possible. For analyses we used the outcome of the (most) affected site. Thermal sensory function was tested using a heat-conducting aluminium rod (diameter 2.0 mm) as a real stimulus (22°C; touch as well as cold sensory function). The sham stimulus was produced by a non-heat-conducting Perspex rod. Tactile sensory function was evaluated using a Semmes-Weinstein monofilament (Semmes-Weinstein Aesthesiometer, Stoelting Co., Wood Dale, IL) with index number 3.22.[15,16] The real stimulus was a touch with the filament. The sham stimulus was achieved by approaching the patient with the device while the filament was turned away. The score for reduced thermal or tactile sensory function was 0 and for normal sensory function 1. A detailed description of this procedure was recently published.[15]

Table 1. Characteristics of the surgery group and the surgery-radiotherapy group. Possible differences in number of patients in the two groups were tested by Chi-square tests.

	Surgery (N=23)	Surgery & Radiotherapy (N=22)	p-value
Pathalogical Tumour stage (pT)			
T1	18	5	
T2	5	9	0.001**
T3	0	4	
T4	0	4	
Resection site			
Tongue	17	10	
Floor of mouth	4	5	
Floor of mouth & Slice mandible	2	4	0.233
Tongue & Floor of mouth	0	2	
Tongue & Floor of mouth & Slice mandible	0	1	
Reconstruction			
Primary closure	17	5	
Local flap	1	0	0.001**
Myocutaneous or free flap	5	17	
Bone graft/flap	0	0	

*** $p < 0.001$

Tongue mobility

Tongue mobility was determined by measuring tongue protrusion and lateralization.[17] Tongue protrusion was rated on a three point scale: the tongue cannot touch the lower lip (0 points); can touch the lower lip (1 point); passes the lower lip (2 points). Lateralization was rated on a three point scale as well: the tongue cannot touch the mouth corner (0 points); can touch the mouth corner (1 point); passes the mouth corner (2 points). The right and left tongue lateralization were averaged for the outcome measure of tongue lateralization.

Maximum tongue force

Maximum tongue forces were measured in cranial direction. The device for measuring the tongue force consisted of a strain gauge mounted on a mouthpiece. The strain gauge had a surface area of 110 mm^2 and a vertical height of 4.5 mm. The strain gauge element was placed between the tongue and the palate at the midline of tongue 5 mm from the tip. The task of the patient was to press the tongue as hard as possible to the palate. The task was performed twice. The highest tongue force of both efforts was used in the study.

Sample size

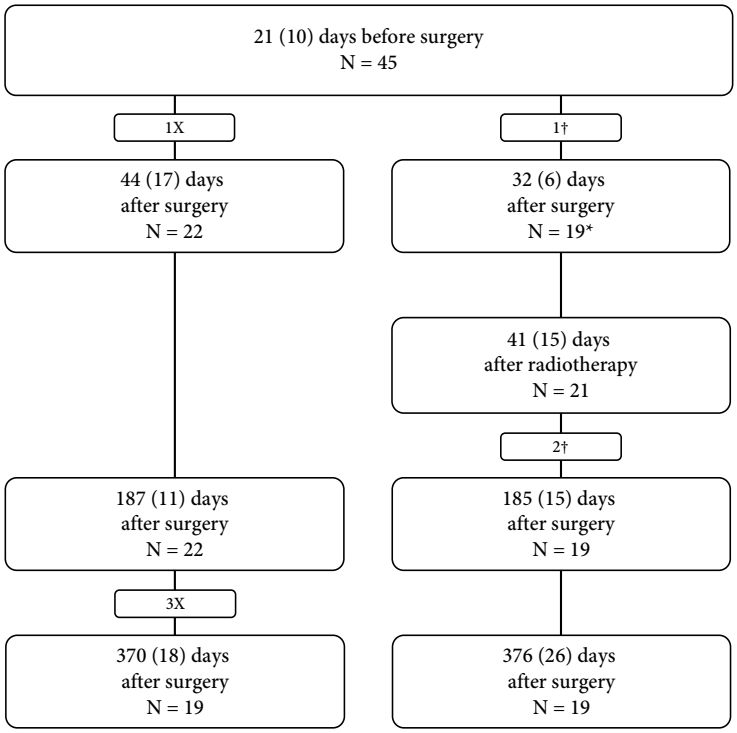
To detect differences between the surgery group (SG) and the surgery-radiotherapy group (SRG), using ANOVA, we assumed a minimal effect size of 0.40 at an α of 0.05 and a power (β) of 0.80. This effect size was used to detect small differences between those two treatment groups. Consequently, using an effect size of 0.40 at least 20 persons were needed per treatment group in this study.

Statistical analyses

The presentation of results is primarily descriptive with means, standard deviations (SD), and standard error of the means (SEM). Characteristics of the two patient groups before intervention were compared by a Chi-square test. In each treatment group (i.e. surgery group and surgery-radiotherapy group) changes in time of sensory function, mobility, and maximum force of the tongue were analyzed by repeated measures analysis of variance (ANOVA) for continuous data and by a Friedman test for ordinal data. Repeated measures ANOVA and the Friedman test determine possible differences among all measurement moments. Therefore, these tests are susceptible for missing data, due to patients who died,

stopped, or missed a measurement. To avoid this disadvantage, we also performed paired *t*-tests (continuous data) and Wilcoxon signed rank tests (ordinal data) to test differences between two measurement moments only. For nominal data we performed McNemar tests between two measurement moments. Differences among the surgery group and the surgery-radiotherapy group, and the healthy controls were analyzed by independent-samples *t*-tests (continuous data), Mann-Whitney U-tests (ordinal data), and Chi-square tests (nominal data). One-way ANOVA and Kruskal-Wallis tests were used to find explanatory factors for the changes of outcomes of tongue function before and shortly after surgery for all patients. Relationships among the various tongue function results before and shortly after surgery were determined with Spearman correlations and Cramer's V tests. A *p*-value less than 0.05 was considered statistically significant. All analyses were performed with SPSS 15.0 software (SPSS, Inc., Chicago, IL).

Figure 1. Flow chart of measurement moments and measured patients [N]



X: patient(s) stopped to participate
†: patient(s) died
*: 2 missing measurements

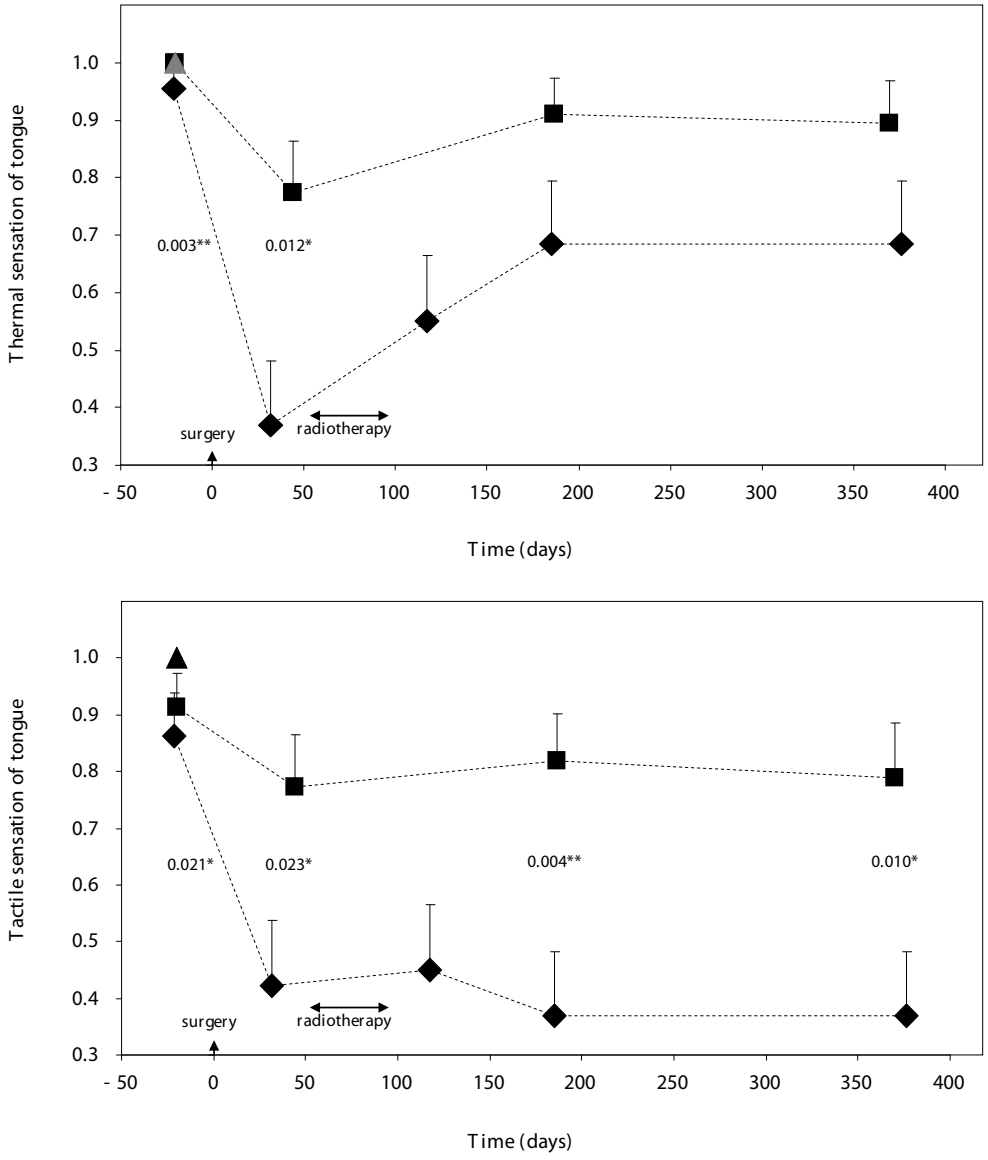


Figure 2. Mean (SEM) thermal and tactile sensory function of tongue for two intervention groups and healthy controls. *P*-values obtained from McNemar tests (within subjects), and Chi-square tests (between subjects). *: $p < 0.05$; **: $p < 0.01$. The score for reduced thermal sensory function was 0 and for normal sensory function 1.◆ : surgery group (before treatment, shortly after, 6, and 12 months) ■ : surgery-radiotherapy group (before treatment, shortly after surgery, shortly after radiotherapy, 6 and 12 months after surgery):▲ healthy controls. The lines are for visual aid only.

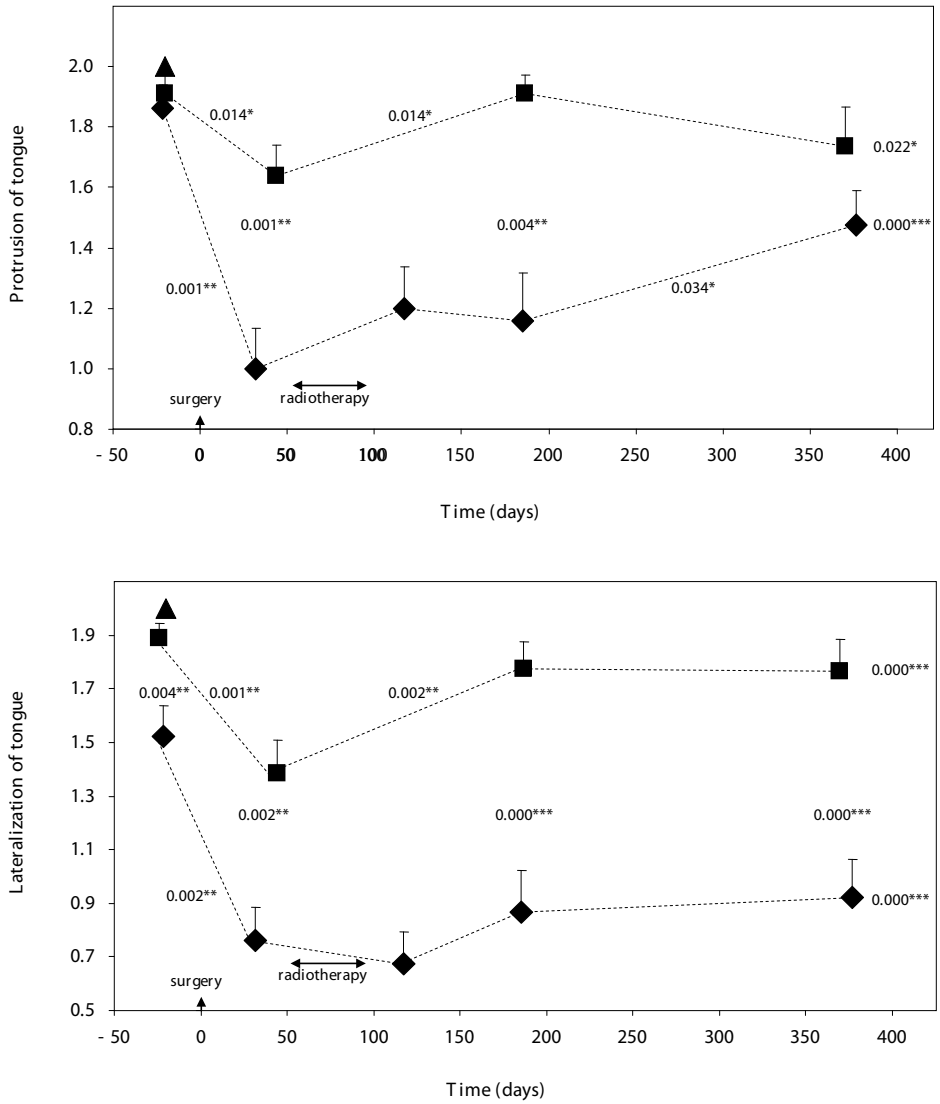


Figure 3. Mean (SEM) protrusion and lateralization of tongue for two intervention groups healthy controls. *P*-values obtained from Friedman tests (longitudinal), Wilcoxon Signed Rank tests (within subjects), and Mann-Whitney U tests (between subjects).*: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$. The degree of tongue protrusion was rated on a three point scale: the tongue cannot touch the lower lip (0 points); the tongue can touch the lower lip (1 point); the tongue passes the lower lip (2 points). The degree of lateralization was rated on a three point scale: the tongue cannot touch the mouth corner (0 points); the tongue can touch the mouth corner (1 point); the tongue passes the mouth corner (2 points). Right and left tongue lateralization were averaged. ◆: surgery group (before treatment, shortly after, 6, and 12 months) ■ : surgery-radiotherapy group (before treatment, shortly after surgery, shortly after radiotherapy, 6, and 12 months after surgery) ▲: healthy controls. The lines are for visual aid only.

