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Surgical reconstruction of the lingual and hypoglossal nerves in oropharyngeal cancer: Anterior oral cavity sensorimotor and quality of life outcomes

by

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Abstract

This study explores the effects of surgical reconstruction and nerve repair on sensorimotor function and quality of life (QOL) for patients with base of tongue (BOT) cancer compared to healthy, age-matched adults. Sensations were tested on the anterior two-thirds of the oral tongue for two-point discrimination, light touch, taste, temperature, form and texture on 30 patients with BOT reconstruction with radial forearm free-flap and on 30 controls. Results indicated sensation for the unaffected tongue side and affected side with lingual nerve intact was comparable to controls, with poorer sensory outcomes for nerve repair. However, lingual nerves repaired with reanastomosis provided superior results to cable-grafting and severed nerves. Patients had decreased motor function only when the hypoglossal and lingual nerves were affected. Patients' QOL responses on the UW-QOL and EORTC QLQ-H&N35 revealed involvement of lingual and hypoglossal nerves resulted in poorer QOL outcomes. QOL interviews revealed additional problematic issues in this population not identified by standardized questionnaires.

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Introduction

Oropharyngeal and oral cancer are significant worldwide diseases with over 400,000 people affected every year and growing (Oliver et al., 2007). Cancer that specifically affects the base of tongue can account for 1.36% of all cancers in the body (Yadav, 2007). In an attempt to achieve a cure, surgeons remove affected tissue and reconstruct the defect with a flap of tissue taken from another area of the body. Radial forearm free flap reconstruction is a well-recognized surgical technique that has been accepted over the years as a versatile and widely used method of reconstruction in the head and neck region (Remco de Bree et al., 2004). Radial forearm free flap surgery involves the use of a portion of the tissue of the forearm to replace the bulk of the base of tongue. During this surgery, the lingual nerve is often severed or damaged on one or both sides, affecting sensation in the preserved, native tissue of the anterior portion of the tongue. The tongue is a highly developed structure and has a specialized sensory system which is paramount to function (Linden, 1990). Therefore, the loss of tongue sensation can dramatically affect a person's quality of life. Concomitantly, the hypoglossal nerve may be damaged or severed which impairs motor function of the tongue and potentially speech, mastication, swallowing, and management of oral secretions (Yadav, 2007). In an attempt to preserve sensation on the affected side of the tongue, surgeons have begun to either anastomize the two ends of the severed lingual nerve or use a sensory nerve graft from either the antebrachial cutaneous nerve from the forearm or the great auricular nerve from the head. In motor nerve repair of the hypoglossal nerve, surgeons have begun using nerve conduits, motor or sensory nerve grafts, or direct anastomosis of the ends of the severed nerve. Further research is necessary to critically examine the success of current surgical procedures used in base-of-tongue reconstruction and their attempts to restore sensory and motor functions in the anterior native tissue. What is also unknown in this patient population is the extent to which resulting oral sensation deficits affect quality of life and whether or not better sensation and tongue movement leads to improved functional outcomes (Yadav, 2007).

Base of Tongue Cancer

Squamous cell carcinoma is the most common cancer of the oral cavity (Yadav, 2007), accounting for 90% of all oropharyngeal neoplasms (Hermans, 2005). In 2002, an estimated 130,000 new cases of oropharyngeal cancer were reported worldwide with evidence of increasing incidence in certain global regions (Parkin, Bray, Ferlay, & Pisani, 2005). In base of tongue cancer, tumours tend to grow silently with the potential to spread anteriorly into the floor of the mouth and/or tongue body, or retrograde along the lingual vessels (Hermans, 2005). Upon clinical examination, the size of tumours in base of tongue cancer is often larger than suspected (Hermans, 2005). Treatment options for patients are typically medical, including surgical removal and/or reconstruction, radiation, chemotherapy, or a combination of treatments. However, whereas surgical techniques and treatment options continue to improve patients' quality of life, the overall survival rate has not changed greatly (Hollows, McAndrew, & Perini, 2000). In order to fully understand the implications of surgical reconstruction and neural grafting, we must first acknowledge the typical sensory and motor pathways that are involved in the oral structures affected, and the mechanisms of neural regeneration in the peripheral nervous system.

Typical Sensory Pathways

The tongue is a highly specialized sensory system with afferent fibres arising from three different cranial nerves. The trigeminal nerve (cranial nerve V) is a mixed (motor and sensory) nerve that breaks off into three major branches: the ophthalmic branch (sensory), the maxillary branch (sensory), and the mandibular branch (mixed), which is the largest of the three trigeminal branches (Kandel, Schwartz & Jessell, 2000). The ophthalmic branch provides sensation to regions surrounding the eyes, and the maxillary branch provides sensation to the palate, upper lip, gums, teeth, and part of the pharynx (Zemlin, 1998). The mandibular branch carries all of the fibres of the motor root to the muscles of mastication (Kandel et al., 2000). The afferent fibres provide sensory information from the lower lip, gums, and teeth, skin of the temples, salivary glands, and anterior portions of the tongue (Zemlin, 1998). The mandibular branch further divides into the lingual and mental nerves, with the lingual nerve providing sensory fibres to the anterior two-thirds of the tongue (Kandel et al., 2000).

Cranial nerve VII, the facial nerve, plays a role in specialized sensory function of the tongue. The facial nerve is a mixed nerve, with somatic motor control of the muscles of facial expression, and visceral motor control of the lacrimal gland, nasal mucous glands, and submandibular and sublingual salivary glands (Kandel et al., 2000). Sensory fibres arise from a branch of the facial nerve, the chorda tympani nerve, which provides afferent fibres to the taste receptors of the anterior two-thirds of the tongue. The chorda tympani nerve travels with the mandibular branch of the trigeminal nerve, where the lingual branches of the facial and trigeminal nerves innervate the anterior two-thirds of the tongue (Kandel et al., 2000). Thus, damage to the lingual nerve could also result in damage to the lingual branch of the chorda tympani nerve, affecting taste sensation.

Cranial nerve IX, the glossopharyngeal nerve, is a mixed nerve that is mostly abundant in sensory fibres. The sensory branch provides afferent fibres to the posterior one-third of the tongue, part of the pharynx, and the palate (Zemlin, 1998). The glossopharyngeal nerve has a lingual branch that innervates the posterior one-third of the tongue, providing afferent fibres for tactile, thermal, and pain sensations, as well as taste (Kandel et al., 2000). The motor branch of the glossopharyngeal nerve provides efferent fibres to the pharyngeal muscles involved in swallowing.

Tongue Sensations

Somatosensory input from the oral cavity provides the central nervous system with the ability to perceive extremely sensitive two-point discrimination, shape, and texture (Miller, 2002). Many different types of sensory receptors are found in the oral cavity, including mechanoreceptors (touch), nociceptors (pain), and thermoceptors (temperature) associated with tactile and thermal sensation (Jacobs, Wu, Goossens, van Loven, van Hees, & van Steenberghe, 2002).

Temperature and nociceptive sensory fibres dominate sensory innervation of much of the oral cavity, which includes the tongue, faucial pillars, and palate

(Miller, 2002). Thermal sensations in the tongue are divided into two categories, warm and cold, which are perceived by specific receptors in the mucosa. Cold receptors are more superficially located than warm receptors, and cold-sensitive spots are more numerous than warm-sensitive spots on the mucosal surface (Jacobs et al., 2002).

Taste sensations are mediated by taste buds which are located on the tongue, palate, pharynx, epiglottis, and upper third of the esophagus. Taste buds on the tongue are located primarily in the papillae, embedded in the epithelium (Kandel et al., 2000). Primary taste sensations are salty, sweet, sour, and bitter, and some research on humans and animal models demonstrates the presence of water receptors in the tongue and pharynx, such that water is processed differently than other tastes (Martini Timmons, & Tallitsch, 2006). The taste receptors of the tongue are most sensitive to bitter compounds and then to acid compounds (sour taste), which are tastes usually associated with poisonous and harmful substances.

Stereognosis involves oral manipulation and palpation of shapes within the oral cavity, and requires cortical evaluation of the sensory input to help differentiate and compare the shapes to previously stored images (Dahan, Lelong, Celant, & Leysen, 2000). Stereognosis is a psychophysical measure of perception that is applicable to the oral cavity (Dahan et al., 2000), even though it also involves sensory receptors in nearby structures such as the muscles, tendons and temporomandibular joints (Jacobs, Bou Serhal, & van Steenberghe, 1998). Recognition of form can be enhanced with training, and there is evidence that performance seems to be affected by age, culture, and dental factors, as well as the orthodontic state of the oral cavity (Dahan et al., 2000).

Two-point discrimination and light touch involve fine touch and pressure receptors of the tongue. However, two-point discrimination also requires higher level processes that help to perceive two points instead of one. The ability of our sensory system to distinguish between two points of stimulation occurs through a mechanism called lateral inhibition (Kuriakose, Loree, Spies, Meyers, & Hicks, 2001). The sensory pathways of the tongue give rise to lateral inhibitory signals through interneurons, limiting “the lateral spread of excitatory signals and increasing the degree of contrast of the sensory pattern perceived by the sensory cortex” (Kuriakose et al., 2001, p 1465). Also important in two-point discrimination is receptor density in the tongue. The tongue has a greater receptor density from other areas of the body, such as the back and arms, which allows for the fine discrimination of two points and lateral inhibition.

Typical Motor Pathways

Cranial nerve XII, the hypoglossal nerve, innervates the extrinsic and intrinsic lingual muscles of the tongue for motor output. The extrinsic lingual muscles include the styloglossus, hyoglossus, genioglossus, and geniohyoid, and the intrinsic lingual muscles include the vertical, horizontal, superior and inferior longitudinal lingual muscles. The hypoglossal nerve has predominantly efferent fibres, and controls voluntary motor movements of the tongue. It exits the occipital bone of the skull and curves in an inferior-anterior direction, and then superiorly to reach the skeletal muscles of the tongue (Martini et al., 2006). The hypoglossal nerve constantly anastomoses with the lingual nerve at the level of the tongue, creating loops or thin plexuses at the anterior border of the hyoglossus muscle (Rusu, Nimigean, Podoleanu, Ivascu, & Niculescu, 2008). These anastomoses allow for the tongue to exhibit a lingual-hypoglossal reflex.

Sensory-Motor Reflexes

A reflex is a hard-wired circuit through the central nervous system, often controlling a set of antagonistic muscles to coordinate a given motor response (Miller, 2002). The coordination of motor movements in speech, swallowing, and mastication are highly complex, and the motor signals to designated muscles are constantly fine-tuned and modulated by continual reflex arcs (Miller, 2002). These sensori-motor interactions and feedback loops highlight the significant role that oral sensation plays in function. There are several reflexes that affect the tongue, most of which are evoked by stimulation of the branches of the trigeminal nerve; thus, these reflexes are referred to as trigemino-hypoglossal reflexes. The lingual-hypoglossal reflex occurs when stimulation of the lingual nerve induces discharges in fibres of the hypoglossal nerve (Miller, 2002). The overall effect of stimulating the lingual nerve is tongue retraction, as mostly excitatory post-synaptic potentials are evoked in the motoneurons innervating the tongue-retracting muscles (hyoglossus and styloglossus muscles), and mostly inhibitory post-synaptic potentials are evoked in the motoneurons innervating the tongue-protruding muscles (Miller, 2000). Stimulation of either lingual nerve will produce a bilateral, asymmetrical movement of the tongue (Miller, 2002), and mechanical stimulation of the tongue will induce the same reflex as direct stimulation of the lingual nerve fibres (Porter, 1967). Most stimuli applied to the anterior oral region will induce tongue retraction, although pressure on other regions or stretching will not synaptically affect the hypoglossal motoneurons (Miller, 2002).

Neural Degeneration

When peripheral nerves are severed or resected, the proximal and distal stumps of the nerve undergo transneuronal degeneration (anterograde and retrograde degeneration). Wallerian degeneration occurs at the distal segment of the nerve, where the myelin sheath fragments and degenerates, and phagocytic cells envelope the axonal debris. Terminal degeneration also occurs distally, as there is no longer any input coming from the neuron. The proximal portion is cut-off from its supply of target-derived trophic factors (Kandel et al., 2000), leading to cell death or a chromatolytic reaction (cell body enlarges and nucleus is displaced) with metabolic changes. Post-synaptic neurons are also affected during axonal degeneration, because of disruptions of major inputs to the target cell. The target muscles of a motor nerve pathway will become denervated, resulting in muscle atrophy and death. However, if the target muscle is only partially denervated, responses will be more subtle. In a sensory nerve pathway, disruption of major inputs to the neuron can lead to synaptic stripping. This happens when the synaptic terminals withdraw from the neuronal cell bodies or the dendrites of chromatolytic neurons, and the terminals are replaced by the processes of glial cells (Kandel et al., 2000). Synaptic stripping depresses synaptic function and can also impair the recovery of function in the nerve.

