University of Alberta

The relationship between sensory outcome and both function and quality of life following microvascular radial forearm free flap reconstruction of the tongue

by

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Always dream and shoot higher than you know you can do. Don't bother just to be better than your contemporaries or predecessors. Try to be better than yourself.

William Faulkner

Abstract

Eight subjects with innervated radial forearm free flap (RFFF) reconstruction of the tongue were compared to 8 age- and gender-matched controls on measures of tongue sensation, mastication and speech intelligibility. Quality of life was evaluated for the patient group. Findings indicated that some sensations were preserved in the reconstructed aspect of the tongue including two-point discrimination and light touch. These sensations require fine discrimination and appeared to be more often related to function and quality of life. Sensations involving the whole mouth (e.g., texture) were not related to function and quality of life. Patients were less effective than controls on the masticatory efficiency task and exhibited differences on chewing kinematics. Patients' speech was less intelligible than controls. Although relationships exist between sensation, functional outcomes and quality of life, other factors including the number of natural tooth pairs and history of radiation therapy play an important role.

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Introduction

In Canada, it is estimated that 4350 new cases of cancer related to the head and neck will occur within the year 2006, and of those, approximately 300 will occur in Alberta.[1] In addition to the fear associated with a diagnosis of cancer, treatment for oral cancer can result in functional complications, which may include difficulty with eating, chewing, drinking, and speaking.[2] The functional complications that result from treatment of head and neck cancer are especially apparent in patients with cancer of the tongue. Currently, one method for treatment of tongue cancer is surgical resection of the diseased tissue, followed by reconstruction using a microvascular free flap, often from the radial forearm. Presently, surgeons are attempting to provide sensory reinnervation to the reconstructed tongue by transferring a sensory nerve with the free flap.

There is an increasing amount of literature on sensory recovery after microvascular free flap reconstruction of the tongue. In studies where patients' tongues were reconstructed with a noninnervated flap, researchers have found sensory recovery, which has been attributed to neural ingrowth from the surrounding nerves. For example, Lvoff and colleagues[3] found that some sensory recovery could be detected in 80% of the patients that were reconstructed with noninnervated radial forearm free flaps after resection for head and neck cancer. Of 40 patients, 15 had reconstruction for the oral tongue. These authors tested a variety of sensations including light touch, pinprick, hot and cold, and static and moving two-point discrimination. Two separate examiners tested each patient. It was found that the recovery of sensation for the 40 patients was unpredictable and variable, but that most did have some recovery of sensation. The authors noted that sensory recovery cannot be expected. This is confirmed by other researchers who have found no return of sensation in noninnervated flaps.[4, 5] In another study, Kerawala and colleagues[6] evaluated sensory ability and quality of life in 50 patients reconstructed with noninnervated radial forearm free flap of oral mucosal defects. A large variety of oral mucosal defects were examined in this study including mandible, tongue, floor of mouth, soft palate, buccal and retromolar deficits. The sensory abilities evaluated included pinprick, two-point discrimination, light touch, and temperature sensitivity. Quality of life was measured using the University of Washington head and neck disease-specific measure. The authors of this study found that those patients with some sensory recovery did not display an enhanced quality of life. However, findings such as these have not halted the use innervated flaps. This is likely due to the hope that innervated flaps will provide patients with superior sensory recovery in the reconstructed tongue and, ultimately, a better quality of life.

Satisfactory return of sensation with an innervated radial forearm free flap has been found by several authors.[7, 8] Santamaria and colleagues[7] found that sensory recovery of the innervated radial forearm flap after hemitongue reconstruction results in sensory abilities that approach normal compared with the intact hemitongue. Twenty-eight patients were tested on static two-point discrimination, light touch, pain, and hot and cold perception at a mean postoperative follow-up time period of 18.2 months (range 6 to32 months). These sensations were tested on several areas of the reconstructed hemitongue and compared to the same areas on the intact hemitongue. They found similar sensory abilities for the reconstructed and intact portions of the tongue. Kuriakose and colleagues[8] report that sensate radial forearm free flaps have superior sensation when compared to the native forearm donor site and closely approach that of the normal tongue. Seventeen patients with tongue resection and reconstruction with reinnervated radial forearm free flaps were included in that study. Eight months post surgery, the patients were tested on six different sensory tasks including subjective ability to sense food, sharp-dull discrimination, pain sensation, light touch, static and moving two-point discrimination and hot-cold perception. The sensations were compared with the residual tongue or adjacent oral mucosa and the contralateral forearm donor side. The authors found that the radial forearm free flap had sensory abilities that more closely resembled the tongue than the contralateral forearm donor site.

Although sensory recovery after reconstruction with an innervated flap is an important outcome, the eventual functional outcome and quality of life likely are more important. Many studies that have explored functional outcomes after radial forearm free flap reconstruction in head and neck cancer include multiple reconstructive sites, subjective reports of function and multiple definitions of functional outcomes. Of studies that use objective measures of functional outcomes after reconstruction within the oral cavity, the outcomes are limited to speech and swallowing without the consideration of sensory ability.[9-12] A study by Matloub and colleagues[13] is one of only a few studies that explored sensory recovery with respect to speech and swallowing outcomes. That study reported two cases in which the sensory measures of light and deep touch, hot and cold temperature and taste were measured, as were swallowing and speech abilities. One subject had a defect that included the right half of the mobile tongue, base of the tongue, epiglottis and the right hemimandible and maxilla. That subject underwent reconstruction of the base of tongue and buccal mucosa with a neurotized lateral arm fasciocutaneous flap initially, followed by bony reconstruction of the orbit, maxillae and mandible. The other patient had a defect that included the left lateral tongue and buccal mucosa that was reconstructed using a lateral arm fasciocutaneous free flap. The authors found that both patients were able to respond appropriately to all of the sensations on the reconstructed side of the oral cavity except for taste, which was limited to detection on the intact portion of the tongue. Both patients had functional swallows; however, both exhibited penetration into the laryngeal vestibule in approximately 15-20% of all swallows. Both patients had poor speech intelligibility. No studies were found that evaluated masticatory ability as a functional outcome after reconstruction with a radial forearm free flap of the oral tongue. Whereas results from the Matloub et. al.[13] study provided some insight into recovery of sensory ability and its relation to function, there are several yet unexplored questions to be answered within a larger and more homogeneous sample. Therefore, the aim of the current study was to further understand the sequela associated with tongue reconstruction, and the interrelationships between sensation, functional outcomes and quality of life in a population of individuals with reconstruction limited to the anterior portion of the tongue.

Purpose

Research in the area of head and neck cancer has been expanding recently, shifting from descriptions of mortality to that of functional outcomes. The functional outcomes literature, however, is sparse in some areas. For example, although a number of studies look at functional outcomes and others look at quality of life, very few look at them in combination. It is important to look at both functional outcomes and quality of life, as these variables are not necessarily indicative of each other. Although it may seem intuitive that better functional outcomes would be related with a higher quality of life, this may not be the case. Furthermore, very few studies[13-15] have related either functional outcomes or quality of life to sensory recovery after reconstruction of the tongue. Therefore, it was the purpose of this study to determine

1. If sensation of the oral tongue, masticatory efficiency, masticatory style and speech intelligibility in patients with innervated radial forearm free flap reconstruction is similar to that of age- and gender-matched controls
2. If sensation of the innervated radial forearm free flap is similar to that of the intact portion of the oral tongue
3. If a relationship exists between sensation and functional outcomes (masticatory efficiency, masticatory style and speech intelligibility) for patients with radial forearm free flap reconstruction of the tongue
4. If a relationship exists between sensation and functional outcomes (masticatory efficiency, masticatory style and speech intelligibility) for age- and gender-matched control subjects
5. If a relationship exists between quality of life and sensation for patients with radial forearm free flap reconstruction of the tongue
6. If a relationship exists between quality of life and functional outcomes (masticatory efficiency, masticatory style and speech intelligibility) for patients with radial forearm free flap reconstruction of the tongue
7. How radiation therapy influences sensation, masticatory efficiency, masticatory style, speech intelligibility and quality of life

8. How dentition influences sensation, masticatory efficiency, masticatory style, speech intelligibility and quality of life

Methods

Subjects

A total of 68 patients with oral cancer were assessed between May 2000 and December 2004 at the Craniofacial Osseointegration and Maxillofacial Prosthetic Rehabilitation Unit (COMPRU) at the Misericordia Community Hospital in Edmonton, Alberta, Canada. Of these patients, 14 were identified as having resection and reconstruction limited to the oral tongue (i.e., the anterior 2/3rds of the tongue) without the involvement of surrounding structures such as the mandible, maxilla, cheek and base of tongue. Some patients had involvement of the floor of mouth in addition to the tongue. These patients were sent an information letter approved by the Health Research Ethics Board at the University of Alberta requesting their participation in this study. Eight of these patients agreed to participate in this study. Of the 6 subjects that did not participate, 5 were unable to be contacted and one declined the offer to participate. All patients in this study were diagnosed with squamous cell carcinoma and had a partial glossectomy (i.e., no more than 75% of tongue tissue removed but no less than 25%) followed by reconstruction with an innervated radial forearm free flap. Of the 8 patients who participated, 4 received adjuvant radiation therapy.

Control subjects in this study were age- and gender- matched to the patients. To be considered age- matched, the control subjects were within 5 years of the age of the patient to whom they were matched. In addition, control subjects were included only if they had no previous history of oral disease or dysfunction. Subject demographic information is listed in Table 1a for patients and 1b for controls.

#	Age	Gender	Cancer stage	Side of reconstruction	Date of Surgery	Radiation therapy	Radiation dosage	Currently smoke	Hx of smoking	# of natural dental pairs	# of prosthetic dental pairs	Total # of dental pairs	Preoperative dentition
1	59	Male	T2	Right	September-01	No	N/A	No	No	0	8	8	CUD
2	69	Male	T2	Left	January-04	No	N/A	No	Yes	3	0	3	Dentate
3	44	Male	T2	Right	December-00	No	N/A	No	No	8	0	8	Dentate
4	62	Female	T3	Right	July-04	Yes	5810 cGy (IMRT)	No	Yes	0	8	8	CUD
5	58	Female	T2	Right	January-03	Yes	5740 cGy (IMRT)	No	Yes	0	8	8	CUD/CLD
6	45	Male	T2	Right	October-03	No	N/A	No	Yes	8	0	8	Dentate
7	61	Male	T3	Right	September-03	Yes	6000 cGy	Yes	N/A	0	0	0	Dentate
8	45	Female	T2	Left	July-03	Yes	6120 cGy	No	No	7	0	7	Dentate

Table 1a. Demographics for patients.

#	Age	Gender	Currently smoke	Hx of smoking	# of natural dental pairs	# of prosthetic dental pairs	Total # of dental pairs
1	58	Male	No	No	10	0	10
2	76	Male	No	No	7	0	7
3	49	Male	No	Yes	10	0	10
4	66	Female	No	Yes	7	0	7
5	54	Female	No	No	7	0	7
6	43	Male	No	No	8	0	8
7	61	Male	No	No	6	0	6
8	44	Female	Yes	N/A	4	0	4
9	69	Female	No	No	4	0	4

Table 1b. Demographics for control subjects.

Procedures

Sensory Function

The same examiner tested all subjects. Subjects were tested in a quiet room on 6 different sensory tasks: light touch, two-point discrimination, temperature, taste, form, and texture. The subjects were blindfolded during presentation of all tasks.

Light Touch

A 2.83 (0.07g/mm^2 of force) Semmes Weinstein touch test sensory evaluator tool (North Coast Medical, Inc, Morgan Hill, CA) was used for this task. The thread of the touch test sensory evaluator was applied perpendicular to the tongue with enough force to cause the monofilament to bend for approximately 1.5 seconds.[16] The subject was asked to indicate if they felt it or not. The procedure was randomized to include trials where the tool was applied to the tongue and trials where it was not. Three trials were completed each at the tip of the tongue and on the lateral dorsal region of the tongue, for both the reconstructed side and the intact side of the tongue. Responses were recorded as either correct or incorrect.

Two-Point Discrimination

Two-point discrimination is the ability to determine that two points of tactile stimulation are indeed separate points. In this task sterilized paperclips with the points set at a specified distance apart were used. The distance that a person feels two points for the right tip of the tongue and the right anterior lateral area of the tongue was determined from three studies.[17-19] The average distance was taken and raised by 1.5 standard deviations to determine the distance to be used. Thus, the distances for two-point application used in this current study for the tip of the tongue was 3 mm and for the anterior lateral areas of the tongue was 6 mm. The subjects were calibrated to the one-point and two-point sensations by initially placing the paperclip on their tongue and informing them if it was one point or two. Subsequently, the subject was asked to indicate by show of fingers if they felt two points or one on their tongue. Three trials were completed each at the tip of the tongue and on the lateral dorsal region of the tongue, for both the reconstructed side and the intact side of the tongue. These trials were randomized. Responses were recorded as either correct or incorrect.

Temperature

Temperature was tested using dental mirrors that were either warmed in water kept at a constant temperature on a hot plate (55^{O}C) or cooled in an ice bath (3^{O}C).[14] The mirrors were kept in the warm water or ice bath for 30 minutes before testing to ensure that the target temperature had been reached. A thermometer was placed in both the warm water and ice bath to document the temperature. The subjects were calibrated to the "warm" and "cold" sensations by initially placing the dental mirror on their tongue and informing them if it was warm or cold. On subsequent trials, subjects were asked to report whether the object placed on their tongue felt warm or cold. Three trials were completed each at the tip of the tongue and on the lateral dorsal region of the tongue, for both the reconstructed side and the intact side of the tongue. All trials were randomized and responses were recorded as either correct or incorrect.