Results

Forty five patients, with a squamous cell carcinoma of tongue and/or floor of mouth, were included in this study. Twenty three patients were included in the surgery group (SG), 9 women and 14 men aged 63.9 ± 14.0 years (mean ± SD). Twenty two patients were included in the surgery-radiotherapy group (SRG), 6 women and 16 men aged 61.8 ± 10.0 years. Characteristics of pathological tumour stage (pT), resection site, and type of reconstruction are listed in Table 1. Chi-square tests revealed that patient numbers were significantly different for both intervention groups with respect to pT and type of reconstruction (Table 1). A flow-chart of the measurement moments and measured patients is depicted in Figure 1. Two patients were not measured between surgery and the start of radiotherapy, because of time constraints. Furthermore, two patients (SG) had an additional resection within a month after surgery. One patient (SRG) had a reconstructive procedure between 6 and 12 months after surgery because of extensive osteoradionecrosis.

Thermal and tactile sensory function of tongue

Significant decreases in thermal and tactile sensory function due to surgery occurred in surgery-radiotherapy patients only (Figure 2). Patients of the SRG had lower thermal and tactile sensory function scores than the surgery patients. Before surgery, patients of both treatment groups had similar thermal sensory function scores as healthy controls. Patients of the SG also had similar tactile sensory function as controls, whereas the patients of the SRG had significantly lower tactile sensory function scores than the controls (Table 2). At all measurement moments after surgery, patients in both treatment groups had significantly worse thermal and tactile sensory function of the tongue as compared to the healthy controls, with the exception of thermal sensory function in the SG 6 and 12 months after surgery.

Tongue mobility

A significant longitudinal change for both treatment groups are observed for both SG and SRG (Figure 3). Protrusion and lateralization of the tongue decreased significantly in both treatment groups due to surgery (Figure 3). Patients of the SRG had lower protrusion and lateralization scores than the surgery patients. A significant recovery of protrusion and lateralization scores was observed for patients of the SG 6 months after surgery.

At all measurement moments both treatment groups showed significant lower tongue lateralization scores than healthy controls (Table 2).

Maximum tongue force

Maximum tongue force showed a significant longitudinal change for the SRG (Figure 4). Tongue force of both groups significantly increased between shortly after treatment and 6 months after surgery. However, in the next 6 months the tongue force significantly decreased in the SRG. Before surgery, patients of the SG had similar tongue force as healthy controls, whereas the SRG had significantly lower tongue force than the controls (Table 2). At all measurement moments after surgery patients of both treatment groups had significantly lower tongue force as compared to the healthy controls excluding 6 months after surgery.

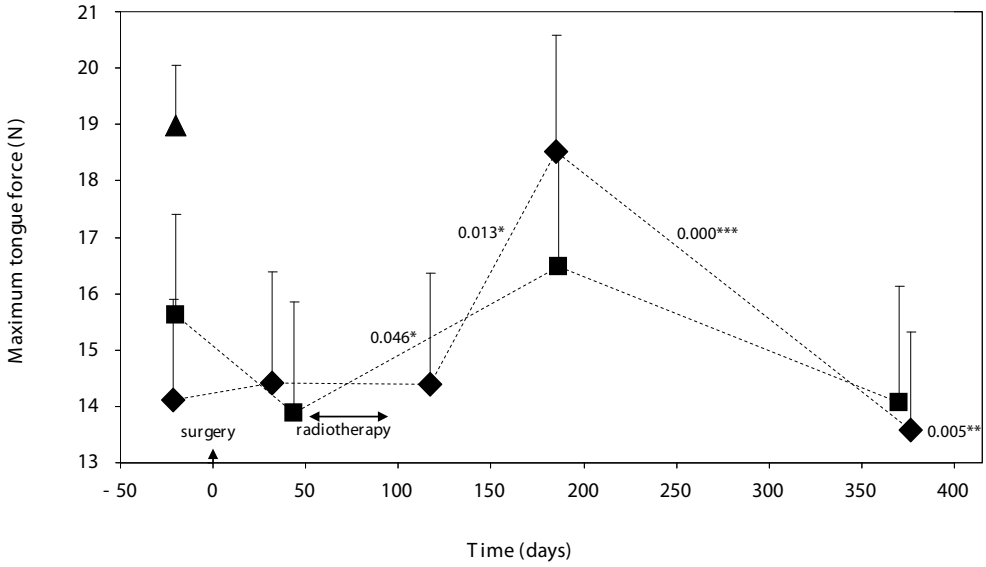


Figure 4. Mean (SEM) maximum tongue force for two intervention groups healthy controls. *P*-values obtained from repeated measurement ANOVA (longitudinal), paired t-tests (within subjects), and independent t-tests (between subjects). *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$. ◆ : surgery group (before treatment, shortly after, 6, and 12 months); ▪ :surgery-radiotherapy group (before treatment, shortly after surgery, shortly after radiotherapy, 6, and 12 months after surgery); ▲ : healthy controls. The lines are for visual aid only.

Table 2. *P*-values for differences of thermal and tactile sensory function, protrusion, lateralization, and maximum force of tongue between the 2 groups of patients (surgery only: N = 23; surgery and radiotherapy: N = 22) and healthy controls (N = 60).

Patients	Surgery	Surgery & Radiotherapy	Surgery	Surgery & Radiotherapy
	Controls	Controls	Controls	Controls
Sensory function [a]	Thermal sensory function		Tactile sensory function	
Before intervention	1.000	0.268	0.074	0.017**
Direct after surgery	0.001**	0.000***	0.001**	0.000***
Direct after radiotherapy	-	0.000***	-	0.000***
Six months after surgery	0.070	0.000***	0.004**	0.000***
Twelve months after surgery	0.056	0.000***	0.003**	0.000***
Tongue mobility [b]	Protrusion		Lateralization	
Before intervention	0.022*	0.004**	0.001**	0.000***
Direct after surgery	0.000***	0.000***	0.000***	0.000***
Direct after radiotherapy	-	0.000***	-	0.000***
Six months after surgery	0.019*	0.000***	0.000***	0.000***
Twelve months after surgery	0.000***	0.000***	0.000***	0.000***
Maximum tongue force [c]	Force			
Before intervention	0.097	0.022*		
Direct after surgery	0.012*	0.044*		
Direct after radiotherapy	-	0.040*		
Six months after surgery	0.199	0.841		
Twelve months after surgery	0.026*	0.015*		

a Chi-square tests
b Mann-Whitney U-test
c Independent t tests
*: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$

Influence of surgery and tongue function

Tumour stage was significantly related to the deterioration of thermal sensory function and protrusion caused by surgery (Table 3). Reconstruction site was also related to the change in protrusion. Furthermore, the deteriorations of thermal and tactile sensory function, thermal sensory function and protrusion, and of lateralization and protrusion of the tongue were significantly associated (Table 4).

Table 3. The influence of tumour stage, resection site, and reconstruction on the change tongue function outcomes before and shortly after surgery was tested with Kruskal-Wallis test and one-way ANOVA. *P*-values of these tests are listed.

	Tumour stage (pT)	Resection Site	Reconstruction
Δ Thermal sensory function [a]	0.028*	0.295	0.344
Δ Tactile sensory function [a]	0.977	0.156	0.413
Δ Protrusion [a]	0.030*	0.920	0.035*
Δ Lateralization [a]	0.130	0.765	0.103
Δ Maximum tongue force [b]	0.284	0.110	0.919

Δ: difference of physical outcomes before and shortly after surgery
a: Kruskal-Wallis test
b: one-way ANOVA
*: $p < 0.05$

Discussion

This study demonstrated a significant decrease in tongue sensory function after surgery in patients with squamous cell carcinoma of tongue and/or floor of mouth (Figure 2). These results concur with an observed drop in tongue sensory function postoperatively in patients treated for oral and oropharyngeal cancer in a longitudinal study.[18] The deterioration in tongue sensory function was most pronounced for surgery-radiation patients (SRG). Some recovery of thermal sensory function occurred shortly after surgery for both groups of patients. During the 12 months period tactile sensory function remained at the low level observed shortly after surgery. After surgery almost all sensory function outcomes were

significantly lower than in healthy controls (Table 2). However, the tactile sensory function levels of the SRG patients remained significantly lower than those of the SG patients. Before surgery tactile sensory function levels were significantly lower for SRG patients than those of healthy controls, whereas no such differences were observed for thermal sensory function. The decrease in thermal sensory function, observed shortly after surgery in all patients in this study, was significantly related to pT (Table 3). Thus, the pT influences the initial decrease in thermal sensory function of the tongue, with larger tumour stages leading to a stronger decrease in thermal sensory function.

Table 4. Cramer's V association and Spearman correlations of changes (before and shortly after surgery) in tongue function outcomes.

		Δ Thermal sensory function	Δ Tactile sensory function	Δ Protrusion	Δ Lateralization
Δ Tactile Sensory function	V_p [a]	0.556			
	p-value	0.000***			
Δ Protrusion	R [b]	0.413	0.232		
	p-value	0.007**	0.144		
Δ Lateralization	R [b]	0.256	0.085	0.616	
	p-value	0.106	0.597	0.000***	
Δ Maximum tongue force	R [b]	- 0.077	0.026	- 0.050	0.009
	p-value	0.632	0.871	0.754	0.956

Δ: difference between outcomes before and shortly after surgery
a: Cramer's V association
b: Spearman correlation
**: $p < 0.01$; ***: $p < 0.001$

An explanation for the different results in tactile and thermal sensory function may be the different effect of compression of the tumour on thick (tactile) and thin (thermal) afferent fibre types. Thick fibres may be more susceptible to compression. Research on sensory function after surgical decompression in carpal tunnel syndrome, for example, showed that recovery of tactile sensory function of the fingers took more time than the recovery of thermal sensory function.[19,20] This phenomenon may also explain the trend of recovery in

thermal sensory function of the tongue after surgery, whereas no such recovery was observed for tactile sensory function. Before surgery tongue protrusion and lateralization was below the levels of healthy controls in all patients (Table 2). All tongue mobility measurements showed deterioration due to surgery (Figure 3). The SRG patients had significantly less tongue mobility than the SG patients. In a cross-sectional study it was demonstrated that loss of tongue mobility was strongly associated with restriction of food intake in patients treated for oral cancer.[21] The decrease in protrusion, observed shortly after surgery in all patients in this study, was significantly related to pT and kind of reconstruction (Table 3). Larger tumour stages and more severe reconstructions will lead to a stronger decrease in protrusion of the tongue. Changes in thermal sensory function and protrusion of the tongue due to surgical intervention were significantly correlated (Table 4).

Maximum tongue force was not significantly influenced by surgery and/or radiotherapy (Figure 4). Similar results were reported in a two month follow-up study in patients treated by oral and oropharyngeal cancer.[7] Six months after surgery we observed a temporary increase in tongue force. This increase was largest SRG patients. However, this increase disappeared in the next 6 months to the levels observed before and shortly after treatment. We observed a significant correlation ($r = 0.52$) between maximum tongue force and masticatory performance[13] for SRG patients 6 months after surgery.[22] Thus, a decreased masticatory performance resulted in an increased tongue force. Apparently, patients "chewed" with the tongue by pressing the food between tongue and palate, compensating for the decreased dental chewing performance. In this way patients inadvertently trained their tongue muscles which resulted in a higher maximum tongue force.