Neural Regeneration

Neural regeneration successfully occurs with motor and sensory nerves in the peripheral nervous system, where restoration of function follows axonal regeneration and formation of functional synapses on their targets (Kandel et al., 2000). Neural regeneration starts at the proximal stump of the nerve with axonal sprouting. The axon grows and enters the distal stump of the nerve, and then sprouts towards the nerve's end-organs (Kandel et al., 2000). Axonal sprouting can occur in peripheral nerves due to three major mechanisms: (a) neurotrophic factors secreted by the Schwann cells which attract axons to the distal stump, (b) adhesive molecules (e.g. immunoglobulins and cadherins) within the distal stump which promote axonal growth and (c) inhibitory molecules (e.g. netrins and semaphorins) in the perineurium which prevent regenerating axons from going astray (Kandel et al., 2000). Once the motor or sensory nerves have undergone axonal sprouting and regeneration, the nerves can form new functional nerve endings upon reaching their targets (Kandel et al., 2000). Motor nerves form new neuromuscular junctions, and sensory nerves can reinnervate muscle spindles. Axons that were demyelinated during degeneration become remyelinated in the process, and chromatolytic somata regain their original appearance (Kandel et al., 2000). However, not all spontaneous nerve regeneration leads to perfect recovery of motor or sensory functions. For example, in motor recovery the strength of the muscle may return, but fine motor movements may still be impaired. Axonal regeneration is not picture-perfect, in that some motor axons may be guided to and form synapses on inappropriate muscle fibers, some may never find their target, and some neurons may die in the process (Kandel et al., 2000).

During reconstructive efforts within the oropharynx, the muscles and mucosa of the tongue can be temporarily denervated if the hypoglossal and lingual nerves are affected by the resection. In order to avoid permanent denervation of oral and oropharyngeal structures, surgeons will often attempt to reinnervate both sensory and motor nerves using microsurgical procedures. Reinnervation can occur by directly anastomizing the distal and proximal ends of the nerves, by using an interpositional sensory or motor graft or by using a nerve conduit. The ultimate goal of reinnervation of sensory and motor nerves is neural regeneration to the target organ. In oropharyngeal resection and reconstruction, the target organ is the anterior two-thirds of the tongue in the anterior oral cavity. Whereas the radial forearm free flap has been used for reconstruction of the tongue for many years, reinnervation of the lingual and hypoglossal nerves is a relatively new procedure.

Radial Forearm Free Flap (RFFF) and Reinnervation Techniques

The radial forearm free flap (RFFF) was first described in 1981 by Yang et al. This surgical technique has established itself over the years as a versatile and widely used method of reconstruction in the head and neck region (Remco de Bree et al., 2004). Radial forearm free flaps are reliable for reconstructing a wide range of oral cavity defects, as they have an acceptable low morbidity rate, predominately hairless skin, and provide adequate bulkiness, pliability and vascularity (Meek, Vermey, Robinson, Lichtendahl, & Roodenburg, 1998). The surgical procedure requires harvesting a skin flap from the forearm of the patient and may involve either the lateral or medial antebrachial cutaneous nerves for reinnervation. However, some oral reconstruction may not require or use a sensate free flap to repair nerve damage. There is no consensus in the literature about the effectiveness of sensate radial forearm free flaps versus noninnervated free flaps in reconstruction of the anterior oral cavity. Boyd et al. (1994), Santamaria , Chen, and Chuang (1999), and Kuriakose et al. (2001) have shown that innervated radial forearm free flaps improve sensation significantly in oral reconstruction and endorse microsurgical reinnervation in free flaps. However, Sabesan, Ramchandani and Ilankovan (2008) and Cicconetti, Matteini, Cruccu, and Romaniello (2000) provide equivocal evidence that excellent or satisfactory sensory recovery occurs in noninnervated free flaps, emphasizing that microsurgical reinnervation in free flaps is unnecessary. Thus, it is apparent from the literature that further investigation and study is required to fully recognize whether sensate free flaps are necessary for the return of sensation in anterior oral reconstructions. To our knowledge, no studies have examined the affected native tissue of the anterior two-thirds of the tongue in base of tongue reconstruction using a radial forearm free flap. However, severed nerves do not spontaneously restore their function unless continuity of the nerve has been re-established through microsurgical intervention (Pfister, Papaloïzos, Merkle, & Gander, 2007). When the reconstruction involves the oropharyngeal cavity, lingual and hypoglossal innervations to the anterior portion of the tongue are at risk. Thus, the issue of reinnervation does not so much concern the flap but rather the native tissues of the intact anterior portion of the tongue.

Microsurgical Techniques for Nerve Repair

During reconstructive surgery of the base of tongue, the hypoglossal nerve will typically be damaged on one side, affecting the efferent innervation of the extrinsic and intrinsic lingual muscles. Damage to the hypoglossal nerve can have profound effects on motor function of the tongue, negatively affecting speech, deglutition, control of oral secretions, and mastication. Major tongue movements can be affected by damage to the hypoglossal nerve, including tongue protrusion, retraction, lateralization, and movements required for oral containment of the bolus and mastication. In order for some recovery of tongue motor function to occur, surgeons may use an artificial (e.g. collagen) or biological (e.g. vein) nerve conduit to guide hypoglossal axonal growth to target muscles, or a motor or sensory nerve graft with microsurgical repair.

Surgical reconstruction also can lead to damage to the lingual nerve. Often the nerve is severed or resected, affecting afferent information from the anterior two-thirds of the tongue. Sensations typically affected are temperature, light touch, two-point discrimination, and to a lesser degree stereognosis (form). Taste can also be impaired, as the chorda tympani nerve is bundled with the lingual nerve innervating the anterior region of the tongue (Martini et al., 2006). The spontaneous recovery of a transected lingual nerve is limited due to the poor opportunity sprouting axons have of extending down their original connective tissue sheaths (Holland, 1996). This is largely the result of the retraction of the cut ends of the lingual nerve within loose connective tissue (Holland, 1996). In order for sensory recovery to occur in the anterior two-thirds of the tongue, microsurgical repair is necessary to re-appose the cut ends of the lingual nerve. For optimal sensory outcomes in observed nerve injuries, research suggests that microsurgical repair should occur immediately rather than waiting (Ziccardi & Steinberg, 2007). Thus, in order for sprouting axons to continue to their target without dying back, the gap between the cut ends of the lingual nerve must be bridged and the two ends re-apposed. Direct anastomosis of the transected nerve or the use of an interpositional graft are the most commonly used surgical techniques in lingual nerve repair. Findings from both animal models and clinical literature confirms that following trigeminal nerve microsurgery, neuronal cells are capable of supporting axonal regeneration resulting in the re-establishment of functional connections with distal nerves (Zuniga, Pate, & Hegtvedt, 1990).

Using microsurgical techniques with radial forearm free flap surgery, nerve repair can occur as a fascicular (perineurial) repair, or as an epineurial repair. A fascicular repair provides superior results to an epineurial repair, but is more challenging to do clinically as greater manipulation of the nerve is required and there is greater potential for things to go wrong (Dvali & Mackinnon, 2007). In a fascicular repair, the surgeon aligns the fascicles of the severed nerve with the fascicles of the nerve graft or distal nerve stump. In an epineurial repair, the surgeon is only required to line up the epineurium of each nerve and suture them together (Dvali & Mackinnon, 2007). A surgeon may use either of these microsurgical techniques in nerve repair, whether he/she is completing direct anastomosis or using a graft to bridge the gap between the severed ends of the nerve.

It is well documented in the literature that direct anastomosis of a severed/resected nerve is preferable to an interpositional graft, unless the nerve is under tension (Pogrel & Maghen, 2001; Dvali & Mackinnon., 2007; Shindo, 1999). Tension at the site of nerve anastomosis must be avoided whenever possible (Haftek, 1976; Pogrel & Maghen, 2001), as tension can have deleterious effects on nerve regeneration, causing scar formation that impedes axonal regeneration beyond the site of repair (Dvali & Mackinnon, 2007; Shindo, 1999). However, there is a lack of consensus derived from animal models about maximum length of the nerve gap or amount of tension the nerve can withstand to ensure successful anastomosis without grafting (Pogrel & Maghen, 2001). There is however, agreement that nerve regeneration is more successful across two tension-free repair sites (e.g. a nerve graft) than across one repair site with tension (Dvali & Mackinnon, 2007).

Nerve grafting has become a common technique over the past two decades for peripheral nerve repair, requiring microsurgical skills and expertise by the surgeon. The use of an interpositional nerve graft usually occurs when the site of nerve repair has a gap too large to use neurorrhapy, or direct nerve anastomosis (Shindo, 1999). Some commonly used donor sensory nerve grafts are the great auricular nerve, and the lateral and medial antebrachial cutaneous nerves found in the subcutaneous fat of the forearm (Shindo, 1999). The surgical procedures for using a cable-graft in sensory nerve repair require the microsurgical skills of the surgeon to suture the transected proximal stump of the lingual nerve to one end of the nerve graft, and the distal stump of the lingual nerve to the other end of the nerve graft. Thus, the cable graft has two regions of anastomosis with the transected lingual nerve and bridges the nerve gap, but does not place the nerve under any tension.

The repair of motor nerves is possible using direct anastomosis, or either a motor or sensory interpositional graft. Typically, sensory nerve grafts such as the sural nerve or antebrachial cutaneous nerve are used to repair motor nerve defects due to their low donor site morbidity as well as their relative ease of harvest (Brenner et al., 2006; Dvali & Mackinnon, 2007). However, animal models show that sensory nerve grafts can disrupt motor axonal regeneration when used in end-end motor nerve repair (Brenner et al., 2006; Nichols et al., 2004; Chu, Du, & Wu, 2008). When nerve injury occurs, motor axons demonstrate preferential motor reinnervation, where motor axons preferentially regenerate down motor nerve branches to reach their end-targets, rather than down sensory nerve branches (Brenner et al., 2006). Dvali and Mackinnon (2007, p 75) state that sensory nerves “may possess phenotypically distinct Schwann cells that can negatively affect the regeneration of motor neurons down sensory pathways”. Animal models show that the repair of a motor nerve will be most successful when a nerve graft of motor origin is used, rather than a nerve graft of sensory origin (Brenner et al., 2006). However, sensory nerve grafts promote axonal growth and regeneration when paired with a sensory nerve repair, due to its distinct neural characteristics. Currently, sensory nerve grafts are commonly used in motor and sensory peripheral nerve repair as they have some advantages to motor nerve grafts: more readily available for use, low donor site morbidity. Further research is required to investigate whether the benefits of grafting motor nerves for the repair of motor nerve lesions are sufficient to justify an increase in associated donor site morbidity (Brenner et al., 2006).

When transected lingual nerves have undergone microsurgical repair during base of tongue reconstruction, there is the possibility of the recovery of taste and some neurosensory function to the anterior two-thirds of the tongue (Rutner, Ziccardi, & Janal, 2005). Motor nerve repair of the hypoglossal nerve also may result in the return of some motor function of the tongue, although full functional recovery after peripheral nerve injury is rarely achieved. However, there are numerous factors that contribute to patient outcomes after nerve reconstruction including: (a) type and extent of injury, (b) the timing of the repair, (c) patient factors such as age, health status, and cancer stage, (d) technical skills of the surgeon and (e) surgical method used (Dvali & Mackinnon, 2007). Moreover, direct end-to-end anastomosis under ideal conditions will generally give superior results over an interpositional graft (Shindo, 1999). However, cable-grafting is the best option when direct nerve repair is unattainable due to a large gap at the site of repair (Dvali & Mackinnon, 2007; Smith & Robinson, 1995). Nerve conduits also offer a surgical option for nerve gaps less than 3cm in length and provide an alternative to harvesting autologous sensory or motor nerve grafts which are connected with issues of donor site morbidity, availability and harvest (Dvali and Mackinnon, 2003).

Peripheral nerve changes can occur in the lingual and hypoglossal nerves when microsurgical repair has been performed. However, it is the higher level processes at the cortical and subcortical levels that control tongue movements and assess sensory input. The basic cortical and subcortical pathways related to the lingual and hypoglossal nerves are important to understand when examining sensation and motor function of the tongue and orofacial muscles.

Higher Level Processes

The motor cortex mediates voluntary control of tongue movement via corticobulbar pathways to the lower motor neurons in the medulla (Corfield et al., 1999). Cell bodies of the lower motor neurons are located within the hypoglossal nuclei, bilaterally, on the dorsal surface of the medulla. The cortical control of tongue movement is represented bilaterally on the inferior aspect of the motor homunculus (primary motor cortex), close to the lateral fissure (Foerster, 1936; Penfield & Boldrey, 1938). The somatosensory cortex perceives and interprets sensory input from the anterior tongue via corticobulbar pathways from the sensory nuclei in the medulla. The sensory nuclei of the trigeminal nerve are: the spinal trigeminal nucleus, extending from caudal to rostral throughout the lateral medulla and into the caudal pons; the principal sensory nucleus, located in lateral parts of the pontine tegmentum at about midpontine level; and the mesencephalic nucleus and the mesencephalic tract, extending rostrally from the principal sensory nucleus along the lateral aspect of the periaqueductal gray (Kandel et al., 2000). Afferent fibres conveying pain, thermal sense, and light touch (nondiscriminative touch) from the anterior two-thirds of the tongue have their cell bodies in the trigeminal ganglion. Afferent fibres conveying taste from the anterior two-thirds of the tongue (cranial nerve VII) have their cell bodies in the geniculate ganglion. The central processes of these afferent fibres form the spinal trigeminal tract, terminating in the spinal trigeminal nucleus. Afferent fibres conveying discriminative touch from the anterior two-thirds of the tongue follow a similar pathway, but the fibres terminate centrally in the principal sensory nucleus. The sensory inputs to the spinal trigeminal nucleus and to the principal sensory nucleus are relayed to the thalamus via the anterior and posterior trigeminothalamic tracts, and then from the thalamus to the somatosensory cortex.