Form

Stereognosis is the ability to determine the shape of an object without visual cues. Stereognosis was tested using acrylic resin forms appended to rods. The forms being used were approximately 5-mm thick and 8-mm in diameter. Subjects were presented with pictures of all potential forms and allowed to study them for 30 seconds. During testing, subjects were allowed to manipulate the object in their mouth for ten seconds and then they were asked to indicate on the picture display which object was placed in their mouth (a response was required within 10 sec). The ten objects were presented in a random order for each subject. Responses were recorded to indicate if a choice was correct, similar in shape or incorrect. This method of stereognosis is similar to the method used by Hirano and colleagues.[20]

Texture

Three acrylic resin forms of varying texture (i.e. one smooth, one bumpy and one rough) were used to measure texture sensation. These forms were appended to rods. The subjects were calibrated to the textures before testing. During testing, each subject was given one form to manipulate in their mouth for ten seconds, and then another form of rougher, smoother or the same texture. The subjects were allowed to manipulate the forms for ten seconds and then were asked to identify if the second form presented was smoother, rougher or the same as the first. Nine trials were given in a random order to account for all of the possible combinations that can be made with pairing of the three forms. Responses were recorded as either correct or incorrect

Taste

The four basic taste sensations: salty (sodium chloride), sweet (sucrose), sour (citric acid) and bitter (quinine hydrochloride/sulfate) were tested. In addition a neutral solution (distilled water) was tested. 30 mg of table salt was added to 1 liter of distilled water to make the sodium chloride solution. Adding 60 mg of refined sugar to 1 liter of distilled water was used to make the sucrose solution. In the citric acid solution, 90mL of commercial lemon juice was added to 1 liter of distilled water. Flattened tonic water was used for the bitter solution. Each solution was kept at room temperature. One milliliter of the solution was dropped from a medicine dropper onto the center of the subject's tongue. A different medicine dropper was used for each of the solutions. Subjects indicated whether the solution placed in the center of their tongue was salty, sweet, sour, bitter or neutral. The solutions were provided in a random order, excluding the bitter taste, which was always presented last because quinine hydrochloride/sulfate tends to alter subsequent taste perception.[21] Between each trial, the subject was given 30 ml of distilled water with which to rinse. One trial of each taste was presented and responses were recorded as either correct or incorrect.

Masticatory Function

This study aimed to investigate masticatory function as a measure of functional outcome. Whereas there are multiple aspects of mastication, this study focused on two of these aspects: the ability to comminute food (masticatory efficiency) and analysis of jaw rotation (masticatory style). The methods for measuring masticatory efficiency and masticatory style are described below.

<u>Masticatory Efficiency</u>

Masticatory efficiency was defined in this study as the subject's ability to break down food in a given number of chewing strokes. The almond, having been used in previous studies of masticatory ability,[22, 23] was determined to be the best natural food for measuring masticatory performance. An almond and six weighing cups were weighed to the nearest thousandth (Mettler Toledo analytical balance Model AB104, Columbus, OH) and the weight was recorded. Then, the subject was asked to brush their teeth and the examiner ensured no foreign particles remained in the subject's oral cavity. The subject was then asked to chew the previously weighed almond five times, after which it was expectorated into a reusable coffee filter with a flat mesh bottom (Today's Housewares Reusable Stainless Steel Coffee Filter) suspended in a beaker. The subjects were then asked to rinse with 30 ml of water and to expectorate it into the same filter. At that time, the examiner checked the subjects' teeth and aided in the removal of additional particles with the use of a dental explorer. The subject then was asked to rinse with 30 ml of water again and to expectorate that into the filter. Again, the examiner checked the oral cavity and aided in the removal of any additional particles using the dental explorer. The subjects rinsed with another 30 ml of water, which was passed through the same filter. Once again the examiner inspected the subject's oral cavity to ensure there were no remaining particles.

The almond in the filter then was rinsed with 500 ml of water. The masticated material was transferred into a non-stick muffin top pan measuring 8 cm in diameter by 1.5 cm deep. A series of pilot studies revealed that transferring the wet particles from the coffee filter to a non-stick surface for drying was the best method to preserve particle integrity during drying. Ten milliliters of water then was added to the pan and the pan was lightly agitated to separate the particles. The material was dried for two hours at 100^{o} C in a Fisher Scientific Isotemp standard oven (Model 625, Indiana PA). 100^{o} C was determined as the temperature at which the almond would dry in the least amount of time without losing its natural moisture properties, as determined through a series of pilot studies. The dried material then was transferred into a series of six sieves (arranged in decreasing-sized mesh from 4 mm, 2.8 mm, 1.7 mm, 1 mm, 815 µm, and 710 µm – see figure 1). The sieves were then vibrated on the Buffalo Dental vibrator (No.1A, Syosset NY) on the high speed setting for 120 seconds.[24-26]

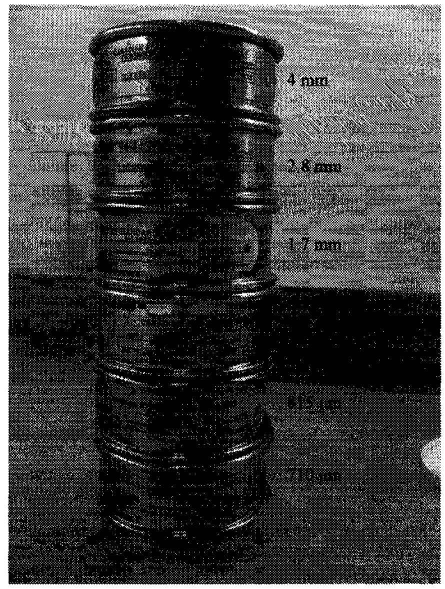


Figure 1. Series of six sieves and aperture size used to determine masticatory efficiency.

The particles from each sieve were transferred into the pre-weighed weighing cups and the weight of the dried particles from each sieve was recorded. The masticatory efficiency was determined by the percentage of total material found on each sieve (see Equation 1).

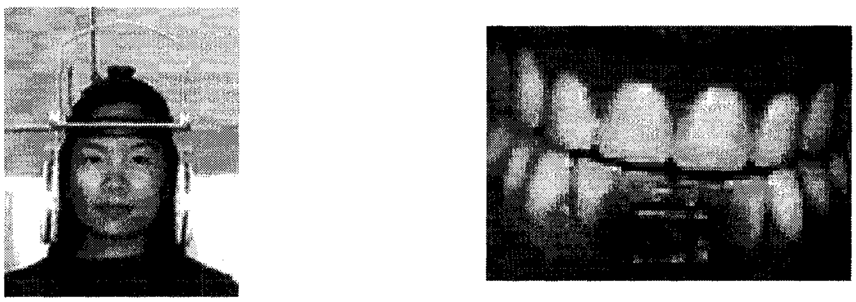
$$\frac{\text{Total weight of material recovered from sieve X}}{\text{Sum of the total weight of material recovered on all sieves}} * 100$$

Equation 1. Masticatory efficiency calculation

This procedure assumes that more effective chewing will result in a higher percentage of food particles captured by the smaller mesh sieves.

<u>Masticatory Style</u>

This next procedure differs from the one above as it looks at quantifying events around each subject's ability to break down food using as much time as needed to complete their regular chewing pattern as opposed to performance within a given number of chewing strokes. Subjects were asked to eat two different forms of food consistency (an almond and a digestive cookie), with two trials of each food consistency. A number of measures to analyze masticatory style were measured using BioPak hardware and software (BioPak version 4.0, Milwaukee, WI). This tool requires an electromagnetic sensory array to be worn on the head and a magnet to be placed on the mandibular incisors (See Figure 2).



(a) (b)

Figure 2. BioPak Device. (a) The electromagnetic sensory array worn by the subject and (b) the magnet that is detected by the sensory array placed on the subjects' mandibular incisors.

This technique uses the sensory array to detect the motion of the magnet placed on the subject's mandibular incisors to measure mandibular movement. The magnet was held in place with a substance called stomadhesive. The masticatory style measures included the total time to complete one chewing cycle, and the amount of time spent opening the mouth, closing the mouth and with the teeth in occlusion. Other measures included the number of chewing strokes taken before the first swallow and the total time taken before the first swallow. In addition the maximum lateral width was measured, indicating the lateral distance that the jaw moved from midline during a chewing cycle. Data were taken from the time the trial item was given (e.g. the almond or cookie) to the initiation of the first swallow. The time before the first swallow and the number of chewing strokes were measured. A more in-depth analysis of chewing patterns was then conducted by taking the mid-10 or -15 strokes for the almond and the cookie (respectively) for further analysis. The software was set to exclude any strokes throughout the masticatory process that deviated beyond three standard deviations of the mean stroke pattern. These strokes were then used to obtain the Average Chewing Pattern (ACP) summary. The ACP summarizes the chewing cycle phases including the average opening time, closing time and occlusal time. In addition the average cycle time and the maximum lateral width (lateral jaw movements from midline) were summarized. The ACP summary also presents the average pathway of mandible movements from both the frontal and sagittal planes. These pathways were analyzed by categorizing them into one of four frontal and two sagittal chewing patterns described by BioResearch.

Speech Intelligibility

Intelligibility of speech was assessed by asking the subjects to read 50 words and 22 sentences, randomly generated from the Computerized Assessment of Intelligibility of Dysarthric Speech (C-AIDS) program.[27] Each subject read a different set of stimuli. These words and sentences were audio recorded with a Digital AudioTape (DAT) recorder and played back to an unfamiliar listener after the testing session. The listeners transcribed what they believed the subject to have said. Their transcriptions were compared to the sentences the subjects actually read. The percent correct words understood by the listener compared to the actual words spoken was calculated. A second naive listener transcribed the words and sentences of half of the subjects to determine reliability.

Quality of Life

The EORTC QLQ-H&N35 survey[28] was administered to the subjects in the experimental group. As well, selected questions from the SWAL-QOL survey[29-31] were administered to supplement the EORTC QLQ-H&N35 survey. The questions from the SWAL-QOL were largely related to personal history. In addition, a personal interview was conducted where 9 open-ended questions were asked regarding issues surrounding the patient's outcome. Patients' responses were audio recorded and qualitatively analyzed. These open-ended questions were designed to gain a better understanding of the impact that treatment had on patients' personal and social life. The quality of life measures (EORTC-H&N35, questions from the SWAL-QOL and open-ended questions) were not conducted for the control subjects.

Ethics

This study was completed with approval from the Heath Ethics Research Board (HREB) at the University of Alberta, Edmonton, Alberta, Canada.

Results

Data Analysis

Whenever possible, data were converted into ratio or interval form (i.e., 2/3 correct responses = 0.667). The between- and within-groups variables were analyzed with a Wilcoxon non-parametric test. Spearman's correlations were calculated to determine relationships among the variables for both the patient and control subjects. All statistical analyses were completed using SPSS (Version 14.0). Table 2 lists the number of subjects that participated in each sensation, functional outcome and masticatory measure, with comments to describe missing data.

Test	# of patients	# of controls	Comment
Sensation	8	8	N/A
Masticatory Efficiency	5	8	One patient could not eat nuts, one could not eat solid food and one had no teeth.
Masticatory Style	4	7	One patient could not eat nuts, one could not eat solid food, one had no teeth, and one had an ill-fitting denture. One control subject was not able to keep the magnet on the teeth.
Speech Intelligibility	8	8	N/A
Quality of Life	8	0	Quality of life questionnaire is cancer specific, therefore not appropriate for control subjects.

Table 2. The total number of patients and controls that participated for each sensation, functional outcome and quality of life task.

Data relative to the study's research aims will be presented in the following sections. Data analyses assessing differences between patients and matched controls will be presented first, followed by data addressing the relationships among tongue sensation and function for patients and control subjects. In addition, the relationships between quality of life and both tongue sensation and function will be reported for the patient subjects. Lastly, potential predictive relationships among tongue sensation, function and quality of life will be presented.

Sensory Abilities of Patients Compared to Controls

A Wilcoxon non-parametric statistical analysis was performed to determine differences between patients and controls on measures of tongue sensation, masticatory efficiency, masticatory style and speech intelligibility. Significant differences were found between patients and controls within each category of measurement. Six tongue sensations were tested in this study. These included two-point discrimination, light touch, temperature, texture, form and taste. The sensation data for patients and control subjects are depicted in Figure 3.

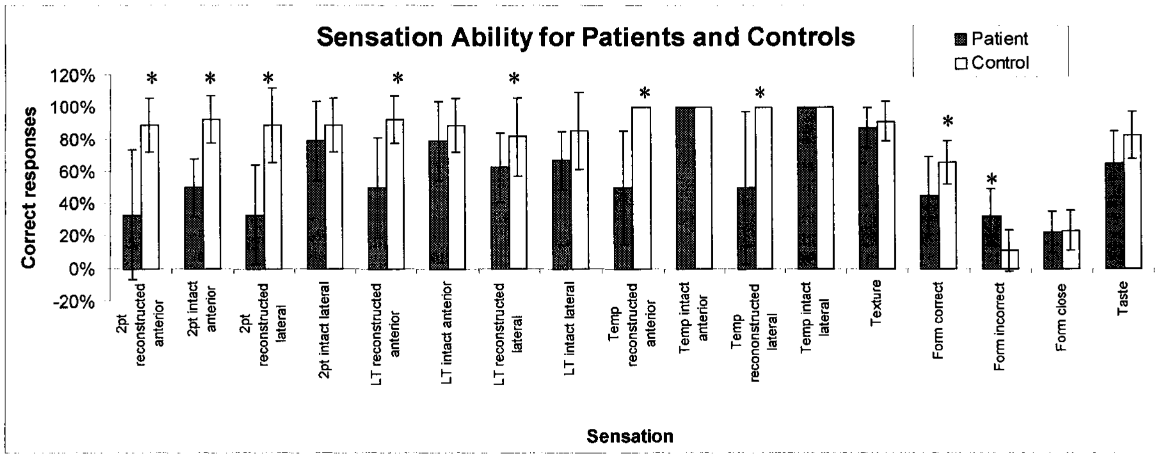


Figure 3. Sensory abilities for patients and control subjects. The sensations tested include two-point discrimination (2pt), light touch (LT), temperature (Temp), texture, the number of forms correctly identified (Form correct), the number of forms incorrectly identified (Form incorrect), the number of forms identified as close to but not the correct form (Form close), and taste. The first three sensations were tested on the reconstructed side of the tongue (reconstructed) and the intact portion of the tongue (intact), and on both the anterior and lateral portions of the tongue. (*) indicates a statistically significant difference.