In this study post-surgical radiotherapy had no significant influence on tongue function in the outcome measures. However, the SRG patients had more advanced pT and received more extensive reconstructions (Table 1). Therefore the decrease in tongue sensory function and mobility was significantly larger in SRG patients than in SG patients. We may conclude that surgical intervention has a large negative impact on tongue function. Further improvement of surgical techniques of tongue and/or floor of mouth tumours is important to preserve specific tongue functions.

Rehabilitation of tongue function is important to optimize mastication, deglutition, and speech after surgical treatment. Research on revalidation interventions, such as orofacial phyiosiotherapy,[23] speech therapy, and dietetics[24] may further improve oral function after oral oncological intervention.

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7

Neck and shoulder function in patients treated for oral malignancies: a 1-year prospective cohort study

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Head and Neck: *under review*

Abstract

Background: Neck and shoulder complaints can be a direct result of a neck dissection. In this study neck and shoulder function was examined in patients treated for oral cancer with or without neck dissection and compared with healthy controls at different moments within a 1-year period.

Methods: Maximal active lateral flexion of the neck, forward flexion and abduction of the shoulder (range of motion), and self-perceived function (questionnaire) were measured in 145 patients.

Results: Patients treated by neck dissection showed a deteriorated neck and shoulder function shortly after intervention ($p < 0.05$). One year after intervention patients treated with bilateral neck dissection still showed deteriorated lateral flexion of the neck. Forward flexion recovered to the level of healthy controls, but abduction of the shoulder was still reduced.

Conclusions: More extended neck dissections induced more deterioration in neck and shoulder function shortly after intervention. Maximal active abduction of the shoulder was affected most.

Introduction

The objectives of treatment of patients with oral cancer are cure and preservation of function. Patients with early stage disease are treated by surgery or radiotherapy. In advanced stage disease, treatment options are surgery with adjuvant (chemo)radiotherapy or radiotherapy with or without chemotherapy with surgical salvage in case of loco-regional failure. A universally accepted adverse independent prognostic factor in head and neck cancer is the presence of cervical lymph node metastasis, and in that case neck dissection (ND) is often indicated. In 1906 George Crile first described the classic radical neck dissection (RND, regions I-V).[1] We have to keep in mind that the philosophy of postoperative radiation therapy was not a common consideration at that time. Various modifications of Crile's RND have been developed over years to improve functional and cosmetic results. Depending on the neck stage and location of the primary tumour these modifications were also developed to maintain or even improve regional control.[2-5] More selective procedures are used nowadays in neck dissection, preserving all nonlymphatic structures within the neck as in the modified radical neck dissection (MRND, regions I-IV). Depending on disease stage, selective neck dissection (SND, regions I-III) will now be indicated in clinically and radiologically N_0-negative neck or N_1-positive neck, without compromising regional recurrence.[4,6] Neck metastases, even if they are occult and the neck is clinically N_0, have a deleterious effect on the survival of patients with head and neck cancer.[7]

Neck and shoulder complaints can be a direct result of a ND and can manifest as pain, reduced range of motion (ROM) of the neck and shoulder, loss of sensation and loss of neck and shoulder function.[8-11] These shoulder complaints may have a large influence on quality of life (QoL)[12-15] and are associated with depression and poor outcome.[16] It has been demonstrated that more extensive surgery in the neck is associated with more postoperative shoulder morbidity.[8,17-19] After a RND, shoulder dysfunction was reported to be the most important source of long-term morbidity for the patient.[20,21] Resection of the spinal accessory nerve (SAN) during RND usually leads to loss of function of the trapezius muscle, which is then unable to perform its primary task of stabilizing the scapula. As a result, the scapula tends to flare out at the vertebral border (scapular winging) and to slip forward and down. This in turn limits the ability of the shoulder to move in a full active ROM. The dropped and protracted shoulder is attributed to atrophy of the trapezius muscle and a stretched levator muscle of the scapula. This has also been reported to account for the shoulder and neck pain

that patients experience.[10] Nevertheless, in some cases the trapezius muscle will function normally,[19] because of the innervation by branches from the cervical plexus. Innervation from the cervical plexus may occur through connections with the SAN, or through an independent double motor supply directly to the trapezius muscle.[22,23] The relation between shoulder morbidity (pain and ROM) and the function of the SAN after neck dissection, however, is not straightforward. Significant shoulder dysfunction continues to arise even with (SAN) sparing neck dissection procedures.[23-25] After neck dissection with preservation of the nerve, neurapraxia, axonotmesis, and/or neurotmesis may result in a, mostly temporary, loss of function of the trapezius muscle. Possible causes of the loss of function are traction during the operation, micro traumata or devascularisation of the nerve during, or as a consequence of the operation.[26,27] Micro traumata may occur because of the anatomical variations in the course of the nerve, particularly in the passage of the sternocleido mastoid muscle (SCM), which may lead to more extensive damage.[23,28]

Radiotherapy may result in troublesome and uncomfortable fibrosis which may worsen with time. Neck mobility may therefore be limited by radiotherapy.[29] However, contradictory results are reported in literature regarding the effect of radiotherapy on shoulder function. Some concordance exists that radiotherapy does not significantly influence the results of instrumentally determined shoulder function.[21,30-33] In contrast, radiotherapy often adversely influenced self-assessed shoulder function outcomes.[34-36] Perhaps the effect of additional radiotherapy on shoulder function may be confounded by the effects of surgical intervention. The aim of this prospective cohort study was to examine and quantify prospectively the effect of neck and shoulder function of patients with malignancies in the oral cavity treated with and without ND. The outcomes of the various ND groups were compared with each other and with the results of the healthy controls. Our hypothesis was that a more extended ND would lead to a more deteriorated neck and shoulder function.

Materials and Methods

Subjects

One hundred forty-five patients with a primary oral carcinoma and 60 healthy controls were recruited for this study in the period from January 2007 till August 2010. Exclusion criteria were previous or synchronous malignancies, pectoralis flap reconstruction, cognitive impairment, and inability to understand Dutch. Sixty healthy people, matched for age and

gender, were recruited in 4 dental practices. More details of the control group were recently published.[37] The patient group consisted of 59 patients in the surgery only group, 66 in the surgery-radiotherapy group, and 20 patients in the radiotherapy only group. Postoperative radiotherapy was given within 6 weeks after surgery when indicated according to the treatment guidelines of the Dutch Cooperative Head and Neck Oncology Group, based on the histology of the resection specimen. Tumour stage (T of TNM), regional lymph node metastasis (N of TNM),[38] oncological intervention, and oral reconstruction were collected from medical data. The protocol was approved by the Ethics Committees of University Medical Center Utrecht and Radboud University Nijmegen Medical Centre. All subjects received a written explanation of the study, and informed consent was obtained from each subject before the start of the study.

Definition of the different NDs

RND refers to the removal of all ipsi-lateral cervical lymph node groups (lymph nodes from levels I through V) including the spinal accessory nerve (SAN), internal jugular vein, and SCM. MRND refers to the excision of all lymph nodes routinely removed by the RND with preservation of one or more nonlymphatic structures (i.e., the SAN, internal jugular vein, and SCM). In SND all nonlymphatic structures are spared and the lymph node groups removed are based on the patterns of metastases. For oral cavity cancers, the lymph nodes at greatest risk are located in levels I, II, and III.[39]

Measurements

Patients were measured maximal 4 weeks before oncological intervention, shortly (4-6 weeks) after intervention, 6 and 12 months after surgery or when patients were treated by radiotherapy only, 6 and 12 months after radiotherapy. The intervention of the measurement moment "shortly after intervention" refers to "surgery" for the patients treated by surgery and surgery/radiotherapy and to "radiotherapy" for the patients treated by radiotherapy only. Healthy persons were measured once. Ranges of motion of neck and shoulder were determined with an electronic inclinometer (MicroFET 6™, Hoggan Health Industries; West Jordan, Utah). Digital inclinometry have shown an Intra Class Correlation (ICC) of 0.83 for shoulder abduction in patients with shoulder pain[40] and an ICC of 0.93 for patients with neck pain.[41] We determined the following ROM variables: active maximal lateral flexion of the

neck to the left and right side in a standardized sitting position and active maximal forward flexion and active maximal abduction of both arms in a standardized standing position starting with the arms relaxed along the body. The end-point in ROM measurements was determined by musculoskeletal restrictions or the subject's complaints about pain. Right and left side were each measured twice. The mean of the two sequential measurements was used for further analysis. Self-assessed neck and shoulder function was determined from a questionnaire (Appendix 1). The side of the patient where the tumour was located will be referred to as the ipsi-lateral side and the opposite site as the contra-lateral side. For healthy controls and patients without ND or with bilateral ND, we averaged the results of the right and left side.

Statistical analyses

Characteristics of the patients of the radiotherapy group, the surgery group, and the surgery-radiotherapy group were compared with a Chi-square test. In each treatment group (i.e., no ND, SND, (M)RND and bilateral ND) changes in time of maximal lateral flexion of the neck, maximal forward flexion and maximal abduction of the shoulder, and the responses from the questionnaire were analyzed by repeated measures analysis of variance (ANOVA) for continuous data and by a Friedman test for ordinal data. Repeated measures ANOVA and the Friedman test determine possible differences among all measurement moments. Therefore, these tests are susceptible for missing data, due to patients who died, stopped, or missed a measurement. To avoid this disadvantage, we also performed paired *t*-tests (continuous data) and Wilcoxon signed rank tests (ordinal data) to test differences between consecutive measurement moments. Differences among the healthy persons and the patient groups with (no) ND were analyzed by independent *t*-tests (continuous data) and Mann-Whitney U-tests (ordinal data). Regression analysis was used to determine possible explanatory factors for the change in outcomes before and shortly after intervention for all patients. A *p*-value less than 0.05 was considered statistically significant. All analyses were performed with SPSS 15.0 software (SPSS, Inc., Chicago, IL).

Results

Eighty-three patients were treated with ND and 62 patients had no ND (Figure 1). Fifty-five patients were treated with a unilateral SND, 16 patients with a unilateral MRND, 3 patients

with a unilateral RND, and 10 patients with a bilateral ND. Because the number of RND patients was low, we combined these patients with the MRND patients in a group called (M) RND. In the bilateral ND group, 6 patients were treated with SND on both sides of the neck, 2 patients had SND on one side and MRND on the other side, 1 patient was treated with MRND on both sides, and 1 patient was treated with MRND on one side and RND on the other side of the neck. Characteristics of tumour stage (T of TNM), regional lymph node metastasis (N of TNM), oncological intervention, and type of reconstruction are listed in Table 1. Chi-square tests revealed that patient numbers were significantly different ($p < 0.005$) for the 4 patient groups (no ND, SND, (M)RND and bilateral ND) with respect to regional lymph node metastasis, oncological intervention, and oral reconstruction. The average age of the 145 patients (65.3 ± 13.0 yrs) was slightly higher than the age of the controls (60.3 ± 7.2 yrs). Twenty-five patients stopped participation, 19 patients died within a year after surgery, and 4 patients were excluded from the study during the follow-up because of a recurrence and a salvage ND as consequence (Figure 1). Six patients had missing data because of time constraints and/or planning errors.

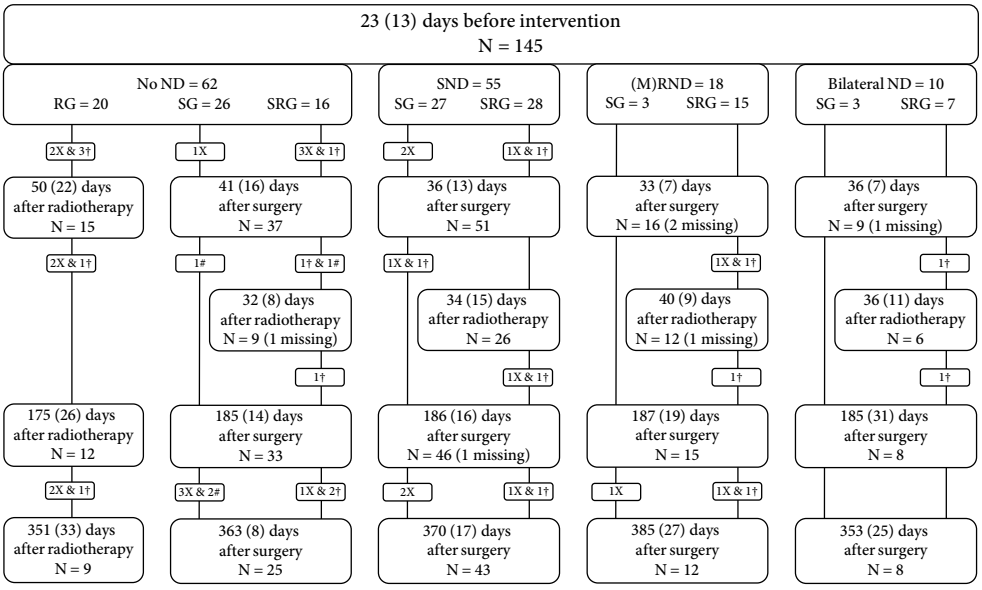

Figure 1. Flowchart of measurement moments (average and SD) and numbers of measured patients (N) for the 4 neck dissection groups.
RG: radiotherapy group; SG: surgery group; SRG surgery-radiotherapy group. X: patient stopped participating; †: patient died; #: salvage neck dissection.