Quality of Life

Quality of life in head and neck cancer has been examined in the literature using standardized self-completed measures and rating scales, as well as informal measures with surveys, interviews, and questionnaires. Patients who have undergone oral reconstruction often have functional problems with speech, mastication, swallowing, and/or xerostomia. The functional outcomes of reconstructive surgery directly or indirectly affect a patient's social, psychological, and emotional well-being, consequently influencing their quality of life.

In a structured review and theme analysis by Rogers, Ahad, and Murphy (2007), the authors examined 165 papers published from 2000 to 2005 on quality of life in head and neck cancer. They established five basic themes from their review, two of which included 1) predictors of quality of life and 2) functional outcomes. They identified the EORTC (European Organisation of Research and

Treatment of Cancer) quality of life questionnaire as the most commonly used self-completed measure of predictors of quality of life in head and neck cancer.

A study by Rogers, Lowe, Patel, Brown and Vaughan (2002) examined over 100 patients who received surgical flaps with and without radiation therapy for previously untreated oral and oropharyngeal squamous cell carcinoma. They performed assessments preoperatively and at 6 and 12 months post-operatively using an 11-item clinical examination, including tongue mobility (lateralization and protrusion) and tongue sensation (light touch). At six months post-treatment, approximately 29% of patients with unrestricted tongue protrusion at baseline had some worsening of function, 30% of patients with unrestricted tongue lateralization at baseline were experiencing restricted movement, 17% of patients with normal tongue sensation at baseline indicated blunted sensation and 33% indicated no sensation. At one year post-treatment approximately 17% of patients still experienced restricted tongue protrusion and 23% experienced restricted tongue lateralization, with 18% experiencing blunted tongue sensation and 26% with no sensation. This study by Rogers et al. (2002) highlights clinically important differences in tongue movements and tongue sensation in patients after oral and oropharyngeal reconstruction, providing evidence for decreased function in tongue sensation, protrusion, and lateralization that could have lasting effects on quality of life. While improvements in oral function have the potential to positively impact many aspects of quality of life in oral cancer patients, the specific relationship of tongue sensation and mobility to quality of life is an area of research that requires further study.

In a study by Winter, Cassell, Corbridge, Goodacre, and Cox (2004), the authors evaluated quality of life in a cohort of patients with squamous cell carcinoma of the base of tongue. Six of the patients had received radial-forearm free flap surgery with no neural anastomoses, and completed the UW-QOL (University of Washington Quality of Life Instrument) self-administered questionnaire. The authors found that the majority of reported problems in function were with saliva and swallowing, although chewing and taste were also reduced in patients. All six patients reported some form of reduction in quality of life, indicating the effects of surgical reconstruction on health and social functioning. However, this study was performed with a small sample of patients using a subjective questionnaire and should be considered cautiously. Further research is required to gain an understanding of the functional outcomes in oropharyngeal cancer and the relationship to quality of life.

Purpose

The purpose of this study will be to critically examine the importance of nerve preservation and reinnervation during radial forearm free flap surgery through testing sensory and motor ability of the anterior tongue in patients with oropharyngeal lesions and collecting patient-perceived outcomes related to quality of life. The primary objective is to determine if sensory differences can be seen between the affected and unaffected sides of the anterior portion of the tongue within the patient population. The objective of investigating these differences within the patient group will be to consider the effectiveness of nerve anastomosis or cable grafting with radial forearm free flap surgery of the base of tongue, and the effects of surgery on the contralateral native tongue tissue. The secondary objective is to determine if tongue sensation and motor function differ between the patient population and age-matched controls. More specifically, it is important to investigate if the non-injured or unaffected side of the tongue in the patient group compares to the control group in sensation measures. Current research practices often use the patients' unaffected side of tongue or residual tongue tissue as their control, implying that the sensation is comparable to normal measures (Kuriakose et al, 2001; Santamaria et al., 1999; Sabesan et al., 2008). However, a study by Loewen, Boliek, Harris, Seikaly, and Rieger (2010) showed that the native tissue of the tongue in hemiglossectomy patients who had undergone radial forearm free flap surgery was different on measures of two-point discrimination from a normal control group. Thus, this study will compare sensation of the residual anterior tongue after reconstructive surgery of the oropharynx to a normal population. Another objective is to determine how lingual and hypoglossal nerve repairs may affect the quality of life for patients who have undergone reconstructive surgery in the oropharynx. Currently, there is a lack of literature reporting on the relation between sensory and motor recovery after surgery in the native tissue of the tongue and the quality of life in patients. Much of the literature has focused on sensory restoration of the flap being used in oral reconstruction, and the debate over sensate flaps versus non-sensate flaps.

Methods

Participants

The patient group consisted of participants with oropharyngeal cancer who underwent primary resection and reconstruction with a radial forearm free flap either with or without adjunctive radiation therapy or chemoradiation. All patients received primary surgery between 2004 and 2009 at the University of Alberta Hospital in coordination with the Institute for Reconstructive Sciences in Medicine (iRSM) located at the Misericordia Community Hospital in Edmonton, Alberta, Canada.

Microsurgical resection and reconstruction may or may not have included nerve repair to the lingual nerve, hypoglossal nerve, or both. Patients were excluded if surgery involved the anterior tongue, maxilla, cheek, or mandible. All patients had a diagnosis of base of tongue cancer lesions with primary tumours that spanned from T1 to T3 stages according to the TNM staging system commonly used in medical facilities (accepted by the National Cancer Institute, International Union Against Cancer and American Joint Committee on Cancer). The participants' surgical outcomes were described based on lingual nerve damage and type of repair, and presence or not of hypoglossal nerve damage with or without repair.

This study was approved by the Health and Research Ethics Board at the University of Alberta for the recruitment and testing of patients and control participants. Information letters (Appendix A) were mailed to patients identified through iRSM according to the inclusion criteria for the study. The primary examiner contacted the patients by phone two weeks after letters were mailed. Patients who were interested in participating in the study booked appointments with the primary examiner. Upon arrival, patients were provided an information letter about the study (Appendix B), given the opportunity to discuss and ask the primary examiner questions, and then signed an informed consent form prior to testing (Appendix C).

A control group was matched to the patient group based on age (+ or – 5 years) and sex, and included participants who had not experienced any prior sensory or motor loss of the tongue and/or oral cavity. Control participants were recruited through posters and advertisements placed at the Misericordia Hospital and University of Alberta campus, and emails sent to students, faculty and staff of Rehabilitation Medicine at the University of Alberta. Control participants were provided with an information letter upon arrival (Appendix D), the opportunity to discuss and ask the primary examiner questions, and then signed an informed consent form prior to testing (Appendix E).

Sample Size

The sample size was restricted by the number of patients available from a convenience sample of 80 people, with an overall sample size of 30 patient participants and a matched control group of 30 participants. Participants in both groups ranged in age from 43 to 74 years, with a 9:1 ratio of males to females. The mean time from surgery for patients participating in this study was 37 months, ranging from 6 – 73 months post-surgery. Patient demographics, including sex and age, treatment modality, surgical defect, TNM stages and classification, nerve repair/resection status and date of surgery are presented in Table 1. A summary of nerve repair/resection status is presented in Table 2.

Table 1.

Patient demographics, TNM classification, surgical defect, and treatment modality

Patient no./sex/ age,y	TNM classification	Base of tongue resected, %	Nerve(s) resected	Primary treatment	Date of surgery, mos/year
1/M/66	T3N0M0	50	L[b]	S-CRT	Aug. 2004
2/F/57	T3N2bM0	33	L[b]	S-CRT	Jan. 2006
3/M/55	T3N0M0	25	L[a]	S-RT	Jan. 2003
4/M/57	T3N3	50	L[b] and H[b]	S-CRT	Oct. 2005
5/M/62	T1N1	50	Nerves intact	Surgery	May 2007
6/M/57	T3N2bM0	100	L[b] and H[b]	Surgery	Mar. 2008
7/M/71	T3N0	25	L[c]	S-RT	Dec. 2005
8/M/46	T1N2aM0	25	Nerves intact	S-RT	Aug. 2008
9/M/63	T1N2M0	50-75	L[a]	S-CRT	July 2007
10/M/66	T3N2	25	L[b]	S-CRT	July 2005
11/M/74	T3N2cM0	100	L[a] and H[b]	S-CRT	Apr. 2007
12/F/44	T2N2M0	75	L[a]	S-CRT	June 2006
13/M/56	T3N2B NMM0	25	L[a]	S-CRT	July 2005
14/M/56	T2N2M0	75	L[a]	S-CRT	Mar. 2007
15/M/60	T1N2M0	50	L[c]	S-RT	Sept. 2003
16/M/54	T3N2bM0	25	L[a] and H[b]	S-CRT	July 2006
17/M/59	T2N2bM0	50	Nerves intact	S-CRT	Feb. 2006
18/M/50	T2N2bM0	50	L[c]	S-CRT	Jan. 2005
19/M/52	T3N2bM0	100	L[c] and H[c]	S-CRT	Feb. 2006
20/M/61	T2N2bM0	50	L[a]	S-CRT	Aug. 2004
21/M/44	T2N3M0	25	L[a] and H[c]	S-RT	Dec.2007
22/M/43	T2N2bM0	25	L[c]	S-CRT	Sept. 2008
23/F/62	T2N1	25	L[a]	S-RT	Oct. 2003
24/M/56	T3N0M0	25	L[a]	S-RT	Aug. 2007
25/M/65	T2N0M0	25	Nerves intact	S-RT	July 2003
26/M/58	T2N3M0	25	L[b] and H[b]	S-CRT	July 2008
27/M/48	T3N1M0	25	L[a]	S-CRT	Oct. 2007
28/M/59	T3N0M0	50	L[b] and H[b]	S-RT	Oct. 2007
29/M/70	T3N1M0	25	L[c]	S-RT	Sept. 2004
30/M/46	T1N2M0	25	Nerves intact	S-RT	Mar. 2003

Notes. Abbreviations: S-CRT, surgery with postoperative chemotherapy and radiotherapy; S-RT, surgery with postoperative radiotherapy

[a] Reanastomosed

[b] Cable-grafted

[c] Severed/cut

Table 2.

Summary of patients with specific nerve involvement

	Nerve involvement						
	Nerves intact	V reanast. & XII intact	V cable-graft & XII intact	V cut & XII intact	V & XII cable-graft	V reanast. & XII cable-graft	V reanast. & XII cut
No. of patients	6	9	3	5	4	2	1

Notes. Abbreviations: V, lingual nerve; XII, hypoglossal nerve; reanast., reanastomosed.

Procedures

Focal sensation measures. This study used four sensation measures to test a focal portion of the tip and dorsolateral anterior regions of the tongue, on the left and right sides. These sensation measures included two-point discrimination, light touch, temperature and taste. All focal sensation measures were taken on the dorsal surface of the tongue, three times each on the right and left tip of the tongue, and three times each on the right and left dorsolateral regions of the anterior two-thirds of the tongue. All participants were blindfolded during sensory testing to ensure response objectivity. All sensations were measured using a series of tests developed and tested previously in this population (Boliek, Rieger, Mohamed, Kickham, & Amundsen, 2007) with the exception of taste.

Two-point discrimination

Using a sterile unfolded paper clip, the experimenter placed one or two ends of the paper clip on the left and right tip of the tongue, and on the left and right dorsolateral regions of the anterior third of the tongue. The fixed distance between the ends of each two-point paper clip was set at 3.0 millimetres, according to the mean of values obtained in other studies of two-point discrimination (Boliek et al., 2007; Loewen, et al., 2010). The order of presentation of one-point or two-points was randomized for each participant. Participants indicated their response by saying “one” or “two” for whether they felt one point or two points. All responses were recorded as either correct or incorrect. Two-point discrimination was further coded into numbers ranging from 0 to 3, due to the nature of the task and combination of correct responses. A score of 2 out of 3 correct could have multiple meanings, such that a participant may have only felt one-point touches, only felt two-point touches, or felt a one-point and a two-point touch and was able to discriminate between the two. The coding system for this task (Appendix F) accounts for all possible combinations of correct responses.

Light touch

The experimenter placed the tip of a 2.83 (0.07g/mm^2 of force) Semmes Weinstein touch test sensory evaluator tool (North Coast Medical, Inc, Morgan Hill, CA) on the tongue, perpendicular to the surface and applied with enough force to make the monofilament bend for approximately 1.5 seconds (Weinstein, Semmes, Ghent, & Teuber, 1958). Measurements were randomized for each trial such that the participant may have been asked to respond when no touch had occurred. Measurements were taken three times each on the areas of interest on the tongue. Participants who did not feel any sensation also were tested with a 6.65 (300g/mm^2 of force) Semmes Weinstein touch test sensory evaluator tool (North Coast Medical, Inc, Morgan Hill, CA) in accordance with the appropriate region, in order to examine deep pressure sensation. All responses were recorded as correct or incorrect. Light touch was further coded into numbers ranging from 0 to 3 (similar to two-point discrimination), due to the nature of the task and combination of correct responses. The coding system for this task (Appendix G) accounts for all possible combinations of correct responses.