Two-Point Discrimination

For the control population, two-point discrimination was measured on four areas of the tongue: the tip and the lateral dorsal aspect on both the left and right side of the tongue. For the patient population, the same procedure was followed except that the portion that was reconstructed with a radial forearm free flap and the other that was composed of intact tongue tissue delineated the two sides of the tongue. No difference was found between patients and controls in their ability to discriminate one point from two points applied to intact tissue on the lateral dorsal portion of the tongue. Patients performed more poorly than controls on two-point discrimination tasks on the tip of the tongue regardless of whether the stimulus was applied to the patient's most anterior portion of the reconstructed tongue ($z=-2.414$; $p=0.016$) or the most anterior portion of the intact lingual tissue ($z=-2.598$; $p=0.009$). Patients also had poor discrimination on the lateral dorsal portion of the reconstructed tongue, exhibiting lower scores than controls for this aspect of the tongue ($z=-2.232$; $p=0.026$).

Light Touch

Light touch was measured using a Semmes-Weinstein monofilament on the same 4 aspects of the tongue as described for two-point discrimination. No difference in light touch sensory ability was found between patients and controls for intact lingual tissue. Patients demonstrated difficulty identifying light touch on both the anterior and lateral aspects of the reconstructed portion of the tongue, performing significantly poorer than control subjects ($z=-2.157$; $p=0.031$ and $z=-2.121$; $p=0.034$, respectively).

Temperature

Temperature discrimination was measured using heated and cooled dental mirrors on the same 4 aspects of the tongue as described for two-point discrimination and light touch. No difference was found between patients and control subjects for their ability to discriminate warm and cold on the intact portion of the tongue. Temperature discrimination on the reconstructed anterior and lateral portions of the tongue in patients was poorer than that achieved by controls ($z=-2.264$; $p=0.024$ and $z=-2.060$; $p=0.039$, respectively). For the reconstructed portion of the tongue, it was observed that patients were more likely to perceive the cold sensation correctly than the warm sensation as 5 of the 8 patients (62%) correctly identified all of the cold trials, whereas only 2 of the 8 patients (25%) correctly identified all of the warm trials.

Texture

Texture was measured by allowing each subject to manipulate an acrylic resin form of one of three textures in their mouth for 10 seconds. This was followed by presentation of another form, which was also manipulated for 10 seconds in the mouth. Subjects were then forced into a paired comparison task where they indicated if the second form was rougher, smoother or the same as the first form. There were no significant differences identified in the ability to discriminate texture between the control subjects and the patients.

Form

Form was measured by allowing each subject to manipulate 1 of 10 acrylic resin shapes in their mouth for 10 seconds. Subjects were then presented with an array of 12 two-dimensional line drawings of shapes and asked to choose the shape that they perceived intraorally. Control subjects were more likely than patients to identify the exact form ($z=-2.121$; $p=0.034$). On the other hand, control subjects and patients did not differ in the number of times that they chose a picture that was close to, but not exactly like, that of the actual form.

Taste

Taste was tested by applying a single drop of a solution onto the middle of each subject's tongue with a medicine-dropper. Subjects then determined what flavor they perceived from a choice of five options: sweet, sour, salty, bitter, or neutral. Control subjects and patients did not differ in their ability to determine the taste of a drop of liquid on their tongue.

Masticatory Efficiency of Patients Compared to Controls

Masticatory efficiency was measured by asking subjects to masticate a single almond for five chewing strokes then expectorate into a filter. Efficiency was then calculated by determining the relative percentage of the total almond recovered on a series of 6 sieves and a bottom plate. Of these 6 sieves, 3 had larger mesh sizes (with aperture decreasing in size across sieves 5, 7, and 12) and 3 had smaller mesh sizes (with aperture continuing to decrease in size across sieves 18, 20, and 25). Figure 4 illustrates the results related to the relative percentage of the total almond recovered on each of the 6 sieves and the bottom plate for patients and control subjects. Control subjects had significantly more almond particles on the bottom plate under the series of sieves (therefore smaller particles) than the patients ($z=-2.023$; $p=0.043$).

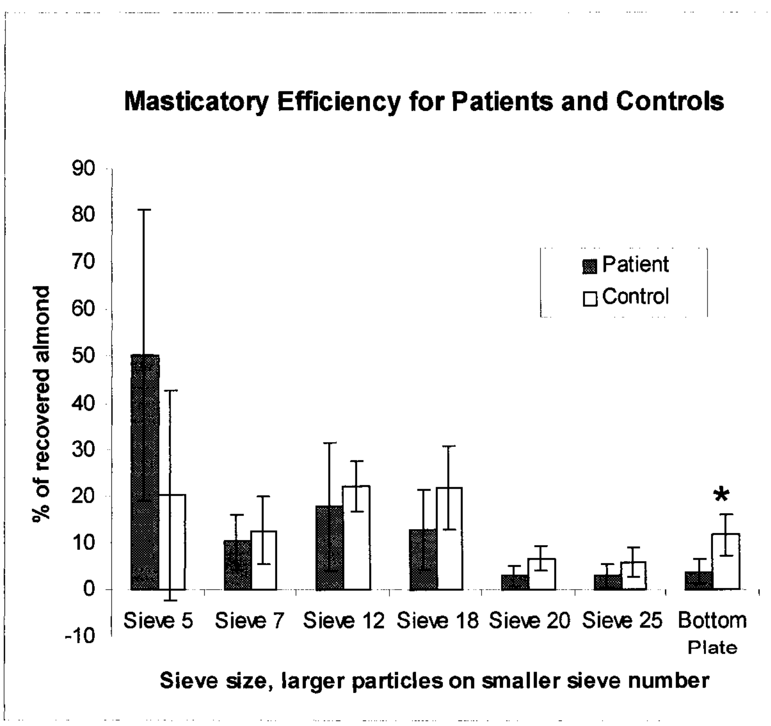


Figure 4. Masticatory efficiency of patients and controls as a percentage of the weight of almond particles on each sieve relative to the total weight of almond recovered. Smaller sieve numbers indicate larger aperture size and larger sieve numbers indicate smaller aperture size (e.g. left to right: large aperture to small aperture.)

Masticatory Style of Patients Compared to Controls

Masticatory style measures were calculated using the BioPak system (BioPak version 4.0, Milwaukee, WI), in which the subject wore a magnet on their lower incisors and a sensory array on their head to track jaw movements as an almond and a cookie were chewed. The masticatory style measures included the total time to complete one chewing cycle, and the amount of time spent opening the mouth, closing the mouth and with the teeth in occlusion. Other measures included the number of chewing strokes taken before the first swallow and the total time taken before the first swallow. In addition the maximum lateral width was measured, indicating the lateral distance that the jaw moved from midline during a chewing cycle. As can be observed in Figures 5a-d, no significant differences were observed between group (e.g. patient vs. control) or consistency (e.g. almond vs. cookie) on any of the masticatory style measures.

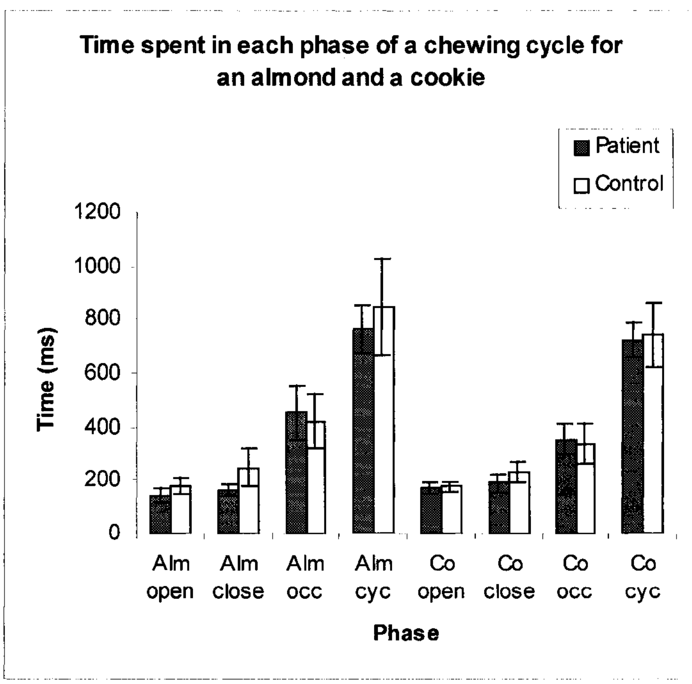


Figure 5a. Time spent in each of the three phases of a chewing cycle including the opening phase (open), the closing phase (close), and the time the teeth are occluded (occ) between patients and controls. The total time to complete one chewing cycle (cyc) is also illustrated. The measures are represented for both an almond (Alm) and a cookie (Co).

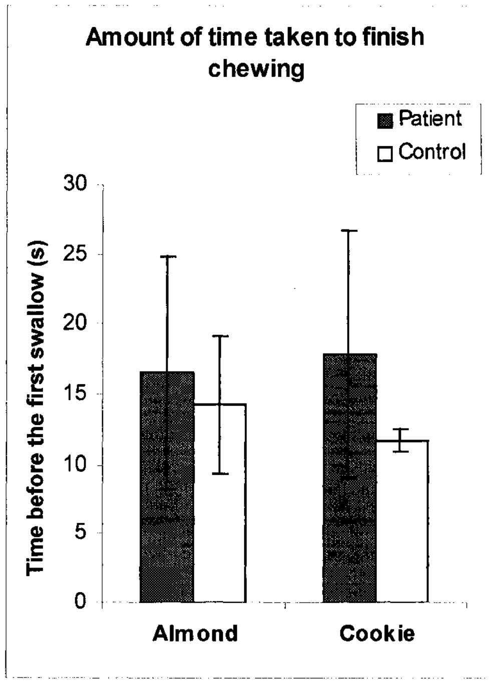


Figure 5b. The total time taken to completely chew an almond and a cookie for patients and controls.

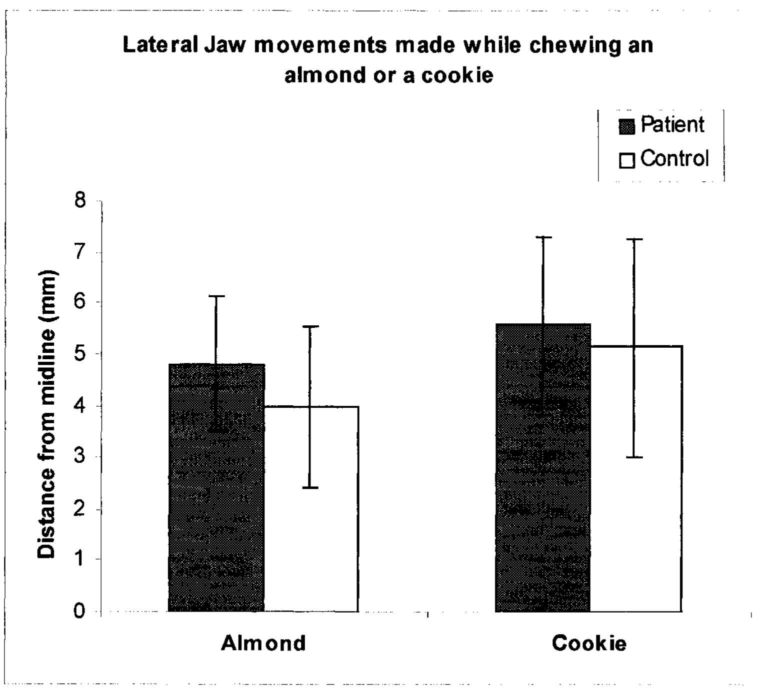
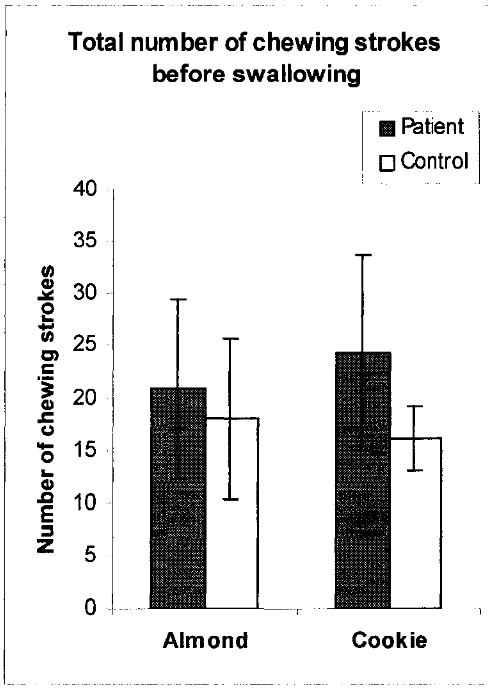


Figure 5c. The maximum lateral jaw movements from midline made while chewing an almond or a cookie for patients and controls.



Figures 5d. The total number of chewing strokes taken before the swallow was elicited for an almond and a cookie for patients and controls.

To better understand the chewing patterns of patient and control subjects, jaw movements were visually analyzed from the frontal plane (right to left view) and sagittal plane (anterior to posterior view) and categorized according to 4 patterns presented in the BioResearch manual (see Table 3).

Frontal Plane

Four patterns exist for the frontal plane. Characteristics of each of these patterns are described in Table 3. Figure 6 indicates the number of patients and controls using each pattern for the almond and the cookie. F-2 was overall the most common pattern used by both patients and control subjects. Interestingly, control subjects rarely used an F-1 pattern and patient subjects never used the F-4 pattern.

Pattern	Opening path shape	Turning point	Separation between opening and closing phases	Opening path crosses midline	Closing path crosses midline
F-1	Concave toward bolus side	Bolus side	Yes	May or may not	No
F-2	Convex toward bolus side	Bolus side	Minimal	No	No
F-3	Concave toward bolus side	Opposite side	Yes	No	May or may not
F-4	Convex toward bolus side	Opposite side	Minimal	May or may not	May or may not

Table 3. Characteristics of the four frontal plane chewing styles as described by BioResearch.