Table 1. Characteristics of groups related to (no) neck dissections. Possible differences in number of patients in the four groups were tested by Chi-square tests.

	No ND	SND	(M)RND	bilateral ND	p-value
Tumour stage (T of TNM)					
T1	23	18	1	3	0.149
T2	13	17	10	3	
T3	3	5	2	0	
T4	23	15	5	4	
Regional lymph node metastasis (N of TNM)					
N0	47	39	1	8	0.000***
N1	3	5	7	0	
N2	10	11	9	2	
N3	2	0	0	0	
Oncological intervention					
Radiotherapy	20	0	0	0	0.000***
Surgery	25	27	4	3	
Surgery & Radiotherapy	16	28	15	7	
Oral reconstruction					
No reconstruction (no surgery)	20	0	0	0	0.002**
Primary closure	27	20	9	2	
Local flap	1	2	1	0	
Myocutaneous or free flap	12	20	7	5	
Bone graft/flap	2	13	2	3	

**: $p < 0.01$; ***: $p < 0.001$

Radiotherapy

No significant difference in observed ROM and self-assessed neck and shoulder outcomes were found within the no ND group between patients treated for radiotherapy only and all patients treated with surgery; before, shortly after, half a year, and one year after intervention. Furthermore, no significant changes were found between shortly after surgery and shortly after radiotherapy in patients treated by surgery and radiotherapy. This applies to the entire group and to the (no) ND groups separately.

Maximal active lateral flexion of the neck

Maximal lateral flexions of the patients of the 4 neck dissection groups are depicted at the various measurement moments in Figure 2. The solid line represents the average angle of the neck movements of the healthy controls. The maximal lateral flexion showed a significant ($p < 0.05$) change at both the ipsi- and contra-lateral side of the SND group over the 1-year

period. Directly after intervention we observed significant decreases in lateral flexions to the ipsi- ($p < 0.01$) and contra-lateral ($p < 0.001$) side for patients of the (M)RND ($p < 0.001$) group (Figure 2). The average decrease in maximal lateral flexion at the contra-lateral side was nearly 25%. During the 1-year period a gradual recovery occurred. Patients of the SND group showed deterioration of maximal lateral flexion of the neck at both the ipsi- and contra-lateral side ($p < 0.01$) between half and one year after intervention. Patients of the bilateral ND group had low maximal lateral flexion values at all measurement moments. Before intervention no significant differences in maximal lateral flexion of the neck were observed between the patients of the 4 ND groups and the controls. Shortly after intervention lateral flexion to the contra-lateral side of the neck of the (M)RND group was significantly lower ($p < 0.05$) than the lateral flexion of the healthy controls, patients with no ND, and contra-lateral lateral flexion in the SND group. One year after intervention the bilateral ND group showed a significantly lower ($p < 0.05$) maximal lateral flexion of the neck than healthy controls and patients without a ND.

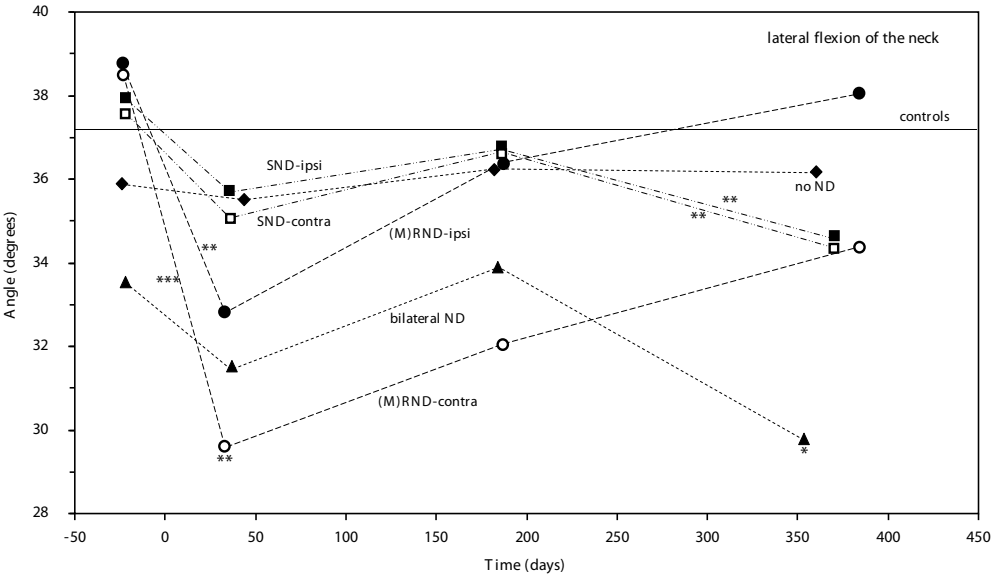

Figure 2. Average maximal lateral flexion of the neck for the 4 neck dissection groups at the various measurement moments.
The solid line represents the average angle of the maximal lateral flexion of the healthy controls. Patient groups: ◆ no ND; ■ and ▫SND (ipsi- and contra lateral); ● and ○(M)RND (ipsi- and contra lateral); ▲ bilateral ND. Measurement moments: before intervention, shortly after intervention, half a year after intervention, and 1 year after intervention. Asterisks close to lines indicate significant differences between measurement moments. Asterisks close to symbols indicate significant differences between patient data and controls.
* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. The lines are for visual aid only.

Maximal active forward flexion of the shoulder

The maximal forward flexion of the shoulder showed significant ($p < 0.01$) changes at the ipsi-lateral side of both the SND and (M)RND groups over the 1-year period (Figure 3). Directly after intervention we observed a significant decrease ($p < 0.05$) in maximal forward flexion in all patient groups except in the SND group at the contra-lateral side.

Before intervention no significant differences in maximal forward flexion were observed between the 4 ND groups and the controls. Shortly after intervention the ipsi-lateral forward flexion for patients of the SND and (M)RND groups, and the average forward flexion of the bilateral ND group was significantly lower ($p < 0.01$) than the forward flexion in healthy controls and patients without a ND. Half a year after intervention the ipsi-lateral maximal forward flexion of the patients of the SND and (M)RND groups was still significantly lower ($p < 0.05$) than the forward flexion of the healthy controls. However, at the end of the 1-year period maximal forward flexion of the patients of all ND groups was near the level of the controls.

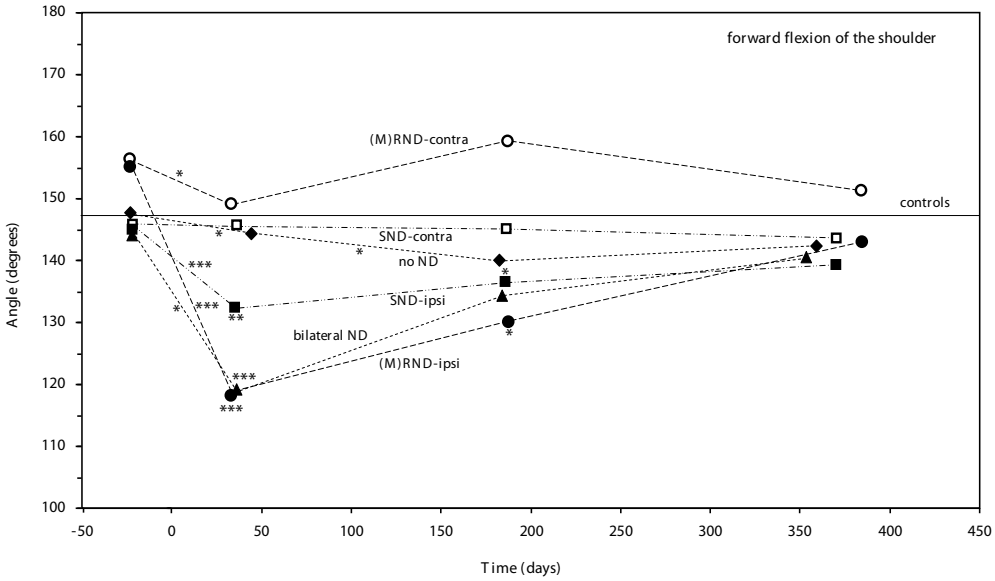

Figure 3. Average maximal forward flexion of the shoulder for the 4 neck dissection groups at the various measurement moments.
The solid line represents the average angle of the maximal forward flexion of the healthy controls. Patient groups: ◆ no ND; ■ and ▫ SND (ipsi- and contra lateral); ● and ○ (M)RND (ipsi- and contra lateral); ▲ bilateral ND. Measurement moments: before intervention, shortly after intervention, half a year after intervention, and 1 year after intervention. Asterisks close to lines indicate significant differences between measurement moments. Asterisks close to symbols indicate significant differences between patient data and controls.
* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. The lines are for visual aid only.

Maximal abduction of the shoulder

Over the one year period the maximal abduction of the shoulder showed significant ($p < 0.05$) changes for all patients groups, except for the contra-lateral side of the (M)RND group (Figure 4). Maximal abduction significantly deteriorated ($p < 0.05$) after intervention in all patients groups, except for the contra-lateral abduction of the patients of the SND and (M)RND groups. The largest decreases in abduction were observed for the ipsi-lateral side of patients in the (M)RND group (about 60°) and for the averaged abduction of the bilateral ND group (about 50°).

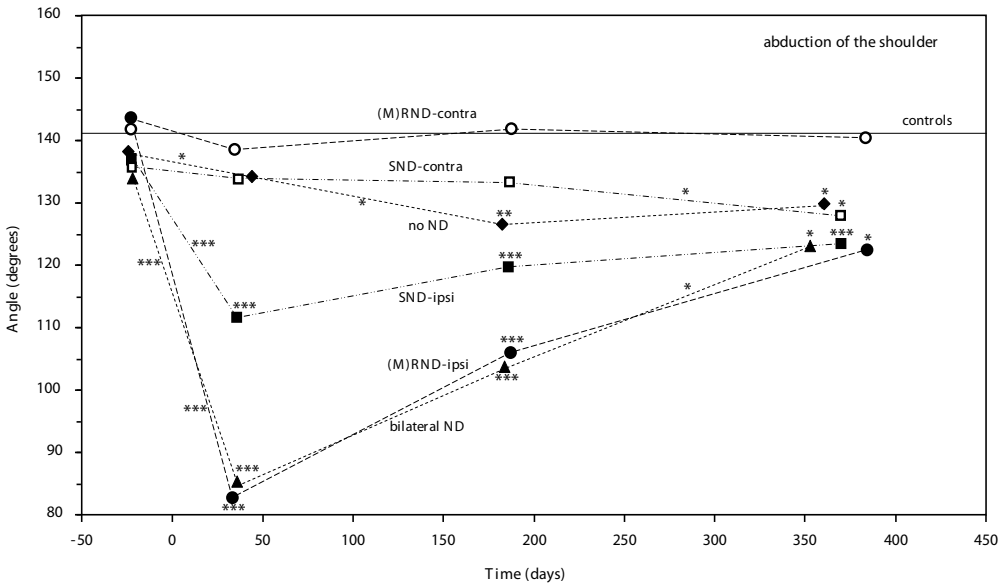

Figure 4. Average maximal abducton of the shoulder for the 4 neck dissection groups at the various measurement moments.
The solid line represents the average angle of the maximal abduction of the healthy controls. Patient groups: ◆ no ND; ■ and ▫ SND (ipsi- and contra lateral); ● and ○ (M)RND (ipsi- and contra lateral); ▲ bilateral ND. Measurement moments: before intervention, shortly after intervention, half a year after intervention, and 1 year after intervention. Asterisks close to lines indicate significant differences between measurement moments. Asterisks close to symbols indicate significant differences between patient data and controls.
* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. The lines are for visual aid only.

Before intervention no significant differences in abduction were observed between the patients of the 4 ND groups and the controls. Shortly after intervention abduction at the ipsi-lateral side of the SND and (M)RND group and the average abduction in the bilateral ND group differed significantly ($p < 0.01$) from healthy controls and the no ND group. Furthermore, the ipsi-lateral abduction of the (M)RND group was significantly lower than

the ipsi-lateral abduction of the SND group ($p < 0.05$). Although recovery occurred in the 1-year period after intervention, the ipsi-lateral abduction (SND and (M)RND groups) and averaged abduction (bilateral ND group) remained significantly below the level of the controls (half- and 1-year measurement). Also the contra-lateral abduction of the SND patients and the average abduction of the no ND patients was significantly below the level of the controls.