Temperature

Dental mirrors were placed into beakers of water kept at constant temperatures either warmed to 55 °C on a hot plate or cooled to 3 °C in an ice bath (Netscher, Armenta, Meade, & Alford, 2000). These temperatures are commonly used in testing thermal receptors of the tongue (Boliek et al., 2006). A mirror was placed three times on the areas of interest on the tongue. The temperatures were randomly selected for each participant, and participants responded by reporting warm or cold. All responses were recorded as either correct or incorrect.

Taste

Taste was tested using five different solutions: citric acid for sour (commercial lemon juice), sucrose for sweet (white sugar), sodium chloride for salty (table salt), quinine hydrochloride/sulphate for bitter (tonic water), and distilled water for neutral. The mixture for the citric acid solution was 90ml lemon juice to 1L of distilled water, the sucrose solution was 60ml sugar to 1L of distilled water, the sodium chloride solution 30ml salt to 1L of distilled water, and the quinine hydrochloride/sulphate solution was flattened tonic water. The experimenter swiped a cotton swab on the region of the tongue that corresponded with the solutions' dominant taste receptors. The participants were asked to leave their mouths open after swabbing and to avoid talking until they had identified the taste by pointing to one of six choices of taste type printed on a piece of paper. This was done in order to isolate taste to that specific area of the tongue and avoid the recruitment of other taste buds through the rest of the tongue and the palate. The experimenter performed the task for each taste (five trials) on the right and left sides of the tongue. The order of solutions and tongue side were randomly chosen for each participant, with the exception of applying the bitter solution at the end of all trials due to the tendency of quinine hydrochloride/sulfate to alter subsequent taste perception (Sato, Endo, & Tomita, 2002). After each application of the solution, the participant was provided a sip of distilled water to cleanse his or her mouth. All responses were recorded as either correct or incorrect and by type of taste response.

Whole mouth sensation measures. Form and texture sensations were only tested as whole mouth measures due to the nature of the tasks and materials used (e.g., resin shapes on rods for texture and form). The participants provided responses according to the type of whole sensation measure being tested. All participants were blindfolded during sensory testing to ensure response objectivity.

Form

Form was tested as a measure of stereognosis using 10 resin shapes fixed to the end of a small rod. Stereognosis is the ability to identify a shape through oral manipulation, and requires tactile sensation as well as higher cortical functioning to encode, recognize, and differentiate the shape from others. Ten acrylic resin forms appended to rods were used in this study and each was approximately 5-mm thick and 8-mm across in length (Figure 1). At the beginning of the task, participants were presented with a page of pictures of all the potential shapes, and were allowed to study the pictures for up to 30 seconds. Next, participants had 10 seconds to manipulate a shape in their mouth while blindfolded, and then were given 10 seconds to look at the picture choices and provide a response. Two extra shapes were included in the 12 picture choices in order to eliminate guessing through the process of elimination. The task was randomized for each participant and responses were recorded as similar in shape, correct or incorrect.

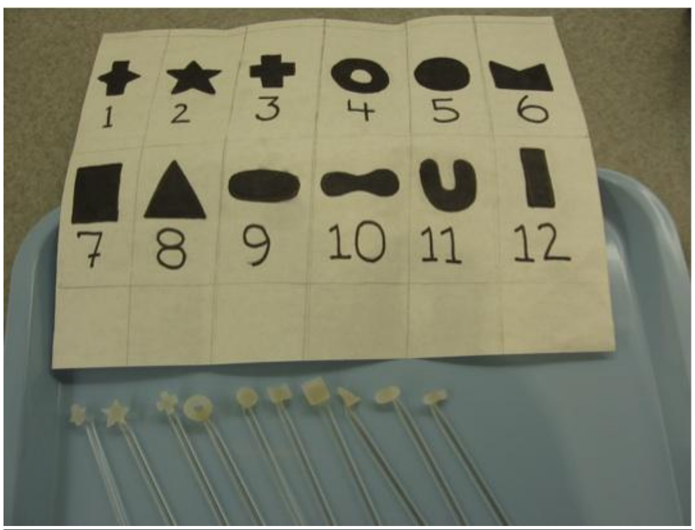


Figure 1. The 10 resin shapes appended to rods and pictures of the 10 shapes (with additional foils, shapes 11 and 12) used to test oral stereognosis (form).

<u>Texture</u>

Texture was tested using three different resin spheres graded as smooth, rough, and bumpy. The second sphere had bumps approximately 1 mm in diameter dispersed across its surface, and the third sphere had substantially more bumps that were closer together and 1 mm in diameter. Each sphere was appended to a small rod so that participants could manipulate the spheres across the surface of their tongue as needed. Participants were calibrated to each texture before the task began. In each trial, participants were given one sphere to manipulate in their mouths, and then a second sphere to compare to the first. Participants were asked to identify the second texture as the same, smoother or rougher from the first. The task was randomized for each participant and performed in nine trials, in order to account for all combinations of the three different textures. All responses were recorded as either correct or incorrect.

Motor function. The experimenter examined the participant's tongue at rest in order to observe any signs of fasciculation or muscle atrophy. Participants were asked to protrude their tongue as far as possible in order for the experimenter to observe any signs of tongue deviation to the left or right. Observations were recorded as the presence or absence of fasciculations, atrophy and/or deviation, and side of tongue in which the dysfunction occurred. For fasciculations and atrophy, bilateral presence was coded as 0, unilateral presence as 1, and absence of dysfunction as 2. For deviation, presence was coded as 0 and absence as 1. A total motor function score was computed by adding the coded scores from all three domains, with the highest score equal to 5 (representing normal function), and the lowest score equal to 0 (representing poorest level of function).

Quality of life. Quality of life was measured using the EORTC QLQ-H&N35 questionnaire (European Organisation for Research and Treatment of Cancer, Quality of Life – Head and Neck) (Appendix H) and UW-QOL questionnaire (University of Washington Quality of Life) (Appendix I) completed by each patient participant. The EORTC and UW-QOL questionnaires are standardized quality of life tools that are commonly used in the head and neck cancer population throughout Europe (EORTC) and North America (UW-QOL). The UW-QOL questionnaire is typically scaled from 0 to 100 with lower scores indicating poorer quality of life outcomes, and the EORTC questionnaire is typically scaled from 0 to 100 with lower scores indicating better quality of life outcomes. In this study both questionnaires were scored and interpreted according to standardized protocol (Lowe and Rogers 2008; Weymuller, Alsarraf, Yueh, Deleyiannis and Coltrera, 2001; Rogers, Gwanne, Lowe, Humphris, Yueh and Weymuller, 2002) with the exception of the UW-QOL scaled to match the EORTC questionnaire where higher scores indicated poorer quality of life outcomes, and lower scores indicated better quality of life outcomes. A DAT (digital audio tape) recorder and microphone were used to record responses to open-ended questions during quality of life interviews (Appendix J). The interview questions addressed such issues as social eating and lifestyle changes since participants' surgery, as well as changes in sensory function of the tongue, and any social-emotional issues since their surgery. The quality of life interviews were transcribed for each patient, and then analyzed and rated by two different examiners for basic themes within and across interviews.

Design

This study was a mixed causal-comparative design with multi-level variables. The independent variables of the study are as follows:

- Side of tongue (affected, unaffected) (within-groups, patients only)
- Surgical nerve intervention (patient group divided based on surgical intervention to the lingual and/or hypoglossal nerves) (within-groups, patients only)
- Tongue placement (tip, dorsolateral body) (within-groups)
- Participant groups (matched control group, patient group) (between-groups)

The dependent variables of the study are as follows:

- Form
- Texture
- Temperature
- Light Touch
- Two-point discrimination
- Taste
- Motor function (atrophy, deviation, fasciculations)
- Quality of life interview (patients only)
- EORTC QLQ-H&N35 survey (patients only)
- UW-QOL survey (patients only)

Statistical Analyses

SPSS was used to analyze quantitative data for sensation measures, the EORTC QLQ-H&N35 and UW-QOL surveys, and motor function measures. To analyze the data related to different research questions, one-way ANOVA's and post hoc multiple comparisons with a Bonferroni correction were used or independent/paired samples *t*-tests with an adjusted Bonferroni correction. For the first research question, one-way ANOVA's and post hoc multiple comparisons with a Bonferroni correction were used to test differences within the patient group on measures of tongue sensation, temperature, light touch, two-point discrimination, taste, form and texture. The patients were divided into groups with specific surgical interventions: 1) lingual nerve intact, 2) lingual nerve reanastomosed, 3) lingual nerve cable-grafted and 4) lingual nerve cut. This was a two-tailed hypothesis with a significant p-value $< .05$ set a priori.

For the second research question, independent samples *t*-tests with a Bonferroni correction were used to compare sensation within the patient group, between the affected and unaffected sides of the tongue. The sensations compared were temperature, light touch, two-point discrimination, taste, form and texture. The patients were divided into groups with specific surgical interventions: 1) lingual nerve intact, 2) lingual nerve reanastomosed, 3) lingual nerve cable-grafted and 4) lingual nerve cut. A Bonferroni correction was calculated by dividing the p-value of .05 by the number of comparisons made with each independent sample *t*-test: tongue side (unaffected, affected) and tongue placement (tip, body) made up four comparisons ($2x2 = 4$). Thus, the p-value was adjusted to .05/4 = .013. The research question involved a one-tailed hypothesis predicting the unaffected sides of the tongue would perform significantly better than the affected sides of the tongue on temperature, light touch, two-point discrimination and taste within the patient group. This question had an adjusted *p*-value < .013.

For the third research question, paired samples *t*-tests were used to analyze focal sensation measures temperature, light touch, two-point discrimination and taste between the right and left tongue tip and body within the control group. There were no significant differences between the right and left sides of the tongue within the control group, thus data were taken from the right side of the tongue used as the comparison to the data from the patient group.

Independent samples *t*-tests with a Bonferroni correction were used to analyze focal sensation measures temperature, light touch, two-point discrimination and taste between the affected and unaffected sides of the tongue in the patient group to that of the matched controls. The patients were divided into groups with specific surgical interventions and then matched to appropriate control participants: 1) lingual nerve intact, 2) lingual nerve reanastomosed, 3) lingual nerve cable-grafted and 4) lingual nerve cut. The Bonferroni correction was calculated by dividing the *p*-value of .05 by the number of comparisons made with each independent sample t-test: tongue side (unaffected, affected), tongue placement (tip, body) and groups (surgical group, matched control group) made up 8 comparisons (2x2x2 = 8). Thus, the significant *p*-value was adjusted to .05/8 = .0063. For the surgical groups with the lingual nerve reanastomosed, lingual nerve cable-grafted, and lingual nerve cut, a one-tailed hypothesis with the prediction that the matched controls would perform significantly better than the surgical groups for the affected side of tongue was used. For the surgical group with the lingual nerve intact, a two-tailed hypothesis was used because a prediction of difference in either direction was not plausible. This question had an adjusted p-value < .0063 for all variables.

For the fourth research question, independent samples *t*-tests were used to analyze whole-mouth sensations, form and texture, between patients and their age-matched controls. The patients were divided into groups with specific surgical interventions and then matched to yoked control participants: 1) lingual nerve intact, 2) lingual nerve reanastomosed, 3) lingual nerve cable-grafted and 4) lingual nerve cut. Each sensation was compared once between two groups and correction for a type one error was unnecessary. This was a two-tailed hypothesis with a significant p-value < .05 set a priori.

For the fifth research question, one-way ANOVA's and post hoc multiple comparisons with a Bonferroni correction were used to compare motor function scores between the patient group and control participants. The patients were divided into groups with specific surgical interventions: 1) lingual and hypoglossal nerves affected (n=7), 2) lingual and hypoglossal nerves intact (n=6), 3) lingual nerve reanastomosed and hypoglossal nerve intact (n=9), 4) lingual nerve cable-grafted and hypoglossal nerve intact (n=3) and 5) lingual nerve cut and hypoglossal nerve intact (n=5). The variance of the control group motor function scores was equal to 0, thus all matched controls had the same score for motor function. Instead of matching controls to patient groups as done previously, statistical analysis involved using a mean number of controls to compare to patient groups, with the control *n* calculated based on the mean number of participants in the surgical groups (n=7 + n=6 + n=9 + n=3 + n=5 -> 30/5 groups = 6; *n* = 6 for the control group). This was a two-tailed hypothesis with a significant *p*-value < .05 set a priori.

For the sixth research question, one-way ANOVA's and post hoc multiple comparisons with a Bonferroni correction were used to analyze the individual quality of life domains within the patient group for the UW-QOL questionnaire. The UW-QOL was also examined based on an overall physical function measure for each participant (Lowe & Rogers, 2008), computed as the average of seven domains: Eating A (chewing) and B (swallowing), speech, taste, saliva A (amount) and B (consistency), and disfigurement (appearance). The patients were divided into groups with specific surgical interventions: 1) lingual and hypoglossal nerves affected, 2) lingual and hypoglossal nerves intact, 3) lingual nerve reanastomosed and hypoglossal nerve intact, 4) lingual nerve cable-grafted and hypoglossal nerve intact and 5) lingual nerve cut and hypoglossal nerve intact. This was a two-tailed hypothesis with a significant *p*-value < .05 set *a priori*. For analysis, higher scores indicated poorer quality of life outcomes, and lower scores indicated better quality of life outcomes to match results of the EORTC questionnaire.