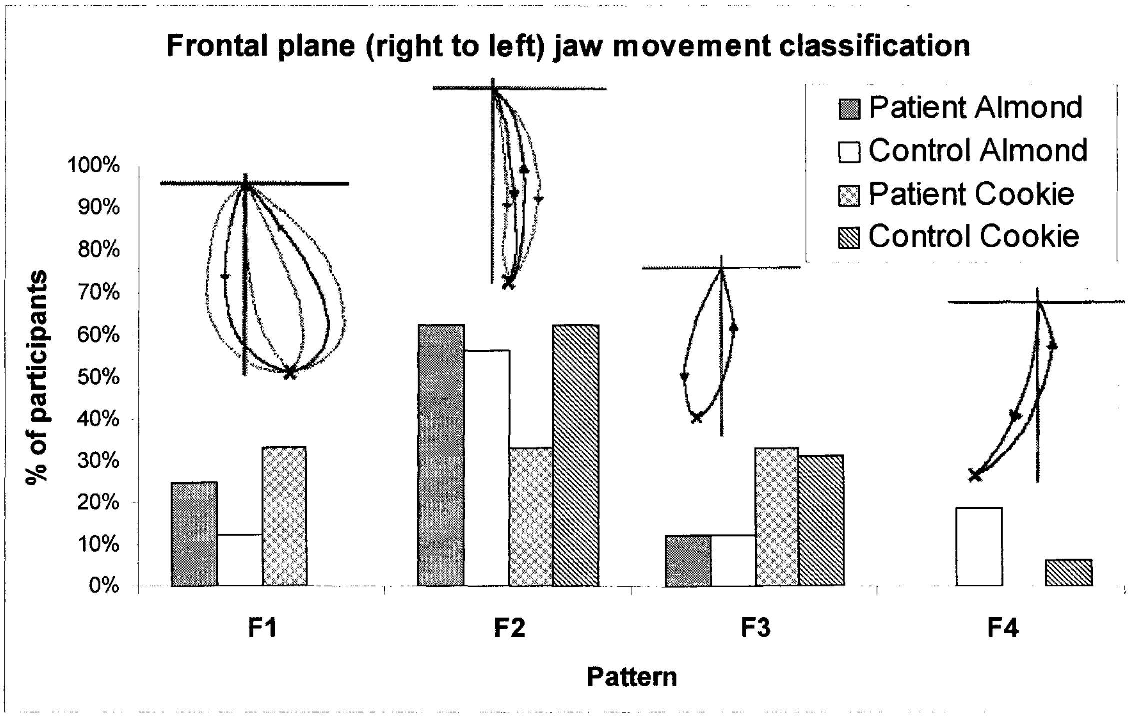


Figure 6. Frontal plane movement patterns used by each subject. Categories listed on the x-axis are described in table 3 and illustrated in this graph.

Sagittal Plane

Two distinct patterns are described by BioResearch for chewing patterns from the sagittal perspective. In the S-1 pattern, the opening phase is distinct and generally anterior to the closing path. Conversely, in the S-2 pattern, the opening and closing paths overlap over the entire pattern. Figure 7 illustrates the sagittal plane patterns used by the patients and control subjects. All of the patients used an S-1 pattern in chewing an almond whereas control subjects used either S-1 or S-2. Patients and control subjects used either S-1 or S-2 patterns while chewing a cookie; however, patients used an S-1 pattern more often and control subjects used an S-2 pattern more often.

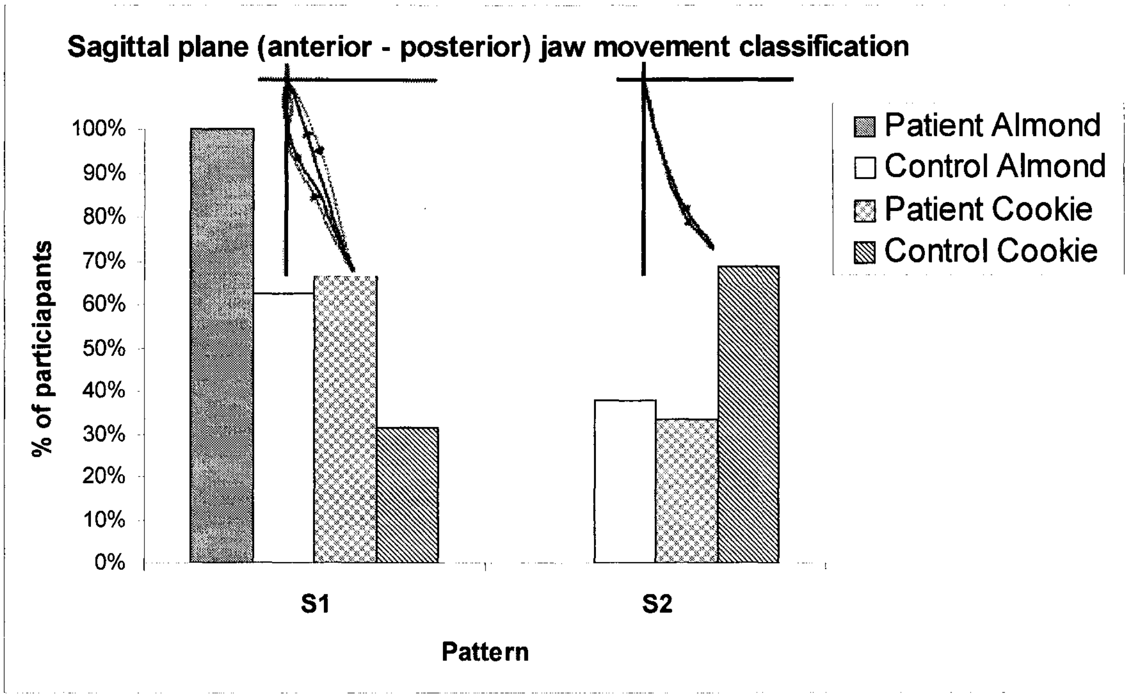


Figure 7. Sagittal plane jaw movements (e.g. anterior – posterior) used by subjects as categorized by the BioResearch method described above for patients and controls chewing an almond or a cookie.

Speech Intelligibility of Patients Compared to Controls

Audio recording of subjects was completed while they read a series of randomly generated words and sentences in order to measure speech intelligibility. The transcriptions and the keys were compared to derive a percentage of words correctly identified for both single-word utterances and sentences. Figure 8 illustrates these results. Control subjects were significantly more intelligible than patients for words (z=-2.366; p=0.018) and sentences (z=-2.103; p=0.035).

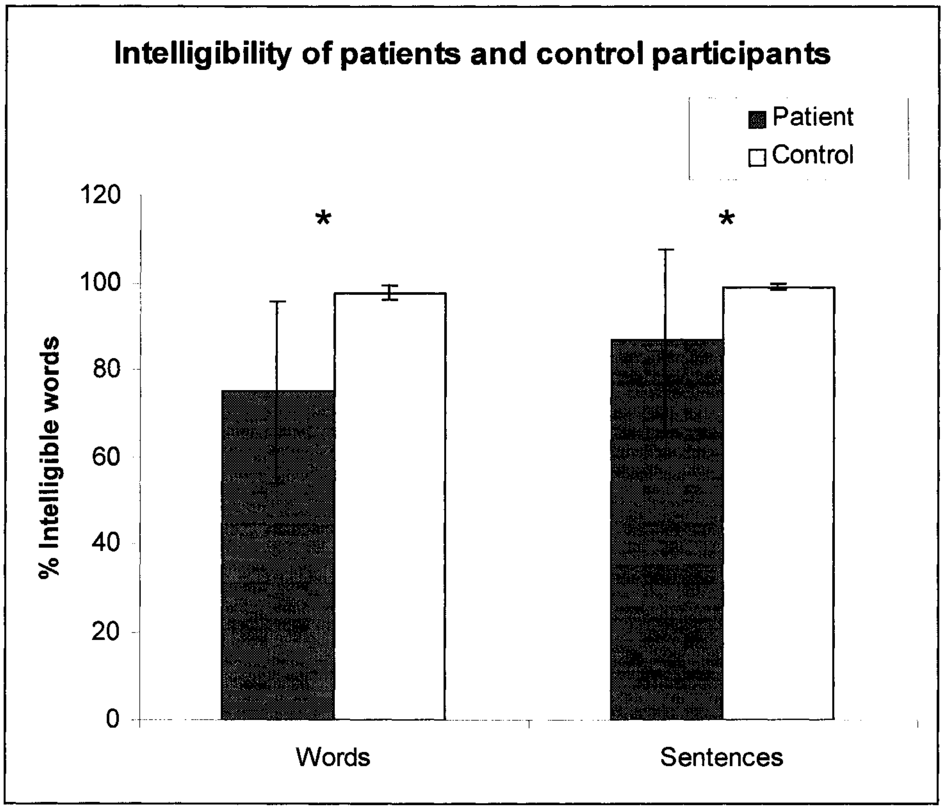


Figure 8. Speech intelligibility for patients and controls as determined as the % of words correctly identified by a naive listener in single words (Words) and within sentences (Sentences). (*) indicates a statistically significant difference.

Sensory Ability of the Reconstructed and Natural Portions of the Tongue

Differences in sensation data between the reconstructed and non-reconstructed portions of the tongue in patients were tested using Wilcoxon non-parametric statistical analyses. Only the sensations of two-point discrimination, light touch and temperature could be compared between the two sides of the tongue, as the other sensations (form, texture and taste) were not limited to one side of the tongue. The comparisons between the reconstructed and non-reconstructed portions of the tongue are depicted in Figure 9a. Differences between the 2 sides of the intact tongue in the control subjects are depicted in Figure 9b. With respect to the lateral dorsal portion of the tongue in patients, two-point discrimination was better on the intact portion of the tongue than it was on reconstructed portion (z=-2.156; p=0.031). There were no differences in two-point discrimination between the intact and reconstructed anterior portions of the tongue. No significant differences were found for patients between the reconstructed and non-reconstructed portions of the tongue for light touch. For both the anterior and lateral dorsal portions of the tongue, temperature discrimination was significantly better on the intact portion than it was on the reconstructed portion (z=-2.264; p=0.024 and z=-2.060; p=0.039, respectively). No significant differences were found between the two sides of the tongue for control subjects.

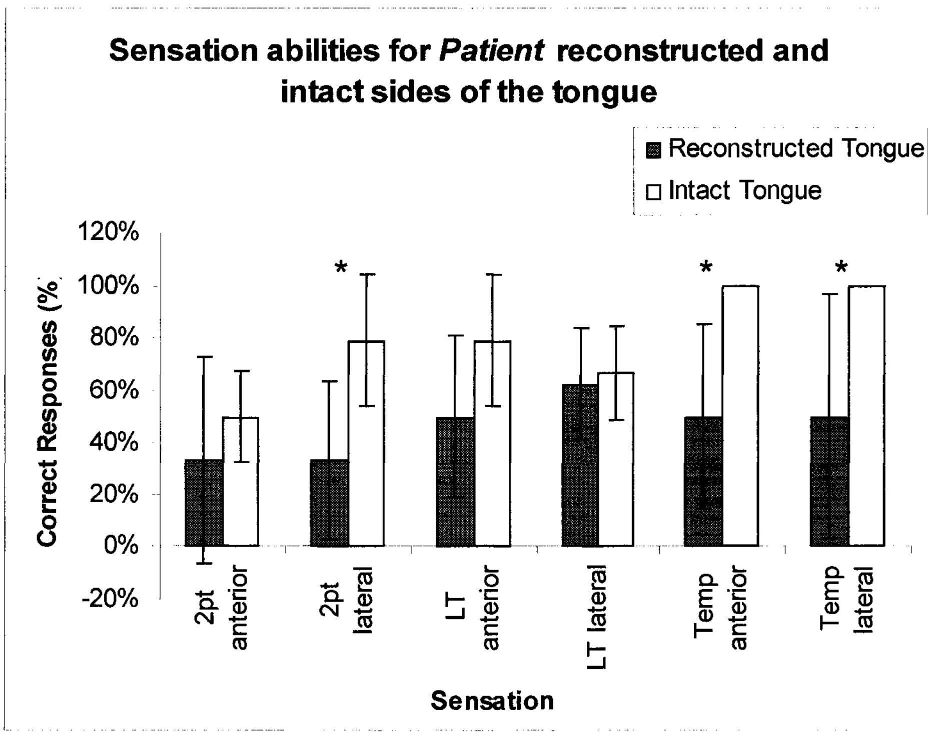


Figure 9a. Sensory abilities of the patients between the reconstructed and intact side of the tongue for three sensations. Sensations include two-point discrimination (2pt), light touch (LT) and temperature (Temp) for the tip (anterior) or lateral dorsal (lateral) portion of the tongue. (*) indicates a statistically significant difference.

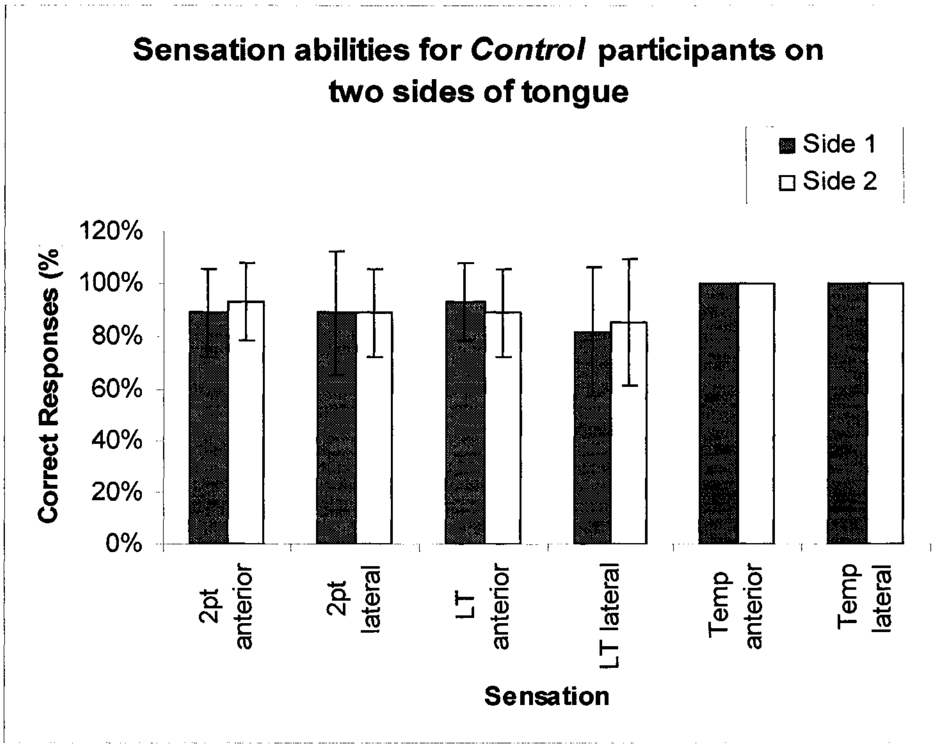


Figure 9b. Sensory abilities of the controls between the two sides of the tongue for three sensations. Sensations include two-point discrimination (2pt), light touch (LT) and temperature (Temp) for the tip (anterior) or lateral dorsal (lateral) portion of the tongue. No statistically significant differences were found.