Questionnaire

Two questions concerning difficulties with head/neck movements (1 and 4; see appendix 1) and three questions on difficulties with right and left shoulder/arm movements (2/3, 5/6 and 7/8) were answered by the participants during each visit. Highly significant correlations ($p < 0.001$) were observed between the answers on head/neck as well as shoulder/arm questions. Therefore, we report only the answers on questions 1 (pain while moving neck) and 2/3 (pain while moving left/right shoulder/arm).

Pain while moving the neck

Figure 5 depicts the results obtained for the head/neck question in the same way as was done in the previous Figures. The pain while moving the neck significantly ($p < 0.001$) changed during the first-year period for the patients of the SND, (M)RND and bilateral ND groups.

A significant increase in pain while moving the neck was reported shortly after intervention by the patients of the SND, (M)RND and bilateral ND groups. The pain scores decreased during the 1-year period for the patients of the SND and bilateral ND groups to the level of the controls, but remained significantly higher than the scores of the controls for the patients of the (M)RND group. The patients of the no ND group reported pain scores comparable to those of the controls.Before intervention no significant differences in pain while scores were observed between the patients of the 4 ND groups and the controls. Shortly after intervention the patients of the SND, (M)RND, and bilateral ND groups scored significantly higher ($p < 0.05$) on pain while moving the neck, than the healthy controls and the patients without a ND. Half a year after intervention the (M)RND and bilateral ND groups still significantly differed ($p < 0.05$) from the no ND group. One year after intervention the patients of the (M) RND group scored significantly higher on pain ($p < 0.05$) than the healthy controls, the no ND and the SND group.

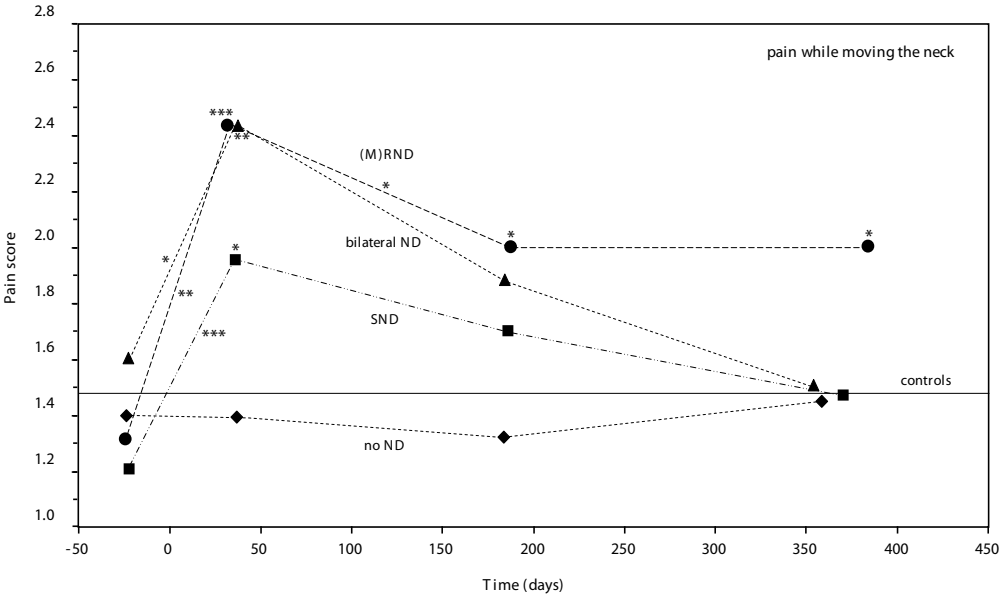

Figure 5. Average scores for "pain while moving the neck" for the 4 neck dissection groups at the various measurement moments.
The solid line represents the average pain score of the healthy controls. Patient groups: ◆ no ND; ■ and ▫ SND (ipsi- and contra lateral); ● and ○ (M)RND (ipsi- and contra lateral); ▲ bilateral ND. Measurement moments: before intervention, shortly after intervention, half a year after intervention, and 1 year after intervention. Asterisks close to lines indicate significant differences between measurement moments. Asterisks close to symbols indicate significant differences between patient data and controls.
* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. The lines are for visual aid only.

Pain while moving the shoulder/arm

Significant changes ($p < 0.01$) over the 1-year period in "pain while moving the shoulder/arm" were reported for the ipsi-lateral side by patients of the SND and (M)RND groups, and for both sides by patients of the bilateral ND group (Figure 6). Shortly after intervention pain during moving the shoulder/arm significantly increased ($p < 0.001$) at the ipsi-lateral side of patients of the SND and (M)RND groups and at both sides for the bilateral ND group. The pain scores of these patients gradually decreased in the one-year period after intervention. Before intervention some of the pain scores of the patients (no ND, contra-lateral SND/(M)RND, and ipsi-lateral SND) were below the level of the controls ($p < 0.05$). Shortly after intervention and half a year after intervention the patients of the SND and (M)RND groups had significantly higher scores on pain at the ipsi-lateral side than controls and patients of the no ND group. Also the patients of the bilateral ND group scored significantly higher at these measurement moments. One year after intervention no longer significant differences in pain scores among patient groups and controls were present.

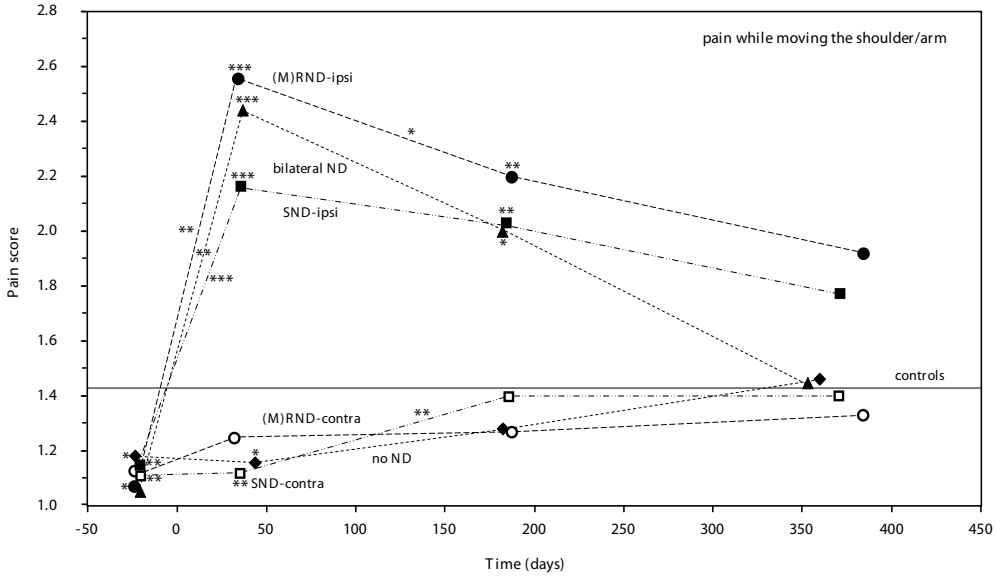

Figure 6. Average pain scores for "pain while moving shoulder/arm" for the 4 neck dissection groups at the various measurement moments.
The solid line represents the average pain score of the healthy controls. Patient groups: ◆ no ND; ■ and SND (ipsi- and contra lateral); ● and ○ (M)RND (ipsi- and contra lateral); ▲ bilateral ND. Measurement moments: before intervention, shortly after intervention, half a year after intervention, and 1 year after intervention. Asterisks close to lines indicate significant differences between measurement moments. Asterisks close to symbols indicate significant differences between patient data and controls.
* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. The lines are for visual aid only.

Influence of T- and N-stage, resection site and oral reconstruction on neck and shoulder function

The deterioration, caused by the intervention, of maximal forward flexion and abduction of the shoulder at the contra-lateral side, was significantly related to reconstruction ($p < 0.01$). Bone flaps were related to the largest reduction in shoulder movement. The reduction in ipsi-lateral maximal forward flexion and abduction of the shoulder was significantly related to regional lymph node metastasis ($p < 0.01$). Furthermore, resection site had a significant influence on the reduction of ipsi-lateral abduction. The deterioration of the ipsi- and contra-lateral lateral flexion of the neck was not significantly correlated to any of the above mentioned factors.

Discussion

The results of this study demonstrated that more extended neck dissections induced more deterioration in neck and shoulder function. A significant decrease in neck and shoulder mobility directly after intervention was followed by a gradual recovery one year later up to levels not so far below those of healthy controls. Our findings complement the existing knowledge in neck and shoulder function after ND obtained from cross-sectional and longitudinal observation studies. To our knowledge, no other studies reported on objective and self-perceived neck and shoulder function in patients treated for oral malignancies until one year after intervention, while comparing patients treated with or without ND to each other and to healthy controls. The reasons for not performing a neck dissection were: wait-and-see regimen for the N_0-negative neck, poor general condition, degree and type of comorbidities, and palliative care.

Shortly after intervention our patients treated with (M)RND and bilateral ND had a significantly worse maximal lateral flexion of the neck than patients treated with SND. Furthermore, the (M)RND and bilateral ND patients reported more pain while moving the neck than the SND patients. One year after intervention the patients treated with bilateral ND still showed significantly reduced lateral flexion of the neck as compared with controls. At that time no significant differences in lateral flexion were observed anymore between the patients of the other ND groups and the controls. One year after intervention patients treated with (M)RND reported significantly more pain while moving the neck than the healthy controls, whereas no such differences were observed for patients of the other groups. In contrast to our findings, a prospective study reported no statistically significant differences in neck mobility (extension + rotation) between patients who underwent SND and (M)RND.[15] On the other hand, in agreement with our findings, a cross-sectional study found that lateral flexion to the contra-lateral side was related to the levels dissected.[42] In a retrospective QoL-study, patients treated by different types of neck dissection reported neck tightness (71% of the patients), which interfered with daily life.[12] Shoulder discomfort and neck tightness had the greatest affect on QoL. Patients with more extended NDs may have more limitations in daily life even after one year. Most studies on mobility and ND report on the consequences of the associated "shoulder syndrome", whereas few studies report on neck mobility after ND. Shoulder forward flexion and abduction and self-perceived pain while moving the shoulder/arm showed the same patterns over the 1-year measurement period. Shortly after

intervention forward flexion and abduction were significantly lower at the ipsi-lateral side in patients treated by ND than in patients without a ND and controls. The largest reduction in forward flexion and abduction was observed for patients of the (M)RND and bilateral ND groups. Furthermore, we observed that the deterioration in shoulder abduction was larger than in maximal forward flexion of the shoulder. This is in concordance with the findings of other studies.[15,30,43,44] In maximal shoulder abduction the trapezius muscle activity is needed to stabilize the scapula, whereas in maximal forward flexion this stabilization is much less important. Resection of the SAN during RND usually leads to loss of function of the trapezius muscle, which is then unable to perform its primary task of stabilizing the scapula. However, also after preservation of the SAN, neurapraxia may result in a loss of function of the trapezius muscle.

One year after intervention the measured maximal forward flexion of the shoulder did not longer differ significantly from the forward flexion of the healthy controls. However, at that time shoulder abduction was still significantly lower in all patient groups as compared with healthy controls, except the contra-lateral side in the (M)RND group. Similar results have been reported in a retrospective study: after MRND 33% of the patients reported shoulder complaints, while this complaint had a prevalence of 20% in patients treated by SND.[18] In a study based on electromyography and ROM of shoulder forward flexion and abduction, it was also found that patients who underwent a SND performed significantly better than those who underwent either a MRND or a RND. A marked difference between these groups occurred 16 weeks after surgery.[24] It has been reported that SAN function was electrophysiologically impaired in all patients who underwent NDs preserving or sacrificing the SAN, although shoulder joint function was clinically better in patients with a preserved SAN than in patients with a sacrificed SAN. Significant shoulder dysfunction occurs even when the SAN is spared during the neck dissection procedure.[30] In a prospective study significant changes were found for shoulder abduction, but not for forward flexion of the shoulder between preoperative and 3 months after surgery.[45] This is in contrast with the results of our study: shortly after intervention shoulder forward flexion was significantly impaired, but recovered within half a year after intervention. In two prospective studies, using the University of Washington Quality of Life questionnaire (UW-QoL), a drop in composite scores was found for all patients treated by ND at 6 months after intervention. The patients who did not receive ND scored better than those who received a ND. Furthermore, a more extensive ND caused a larger

drop in QoL scores.[34] In one of these prospective studies, at 12 and 18 months after surgery, there was a gradual increase in composite scores of the UW-QoL within all subgroups, but the gradation between the ND groups was still maintained.[34] One year after intervention we observed similar outcomes for neck and shoulder mobility in al patient groups. However, QoL is related to more aspects than neck and shoulder function.