For the seventh research question, one-way ANOVA's and post hoc multiple comparisons with a Bonferroni correction were used to analyze the individual quality of life domains within the patient group for the EORTC QLQ-H&N35 questionnaire. The patients were divided into groups with specific surgical interventions as before. This was a two-tailed hypothesis with a significant *p*-value $< .05$ set a priori. For analysis, higher scores indicated poorer quality of life outcomes, and lower scores indicated better quality of life outcomes.

Results

Patient Group – Lingual Nerve Involvement and Sensation

Research question one was established to determine if there were significant differences for sensation based on lingual nerve involvement within the patient group. The sample sizes of each surgical group based on lingual nerve intervention are presented in Table 3. Results showed that for all significant differences, the patient group with the lingual nerve intact performed significantly better than the other groups on temperature and 2-point discrimination applied to the affected tongue tip and/or body. There were no significant differences between nerve repair groups for light touch, taste, form or texture.

A significant main effect between nerve repair groups was found for temperature on the affected tongue tip $F(3, 26) = 4.55$, $p < .01$ (Figure 2). Post hoc tests showed that the lingual nerve intact group performed significantly better ($p < .01$) than the lingual nerve cable-grafted group and the lingual nerve cut group ($p < .05$). There were no significant main differences between surgical groups for temperature on the tongue body.

Table 3

Sample sizes for each patient group based on type of lingual nerve intervention.

	V intact	V reanastomosed	V cable-grafted	V cut
Number of patients	6	12	7	5

Note. Abbreviations: V, Lingual nerve.

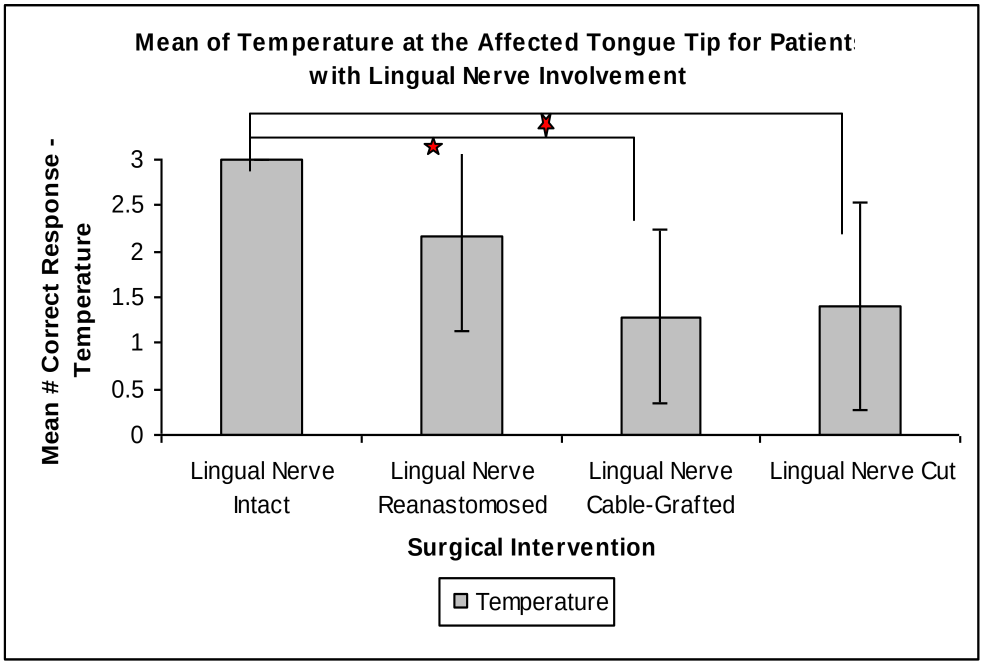


Figure 2. Bar graphs representing mean of temperature at affected tongue tip with significant differences (* $p < .05$) between patient surgical groups based on lingual nerve involvement.

Results for two-point discrimination showed a main effect for the affected tongue tip $F(3, 26) = 6.971$, $p < .01$ and affected tongue body $F(3, 26) = 7.918$, $p < .001$. Post hoc tests showed three significant interactions for the affected tongue tip (Figure 3): the patient group with the lingual nerve intact performed significantly better than the lingual nerve reanastomosed patient group ($p < .05$), the lingual nerve cable-grafted group ($p < .01$) and the lingual nerve cut group ($p < .01$).

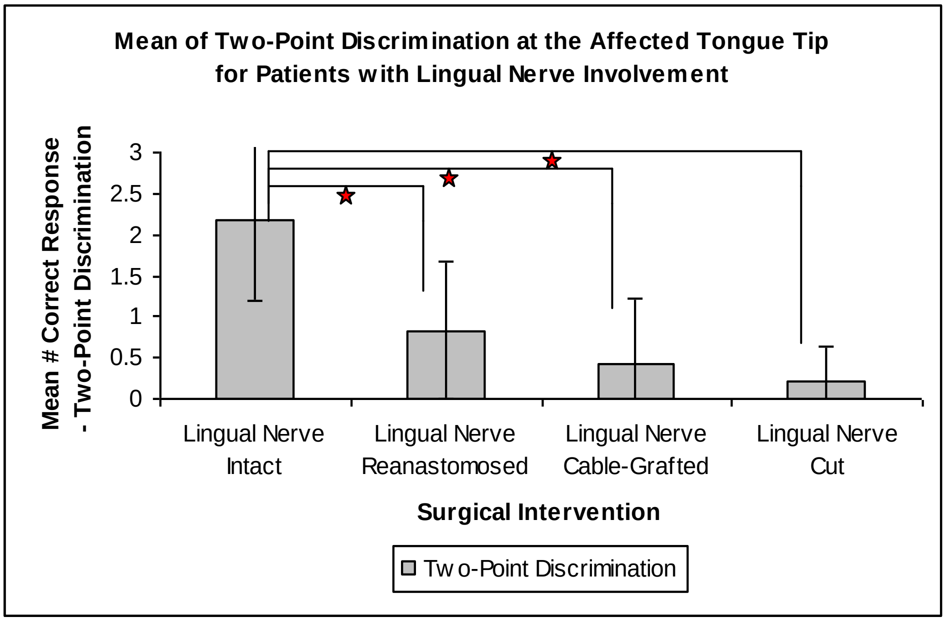


Figure 3. Bar graphs representing mean of two-point discrimination at affected tongue tip with significant differences (* $p < .05$) between patient surgical groups based on lingual nerve involvement.

Post hoc tests for two-point discrimination of the affected tongue body also revealed three significant interactions between groups (Figure 4): the patient group with the lingual nerve intact performed significantly better ($p < .001$) than the lingual nerve reanastomosed group, the lingual nerve cable-grafted group ($p < .01$) and the lingual nerve cut group ($p < .01$).

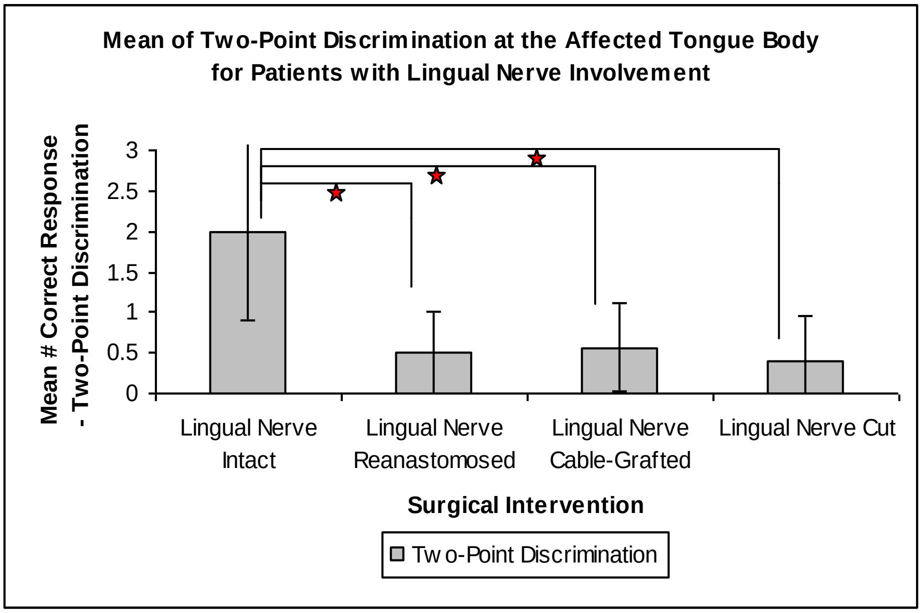


Figure 4. Bar graphs representing mean of two-point discrimination at affected tongue body with significant differences (* $p < .05$) between patient surgical groups based on lingual nerve involvement.

Means and SD for focal and whole-mouth sensations are presented in Table 4 for patients with specific lingual nerve involvement and their matched control groups, including scores for the affected and unaffected tongue sides, and the tongue tip and body.

Table 4

Mean and SD for patient groups and matched controls for whole mouth sensations and the focal sensations on the affected and unaffected tongue sides.

Groups	Temperature				Light touch				Two-point discrimination				Taste		Form	Texture
	Aff. Tip	Unaff tip	Aff. body	Unaff body	Aff. tip	Unaff tip	Aff. body	Unaff body	Aff. tip	Unaff tip	Aff. body	Unaff body	Aff. side	Unaff side		
V intact	3.00 (0.00)	3.00 (0.00)	2.67 (0.82)	3.00 (0.00)	1.83 (0.98)	2.67 (0.82)	1.67 (0.82)	2.00 (1.10)	2.17 (0.98)	2.67 (0.82)	2.00 (1.10)	2.60 (0.89)	36.67 (15.06)	56.67 (15.06)	11.00 (3.85)	8.33 (0.82)
Control (V intact)	_____	3.00 (0.00)	_____	3.00 (0.00)	_____	2.67 (0.52)	_____	1.50 (1.05)	_____	2.40 (1.34)	_____	2.33 (0.82)	_____	60.00 (30.98)	16.67 (1.63)	7.83 (0.75)
V reanast	2.17 (1.03)	3.00 (0.00)	2.17 (0.84)	2.92 (0.29)	1.17 (0.72)	2.91 (0.30)	1.17 (0.58)	2.75 (0.45)	0.83 (0.84)	2.17 (1.12)	0.50 (0.52)	1.58 (1.00)	21.67 (13.37)	46.67 (27.41)	12.75 (4.20)	8.17 (0.84)
Control (V reanast)	_____	3.00 (0.00)	_____	3.00 (0.00)	_____	2.42 (1.00)	_____	2.33 (0.78)	_____	2.42 (1.00)	_____	1.30 (0.48)	_____	48.33 (23.29)	13.17 (5.06)	8.33 (1.16)
V cable-graft	1.29 (0.95)	3.00 (0.00)	1.57 (1.51)	3.00 (0.00)	1.43 (0.79)	2.29 (0.76)	1.14 (0.69)	2.29 (0.95)	0.43 (0.79)	1.67 (1.03)	0.57 (0.54)	1.57 (0.98)	25.71 (19.02)	48.57 (19.52)	10.86 (2.85)	7.43 (0.98)
Control (V cable)	_____	3.00 (0.00)	_____	3.00 (0.00)	_____	2.57 (1.13)	_____	1.57 (0.54)	_____	2.43 (0.79)	_____	1.33 (0.82)	_____	62.86 (26.90)	14.29 (2.43)	7.57 (1.40)
V cut	1.40 (1.14)	3.00 (0.00)	1.20 (1.30)	2.40 (1.34)	1.20 (0.45)	2.20 (0.84)	1.00 (0.00)	2.20 (1.10)	0.20 (0.45)	2.20 (1.10)	0.40 (0.59)	1.80 (1.30)	20.00 (14.14)	44.00 (32.86)	10.30 (5.31)	7.60 (0.55)
Control (V cut)	_____	3.00 (0.00)	_____	3.00 (0.00)	_____	2.80 (0.45)	_____	2.20 (0.84)	_____	2.20 (1.10)	_____	2.00 (1.00)	_____	64.00 (16.73)	14.00 (2.35)	8.40 (0.55)

Notes. Blank cells for the control groups affected tongue side due to data taken only from one side of the tongue to compare to matched patient groups

Patient Group – Affected versus Unaffected Side of the Tongue

Research question two was established to determine if there were significant differences for focal sensation measures within the patient group, between the affected and unaffected sides of the tongue. Mean, SD, t and *p*-values for the affected and unaffected tongue tip and body for the variables temperature, light touch, two-point discrimination and taste are presented in Tables 5a and b. Paired-samples *t*-tests for all dependent variables revealed that the unaffected side of the tongue (tip and body) performed significantly better than the affected side of the tongue.