Interrelationships between Sensation, Functional Outcomes and Quality of Life

The following sections explore the interrelationships between sensation, functional outcomes and quality of life. A Spearman's non-parametric correlation analysis was performed. Significant relationships were found and are discussed first for the relationships between sensation and functional outcomes, next for the relationships between quality of life and sensation, followed by quality of life and functional outcomes. As the quality of life measure is disease-specific, results are discussed for the patient population only.

Relationships between Sensation and Functional Outcomes

In the next two sections, sensation and its relationships to functional outcomes will first be described for the patient subjects followed by the control subjects. As no significant differences exist between the two sides of the tongue for control subjects on the sensory tasks, the control subject results are discussed omitting side of tongue specification.

<u>Sensation and Masticatory Efficiency – Patients</u>

Several relationships were found between sensation and masticatory efficiency within the patient population. These results are depicted in Table 4.

Sensation Measure	Masticatory Efficiency	Statistical Significance of
↑ texture discrimination	↑ food particles on larger meshed sieves	r=0.894; p=0.041
↑ form identification	↓ food particles on larger meshed sieves	r=-0.894; p=0.041

Table 4. Relationships between sensation and masticatory efficiency for the patient population.

<u>Sensation and Masticatory Style – Patients</u>

Several relationships were found between sensation and masticatory style within the patient population. These results are depicted in Table 5.

Sensation Measure	Masticatory Style	Statistical significance of correlation
↑ two-point discrimination on the reconstructed lateral tongue	↓ duration to complete one chewing cycle for a cookie	r=–0.894; p=0.041
	↓ duration to masticate a cookie before the first swallow	r=–0.894; p=0.041
↑ two-point discrimination on the intact lateral tongue	↑ duration of the closing phase for a cookie	r=0.949; p=0.014
↑ temperature discrimination on the reconstructed lateral tongue	↓ chewing strokes taken for a cookie before the first swallow	r=–0.894; p=0.041
	↓ duration to masticate a cookie before the first swallow	r=–0.894; p=0.041
↑ texture	↓ duration of the closing phase for a cookie	r=–0.975; p=0.005

Table 5. Relationships between sensation and masticatory style for the patient population.

Sensation and Speech Intelligibility – Patients

Sensation and speech intelligibility were measured as previously described for the between group comparisons. No relationships were found between any of the sensation measures and intelligibility of speech for the patient population.

Sensation and Masticatory Efficiency – Controls

With respect to sensation and masticatory efficiency, a number of significant relationships exist. These relationships are depicted in Table 6.

Sensation Measure	Masticatory Efficiency	Statistical significance of correlation
↑ two-point discrimination on the anterior tongue	↑ food particles on larger meshed sieves	r=0.732; p=0.039
↑ two-point discrimination on the lateral tongue	↑ food particles on smaller meshed sieves	Sieve 20, r=0.756; p=0.03 Sieve 25, r=0.756; p=0.03
↑ light touch on the lateral tongue	↓ food particles on smaller meshed sieves	Sieve 18, r=-0.784; p=0.021 Sieve 20, r=-0.825; p=0.012 Sieve 25, r=-0.825; p=0.012
↑ form identification	↓ food particles on larger meshed sieves	r=-0.778; p=0.023
↑ forms that were identified as forms similar to the correct form	↑ food particles on larger meshed sieves	r=0.766; p=0.027

Table 6. Relationships between sensation and masticatory efficiency for the control population.

Sensation and Masticatory Style – Controls

A number of relationships existed for control subjects between sensation and masticatory style. These are described in Table 7.

Sensation Measure	Masticatory Style	Statistical significance of correlation
↑ light touch on the lateral dorsal portion of the tongue	↑ duration of the occlusal phase for an almond	r=0.866, p=0.012
	↑ duration of the opening phase for a cookie	r=0.866, p=0.012
	↑ duration of the closing phase for a cookie	r=0.866, p=0.012 r=0.777, p=0.04
	↑ duration of the occlusal phase for a cookie	r=0.866, p=0.012
	↑ duration to complete one chewing cycle for a cookie	r=0.866, p=0.012
	↓ chewing strokes taken before the first swallow for a cookie	r=-0.874, p=0.01
↑ texture	↓ lateral jaw movements for an almond	r=-0.896, p=0.006
	↓ chewing strokes taken before the first swallow for an almond	r=-0.784, p=0.037
	↓ lateral jaw movements for a cookie	r=-0.777, p=0.04
↑ taste	↑ lateral jaw movements for an almond	r=0.805, p=0.029

Table 7. Relationships between sensation and masticatory style for the control population.

Sensation and Speech Intelligibility – Controls

Speech had no significant relationships with sensory ability for the control subject group.

Relationships between Quality of Life, Sensation and Functional Outcomes

As the quality of life measures are disease specific, results are discussed only for the patient population. To determine how sensory ability and functional outcomes are related to quality of life for the patient population, the EORTC-QOL H&N35 was administered as a standardized measure of quality of life and a Spearman's non-parametric correlation analysis was performed across variables. The EORTC-QOL

H&N35 questionnaire is scored and 18 summary scores for areas of quality of life are calculated. These 18 areas include: pain, swallowing (if they have had problems swallowing liquids, pureed food, solid food or if they have choked while swallowing), difficulties with senses (taste and smell), speech problems, trouble with social eating, trouble with social contact (patients were asked a series of questions relating to social contact including questions about how their appearance has bothered them, if they have had trouble with social or physical contact with friends or family, or trouble going out in public), less sexuality (asked if they felt less interest in sex or less sexual enjoyment), trouble with teeth ("have you had problems with your teeth?"), difficulties opening mouth ("have you had problems opening your mouth wide"), dry mouth, sticky saliva, coughing, illness, pain killers, nutritional supplements, feeding tube, weight loss and weight gain. The significant relationships found between quality of life and sensation, masticatory efficiency, masticatory style, and speech intelligibility are discussed in the following four sections.

Quality of Life and Sensation

A number of relationships existed between quality of life and sensation. These are described in Table 8.

Quality of Life EORTC-H&N 35	Sensory Measure	Statistical Significance of Correlation
↑ pain in head and neck region	↑ 2-point discrimination on **intact** anterior tongue	r=0.849; p=0.008
↑ difficulty with speech	↓ 2-point discrimination on **reconstructed** lateral tongue	r=-0.763; p=0.028
↑ trouble with social contact	↑ 2-point discrimination on **intact** anterior tongue	r=0.718; p=0.045
	↓ light touch identification on **intact** lateral tongue	r=-0.718; p=0.045
	↓ ability to discriminate taste	r=-0.800; p=0.017
↑ negative perception of sex life	↑ 2-point discrimination on **intact** anterior tongue	r=0.750; p=0.032
↑ difficulty opening mouth	↓ light touch identification on **intact** anterior tongue	r=-0.843; p=0.009
	↓ form identification	r=-0.708; p=0.05
↑ dry mouth	↓ 2-point discrimination on **reconstructed** lateral tongue	r=-0.723; p=0.043
↑ sticky saliva	↓ 2-point discrimination on **reconstructed** lateral tongue	r=-0.724; p=0.031
	↑ light touch identification on **reconstructed** anterior tongue	r=0.723; p=0.043
	↓ temperature recognition on **reconstructed** anterior tongue	r=-0.723; p=0.043
↑ use of painkillers	↓ taste	r=-0.793; p=0.019
↑ weight loss	↓ taste	r=-0.784; p=0.021

Table 8. Relationships between quality of life and sensation for the patient population.

Quality of Life and Masticatory Efficiency

Only one significant relationship exists between quality of life and masticatory efficiency. Patients who report dry mouth, have significantly fewer almond particles filtered onto one of the larger mesh sieves, sieve 7 ($r=-0.894$; $p=0.041$).

Quality of Life and Masticatory Style

Several relationships between quality of life and masticatory style were found and are described in Table 9. These relationships exist only for masticatory style while chewing a cookie. The same relationships were not found when chewing an almond.

Quality of Life Measure EORTC-H&N 35	Masticatory Style	Statistical significance of correlation
↑ difficulties swallowing	↑ duration of the occlusal phase for a cookie	r=0.894; p=0.041
	↑ duration of the chewing cycle for a cookie	r=0.894; p=0.041
	↑ duration to masticate a cookie before the first swallow	r=0.894; p=0.041
↑ difficulties with senses (taste and smell)	↑ chewing strokes taken before the first swallow for a cookie	r=0.894; p=0.041
↑ difficulties with speech	↑ duration of the occlusal phase for a cookie	r=0.894; p=0.041
	↑ duration of the chewing cycle for a cookie	r=0.894; p=0.041
	↑ duration to masticate a cookie before the first swallow	r=0.894; p=0.041
↑ problems with teeth	↓ duration of the opening phase for a cookie	r=-0.894; p=0.041

Table 9. Relationships between quality of life and masticatory style for the patient population.

Quality of Life and Speech Intelligibility

No meaningful significant relationships existed between quality of life and speech intelligibility.

Effect of Radiotherapy in the Patient Population

Radiation therapy was found to play a role in the quality of life measures for the patients. Figure 10 illustrates the effect of radiotherapy. Of the 8 patients who participated in this study, 4 had undergone adjuvant radiation therapy. To determine what effect radiation therapy had on outcomes, a Wilcoxon non-parametric statistical analysis was performed between groups. The only variables that showed a difference between patients who have had radiation therapy and those who did not were the quality of life measures. None of the sensation, chewing or speech intelligibility measures discriminated between the two groups of patients. On the quality of life measure, patients who underwent radiation therapy were more likely to report problems with their swallowing (such as if they have had problems swallowing liquids, pureed food, solid food or if they have choked while swallowing) than patients who received surgery only (z=-2.247; p=0.025). When patients were asked questions regarding social eating (i.e., have you had trouble eating?, have you had trouble eating in front of your family or friends? or have you had trouble enjoying your meal?), patients who had radiation therapy were more likely to report problems than patients who had no radiation therapy (z=-2.352; p=0.019). Patients with radiation therapy reported significantly more trouble with teeth (z=-2.223; p=0.026), and reported greater difficulty with dry mouth more often than patients without radiation therapy (z=-2.428; p=0.015). Patients who had radiation therapy also reported significantly more trouble with sticky saliva (z=-2.000; p=0.046), more coughing (z=-2.646; p=0.008) and use nutrition supplements more so than patients who did not have radiation therapy (z=-2.646; p=0.008).

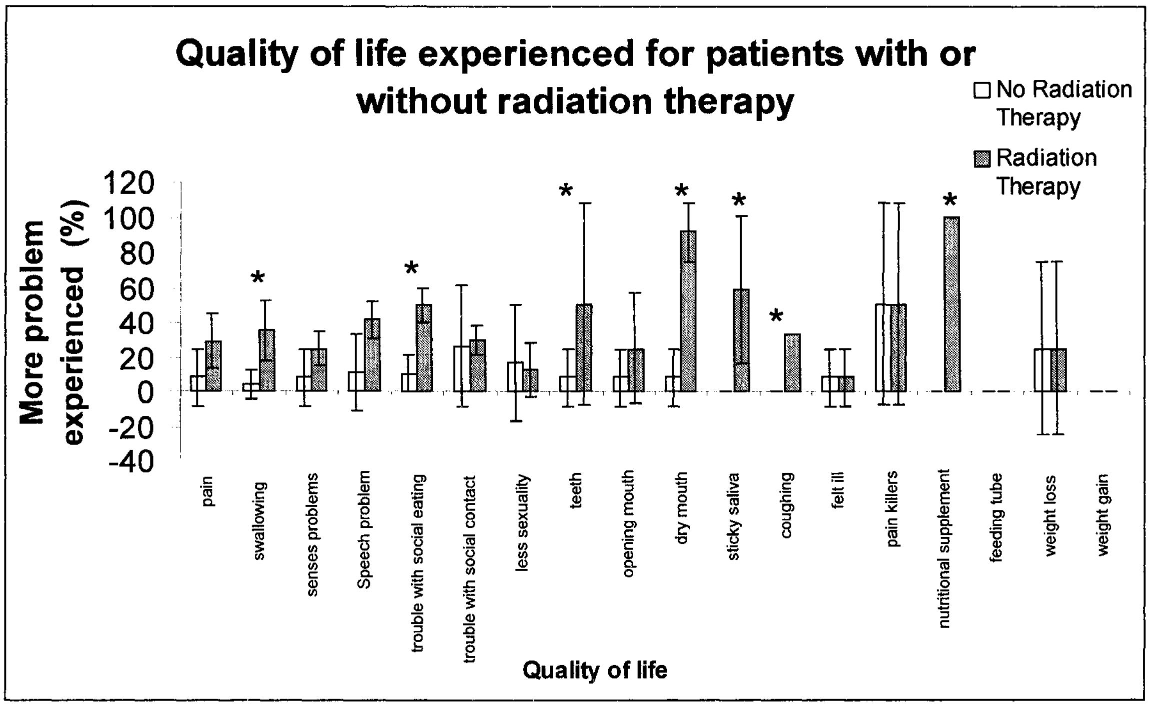


Figure 10.Quality of life for patients who have undergone radiation therapy and patients who have not. A higher score indicates poorer quality of life. (*) denotes a statistically significant difference.