Both in objective measurements as in self-perceived neck and shoulder function no significant changes in neck and shoulder function were found between shortly after surgery and shortly after radiotherapy in the present study. These findings are in accordance with results of a retrospective study on reduced ROM and loss of function in patients treated by ND.[18] The results of that study were retrospectively obtained from a questionnaire. Logistic regression analyses learned that radiotherapy did not significantly contribute to the prediction of shoulder complaints if type of surgery was entered before radiation therapy in the model.[18] Another study where patients were measured at least 6 months after surgery or 3 months after radiotherapy no negative effects of radiotherapy on motion of shoulder joint, shoulder muscle strength, and degree of denervation were found.[30] In a cross-sectional study, with patients included 6-122 months after ND, both the use of adjuvant radiotherapy and the dose used, if adjuvant radiotherapy was given, did not affect shoulder morbidity.[33] Also in other cross-sectional studies no influence of radiotherapy on shoulder ROM was found.[31,32,43] As mentioned in the introduction, radiotherapy often adversely influenced self-assessed shoulder function outcomes.[34-36] Perhaps the effect of additional radiotherapy on shoulder function may be confounded by the surgical intervention. On the other hand, in a prospective QoL-study, with measurements before, half a year, and one year after intervention, it was found that adjuvant radiotherapy had no association with shoulder dysfunction.[17] Also in a cross-sectional study, with patients treated at least one year previously, radiotherapy was not significantly associated with shoulder pain or disability by using the shoulder disability questionnaire (SDQ).[46] There is growing evidence that adjuvant radiotherapy has no significant influence on shoulder function.

Physiotherapy plays an important role in promoting function, improving scapular stability and reducing pain by maintaining the length of muscles, range of movement and by preventing frozen shoulder symptoms.[42,47] Evidence has been presented that such a postoperative treatment policy aids in reducing adverse shoulder symptoms after any type of neck dissection.[48-50] The effect of physiotherapy on neck symptoms has not yet been

examined. After discharge only patients with clear complaints were referred to physiotherapy in the University Medical Center Utrecht and Radboud University Nijmegen Medical Center. It is important that future prospective research focuses on the necessity and effectiveness of physiotherapy for the different ND groups.

The results of this study should not be interpreted as recommendations as to whether or which type of a neck dissection or radiotherapy is indicated for a particular clinical scenario. The type and extent of dissection is dictated by the tumour site, size, and stage. However, from a functional perspective, neck dissections should be as selective as possible to reduce shoulder and neck complaints, particularly shoulder abduction. From the results of our study we may conclude that more extended neck dissections induced more deterioration in neck and shoulder function shortly after intervention. One year after intervention patients treated with bilateral ND still showed deteriorated lateral flexion of the neck, while patients treated by unilateral (M)RND still reported pain while moving the neck. Maximal forward flexion of the shoulder returned to the level of healthy controls at one year after intervention. On the other hand, all patients, also the no ND group, showed significant lower maximal abduction of the shoulder than controls at one year after intervention.

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Apendix 1. Questionnaire: neck and shoulder mobility

During last week:

	Never	Sometimes	Often	Always
1. Did you experience any pain while moving your neck?	1	2	3	4
2. Did you experience any pain while moving your left shoulder/arm?	1	2	3	4
3. Did you experience any pain while moving your right shoulder/arm?	1	2	3	4
4. Did you experience any difficulties turning your head in traffic?	1	2	3	4
5. Did you experience any difficulties when grabbing something above your head with your left arm?	1	2	3	4
6. Did you experience any difficulties when grabbing something above your head with your right arm?	1	2	3	4
7. Did you experience any difficulties carrying a shopping bag in your right hand?	1	2	3	4
8. Did you experience any difficulties carrying a shopping bag in your left hand?	1	2	3	4

8

Summary, conclusions and future research

Introduction

In the Netherlands, the incidence of oral cancer is increasing.[1] Progress in (reconstructive) surgery, radiotherapy and chemotherapy, however, has improved survival and loco-regional control while trying to preserve or restore oral function and quality of life.[2] Despite the progress in treatment, patients are still confronted with impairment or loss of essential oral functions such as mastication, tongue function, lip competence, speech and swallowing.[3-9] Neck and shoulder function may also be affected, when neck dissection is indicated.[10-13] The deterioration of function may be caused by the tumour itself, but may also be induced by the oncological therapy. Surgery may result in tissue defects dependent on the localization, tumour size and cervical lymph node metastasis, whereas radiotherapy may result in troublesome and uncomfortable fibrosis which may worsen with time.

Clinical experience has revealed that the primary location of the tumour will influence the outcomes of oral function in different ways (unpublished data). In this study, therefore, patients were divided into three anatomical groups, based on the location of the cancer: (1) maxilla, hard/soft palate, maxillary tuber, and/or superior alveolar process, (2) buccal mucosa of the cheek, retro molar trigone, and/or inferior alveolar process, and (3) tongue and/or floor of mouth. First, a retrospective study was performed on self-perceived function of 158 patients treated for oral malignancies, in order to get information on the way these patients experience their oral abilities five years after oncological intervention. Secondly, in the period from January 2007 till August 2010, 145 patients with a primary oral carcinoma were recruited for prospective evaluation of oral and oral-related functions: 34 patients with malignancies of the maxilla, hard/soft palate, maxillary tuber, and/or superior alveolar process; 56 patients with malignancies of the buccal mucosa of the cheek, retro molar trigone, and/or inferior alveolar process; and 55 patients with malignancies of the tongue and/or floor of mouth. Exclusion criteria were previous or synchronous malignancies, cognitive impairment, and inability to understand Dutch. In addition 60 healthy people, matched for age, were recruited so that the outcomes of the patients could be compared with those of healthy controls.

This thesis describes investigations into the effects of oral oncological intervention, reconstruction and rehabilitation on function of the mouth, neck and shoulders. The outcomes are based on self-perceived experiences and objectively measured function in patients treated for oral cancer. Using self-perceived and objective outcomes, it was the intention to improve the knowledge of deterioration and recovery of function of these patients after oncological therapy, reconstruction and rehabilitation.

Oral function after oncological intervention in the oral cavity: a retrospective study (chapter 2)

Knowledge of self-perceived function of patients treated for oral malignancies is important for clinicians. It gives information on how patients experience their oral abilities after oncological intervention. Five years after oncological intervention patients were interviewed by telephone. They answered in retrospect questions on their oral function in various phases of their treatment, before and after oncological intervention and at present. The following 11 items were addressed: dentition, chewing, pain during chewing, lip competence, xerostomia, weight loss, tube nutrition, swallow complaints, choke, pain during swallowing, and speech. Patients treated for malignancies in maxilla, hard/soft palate, maxillary tuber, and/or superior alveolar process reported that they experienced more difficulty in chewing food directly after oncological intervention. However, after five years follow-up a significant improvement in chewing was reported. Patients treated for malignancies of the buccal mucosa of the cheek, retro molar trigone, and/or inferior alveolar process experienced deterioration in chewing, lip competence, and xerostomia directly after intervention. Five years later they still reported these problems and a deterioration in their dental state. Patients treated for malignancies in tongue and/or floor of mouth experienced problems on nearly all interviewed items directly after oncological intervention. In the five years of follow-up improvement was reported on several aspects of oral function, although they still experienced problems on dental state, chewing, and xerostomia. These patients reported more complaints on oral function than patients of the other two groups shortly after intervention, notwithstanding that their tumours were on average less extended and that less reconstruction and less radiotherapy was needed. We may conclude that a retrospective interview may help to add information to incomplete data obtained from patient files.

Mixing ability test compared with a comminution test in persons with normal and compromised masticatory performance (chapter 3)

To quantify masticatory function objectively, a new mastication test was developed, suitable for patients with compromised masticatory performance. The new test food should form a bolus and should be soft enough to be chewed by persons with compromised oral function. Existing comminution tests did not meet these criteria. The test food Optocal, which is commonly used in comminution tests, does not form a coherent bolus and the chewing force to fragment Optocal particles is too high for patients with oral cancer.[14] This makes the Optocal comminution test unsuitable for patients with a mutilated oral cavity. We developed a mastication test that measures how well a person can mix and knead a food bolus. Tablets with a diameter of 20 mm were made, that consist of a red and a blue wax layer. The wax tablets are easy to chew and form a coherent bolus. The degree of mixing of the two colours has been determined by computer analysis of digital images of the chewed wax. The results of the new mixing ability test were compared with the results of the Optocal comminution test. Tablets of two-coloured wax and Optocal particles were chewed by 60 healthy participants divided in three groups of 20 subjects (matched for age and gender) based on their dentition: full natural dentition, maxillary dentures plus implant supported mandibular overdentures, and complete dentures. Both tests showed that the natural dentition group chews better than the two denture-wearer groups. The mixing ability test showed better results for the denture wearers with implant support than for the complete-denture wearers. The comminution test, however, showed no significant difference in chewing performance between the two denture groups. The results indicate that the mixing ability test is capable of discriminating the masticatory performance between different groups of subjects with compromised oral function. We may expect that the mixing ability test will be suitable for evaluating masticatory performance of patients with oral cancer.

Digital image processing versus visual assessment of chewed two-colour wax in mixing ability tests (chapter 4)

The objective of this study was to compare the results of computer analysis of digital images of chewed two-colour wax with the results of visual assessment of these images. The degree of colour mixing of the chewed two-colour wax tablets of the previous study (chapter 3) was determined by digital image processing and by visual assessment from five examiners.

Digital images of both sides of the chewed bolus were captured using a flatbed scanner. The digitized images of the chewed wax were processed and a measure for the mixing of the wax was determined from the intensity distributions of the mixed colours: the mixing index. The degree of colour mixing of the same digital images was rated into categories by five examiners according to five reference samples. Digital processing of the images resulted in significantly different mixing abilities for the two full-denture groups, whereas no such differences could be detected by visual assessment. Both methods were capable of discriminating the mixing results of the dentate subjects and full denture wearers. It was concluded that digital image processing is preferred over visual assessment in comparing chewing results of groups of persons with compromised masticatory performance.

Mastication in patients treated for malignancies in tongue and/or floor of mouth: a 1-year prospective study (chapter 5)

Our study on the oral function of patients with malignancies in tongue and/or floor of mouth region demonstrated a significant decrease in dentition index, maximum bite force, and masticatory performance (i.e. mixing ability) after surgical intervention. Oral rehabilitation restored the dental status significantly and for patients treated by surgery only it reached pre-treatment levels one year after surgery. In patients treated by surgery and radiotherapy, however, the dentition index remained below the pre-treatment level. The maximum bite force of the surgery group was not significantly affected by surgical intervention. In the surgery-radiotherapy group, shortly after surgery the bite force had temporarily decreased to a level below that of the healthy full denture wearers. Although some recovery occurred, the bite force of the surgery-radiation group remained significantly below the pre-surgical level. The decrease in maximum bite force, observed shortly after surgery in all patients in this study, was significantly related to the resection site and the extent of reconstruction. Thus, the resection site will influence the initial decrease in maximum bite force, with larger reconstructions leading to a stronger decrease in maximum bite force. Masticatory performance, as measured from the mixing index of two-coloured wax, showed a large deterioration as a result of surgery. A further decrease occurred after radiotherapy. The patients of the surgery-radiotherapy group performed significantly worse than the surgery group. We may conclude that surgical intervention has a large negative impact on oral function. The deterioration of oral function was significantly larger for patients treated

by surgery and radiotherapy as compared to the patients who had surgery only. Also the recovery of oral function was less prominent for the surgery-radiotherapy group than for the surgery group. On average patients treated by surgery and radiotherapy had larger tumours, more extended resections. Half a year after surgery we observed no further improvement in maximum bite force and masticatory performance.

Tongue function in patients treated for malignancies in tongue and/or floor of mouth: a 1-year prospective study (chapter 6)

The tongue plays a major role in mastication, deglutition, oral hygiene, and speech. A significant decrease was found in tongue sensory function after surgery in patients with squamous cell carcinoma of tongue and/or floor of mouth. Tongue mobility decreased significantly after surgery in patients treated by surgery and radiotherapy. During the 1-year period tactile sensory function remained at the low level observed shortly after surgery. The decrease in thermal sensory function, observed shortly after surgery for all patients in this study, was significantly related to pathological tumour size (pT). All tongue mobility measurements showed deterioration due to surgery. The decrease in protrusion, observed shortly after surgery in all patients in this study, was significantly related to pT and type of reconstruction. Maximum tongue force was not significantly influenced by surgery and/or radiotherapy. Six months after surgery a temporary increase in tongue force was observed. This increase, however, disappeared in the next six months to the levels observed before and shortly after treatment. A decreased masticatory performance resulted in an increased tongue force. Apparently, patients "chewed" with the tongue by pressing the food between tongue and palate, compensating for the decreased dental chewing performance. In this way patients inadvertently trained their tongue muscles which resulted in a higher maximum tongue force. In this study additional post surgical radiotherapy had no significant influence on tongue function in the outcome measures. However, the patients treated by surgery and radiotherapy had more advanced pT and received more extensive reconstructions. Therefore, the decrease in tongue sensory function and mobility was significantly larger in patients treated by surgery and radiotherapy than in patients treated by surgery only.