Table 5a

Mean, SD and significant t and p-values for focal sensations at the tongue tip and body between the affected and unaffected sides of the tongue within the patient group

Sensation	Mean and (SD)			
	Tongue tip		Tongue body	
	*Affected	Unaffected	**Affected	Unaffected
Temperature	*2.00 (1.08)	3.00 (0.00)	**1.97 (0.21)	2.87 (0.10)
	$t(29) = -5.06$, $p < .001$		$t(29) = -4.06$, $p < .001$	
Light touch	*1.38 (0.78)	2.59 (0.68)	**1.23 (0.63)	2.40 (0.86)
	$t(28) = -6.01$, $p < .001$		$t(29) = -6.07$, $p < .001$	
Two-point discrimination	*0.93 (0.19)	2.17 (0.19)	**0.72 (0.15)	1.79 (0.20)
	$t(28) = -5.41$, $p < .001$		$t(28) = -5.24$, $p < .001$	

Note. * Significant differences (p < .013) between affected and unaffected tongue tip
** Significant differences (p < .013) between affected and unaffected tongue body
( ) Standard deviation

Table 5b

Mean, SD and significant t and p-values for taste between the affected and unaffected sides of the tongue within the patient group

Sensation	Mean and (SD)	
	*Affected side of tongue	Unaffected side of tongue
Taste	*25.33 (15.70)	48.67 (23.89)
	$t(28) = -5.30$, $p < .001$	

Note. * Significant differences (p < .013) between affected and unaffected side of the tongue
(   ) Standard deviation

Patients with Lingual Nerve Involvement versus Matched Controls – Focal Sensations

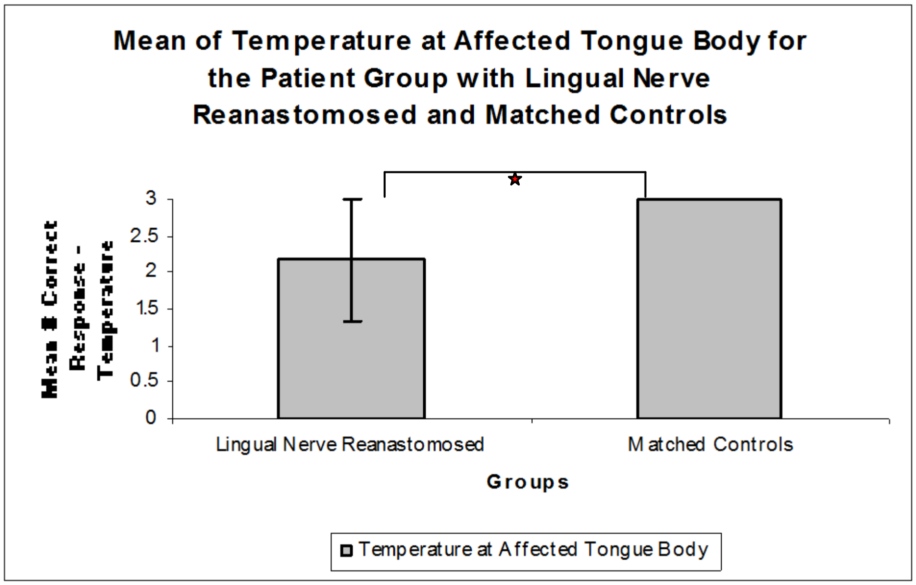
Research question three was established to determine if there were significant differences between patient groups with lingual nerve involvement and matched control participants for focal sensations, comparing the affected and unaffected sides of the tongue in the patient group to the right side of the tongue in the control group. Results showed significant differences ($p < .0063$) between the lingual nerve reanastomosed, lingual nerve cable-grafted and lingual nerve cut groups and their matched controls, with the control group performing significantly better than the patient groups on the affected tongue side. However, there were no significant differences between the lingual intact patient group and its matched controls for the affected tongue side. There were also no significant differences between the patient groups and matched controls for the unaffected tongue side. Descriptive data (means and SD) for patient surgical groups and matched controls based on focal sensation and tongue location is presented in

Table 4. Specific results for the significant findings across all sensations are presented next.

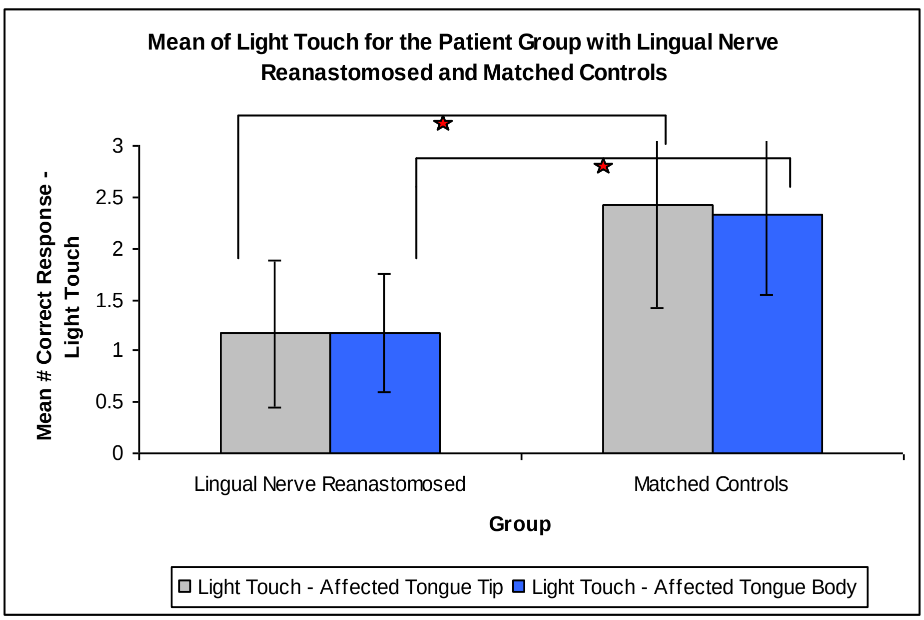
Lingual nerve reanastomosed versus matched controls

Independent samples t-tests for temperature showed that there was a significant difference $t(11) = -3.46$, $p < .005$ for the affected tongue body between the lingual nerve reanastomosed group and the matched control group (Figure 5a). Results for light touch showed a significant difference $t(22) = -3.53$, $p < .001$ for the affected tongue tip between the lingual nerve reanastomosed group and the matched control group. There also was a significant difference $t(22) = -4,17$, $p < .001$ for the affected tongue body between groups (Figure 5b). Results for two-point discrimination showed a significant difference $t(22) = -4.22$, $p < .001$ for the affected tongue tip between the lingual nerve reanastomosed group and the matched control group. There also was a significant difference $t(20) = -3.70$, $p < .001$ for the affected tongue body between groups (Figure 5c). Results for taste showed a significant difference $t(22) = -3.44$, $p < .001$ for the affected side of the tongue between groups (Figure 5d). No other differences were found.

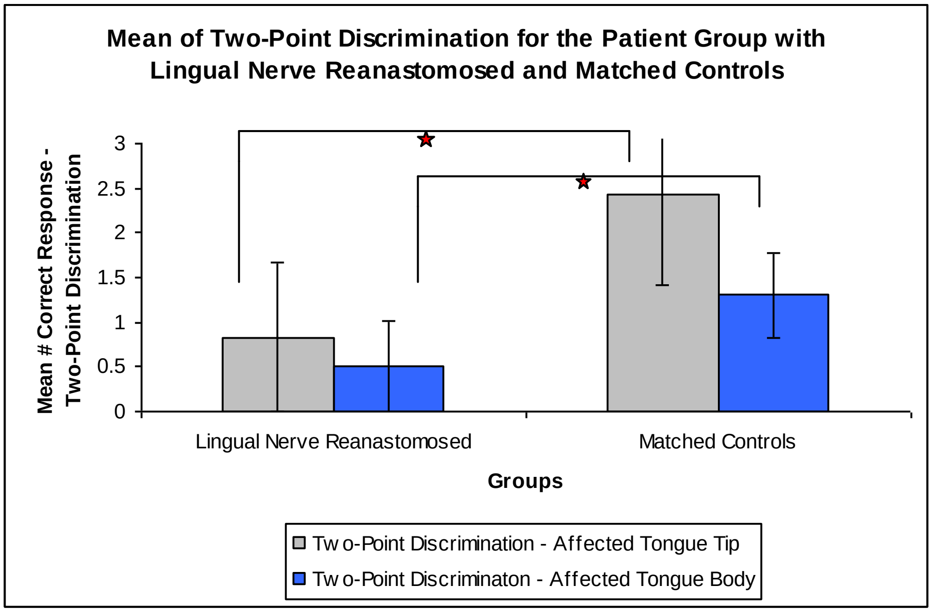
a


Mean of Temperature at Affected Tongue Body for the Patient Group with Lingual Nerve Reanastomosed and Matched Controls
Mean # Correct Response - Temperature
3
2.5
2
1.5
1
0.5
0
Lingual Nerve Reanastomosed
Matched Controls
Groups
Temperature at Affected Tongue Body

b


Mean of Light Touch for the Patient Group with Lingual Nerve Reanastomosed and Matched Controls
Mean # Correct Response - Light Touch
3
2.5
2
1.5
1
0.5
0
Lingual Nerve Reanastomosed
Matched Controls
Group
Light Touch - Affected Tongue Tip
Light Touch - Affected Tongue Body

c



d

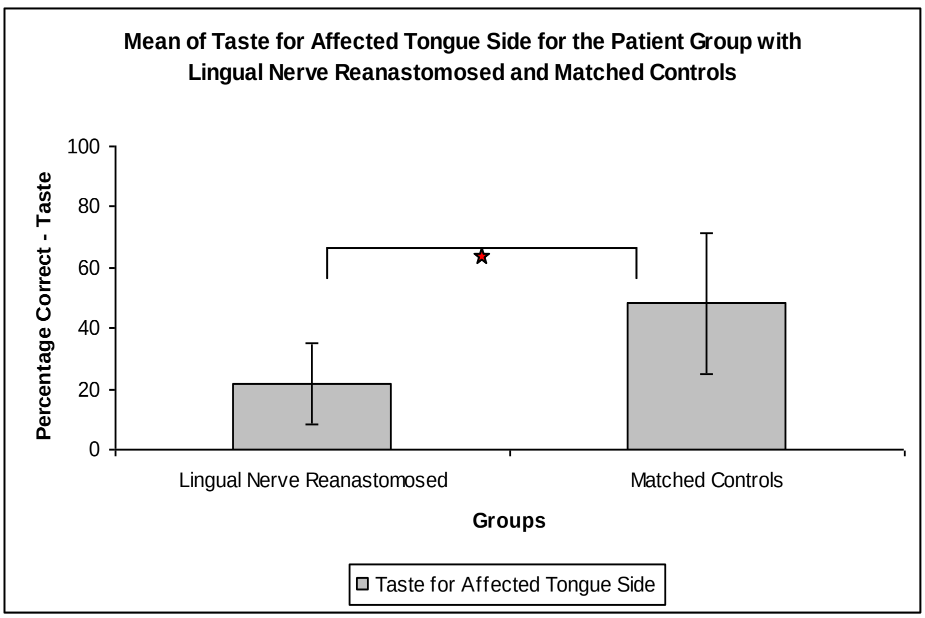
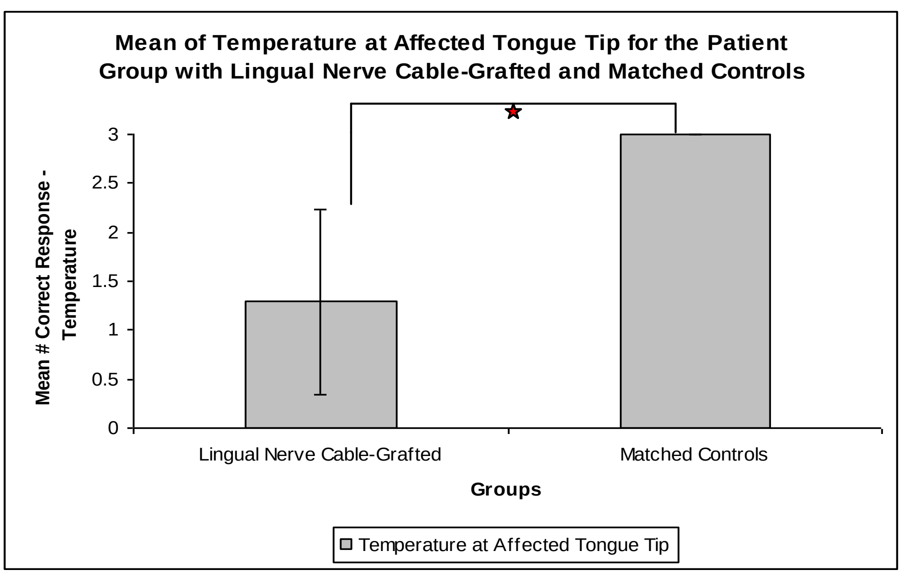


Figure 5. Bar graphs representing significant differences (* $p < .0063$) in measures of focal sensation between patient surgical groups and matched control participants. **a** mean of temperature at affected tongue body. **b** mean of light touch at affected tongue body. **c** mean of two-point discrimination at affected tongue tip. **d** mean of taste on affected tongue