Effect of Dental Status in the Patient Population

Dental status was found to influence mastication and quality of life. The number of occluding natural and prosthetic post-canine tooth pairs was recorded for all patients, as well as the control subjects. All control subjects had all of their natural dentition, thus, due to the lack of variation in the control population, statistical analyses were not revealing. To determine the effect of teeth on outcomes in the patient population, a Spearman's non-parametric correlation analysis was performed. The number and type of teeth (natural or prosthetic) were related to some measures of sensation, masticatory efficiency, and quality of life, but not to masticatory style or speech intelligibility.

Dental Status and Sensation

Significant correlations existed between only one sensation (form identification) and teeth, such that the more prosthetic teeth a patient had, the less able they were to correctly identify the shape of acrylic resin forms (r=-0.725; p=0.042).

Dental Status and Masticatory Efficiency

Significant correlations were present between the number of natural teeth and the amount of almond particles found on each of a series of 6 sieves ranging from large mesh size to a small mesh size. These results are displayed in Table 10.

Teeth	Masticatory Efficiency	Statistical Significance of Correlation
↑ ***natural*** tooth pairs	↓ food particles on the largest mesh sieve	r=-0.949; p=0.014
↑ ***natural*** tooth pairs	↑ food particles on smaller meshed sieves	Sieve 18, r=0.949; p=0.014
		Sieve 20, r=0.949; p=0.014
		Sieve 25, r=0.949; p=0.014
↑ ***natural*** tooth pairs	↑ food particles on the bottom plate under the sieves	r=0.949; p=0.014

Table 10. Relationships between teeth and masticatory efficiency for the patient population.

Dental Status and Masticatory Style

No relationships were found between dental status and masticatory style.

Dental Status and Speech Intelligibility

No relationships were found between dental status and speech intelligibility.

Dental Status and Quality of Life

Interestingly, the number of teeth a patient had was related to only a few quality of life issues. The more natural teeth a patient had, the fewer difficulties they reported with senses (includes taste and smell) (r=-0.845; p=0.008), and the fewer difficulties they reported with opening their mouth ($r=-0.708$; $p=0.05$). The more prosthetic teeth that a patient had, the more difficulties they reported with opening their mouth ($r=0.976$; $p=0.00$).

Discussion

The major aim of this study was to determine how sensation of the tongue is related to function and quality of life after reconstructive surgery in patients with head and neck cancer. Secondary aims of this study were to determine if the sensory abilities and functional outcomes of patients differ from age- and gender- matched controls. In addition, differences in sensation between the reconstructed and non-reconstructed sides of the tongue in patients were explored. The results of this study contain pertinent information for surgeons who specialize in tongue reconstructions and their current and future patients.

In general, the results indicate that sensation relates to masticatory efficiency and style as well as to quality of life. Patients tend to have poorer tongue sensory abilities, poorer masticatory efficiency and poorer speech intelligibility when compared to the control subjects. In addition, the reconstructed side of the tongue appears to function as well as the intact side of the tongue for some sensations but not all thus indicating partial recovery of sensory abilities.

Sensation

Although all patients who participated in this study were reconstructed with innervated microvascular free flaps, the resulting sensory ability of the flap was different from the sensory ability found within control subjects and within the intact side of the tongue in patients for some of the tested sensations applied to one side of the tongue (two-point discrimination, light touch, or temperature). In general, tests of sensations that required application of stimuli to the whole mouth (i.e., texture and taste) resulted in equivalent scores between the control and patient groups. A more in depth look at the results found for each sensation within the patient group, and as compared to the control group, reveals interesting patterns that may have bearing on the functional and quality of life outcomes that were observed in this study.

The ability of subjects to discriminate between one and two points is related to the density of sensory receptors in one area. A higher density of sensory receptors allows the two-points to activate two separate populations of neurons resulting in the perception of two separated points. When the distance between two separate points feels like a single point, there no longer is activation of separate populations of neurons secondary to a reduced density of sensory receptors.[32, 33] With respect to the patient group, Kuriakose and colleagues[8] and Santamaria and colleagues[7] found similar results for two-point discrimination as was found in the present study. The authors concluded that two-point discrimination is similar between the reconstructed and intact portions of the tongue. The present study found that on the anterior portion of the tongue two-point discrimination abilities are similar between the reconstructed and intact portions of the tongue. However, the results from the present study also reveal that two-point discrimination was significantly poorer on the lateral reconstructed portion of the tongue when compared to the lateral intact portion of the tongue. The results may differ from the Santamaria[7] and Kuriakose[8] studies because, in those studies, subjects were tested on a continuum of distances between two points. In the present study, subjects were tested on two points that were a set distance apart based on typical abilities from previous literature.[17-19] The two points were set 3mm apart and 6mm apart for the anterior and lateral portion of the tongue, respectively. In the Kuriakose[8] study, recovery of two-point discrimination was on average 12mm for the reconstructed tongue. In the current study, on the reconstructed portion of the tongue, 33% of patients identified two points at 3mm on the anterior portion of the tongue and 33% identified 6mm on the lateral portion of the tongue. The Kuriakose[8] study found recovery of two-point discrimination was on average 9mm for the intact tongue. On the intact portion of the tongue in the current study, 50% correctly identified two points at 3mm on the anterior portion of the tongue and 79% correctly identified two points 6mm apart on the lateral portion of the tongue.

In the present study patients were compared with controls for two-point discrimination. It was found that patients performed significantly poorer than controls in their ability to identify two separate points on the reconstructed portion of the tongue on both the anterior and lateral portions of the tongue. Patients also had poorer two-point discrimination on the intact portion of the tongue when compared to control subjects on the anterior portion of the tongue. These results suggest that the innervated radial forearm free flap does not allow patients to have two-point discrimination at the level of the controls and that this reconstruction may actually have a negative impact on the intact anterior portion of the tongue.

Hairy skin that covers most of the body including the radial forearm has fewer sensory receptors than glabrous skin (which is hairless) including the tongue. Glabrous skin has a higher number of sensory receptors and a larger area of somatosensory cortex devoted to it; thus, it is more sensitive. For example, the distance between two points that is required to distinguish them as two points on the forearm is approximately 39mm.[33] For the tip of the tongue the difference necessary to discriminate two points is 3mm and for the lateral dorsal portion of the tongue is 6mm. In a study by Shibahara and colleagues,[34] mucosa-like changes occurred in the radial forearm free flap tissue approximately 10 months after reconstruction. These changes included shrinking of the hair follicles and sebaceous glands in the connective tissue layer. In review of the literature, no research has been conducted on further histological changes to indicate if a greater number or different types of sensory receptors develop in this tissue. However it has been shown that two-point discrimination on the innervated radial forearm free flap is more similar to residual tongue tissue than the tissue on the contralateral forearm donor site.[8]

The subjects' ability to identify the presence of $0.07 g/mm^2$ of force was tested using a Semmes – Weinstein monofiliment (#2.83). This was considered to be a measure of the subject's ability to identify light touch. The results of the current study found no difference between control subjects and patients on the intact portion of the tongue. However, patients were poorer at identifying light touch on both the anterior and lateral portion of the reconstructed portion of the tongue. In addition, light touch abilities were similar between the reconstructed and intact tongue in the patient population for both the anterior aspect (50% reconstructed, 79% intact) and the lateral aspect (62% reconstructed, 66% intact). These findings were similar to that of a study completed by Santamaria and colleagues.[7] Both the Santamaria[7] study and the present study found that light touch ability was similar on both the reconstructed and intact portions of the tongue. Both studies used the Semmes – Weinstein monofilament test for light touch sensation and both included innervated radial forearm free flaps. The results from both studies are logical for two reasons. First, the same sensory receptors that identify light touch are found in the skin of the lateral forearm and the mucosa of the tongue (free nerve endings, Merkel's disks and Meissner's corpuscles). Second, the innervation involves anastomizing the lateral antebrachial cutaneous nerve of the arm to the lingual branch of the trigeminal nerve (CN V), which is responsible for general sensation on the anterior 2/3 of the tongue. However, the light touch findings from the present study differ from the results of Netscher and colleagues.[14] Those authors found that 71% of subjects with innervated radial forearm free flaps could detect light touch. In the present study 50% of subjects with innervated radial forearm free flaps could detect light touch on the anterior reconstructed portion of the tongue and 62% could detect light touch on the lateral reconstructed portion of the tongue. These differences may be due to the differences in methods that were used to assess light touch between the 2 studies. Netscher and colleagues[14] stroked the center of the flap with a cotton swab. The present study used a Semmes-Weinstein monofilament and tested both the anterior and lateral portion of the flap. These methods may produce different results as the Semmes – Weinstein monofilament measures the light touch sensation for a single point/ receptor on the tongue whereas stroking the center of the flap with a cotton swab will stimulate multiple receptors as it moves along the flap. The cotton swab method may then allow recruitment of a number of receptors to aid in the identification of the presence of stimuli.

Light touch abilities on the intact portion of the tongue in patients are similar to the light touch abilities of the control subjects. However, the light touch ability for the patients on the reconstructed portion of the tongue was significantly poorer than control subjects. This seeming inconsistency can be explained by exploring the means and standard deviations of the data. No significant differences in light touch ability between the reconstructed and intact portions of the tongue were found in the patient group leading one to believe that light touch sensation may be within normal limits on both sides of the tongue in that group. However, the patients perform only moderately-well on this task for both the reconstructed and intact portions of the tongue. Therefore, when patients are compared to controls, their performance on this task, in general, is poorer than the controls, although only significantly so for the reconstructed portion of the tongue.

The temperature findings in the current study differed somewhat from the current literature. Kerawala and colleagues[6] found the best recovery of hot sensation, followed by cold and then pain in patients with non-innervated radial forearm free flaps for oro-pharyngeal reconstruction including mandible, tongue, floor of mouth, soft palate, retromolar, and buccal sites. Likewise, Shindo and colleagues[4] found better recovery of hot sensation than cold sensation in patients with non-innervated radial forearm free flap reconstruction of the floor of mouth, total glossectomy, pharyngectomy, full-thickness cheek and facial skin. Patients in the present study were more likely to correctly identify the cold sensation over the warm sensations. The results might be discrepant because the previous studies used cold sensory methods that were not as cold as those used in the present study. The Kerawala[6] study used laryngoscopy mirrors immersed in water at $40^{O}C$ to measure cold sensation and the current study had dental mirrors immersed in water at $3^{O}C$ to measure cold sensation. It might be that $40^{O}C$ is not perceived as cold. A study by Manrique and Zald[35] measured the hot and cold thresholds of the tongue for

76 healthy individuals and found the threshold at which subjects perceived cold sensation was 32.14^{O}C. Discrimination of warm temperature was tested at 60 ^{O}C in the Kerwala[6] study and at 55^{O}C in the present study. The Shindo[4] study did not describe the temperature of the mirrors used, only that they were heated or cold mirrors. Another possibility for the differences found between the Kerwala[6] study and the present study may, in fact, be a result of the type of sensory re-innervation. The Kerawala[6] and Shindo[4] studies included patients with non-innervated free flaps and the current study included patients with innervated free flaps. Perhaps reinnervation enhances the sensory perception of hot as temperature sensation is conveyed via the trigeminal nerve (CN V). In the present study the radial forearm free flaps were innervated by connecting the lateral antebrachial cutaneous nerve to the lingual branch of the trigeminal nerve (CN V), which relays temperature sensation. The temperature results from the present study are in accordance with the study by Netscher and colleagues.[14] The Netscher[14] study compared sensory abilities between innervated and non-innervated radial forearm free flaps. They found that 100% of subjects with innervated radial forearm free flaps were able to identify cold sensation and 86% were able to identify heat. Although the subjects in the present study did not score as well as the patients with reinnervation in the Netscher[14] study, a similar pattern was observed. Patients in the present study were able to identify cold more often than hot (62% and 25%, respectively). Interestingly, the patients in the Netscher[14] study with non-innervated radial forearm free flaps did not follow the same pattern as the patients with non-innervated radial forearm free flaps in the Kerawala[6] or Shindo[4] studies. Netscher[14] found better recovery of cold sensation even in the non-innervated patients. However, when comparing the temperatures used in the Kerawala[6]

and Netscher[14] studies, the "hot" temperature in the Netscher[14] study is the same as the "cold" temperature of the Kerawala[6] study ($40^{O}C$).

Patients and control subjects did not differ in their ability to identify texture, however controls were better at correctly identifying the shape of acrylic resin forms. In review of the literature, no research has compared the texture or stereognosis abilities between patients with surgical reconstruction of the tongue and control subjects. It appears that texture is a whole mouth sensation; thus, it appears that both groups were able to take advantage of sensory feedback from a large portion of the oral cavity. On the other hand, oral stereognosis appears to rely heavily on sensory feedback from the tip of the tongue. Colletti and colleagues[36] have described this in normal children who were observed to use their tongue tip more frequently and accurately when performing oral stereognosis tasks than children with a tongue thrust. The patients in the current study all had a hemiglossectomy that encroached on the tip of the tongue; thus, their ability to use sensory feedback from the tip of the tongue to identify objects was likely impaired either directly from the loss of tissue in that area, or from sensory disruption directly related to surgery in the area.