Neck and shoulder function in patients treated for oral malignancies: a 1-year prospective cohort study (chapter 7)

Neck and shoulder complaints can be a direct result of a neck dissection (ND) and can manifest as pain, reduced range of motion of the neck and shoulder, loss of sensation, and loss of neck and shoulder function. Patients without a ND, and patients treated by a selective neck dissection (SND), (modified) radical neck dissection ((M)RND), and bilateral ND participated in this study. Their results were compared with the results of a group of healthy controls. From the results of our study we may conclude that more extended neck dissections induced more deterioration in neck and shoulder function shortly after intervention. A significant decrease in neck and shoulder mobility directly after intervention was followed by a gradual recovery during the 1-year period up to levels not so far below those of healthy controls. However, one year after intervention patients treated with bilateral ND still showed deteriorated lateral flexion of the neck, while patients treated by unilateral (M)RND still reported pain while moving the neck. One year after intervention maximal forward flexion of the shoulder returned to the level of healthy controls in all patients. On the other hand, all patients, also the no ND group, showed one year after intervention significant lower maximal abduction of the shoulder than controls.

Conclusions

This thesis showed that more deterioration in function occurred when patients had larger tumours and had a higher degree of cervical lymph node metastasis. Larger tumours and more extended cervical lymph node metastasis have to be treated by more extended therapy. In our study we observed no further significant deterioration of function as a result of adjuvant radiotherapy in the period between shortly after surgery and shortly after radiotherapy. Thus, no significant short term effects of radiotherapy on function were observed. Possible effects of radiotherapy on function, however, may have been concealed by the ongoing effects of the surgical intervention. Within a year after intervention, function partly recovered depending on which function was performed. Recovery of function was less evident in patients with more intensive surgical intervention. It can be assumed that recovery will take more time for these patients. Our retrospective study learned that after five years part of the patients treated for oral cancer still reported deterioration in xerostomia, dental state, chewing, and lip competence.

Future research

In addition to the data reported in this thesis, data on several other parameters have been collected for the group of 145 patients with oral cancer during the 1-year period. Data were collected on self-perceived Quality of Life (QoL) according to the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30 Head and Neck 35-questions (EORTC QLQ H&N C30). Furthermore, we assessed degree of depression according to the Center for Epidemiological Studies-Depression Scale (CES-D), and coping style according to the Coping Inventory for Stressful Situations Questionnaire. Analysis of these data will give more insight in how patients perceived the various aspects of oncological treatment during the 1-year period. Besides self-perceived data, the following objective parameters have been measured: swallowing time, speech, lip mobility, lip competence, sensation of the lips, maximum mouth opening and salivary flow. Analysis of these new data in combination with the data reported in this thesis, will give more detailed understanding of subjective and objective function of patients with oral cancer.

To complement the data of our retrospective study on self-perceived oral function, it is recommended to perform a 5-year follow-up study to determine all subjective and objective parameters on function of the patients participating in our prospective cohort study. This will give detailed long-term information on how patients perceive their function and on how patients are able to perform oral, neck and shoulder function.

In our prospective cohort study it was found that between 6 and 12 months after surgery no (further) recovery was observed for oral function (i.e., maximum bite force, masticatory performance, tongue mobility, and sensation of the tongue) in the group of 45 patients treated for malignancies in tongue and/or floor of mouth. Neck and shoulder function recovered partly in the 145 patients treated for oral cancer. Research on revalidation interventions, such as (orofacial) physiotherapy,[15,16] speech and swallow therapy,[17] and dietetics[18] is needed to further improve (oral) function after intervention. The physiotherapist, specialized in training and optimization of the mobility of the musculoskeletal system, may help to maximize rehabilitation of (oral) functions. Evaluating physiotherapy interventions, preferably by randomized clinical trials, will give information on whether rehabilitation treatment is successful in further reducing function deficits.

Samenvatting, conclusies en toekomstig onderzoek

Samenvatting

Introductie

In Nederland neemt de incidentie van mondkanker steeds meer toe.[1] Vooruitgang in (reconstructieve) chirurgie, radiotherapie en chemotherapie zorgt echter voor een toename van de overleving en betere locoregionale controle. Daarnaast wordt gewerkt aan behoud en herstel van de orale functie en kwaliteit van leven na de behandeling van de kanker.[2] Desondanks worden patiënten nog steeds geconfronteerd met verslechtering of verlies van essentiële orale functies, zoals kauwen, tongfunctie, lipsluiting, spreken en slikken.[3-9] Wanneer een nekdissectie nodig was, kan ook de nek- en schouderfunctie aangedaan zijn.[10-13] De afname van functie kan worden veroorzaakt door de tumor zelf, maar ook door de oncologische interventie. Chirurgie kan resulteren in defecten van het weefsel, afhankelijk van de locatie en grootte van de tumor en eventuele cervicale lymfklier metastase. Radiotherapie kan bijvoorbeeld leiden tot problematische fibrosering, die in de loop van de tijd kan verergeren.

Uit klinische ervaring is gebleken dat de primaire locatie van de tumor van invloed is op het verloop van de orale functie (ongepubliceerde gegevens). Op basis van deze kennis werden in dit onderzoek de patiënten ingedeeld in drie anatomische groepen, afhankelijk van de locatie van de tumor: (1) maxilla, hard/zacht palatum, tuber maxillare en/of processus alveolaris superior, (2) buccale mucosa van de wang, trigonum retromolare en/of processus alveolaris inferior en (3) tong en/of mondbodem. Allereerst werd een retrospectief onderzoek uitgevoerd naar de beleving van de orale functie bij 158 patiënten die werden behandeld voor orale oncologie. Op deze wijze werd informatie verkregen over het oraal functioneren van deze patiënten over de periode tot vijf jaar na de oncologische interventie. Daarnaast werden 145 nieuwe patiënten met mondkanker geworven voor een prospectieve evaluatie van de orale functie: 34 patiënten met maligniteiten in maxilla, hard/zacht palatum, tuber maxillare en/of processus alveolaris superior; 56 patiënten met maligniteiten in buccale mucosa van de wang, trigone retromolare en/of processus alveolaris inferior en 55 patiënten met maligniteiten in tong en/of mondbodem. Exclusiecriteria waren eerdere of gelijktijdige

tumoren, cognitieve stoornissen en onvermogen tot het begrijpen van de Nederlandse taal. Tevens werden 60 gezonde mensen van overeenkomstige leeftijd gerekruteerd om hun resultaten te vergelijken met die van de patiënten die behandeld werden voor mondkanker.

Dit proefschrift beschrijft wetenschappelijk onderzoek naar de effecten van de oraal oncologische interventie, reconstructie en rehabilitatie op de functie van de mond, nek en schouders. De resultaten van het onderzoek zijn gebaseerd op ervaringen van de patiënten en op objectief gemeten functies van de patiënten vóór en na behandeling van de mondkanker. De resultaten vergroten de kennis omtrent de verslechtering en het herstel van de mondfunctie bij patiënten behandeld voor mondkanker na interventie, reconstructie en rehabilitatie.

Oraal functioneren na oncologische interventie in de mondholte: een retrospectieve studie (hoofdstuk 2)

Het is belangrijk dat clinici weten hoe patiënten, die worden behandeld voor mondkanker, zelf hun orale vaardigheden ervaren. Daarvoor is het nodig deze patiënten te vragen naar hun oraal functioneren. Vijf jaar na oncologische interventie werden patiënten telefonisch geïnterviewd. Zij beantwoordden vragen over hun oraal functioneren in verschillende fasen van hun behandeling: vóór en na interventie en op het moment van het telefonisch interview. De volgende 11 items kwamen aan de orde: dentitie, kauwen, pijn tijdens kauwen, lipsluiting, xerostomia, gewichtsverlies, sondevoeding, slikklachten, verslikken, pijn tijdens het slikken en spraak.

Patiënten die waren behandeld voor maligniteiten in maxilla, hard/zacht palatum, tuber maxillare en/of processus alveolaris superior rapporteerden dat het kauwen van voedsel direct na de oncologische interventie moeilijker was geworden. Echter vijf jaar later werd een significantie verbetering in de kauwfunctie gemeld. Patiënten behandeld voor maligniteiten in de buccale mucosa van de wang, trigone retromolare en/of processus alveolaris inferior rapporteerden een verslechtering in kauwen, lipsluiting en speekselproductie direct na de interventie. Vijf jaar later meldden deze patiënten nog steeds deze problemen met daarbij een verslechtering van de dentale status. Patiënten behandeld voor maligniteiten in tong en/of mondbodem hadden problemen met vrijwel alle items uit de enquête direct na de oncologische interventie. Vijf jaar na de interventie meldden deze patiënten dat zij nog steeds problemen hadden met hun dentale status, kauwfunctie en speekselproductie. Deze

patiënten rapporteerden meer klachten over hun orale functie dan de andere twee groepen kort na interventie, terwijl de tumoren gemiddeld kleiner waren, minder reconstructie had plaatsgevonden en minder patiënten radiotherapie hadden gekregen. Daarnaast concludeerden we dat een retrospectief interview kan helpen om informatie toe te voegen aan onvolledige gegevens die verkregen zijn uit de patiëntendossiers.

Kleurenmengtest vergeleken met een deeltjesverkleiningtest bij personen met een normaal en met een verminderd kauwvermogen (hoofdstuk 3)

Voor het objectief kwantificeren van kauwfunctie werd een nieuwe kauwtest ontwikkeld, geschikt voor patiënten met een verminderd kauwvermogen. Het nieuwe testvoedsel diende een samenhangende bolus te vormen en moest zacht genoeg zijn om te kunnen worden gekauwd door personen met een verslechterde mondfunctie. Bestaande tests, waarin deeltjes worden verkleind door erop te kauwen, voldeden niet aan deze criteria. Het testvoedsel Optocal, dat gewoonlijk wordt gebruikt voor deze tests, vormt geen coherente bolus en de bijtkracht die nodig is voor het verkleinen van de Optocal deeltjes is te groot voor veel patiënten die behandeld zijn voor orale maligniteiten.[14] Dit maakt de test met kauwen op Optocal ongeschikt voor patiënten met een gemutileerde mondholte. We ontwikkelden een test die meet hoe goed een persoon een voedselbolus kan mengen en kneden. Deze test maakt gebruik van tabletten met een doorsnede van 20 mm die bestaan uit een laag rode en een laag blauwe was. De wastabletten zijn makkelijk te kauwen en vormen een coherente bolus. De mate van vermenging van de twee kleuren wordt bepaald door computer analyse van digitale beelden van de was. De resultaten van de nieuwe kleurenmengtest werden vergeleken met de resultaten van de test met verkleining van Optocal deeltjes. De twee-kleuren wastabletten en de Optocal deeltjes werden gekauwd door 60 gezonde deelnemers, verdeeld in drie groepen van 20 proefpersonen gematcht voor leeftijd en geslacht. De verdeling van de deelnemers geschiedde op basis van dentale status: (1) volledige natuurlijke dentitie, (2) bovenkaakprothese plus implantaat gedragen overkappingsprothese voor de onderkaak en (3) volledige protheses.

Beide testen wezen uit dat de groep met volledige natuurlijke dentitie beter kauwt dan de twee groepen prothese dragers. De kleurenmengtest toonde betere resultaten voor de groep met implantaat gedragen prothesen in de onderkaak dan voor de groep zonder implantaat gedragen prothesen. De deeltjesverkleiningtest liet echter geen significant verschil zien

tussen de twee prothese groepen. De resultaten geven aan dat de kleurenmengtest beter verschillen in kauwfunctie kan detecteren tussen verschillende groepen deelnemers met een verminderd kauwvermogen, dan de deeltjesverkleiningtest. Daarom verwachtten we dat het evalueren van de kauwefficiëntie van patiënten behandeld voor mondkanker goed te meten zou zijn met de kleurenmengtest.

Digitale beeldverwerking versus visuele beoordeling van gekauwde twee-kleuren was in kleurenmengtest (hoofdstuk 4)

Deze studie vergelijkt de resultaten van de computer analyse van digitale beelden van gekauwde twee-kleuren was met de resultaten van de visuele beoordeling van deze beelden. Daarvoor werden de beelden gebruikt van gekauwde twee-kleuren was uit de vorige studie (hoofdstuk 3). Hierin werden met een flatbed scanner digitale beelden gemaakt van beide zijden van de gekauwde was. Een computer programma bepaalde uit deze beelden een maat voor de vermenging van de was op basis van de intensiteitsverdeling van de twee kleuren: de mengindex. Daarnaast werd de vermenging van de kleuren beoordeeld door vijf personen. Op grond van vijf referentiebeelden verdeelden zij de beelden van de gekauwde was in vijf categorieën, van zeer goed tot zeer slecht gemengde kleuren.