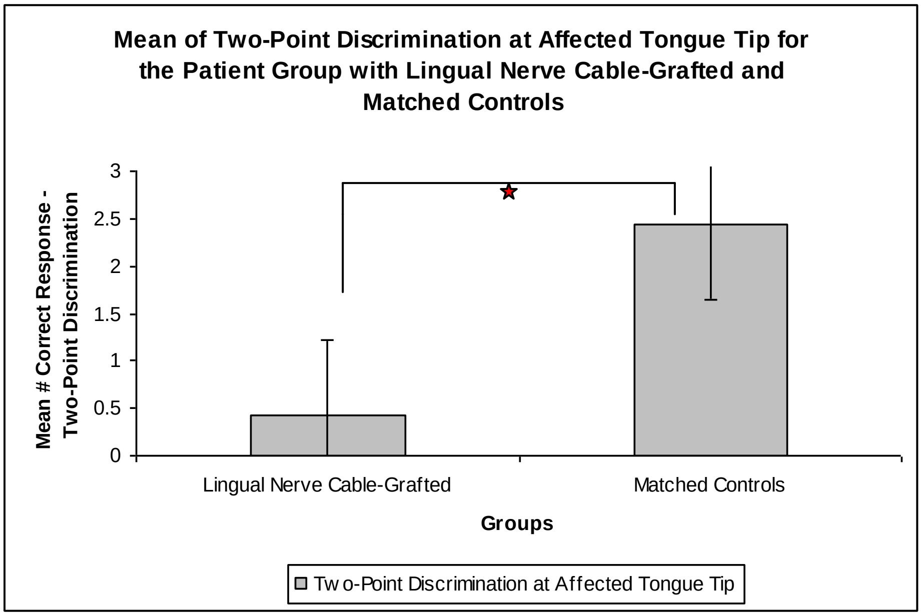
Lingual nerve cable-grafted versus matched controls

Independent samples t-tests for temperature showed a significant difference $t(6) = -4.77$, $p < .005$ for the affected tongue tip between the lingual nerve cable-grafted group and the matched control group (Figure 6a). Results for two-point discrimination showed a significant difference $t(12) = -4.76$, $p < .001$ for the affected tongue tip between the lingual nerve cable-grafted group and the matched control group (Figure 6b). Results for taste showed a significant difference $t(12) = -2.98$, $p < .006$ for the affected side of the tongue between the lingual nerve cable-grafted group and the matched control group (Figure 6c). When data were collapsed for overall taste scores, a trend appeared with the lingual nerve cable-grafted group ($M = 37.14$, $SD = 16.04$) showing worse results than the matched controls ($M = 65.71$, $SD = 17.18$) with $t(11) = -3.22$, $p < .007$. There were no significant differences found between the lingual nerve cable-grafted group and the matched control group for light touch on the affected and unaffected tongue tip and body.

a



b



c

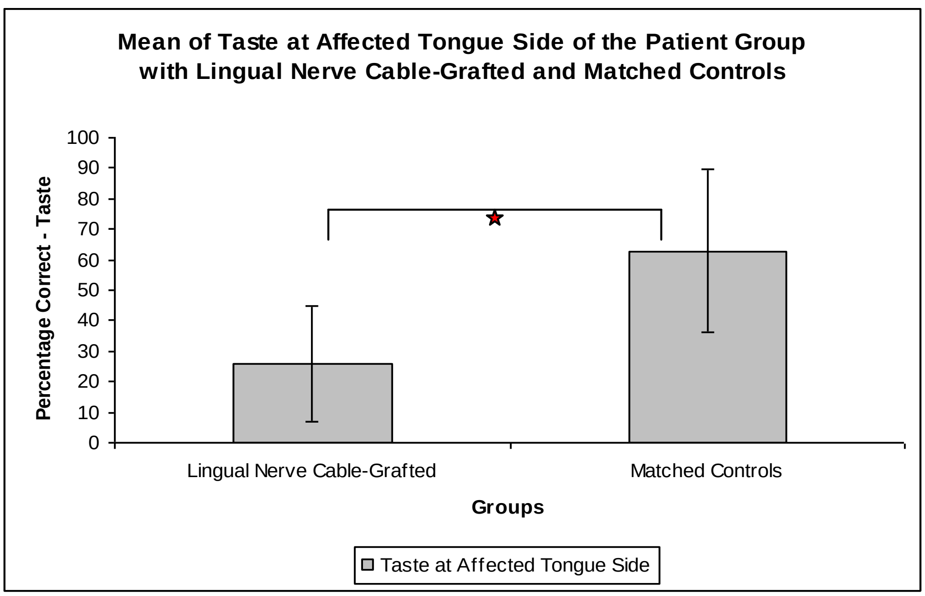
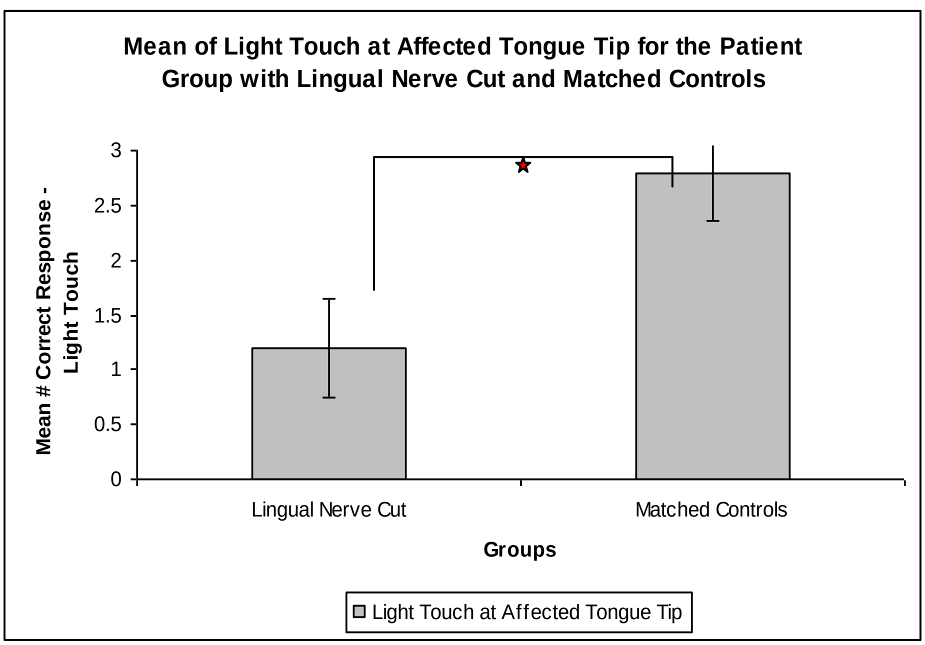


Figure 6. Bar graphs representing significant differences (* $p < .0063$) in measures of focal sensation between patient surgical groups and matched control participants. **a** mean of temperature at affected tongue tip. **b** mean of two-point discrimination at affected tongue tip. **c** mean of taste on affected tongue side.

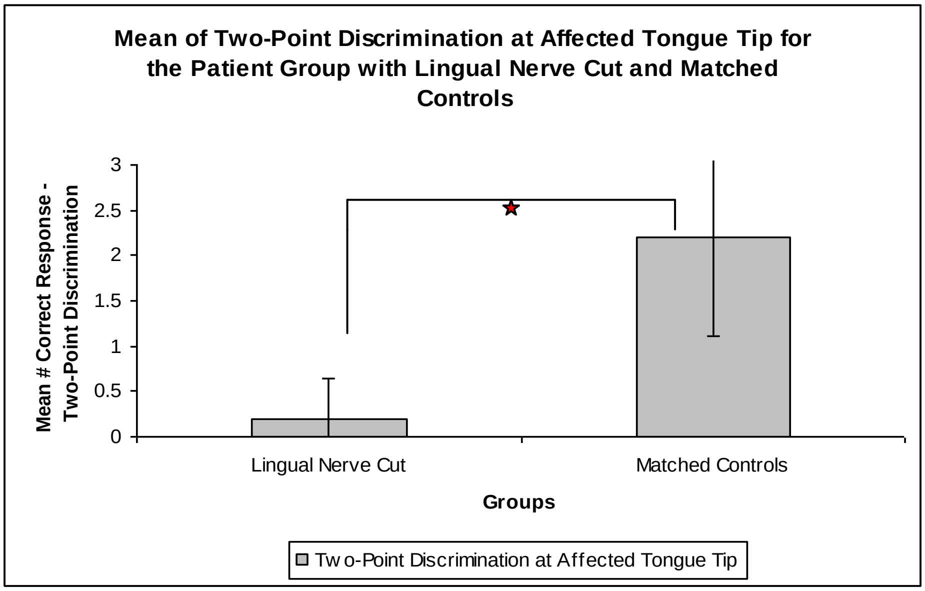
Lingual nerve cut versus matched controls

Independent samples t-tests for light touch showed a significant difference $t(8) = -5.66$, $p < .001$ for the affected tongue tip between the lingual nerve cut group and the matched control group (Figure 7a). Results for two-point discrimination showed a significant difference $t(5) = -3.78$, $p < .006$ for the affected tongue tip between the lingual nerve cut group and the matched control group (Figure 7b). A trend was noted for the affected tongue body with $t(8) = -3.14$, $p < .007$) between the lingual nerve cut group and matched controls. Results for taste showed a significant difference $t(8) = -4.49$, $p < .001$ for the affected side of the tongue between the lingual nerve cut group and the matched control group (Figure 7c). There were no significant differences found between the lingual nerve cut group and the matched control group for temperature on the affected and unaffected tongue tip and body.

a



b



c

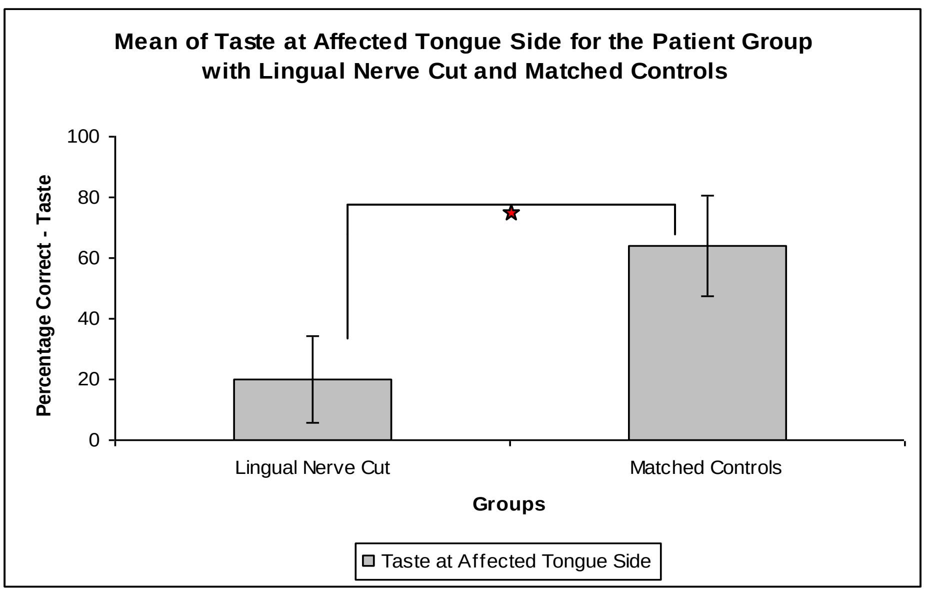


Figure 7. Bar graphs representing significant differences (* $p < .0063$) in measures of focal sensation between patient surgical groups and matched control participants. **a** mean of light touch at affected tongue tip. **b** mean of two-point discrimination at affected tongue tip. **c** mean of taste on affected tongue side.

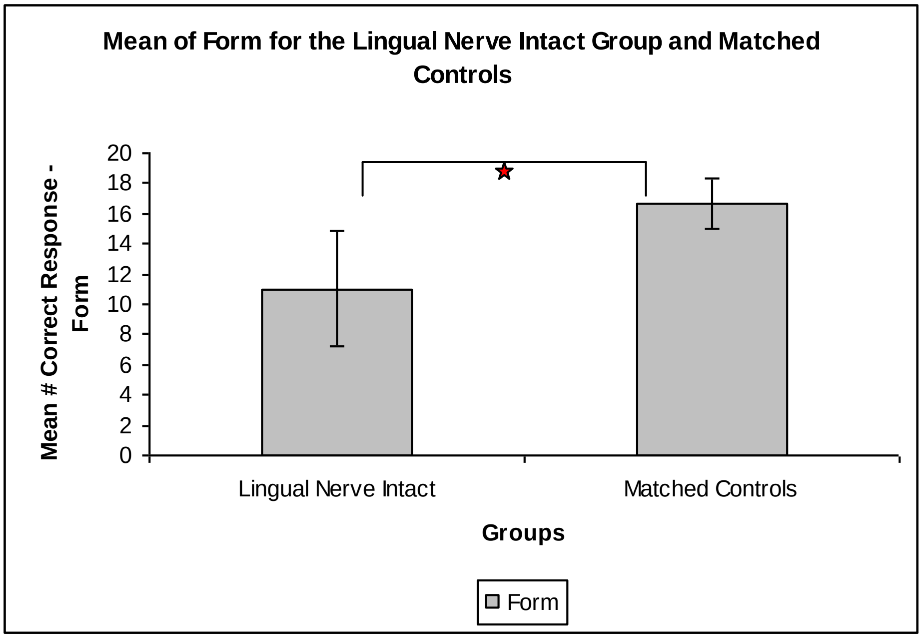
Lingual nerve intact versus matched controls

There were no significant differences found between the lingual nerve intact group and their matched control group on all four dependent variables: temperature, light touch, two-point discrimination and taste.