Findings for taste sensations in this study are consistent with the literature. In review of the literature no previous literature exists on taste sensation with innervated radial forearm free flaps in the oral tongue. However, information in the literature exists on taste sensation after non-innervated reconstruction of the oral tongue that we can draw upon. In a study by Shibahara and colleagues,[37] taste sensation after tongue reconstruction with a non-innervated radial forearm free flap was evaluated. The authors found that overall taste abilities were close to normal however the taste sensations were essentially absent on the reconstructed portion of the tongue. They also found that the taste ability on the intact portion of the tongue also was slightly impaired, concluding that the compensatory mechanism for taste sensation occurs elsewhere in the oral cavity. Shibahara and colleagues[37] suggest that no recovery of taste sensation occurs on the reconstructed portion of the tongue as this region lacks the vallate and fungiform papillae that contain taste buds. In addition, they suggest that the impaired taste abilities on the intact portion of the tongue may be due to changes in the taste receptors from radiation therapy or chemotherapy, or from operative disruption of nerves on the intact portion of the tongue. In the present study, the radial forearm free flaps were innervated through the lingual branch of the trigeminal nerve (CN V). The lingual branch of the trigeminal nerve, however, is not responsible for taste sensation. Instead, taste on the anterior 2/3 of the tongue is detected by the chorda tympani of the facial nerve (CN VII) and by the glossopharyngeal nerve (CN IX) for the posterior 1/3 of the tongue.[38] Thus, one would expect that the innervation would not provide any benefit to the patient in terms of taste. Because this study found that whole-mouth taste sensation was similar to the control population, it can be presumed that the surgical resection had little effect on taste and that the remaining taste ability resulted from compensatory mechanisms elsewhere in the oral cavity as suggested by Shibahara and colleagues.[37]

One theory that may explain compensatory sensation in the intact portion of the tongue or other oral mucosa is the knowledge that the somatosensory cortex has an element of plasticity.[32] Sensory changes in the cortex are often seen in limb amputees. The area of the somatosensory cortex previously dedicated to the amputated limb no longer receives its sensory input. This area of the cortex is then reorganized and receives input from other areas of the body, usually the areas that are represented adjacently in the somatosensory cortex. Thus, the surrounding areas have more cortex dedicated to them. In the case of reconstruction of the tongue, compensation for the loss of taste receptors from the resected portion of the tongue may occur if the associated sensory cortex is reorganized to receive input from healthy surrounding areas in the oral cavity containing appropriate taste receptors.

Masticatory Efficiency

On the whole, control subjects were more efficient masticators than were the patients. A study by Namaki and colleagues[39] that explored masticatory efficiency after surgery in oral cancer patients supports the findings of the present study. The authors found that patients, who had tongue defects not involving the mandible, had poorer masticatory efficiency than controls. The results of the present study also are supported by the findings of Kapur and colleagues[40] in which the authors tested healthy subjects before and after unilateral anesthesia of the inferior alveolar, lingual and long buccal mucosa. The authors found that chewing efficiency was poorer after anesthesia. The Kapur[40] study also supports the theory that sensory abilities are of great importance to masticatory efficiency as anesthesia altered masticatory efficiency.

Whole mouth sensations including texture and the correct identification of forms, were more indicative of masticatory efficiency for patients, whereas light touch and two-point discrimination were more indicative of masticatory efficiency for controls. These results suggest that in the intact oral tongue, the fine senses on the lateral dorsal portion of the tongue have a greater influence on the ability to break down an almond for control subjects. For example, better performance on the two-point discrimination task was related to smaller particles of food following mastication. Form discrimination also was found to be important for both patient and control groups for masticatory efficiency. The results suggest that more particles land on the finer sized sieves when more forms are correctly identified. These results are supported by Hirano and colleagues[20] who found that oral stereognosis ability (i.e., the ability to determine the shape of an object in the mouth) is correlated with masticatory efficiency (i.e., how small can food be broken down) but not with masticatory ability (i.e., can food be broken down at all). The results from these studies support stereognosis as an important sensation for mastication. Engelen and colleagues[41] also support the notion that sensation and motor movements are related. In their study, they found that the ability to perceive the size of a steel ball in the mouth was positively correlated with masticatory ability measured by the median particle size after 15 chewing strokes.

As both stereognosis and texture follow the same neural pathway via the mandibular branch of CN V, the findings in the present study related to texture were somewhat unexpected. The results suggest that texture discrimination has the opposite trend as previously discussed for stereognosis. That is to say that the better a patient was at discriminating texture, the poorer their ability to break down an almond. This may indicate that for this type of masticatory task the ability to recognize form was more important than the ability to discriminate texture. It is possible that the neuronal insult in the tongue resulted in hypersensitivity to texture. Support for this theory can be found in animal studies where trigeminal sensory nerve injury has been induced. For example, Piao and colleagues[42] found that the whisker pads of rats were hypersensitive to tactile stimulation after trigeminal sensory nerve injury.

Masticatory Style

Although patients appear to be less efficient masticators, their chewing style did not differ from control subjects (e.g. time it takes to complete any phase of a chewing cycle, the time it takes to complete a full chewing cycle, the time it takes to finish chewing, the maximum lateral jaw excursion or the total number of chewing strokes before eliciting a swallow). These results are supported in a number of studies. For example, in a study by Engelen and colleagues,[41] it was found that poorer chewers do not compensate for their reduced chewing performance by using more chewing strokes. The present study found that patients did not differ significantly from controls for either the almond or the cookie on number of chewing strokes, however patients were determined to have significantly poorer masticatory efficiency.

The current study found that the visually-analyzed chewing patterns differed slightly between patients and controls. Most subjects (controls and patients) in this study used an F2 frontal chewing pattern. The difference lies within the subjects that used the other styles. No patients used an F4 chewing pattern while masticating either an almond or a cookie. No controls used an F1 pattern while masticating a cookie. Woda and colleagues[43] and Lewin[44] both suggest that the mandibular movement in the frontal plane typically follows a drop-shaped path. This path appears similar to the F1 and F3 patterns described by BioResearch. Interestingly, the F1 pattern was not the most common pattern used by either control or patient subjects in the current study. Lewin[44] describes two types of chewing patterns that occur depending on bolus consistency. The first is punctate or chop strokes. These are more common for soft boluses. The punctate strokes are characterized by minimal separation between the opening and closing phase and are similar to the F2 and F4 strokes described by BioResearch. The other type of stroke is the grinding type. This stroke is seen more often for hard boluses and is characterized by a larger separation between the opening and closing phase of a chewing cycle. Grinding strokes visually look like the F1 and F3 frontal patterns described by BioResearch. Lewin[44] also describes the process of coning in which the chewing pattern switches from a grinding pattern to a punctate pattern, as a hard bolus becomes softer during the tests. These descriptions help to interpret the results of the current study. The digestive cookie used, while initially a hard bolus, quickly becomes softer as it is mixed with saliva. Most controls used a punctate pattern while masticating a cookie. The patients on the other hand, used a grinding pattern (F1 and F3) more often than a punctate pattern (F2 or F4). This may suggest that patients are less able to adapt their chewing style to the changing bolus consistency. Almonds, a harder bolus, present with a punctate pattern of chewing most often as well (F2). A review paper by Yamashita and colleagues[45] may help explain these results. They found that chewing cycles are influenced by a number of factors including bolus consistency and bolus size. They found that with increased bolus size, the chewing cycle appears to increase the lateral component of its movement. Thus, although almonds are a hard consistency, they also are relatively small, resulting in a punctate pattern of chewing. Controls and patients in the present study differed slightly with respect to the chewing patterns of the almond. For example it appears that about 75% of controls used a punctate pattern (F2 and F4) while chewing an almond, whereas only about 60% of patients used a punctate pattern. In addition, it was found that controls used a wider variety of chewing strokes than patients. These chewing patterns are very difficult to interpret as there is a high amount of variability between individuals in their masticatory style.[43, 45]

More relationships are found between sensory abilities and masticatory style for the reconstructed side of the tongue in patients. In general, the better the tongue sensation on the reconstructed side of the tongue the less time is required for mastication. It is interesting that, for two-point discrimination, the better the sensation on the intact lateral dorsal side of the tongue, the more time was required for mastication. The increased sensory ability associated with this side of the tongue may have resulted in heightened awareness of particle size, and a concomitant increase in awareness on the part of the patient to reduce particles to a size that would be safe for swallowing.

Control subjects had significant relationships between chewing style, texture, taste, and light touch on the lateral tongue. The results suggest that the finer sensory tests (such as light touch) are more highly related to the phases of chewing cycles, whereas the sensations that use the whole mouth (such as texture and taste) seem to be more highly related to how the jaw moves. The finding that better texture discrimination results in less lateral jaw movement is supported by Lewin[44] in which the author explains the process of coning, a switch from grinding chewing patterns (larger lateral movements) to punctate chewing patterns (smaller lateral movements) as the consistency of the bolus changes as it is masticated and mixed with saliva. Thus, it is likely that better texture sensation allows for controls to adapt their masticatory style as the bolus changes.

Speech Intelligibility

Control subjects were found to be significantly more intelligible speakers than patients when evaluated objectively by a naïve listener. Haughey and colleagues[46] found that speech intelligibility scores were poorer for patients with oral tongue reconstructions than patients with tongue base reconstructions. In a study by Uwiera and colleagues[9] the authors found that there was poorer single word intelligibility in the postoperative period versus the preoperative time. These studies support the results that patients have poorer speech intelligibility than controls in the present study. It is not surprising that a perturbation to the anterior portion of the tongue would result in decreased speech intelligibility seeing as how this portion of the tongue is most important for speech articulation.

Interestingly, only the whole mouth sensations and intelligibility in sentences were related. For example, our results suggest that the better the taste abilities, the better the speech intelligibility in sentences. This is confirmed by the findings of Zuydam and colleagues[47] in which they found a moderate degree of correlation between speech and taste. Speech had no significant relationships with sensory ability for the control subject group. This is likely due to the fact that control subjects all scored close to 100% intelligible with almost no variation within the group.

Quality of Life

Quality of life is a concept that may be influenced by many factors. Disease specific quality of life measures compare issues that are assumed to influence a patient's quality of life. While acknowledging this limitation of quality of life surveys, a standardized quality of life survey (EORTC H&N35) was used as a method to compare patient outcomes. More positive relationships were seen between the quality of life measures and the finer sensory discriminations as opposed to the more global whole mouth sensations (form, texture and taste). Perhaps this is due to the fact that global sensations can be compensated for using the whole mouth or maybe it is indirectly related to other factors such as the finer sensations as these were found to influence mastication, which may in turn influence quality of life. Interestingly two-point discrimination, light touch and taste are most often related to quality of life issues. This may be due to the fact that it is the finer sensations that are less able to be compensated for using other areas of the oral cavity. Taste appears to have a great impact on quality of life issues including social contact, use of painkillers and weight loss.

Although only one significant relationship exists between quality of life and masticatory efficiency, an interesting trend was also noted. The trend suggests that as a patient is able to break an almond down into finer particles, they show fewer difficulties with swallowing, senses (taste and smell) and mouth opening (trismus). Conversely, the more particles that are found on the highest level sieve (large particles), the more difficulties the patients report with swallowing, senses (taste and smell) and mouth opening.

Engelen and colleagues41 who conclude that poor chewers swallow larger particles than good chewers support these findings. In the present study, poor chewers reported more difficulties with swallowing. It is suggested that the upper size limit of particles that are swallowed is determined by the individual's tolerance of discomfort from distension of soft tissue in the pharynx and esophagus.[48] Thus, it may be the case in the current study that subjects with poorer chewing abilities end up swallowing larger pieces resulting in more complaints of swallowing problems.

Effect of Radiotherapy in the Patient Population

Radiotherapy has often been reported as having a negative effect on functional ability, including chewing and swallowing. The results from the present study suggest that patients who have undergone radiation therapy have more difficulties with quality of life issues, including swallowing, difficulties eating, trouble with their teeth, dry mouth, sticky saliva, coughing more often, and taking more nutrition supplements, than patients who did not have radiation therapy. These results are supported in a study by Epstein and colleauges.[49] The Epstein[49] study found that oral complications are common after radiation therapy and have a negative effect on quality of life. Specifically, patients report difficulty chewing or eating, dry mouth, change in taste, dysphagia, altered speech, difficulty with dentures, increased tooth decay and pain. In addition, Fang and colleagues[50] found that problems with swallowing, dry mouth and sticky saliva become more serious 1 year after radiation therapy.

Radiation therapy did not have an effect on sensory ability or speech intelligibility in the patient population in the present study. These results contradict the results of a study by Bodin and colleagues[51] in which the authors found that radiation therapy resulted in poorer sensory ability on both the operated tumor side of the tongue and the irradiated non-tumor side. The discrepancy may be in the interpretation of the Bodin[51] study. In the Bodin[51] study, patients received preoperative full-dose radiotherapy followed by surgery according to a standard protocol. The timeline for testing in the Bodin[51] study was first prior to all treatment, then within one month after radiotherapy, six months after surgery and one year after surgery. The poor sensory abilities were found not at the time period post radiation therapy but at the time period 6 months post surgery. The authors concluded that this was due to radiation therapy as both the tumor and non-tumor sites were affected. However, it could be that the poor sensory ability on the non-tumor site is actually a result of surgery. The Shibahara[37] study found that taste perception after surgical reconstruction of the tongue was essentially absent on the reconstructed portion but also that the taste sensation was decreased on the intact portion of the tongue. These discrepancies in the results between the current study and the Bodin[51] study also may be due to the time period post-treatment. The patients in the present study were minimum 2 years post surgery and in the Bodin[51] study, patients were tested up to 1-year post surgery.

Effect of Dental Status in the Patient Population

Mastication is a process of sensory-motor interactions. The sensory feedback involves not only the sensory information conveyed by the oral mucosa but also the sensation from the periodontal ligament.[52] Denture-wearers no longer have the sensory feedback from the periodontal receptors, thus natural dentition plays an important role in masticatory function.[52] The results of the present study suggest that the more natural teeth and less prosthetic teeth a patient has, the fewer large unbroken almond pieces will be present and the more small particles will be present. This suggests that having natural teeth is very important for masticatory efficiency. It is noteworthy here as well that no correlations occurred with the total number of teeth, suggesting that even if a patient has a full set of dentures they are less efficient at breaking down an almond than patients who have natural teeth. These results are similar to findings in the literature that suggest that denture wearers have poorer masticatory efficiency than subjects with natural dentition.[43, 53] Contrary to the results of the present study, the Namaki[39] study found no difference in masticatory efficiency between a control group of individuals with all natural teeth and a group of individuals with complete natural maxillary teeth but reduced mandibular molars and/or premolars on one side. These results are likely due to the fact that all subjects had natural opposing tooth pairs on at least one side for mastication.