Computeranalyse van de beelden resulteerde in een significant verschil in mengvermogen tussen de twee prothese dragende groepen, terwijl de beoordelaars dit verschil niet konden detecteren. Beide methoden waren geschikt om onderscheid te maken tussen personen met een volledige natuurlijke dentitie en volledige prothese dragers. De conclusie is dat computeranalyse van de beelden met gemengde was de voorkeur heeft boven visuele beoordeling, wanneer het gaat om bepaling van kauwresultaten van personen met een verminderd kauwvermogen.

Kauwfunctie bij patiënten behandeld voor maligniteiten in tong en/of mondbodem: een prospectieve studie van één jaar (hoofdstuk 5)

Onze studie van de orale functie van patiënten met maligniteiten in de tong en/of mondbodem liet zien, dat na de chirurgische ingreep de gebitsindex, de maximale bijtkracht en de kauwfunctie (mengvermogen) significant verslechterden. Na orale rehabilitatie was de dentale status significant verbeterd. De patiënten die alleen chirurgisch werden behandeld, bereikten één jaar na de behandeling weer het niveau van voor de chirurgische ingreep.

De maximale bijtkracht van deze groep patiënten werd niet significant beïnvloed door de chirurgische interventie. In de groep patiënten die naast chirurgie ook radiotherapie ondergingen, daalde de bijtkracht, kort na de chirurgische ingreep, tijdelijk tot onder het niveau van de gezonde controles met een volledig kunstgebit. Hoewel er enig herstel optrad in de chirurgie-radiotherapie groep, bleef de bijtkracht significant lager dan het niveau voor de operatie. De afname in maximale bijtkracht kort na chirurgie was significant gerelateerd aan de locatie van de resectie en de omvang van de reconstructie voor alle patiënten binnen deze studie. De locatie van de resectie heeft dus invloed op de aanvankelijke afname van de bijtkracht en de afname in bijtkracht is groter naarmate de reconstructie groter is. De kauwfunctie, gemeten met de kleurenmengtest, liet een sterke afname zien als gevolg van de chirurgische ingreep. Radiotherapie had een verdere verslechtering van het kauwvermogen tot gevolg. De patiënten in de chirurgie-radiotherapie groep presteerden slechter dan de patiënten in de chirurgie groep. We concluderen uit deze studie dat een chirurgische ingreep een grote negatieve impact heeft op de orale functie. De orale functie verslechterde significant sterker bij patiënten die werden behandeld met chirurgie en radiotherapie, vergeleken met patiënten die alleen chirurgie hadden ondergaan. Ook het herstel was minder prominent in de chirurgie-radiotherapie groep dan in de chirurgie groep. De patiënten behandeld met chirurgie en radiotherapie hadden over het algemeen grotere tumoren en ondergingen uitgebreidere resecties. Een half jaar na chirurgie vonden we geen verder herstel van maximale bijtkracht en kauwfunctie in beide groepen.

Tongfunctie bij patiënten behandeld voor maligniteiten in tong en/of mondbodem: een prospectieve studie van één jaar (hoofdstuk 6)

De tong speelt een belangrijke rol tijdens het kauwen, slikken, de mondhygiëne en het spreken. Bij patiënten met een plaveiselcelcarcinoom van de tong en/of mondbodem werd na chirurgie een significante afname gevonden in de sensorische functie van de tong. Bij patiënten die naast chirurgie ook met radiotherapie behandeld werden, nam na chirurgie ook de tongmobiliteit significant af. Gedurende het jaar na de oncologische interventie bleef de tactiele sensorische functie op hetzelfde lage niveau dat werd waargenomen kort na chirurgie. De afname in thermische sensorische functie, waargenomen kort na de operatie bij alle patiënten in dit onderzoek, was significant gerelateerd aan de pathologische tumorgrootte (pT). Alle mobiliteitsmetingen van de tong toonden een verslechtering na de chirurgische

ingreep. De daling van het vermogen om de tong uit te steken, waargenomen kort na de operatie bij alle patiënten in deze studie, was significant gerelateerd aan de pathologische pT en het type reconstructie. Maximale tongkracht werd niet significant beïnvloed door chirurgie en/of radiotherapie. Zes maanden na chirurgie werd een tijdelijke toename in tongkracht waargenomen. Deze toename verdween echter in de volgende zes maanden, zodat de tongkracht daalde tot het niveau dat gevonden werd voor en kort na de behandeling. Een verminderde kauwfunctie resulteerde in een toegenomen tongkracht. Het bleek dat patiënten "kauwden" met de tong door het voedsel met de tong tegen het gehemelte te drukken als compensatie voor de verminderde dentale kauwfunctie. Op deze manier trainden patiënten hun tongspieren onbewust, hetgeen resulteerde in een toegenomen maximale tongkracht. Additionele postchirurgische radiotherapie had geen significante invloed op de tongfunctie, zoals gemeten in dit onderzoek. Echter de patiënten behandeld met chirurgie en radiotherapie hadden grotere tumoren en ontvingen uitgebreidere reconstructies. Daardoor was bij deze patiënten de afname in sensorische functie van de tong en tongmobiliteit groter dan bij patiënten die alleen chirurgisch behandeld werden.

Nek- en schouderfunctie bij patiënten behandeld voor orale maligniteiten: een prospectieve studie van één jaar (hoofdstuk 7)

Nek- and schouderklachten kunnen het directe gevolg zijn van een nekdissectie en kunnen zich manifesteren als pijn, verminderde beweeglijkheid van nek en schouders, verminderde gevoeligheid en verminderde nek- en schouderfunctie. In dit onderzoek participeerden patiënten zonder een nekdissectie, patiënten behandeld middels een selectieve nekdissectie, patiënten met een (gemodificeerde) radicale nekdissectie en patiënten die een bilaterale nekdissectie ondergingen. De resultaten van de patiënten werden vergeleken met de resultaten van een groep gezonde proefpersonen. De resultaten laten zien, dat uitgebreidere nekdissecties kort na interventie leidden tot een grotere afname in nek- en schouderfunctie. Een significante afname in nek- en schoudermobiliteit kort na de interventie werd gevolgd door een geleidelijk herstel in het eerste jaar na interventie tot vlak onder het niveau van de gezonde controles. Echter, patiënten behandeld met een bilaterale nekdissectie hadden een jaar na interventie nog steeds een verslechterde lateroflexie van de nek, terwijl patiënten die behandeld werden voor een enkelzijdige (gemodificeerde) radicale nekdissectie nog steeds pijn meldden tijdens het bewegen van de nek. De maximale anteflexie van de schouder was

een jaar na interventie bij alle patiënten terug op het niveau van gezonde controles. Echter, alle patiënten, ook de patiënten zonder een nekdissectie, hadden een significant lagere schouder-abductie dan de controle personen.

Conclusies

Het onderzoek in dit proefschrift toonde aan dat een sterkere achteruitgang in functie optreed bij patiënten met grotere tumoren en een hogere mate van lymfkliermetastasen. Grotere tumoren en uitgebreidere lymfkliermetastasen in de nek worden met een uitgebreidere therapie behandeld. In ons onderzoek zagen we geen verdere significante functieafname als gevolg van de radiotherapie in de periode kort na chirurgie en kort na radiotherapie. Op korte termijn had bestraling dus geen significant effect op de functie. Echter, op dat moment zouden mogelijke effecten van radiotherapie op de functie overschaduwd kunnen zijn door de gevolgen van de chirurgische ingreep. Een aantal functies herstelden gedeeltelijk in het eerste jaar na de interventie. Herstel van functie was minder evident bij patiënten met een meer intensieve chirurgische ingreep. Waarschijnlijk heeft herstel meer tijd nodig voor deze patiënten. Onze retrospectieve studie leerde dat na vijf jaar een deel van de patiënten behandeld voor mondkanker nog steeds een verminderde speekselproductie, dentale status, kauwfunctie en lipcompetentie rapporteert.

Toekomstig onderzoek

Naast de gegevens gerapporteerd in dit proefschrift, zijn gegevens van verschillende andere parameters verzameld voor de groep van 145 patiënten gedurende de periode tot één jaar na de oraal oncologische interventie. De patiënten werd gevraagd hoe zij hun kwaliteit van leven (KvL) ervaren met behulp van de Europese Organisatie voor Onderzoek en Behandeling van Kanker Kwaliteit van Leven Vragenlijst-Versie 30 Hoofd-Hals 35 vragen (EORTC QLQ H&N C30). Verder onderzochten we de mate van depressie, met behulp van de schaal van het Centrum voor Epidemiologische Studies-Depressie (CES-D), en de coping stijl volgens de Coping Inventarisatie voor Stressvolle Situaties vragenlijst. Analyse van deze gegevens zal meer inzicht geven in hoe patiënten de verschillende aspecten van hun oncologische behandeling hebben ervaren gedurende het eerste jaar na de behandeling. Naast door de patiënten gerapporteerde data werden de volgende objectieve parameters gemeten: slikduur,

spraak, lipmobiliteit, lipsluiting, sensorische functie van de lippen, maximale mondopening en speekselproductie. Analyse van deze gegevens in combinatie met de gerapporteerde gegevens in dit proefschrift zal meer gedetailleerd inzicht geven in het subjectief en objectief functioneren van patiënten die behandeld zijn voor mondkanker.

Ter aanvulling op de gegevens van de gerapporteerde orale functie uit onze retrospectieve studie verdient het aanbeveling om een 5-jaars follow-up studie uit te voeren bij de patiënten die deelnemen aan ons prospectief cohort onderzoek. De subjectieve en objectieve parameters zullen een gedetailleerd beeld geven over hoe patiënten op de lange termijn hun functie ervaren en hoe goed zij die functie kunnen uitvoeren.

In onze prospectieve cohort studie werd vastgesteld dat tussen de 6 en 12 maanden na behandeling geen (verder) herstel werd waargenomen voor de orale functie (maximale bijtkracht, kauwfunctie, tongmobiliteit en tongsensatie) in de groep van 45 patiënten behandeld voor maligniteiten in tong en/of mondbodem. De nek- en schouderfunctie herstelde gedeeltelijk in de 145 patiënten behandeld voor mondkanker. Onderzoek naar revalidatie-interventies, zoals (orofaciale) fysiotherapie,[15,16] logopedie[17] en dietetiek,[18] is van belang voor een verdere verbetering van de (orale) functie na interventie. De fysiotherapeut, gespecialiseerd in training en optimalisatie van de mobiliteit van het muskuloskeletale stelsel, kan helpen om herstel van (orale) functies te maximaliseren. De evaluatie van fysiotherapeutische interventies, bij voorkeur door gerandomiseerde klinische studies, kan informatie verschaffen of deze revalidatiebehandeling succesvol is bij het verder verminderen van de beperkingen in functie.

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Curriculum vitae

Caroline Margina Speksnijder was born on January 28, 1977 in Rotterdam, the Netherlands. After completing secondary school in 1994 she started studying Physiotherapy at the Rotterdam University of Applied Sciences. She graduated as a physiotherapist in 1998. Since that time she worked as a physiotherapist in physiotherapy practices. Additionally, she started studying Human Movement Sciences (in 1998) and Epidemiology A (in 2000) at Maastricht University. In 2002, she earned her degree with a scientific paper on the effect of a physiotherapeutic exercise intervention in patients with aspecific repetitive strange injuries (supervised by prof. dr. H. Kuipers and prof. dr. R.A. de Bie, Department of Human Movement Sciences and Epidemiology of Maastricht University). From 2002 to 2004 she worked as a scientist at the Department of Orthopedics at the Academic Hospital of Maastricht on foot plantar pressure measurements and foot problems (supervised by prof. dr. G.H.I.M. Walenkamp and prof. dr. R.A. de Bie). In 2005 she started her PhD research at the Department of Oral and Maxillofacial Surgery, Prosthodontics and Special Dental Care, University Medical Center Utrecht in collaboration with the Department of Oral and Maxillofacial Surgery, Radboud University Nijmegen Medical Centre. This research was supervised by prof. dr. R. Koole, prof. dr. M.A.W. Merkx and dr. A. van der Bilt. In 2007 she started as a university teacher at Clinical Health Sciences, Faculty of Medicine, Utrecht University. In 2010 she became a senior university teacher at Clinical Health Sciences. She obtained her speciality in Orofacial Physiotherapy at the HAN University of applied sciences in 2008 and the Qualification of University Teaching at the Utrecht University in 2009. Since 2011 she has been a postdoctoral fellow at the Department of Oral and Maxillofacial Surgery, University Medical Center Utrecht

List of Publications

van der Bilt A, **Speksnijder CM**, de Liz Pocztaruk R, Abbink JH. Digital image processing versus visual assessment of chewed two-colour wax in mixing ability tests. Journal of Oral Rehabilitation; *under review*

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