The results from the present study indicate that the more prosthetic teeth a patient had, the less acrylic resin forms they are able to correctly identify. It may be the case that patients with dentures are less able to compensate for loss of sensation of their tongue by using alternative mucosa for sensation as an upper denture prevents the use of sensory feedback from the palate. However, these results are contradictory to studies evaluating oral stereognosis ability in denture wearers. The results reported by Mantecchini and colleagues[54] and by Garrett and colleagues[55] suggest that the placement of dentures does not inhibit a patient's ability to identify form. The discrepancy between these results may be that the patients with dentures in the present study were not only unable to use the sensory information from the palate but they also had reduced sensory information from their tongue. Thus, perhaps when just the palate is unable to contribute sensory information, patients can compensate with information from the tongue only. However, the combined lack of sensation from the palate and reconstructed tongue may lead to more pronounced sensory deficits.

The results of the current study suggest that natural teeth specifically are important for chewing style. These results indicate that the more natural teeth a patient has, the less time is taken for mastication. Also, the more natural teeth that are present, the more lateral jaw movements are seen, suggesting a more rotary chewing pattern. These results, in combination with the masticatory efficiency results suggest that natural teeth not only allow a patient to comminute a bolus to a greater extent but also in less time. The result that natural teeth reduces the number of chewing strokes differ from the results of Engelen and colleagues[41] who found that poor chewers did not compensate by taking more chewing strokes. This difference however may be due to the fact that that the subjects in the Engelen[41] study were all healthy volunteers and it was not reported that any of these subjects wore dentures.

Dental Status and Quality of Life

The findings from this study suggest that the more natural teeth a patient had, the fewer difficulties they experienced with swallowing, senses and opening their mouth as measured through a quality of life instrument. In contrast, the more prosthetic teeth a patient had the more difficulties they experienced with opening their mouth. The importance of dental status for quality of life is supported by a study by Duke and colleagues[56] in which the authors found that dental status has a persistent impact on subjective quality of life.

Limitations

This section will discuss limitations of this study including sample size, type I and type II errors, and threats to internal and external validity.

Sample Size

This study employed a small sample size (N=8 patients; N=9 controls). The patient population was chosen from a convenience sample of patients who were treated at

COMPRU and was based on strict criteria limiting the population of possible participants (e.g., patients with partial resection of the oral tongue only and reconstruction with radial forearm free flap). The strict criteria allowed for elimination of other confounding factors such as reconstruction in other areas of the oral cavity and therefore provide description of outcomes specific to this type of treatment. To increase the statistical power of the study, a total of 25 participants per group or more would have been ideal especially because the data were not normally distributed. Taken together, the results from this study are predominantly descriptive and have limited generalization.

Type I and Type II Errors

Setting α to 0.05 or p=0.05 means that the chance of committing a Type I error (rejecting a true null hypothesis) is low, however β (chance of committing a Type II error – accepting a false null hypothesis) is high due to the small sample size. The only way to decrease both α and β at the same time is to increase the sample size, which in this case was not possible. Another concern regarding a Type I error was encountered within this study and was related to the number of tests for significance that were applied to the data. A danger does exist when looking for multiple effects in the data. The more effects that are examined, the more likely an effect will be found. One way to adjust for this is to adjust the p-value by dividing the p-value (e.g. $p>0.05$) by the number of tests. This will reduce the chance of making a Type I error.

Threats to Internal and External Validity

Internal and external validity are discussed in this section to critically evaluate if indeed the independent variable (innervated radial forearm free flap reconstruction of the tongue) resulted in the observed changes and the extent to which these results can be generalized to other patients.

Internal Validity

Internal validity is the extent to which we can conclude that the independent variable resulted in the observed change. According to Schiavetti and Metz[57] six potential threats to internal validity exist. These include history, maturation, testing or test-practice effects, instrumentation, differential subject-selection and mortality. The threats of history, maturation, testing or test-practice effects and mortality were not issues in the current study the current study is cross-sectional as opposed to longitudinal therefore no pre or post measures were given. Instrumentation was considered and controlled for by using the same experimenter to test all subjects and providing the same instructions to all subjects. In addition, a standardized questionnaire was used to control for this threat to internal validity. Statistical regression was not an issue in the current study as patients were not chosen based on test scores. To avoid the threat of differential subject-selection, subjects are often randomly assigned to each group. Due to the nature of the current study, subjects were not randomly assigned. To control for this threat to internal validity, age- and gender- matched controls were used.

External Validity

External validity is the extent to which the results of a study can be generalized across different persons, settings and times. Schiavetti and Metz[57] describe four threats to external validity. These include subject selection, reactive or interactive effects of pretesting, reactive arrangements and multiple-treatment interference. The threat of subject-selection may apply in the current study. It is possible that the patients who agreed to participate in this study were different in some way than the patients that were not able to be contacted or who did not agree to participate, thereby resulting in outcomes that are not be representative of the patient population as a whole. In addition the sample size was very small. Of the 16 patients identified as having solely partial glossectomy and reconstruction with a RFFF, only 8 participated. The characteristics of the subjects in this study were thoroughly outlined in the methods section to help determine the population for which these results may be generalized. Multi-center research would help in recruiting more subjects and better generalization of results.

Reactive or interactive effects of pre-testing is not applicable in the present study, as the study was cross-sectional as opposed to longitudinal. The threat of reactive arrangements relates to the ability to generalize to other settings or areas. This could be relevant in the current study as the results may only be generalized to patients receiving radial forearm free flap reconstruction of the oral portion of the tongue who were treated in Edmonton, Alberta. For example, other surgeons in other areas may use slightly different techniques and medical follow-up, (e.g., type of radiation therapy used, other medical interventions, etc.).

Multiple treatments may interact to have an effect on the dependant variable thus limiting the ability to generalize results to these treatments. This could be an issue in the current study as some patients had both surgery and radiation therapy. To control for this, patients with and without radiation therapy were compared; however, the sample size within each patient group was very small (i.e., 4 patients per group). While radiation therapy seemed to be influential on some areas of function, the limited sample size prevents any firm conclusions from being reached about the effects of this treatment on this patient population.

Critical Evaluation of Study

While this study provided an in depth description of outcomes for this selected patient group, it also raised some additional questions. A critique of the method and new questions arising from the current study will be addressed within the context of the experimental variables measured.

Sensation

Light Touch

This measure appeared to be adequate in revealing similar sensory abilities between the two sides of the tongue when patients were presented with one level of force and asked to respond in a forced choice detection paradigm. The Semmes-Weinstein monofilament method could have been exploited to determine the sensation threshold if trials for each of the Semmes-Weinstein monofilaments were given to determine exactly what level of force is required for each participant to feel the light touch.

Two-Point Discrimination

In this method, the time of stimulus application was controlled whereas the actual force applied was not. It has been previously described that tactile sensitivity varies with the force applied.[58] However, Vriens and van der Glas[59] studied the relationship between facial two-point discrimination and applied force using a modified version of both the Disk-Criminator and the Aesthesiometer to include a force transducer. The Vriens and van der Glas study[59] found that although there was great variability in the force applied by examiners testing facial two-point discrimination, this did not have an influence on the threshold pin distance of two-point discrimination. Therefore, while it may be ideal to control for both time of stimulus application and level of force applied to decrease the standard error of measurement, it may not be necessary.

Temperature

This method appeared to be adequate in determining temperature discrimination as controls were able to correctly identify hot and cold 100% of the time. Conversely, the ability of patients to sense temperature on the reconstructed side of the tongue was impaired. For example, patients were somewhat successful in identifying cold temperature changes on the reconstructed side of the tongue, whereas the identification of warm temperature proved more difficult for the majority of the patients. This may be the direct result of the surgery or may be due to the method used to measure temperature. Intuitively, one way to improve this method may be to use a hot temperature that is much warmer than the natural intra-oral temperature. However, this would not be in the patient's best interest as, from a review of the literature, it appears that temperatures $>52^{O}C$ will result in tissue damage[60, 61] and the cutaneous heat pain threshold has been reported to range from 42-50^{O}C.[62-64] In addition, use of a hotter temperature in this study may not have improved this method as the warm temperature was correctly identified by 100% of control subjects. Taken together, these results indicate that the inability to identify warm temperature is likely the result of surgery in the patient population.

Form

The forms used appeared to be an adequate measure of oral stereognosis and have been used in previous studies. This method, while initially thought to be a measure of "whole-mouth" sensation, appeared to rely heavily on exploration via the tip of the tongue. The current findings suggest that when the tip of the tongue is compromised, compensation by other areas of the oral cavity is limited. Therefore, individual strategies used during this task may be important to note. In addition, to determine the influence of the sensory ability of the tip of the tongue and the portion of the tongue that is affected by reconstruction, an examiner may wish to instruct the subjects to determine the shape of the object using only the reconstructed vs. intact vs. tip of the tongue.

Texture

This method appeared to reveal a preserved sensation in subjects with radial forearm free flap reconstruction of the oral tongue. Another method of texture discrimination has been described in the literature using natural food with varying textures.[65] It would be interesting to determine if using actual substances of varying texture or using contrived objects of varying texture makes a difference in sensing different textures.

Taste

Applying taste solutions to the middle of the tongue is effective if the solution is allowed to mix with saliva and then move around the mouth in order to reach more taste buds. To control for individualized strategies for moving solutions around in the mouth, a "whole mouth rinse" could be used. Another possible method for measuring taste sensation that has been reported to have many advantages and few limitations is the electrogustometric technique.[66] This technique allows for iontophoretic taste stimulation of the tongue while differentiating taste and lingual somatosensory modalities. This technique provides a rapid evaluation of gustatory thresholds in wide samples of human subjects.[66]

Speech Intelligibility

While the method used to assess speech intelligibility in the current study is objective in nature, it did not take into account facial expression, gestures and mouth movements that aid in the overall intelligibility of a person. Perhaps a better measure of speech intelligibility would be to use videotape for recording and play back to a judge. A research design comparing audio only to audio-visual recordings could be used to test the impact of video information on overall speech intelligibility.

Masticatory Efficiency

Through pilot work, the almond was determined to be the best natural food for sieving. The results from the current study pointed to the importance of natural dentition versus dentures for mastication. Future research in this area would require evaluation of control patients with dentures. In addition, evaluation of these patients after they receive dental implants would provide pertinent information as to the influence of more securely-retained dentition on masticatory efficiency. By employing larger groups that vary on the type and number of teeth, one may be better equipped to determine the relative contribution of these variables and reconstruction of the oral tongue to overall masticatory efficiency.

Masticatory Style

The foods used and the manner for tracking chewing did not serve to discriminate the experimental from the control group. Both groups used a punctate pathway of chewing over the rotary type of movement. This method was not designed tease apart the masticatory motion based on a hard-wired neurological pathway vs. the consistency of food chosen for chewing. For example, the cookie changed consistency over time, which may have lead to changes in mastication during communition of the bolus. Previous studies have used chewing gum and wine gum candies, because the consistency past the initial stage does not change. Another example of the influence of food choice on mastication was related to the size of the bolus. The almond was very small and, therefore, a punctate pattern of mastication might have been used as a result. Picking larger nuts like walnuts or other foods of a larger bolus size could impact the nature of chewing movement. However, for the purpose of comparing across conditions (i.e., mastication efficiency and mastication style) a single type of stimulus had to be employed.

A surprising result from this study was that patients and controls did not differ in the time taken before the first swallow, yet patients continually report needing more time to eat as a functional issue. The discrepancy may be in the method used. Rather than measuring the time taken from the food entering the oral cavity to the time when the first swallow occurred, the examiner could have measured the duration of time that was required to clear all food particles from the mouth. This method may show a difference between the two groups where patients require not only more time, but also an increased number of swallows to clear the bolus than control subjects. The finding that patients take the same amount of time to reach the first swallow as controls but are less efficient at breaking a bolus into smaller pieces raises two additional questions. First, is it that the patients are unable to feel the size of the particles and therefore swallow larger particles? Or is it that when patients chew, the timing aspect of mastication exists in the engram or central pattern generator that manages mastication and swallowing outweighs the efficiency of chewing? For example, does the central pattern generator dictate how long one must masticate before a swallow is initiated regardless of particle size? Replicating the mastication tasks within this study in normal subjects with induced anesthesia in half of the tongue, could provide insight into these questions.

Quality of Life

The EORTC-QLQ H&N35 is a standardized measure of quality of life for head and neck cancer patients. While it was thought necessary to use a standardized instrument to measure this aspect of function, a semi-structured interview method was also employed. It would be interesting to correlate the responses from the EORTC with responses and concerns raised in the open interviews, as the responses to the questions on the EORTC did not seem to always reflect what patients were saying in an open-ended format. The major advantages of using a standardized quality of life measure are to control for differences that may be found secondary to the questions asked and to provide a numerical score that can be statistically compared within and between groups. The advantage of using open-ended questions is to allow patients to expand on their answers and provide insight into the experience of the patients. The open-ended questions asked in this study were intended to supplement the standardized questionnaire and to broaden the scope of the quality of life aspect of this study.

Histology

The results of this study provide some insight into the sensory outcomes, functional outcomes and quality of life after radial forearm free flap reconstruction of the tongue. However, questions remain pertaining to changes in actual nerve and tissue of the reconstructed site. For example, are more sensory receptors generated in the transferred tissue? Does neural in-growth occur from surrounding tissue? Are there more neural branches in the tissue after it is transferred as opposed to when it is in its natural habitat? These questions also lead to questions regarding what changes are occurring in the somatosensory cortex of the brain and how might these changes be evaluated. Future studies of histological changes would require that animal models of surgical resection and reconstruction be employed. Studies of changes in the somatosensory cortex of the brain in humans could be exploited using technologies such as transcranial magnetic stimulation.

Conclusion

Although this study presents with limitations including a small sample size and some methodological constraints, it provides a base on which to build future research and presents some interesting initial findings. For example, some sensations appear to be preserved in the reconstructed aspect of the tongue such as two-point discrimination and light touch. These sensations that require fine discrimination appear to be important for function and quality of life as they are more often related to function and quality of life, while those that involved sensation of the whole mouth (e.g., texture) appeared less salient. Although relationships exist between sensation, functional outcomes and quality of life, other factors including the number of natural tooth pairs and a history of radiation therapy may play a very important role.

The limitations of this study highlight the importance of multi-center-based research to improve the generalizability of the research findings to the larger population of patients with head and neck cancer. This study has presented multiple future research questions that will need to be answered to fully understand the scope of reconstructive surgery on functional outcomes related to the anterior 2/3s of the tongue.

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