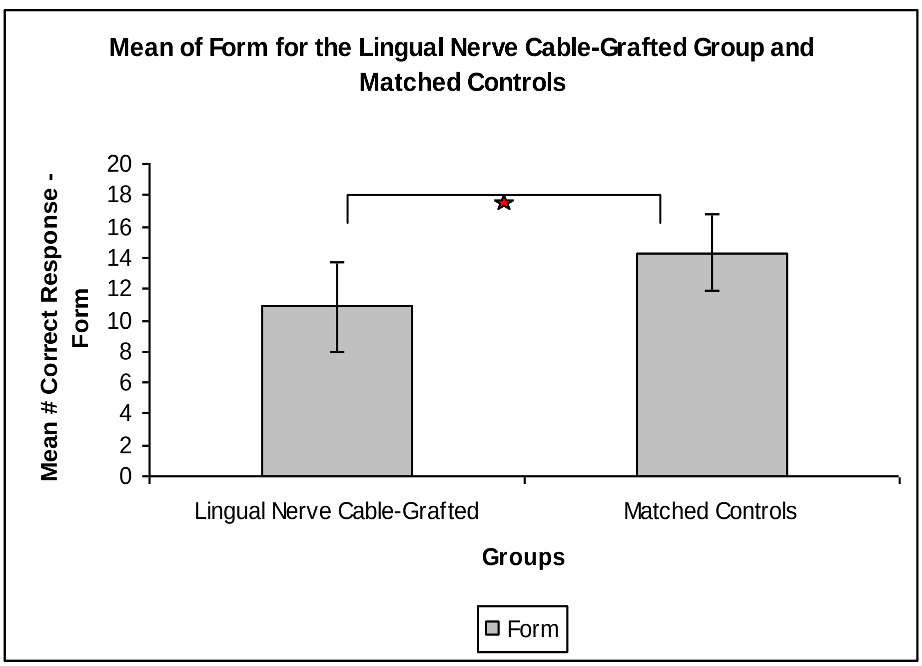
Patients with Lingual Nerve Involvement versus Matched Controls – Whole Mouth Sensations

Research question four was established to determine if there were significant differences between patient surgical groups and matched control participants for whole mouth sensations (form and texture). Significant results for form and texture revealed that the matched control groups always performed better than their corresponding surgical patient groups. Means and SD for whole mouth sensations for patient surgical groups and matched controls is presented in Table 4. Graphical information for significant comparisons between matched groups and patients for whole mouth sensations is presented in Figure 8. There was a significant difference for form between the lingual nerve intact group $t(10) = -3.32$, $p < .01$ and the matched control group (Figure 8a), with no significant differences between groups for total texture scores. There was also a significant difference for form between the lingual nerve cable-grafted group $t(12) = -2.42$, $p < .05$ and the matched control group (Figure 8b), with no significant differences between groups for texture. Significant differences were found for texture $t(8) = -2.31$, $p < .05$ (Figure 8c) between the lingual nerve cut group and the matched control group, though no significant differences were found for form. There were no significant differences found between the lingual nerve reanastomosed group and the matched control group for form and texture.

a



b



c

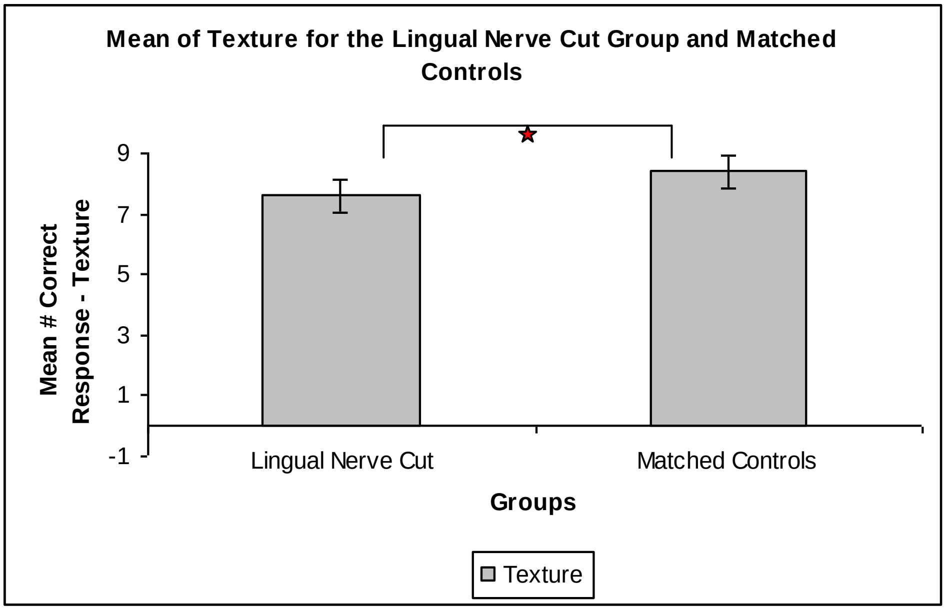


Figure 8. Bar graphs representing significant differences (* $p < .05$) in measures of whole mouth sensation between patient surgical groups and matched controls **a** mean of form for lingual intact group and matched controls **b** mean of form for lingual cable-grafted group and matched controls **c** mean of texture for lingual cut group and matched controls.

Patients with Lingual and/or Hypoglossal Nerve Involvement versus Controls – Motor Function

Research question five was established to determine if there are significant differences for motor function between patients based on lingual and/or hypoglossal nerve involvement and the control group. Results showed no significant interaction between groups for patients with only the lingual nerve affected. The sample sizes for each group and mean and SD for motor function scores between patient groups and controls are presented in Table 6.

Table 6

Sample sizes and the mean and SD of motor function scores between patient surgical groups and controls

Groups	Sample Size	Mean and (SD) Motor function
V & XII affected	7	3.00 (0.58)
V & XII intact	6	4.50 (0.55)
V reanastomosed & XII intact	9	3.89 (1.17)
V cable-grafted & XII intact	3	3.33 (0.58)
V cut & XII intact	5	4.00 (0.71)
Control group	6	5.00 (0.00)

Notes. Abbreviations: V, Lingual nerve; XII, Hypoglossal nerve
( ) Standard deviation

For hypoglossal nerve involvement, there was a significant interaction between groups $F(5, 30) = 5.60$, $p < .001$ on measures of motor function. Post hoc tests revealed that the surgical group with both lingual and hypoglossal nerves affected performed significantly worse ($p < .05$) than the surgical group with both lingual and hypoglossal nerves intact and significantly worse ($p < .001$) than the control group (Figure 9).

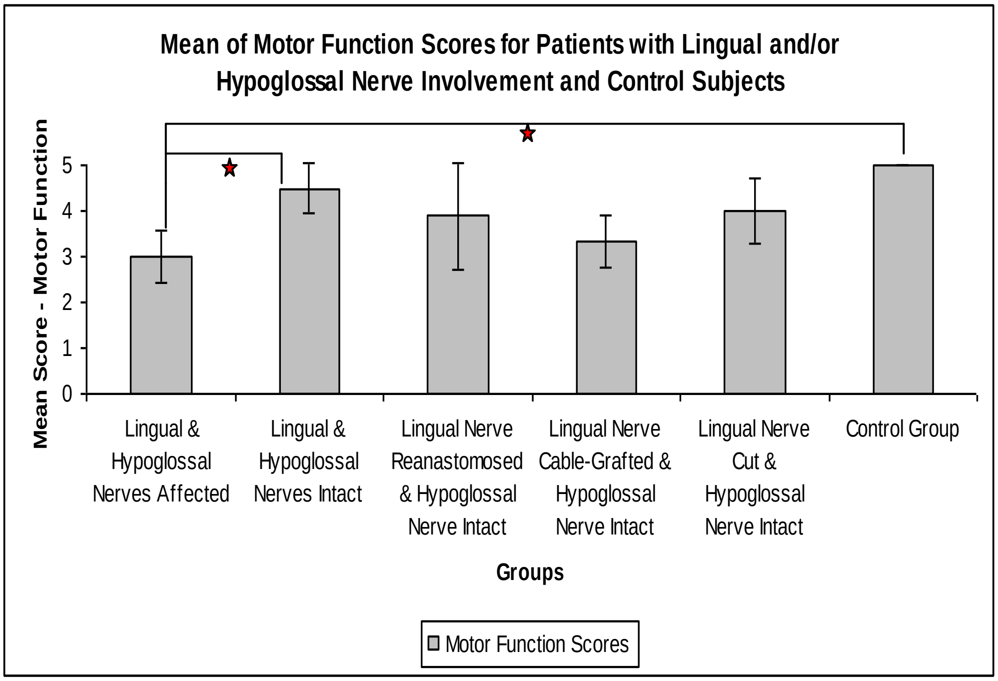


Figure 9. Bar graphs representing significant differences (* $p < .05$) in measures of motor function between patient surgical groups and matched control participants.

Patient Group - Lingual and/or Hypoglossal Nerve Involvement versus UW-QOL scores

Research question six was established to determine if there were significant differences between patients based on lingual and/or hypoglossal nerve involvement for quality of life domains on the UW-QOL questionnaire. Means and SD for the EORTC and UW-QOL surveys for statistically significant quality of life domains are presented in Table 7.

Table 7

Mean and SD for patient surgical groups for statistically significant (p < .05) QOL domains from the EORTC QLQ-H&N35 questionnaire and the UW-QOL questionnaire.

	Mean and (SD)					
Groups	EORTC QLQ-H&N35 Domains				UW-QOL Domains	
	Swallowing	Trouble with social eating	Less sexuality	Dry mouth	Pain B	Saliva A
V & XII affected	50.00 (18.63)	63.10 (26.73)	54.76 (34.31)	85.71 (17.82)	7.14 (12.20)	87.57 (12.50)
V & XII intact	18.06 (13.35)	23.61 (18.57)	5.56 (13.61)	44.44 (27.22)	4.17 (10.21)	33.33 (34.16)
V reanast & XII intact	15.74 (14.10)	16.67 (10.21)	20.83 (23.15)	44.44 (16.67)	0.00 (0.00)	77.78 (31.73)
V cable-graft & XII intact	33.33 (14.43)	38.89 (9.62)	44.44 (50.92)	66.67 (33.33)	41.67 (52.04)	66.67 (38.19)
V cut & XII intact	21.67 (13.94)	28.33 (23.27)	20.00 (21.73)	73.33 (36.51)	5.00 (11.18)	90.00 (13.69)

Results showed a significant main effect for the domain “Pain B” $F(4, 25) = 3.50$, $p < .05$. Post hoc tests revealed that patients with the lingual nerve reanastomosed and the hypoglossal nerve intact and patients with both nerves intact performed significantly better ($p < .05$) than the group with the lingual nerve cable-grafted and hypoglossal nerve intact (Figure 10).

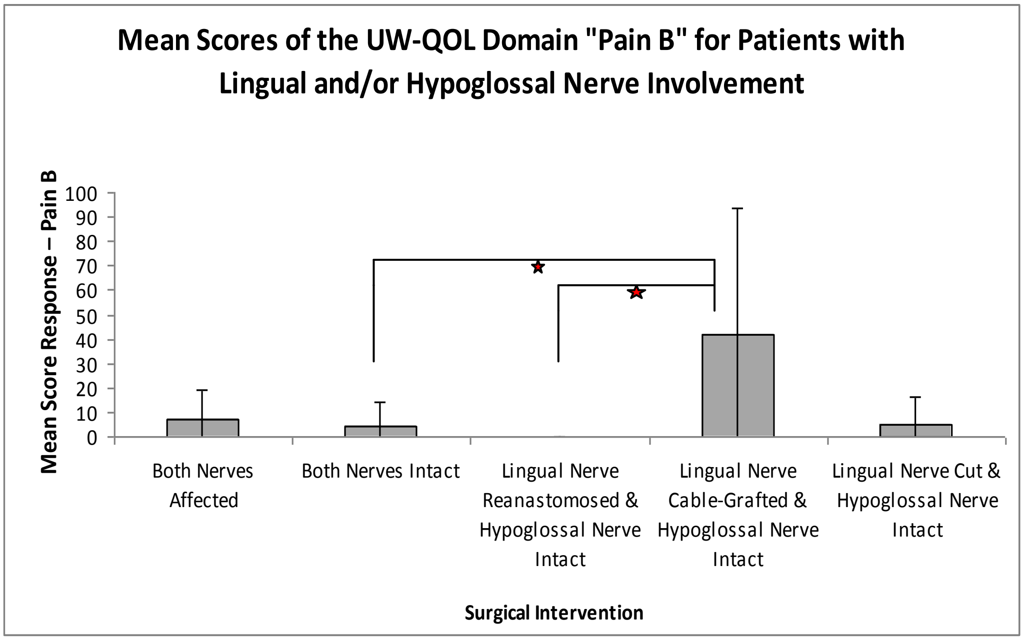


Figure 10. Bar graphs representing the mean score responses for the UW-QOL domain "Pain B" with significant differences (* $p < .05$) between patient surgical groups based on lingual and/or hypoglossal nerve involvement. *Notes*. Higher scores indicate poorer quality of life outcomes.

Results showed a significant main effect for the domain "Saliva A" $F(4, 25) = 4.28$, $p < .001$. Post hoc tests revealed that the patient group with both the lingual and hypoglossal nerves intact performed significantly better ($p < .05$) than the group with the lingual nerve cut and the hypoglossal nerve intact, the group with the lingual nerve reanastomosed and hypoglossal nerve intact, and significantly better ($p < .05$) than the group with both the lingual and hypoglossal nerves affected (Figure 11).

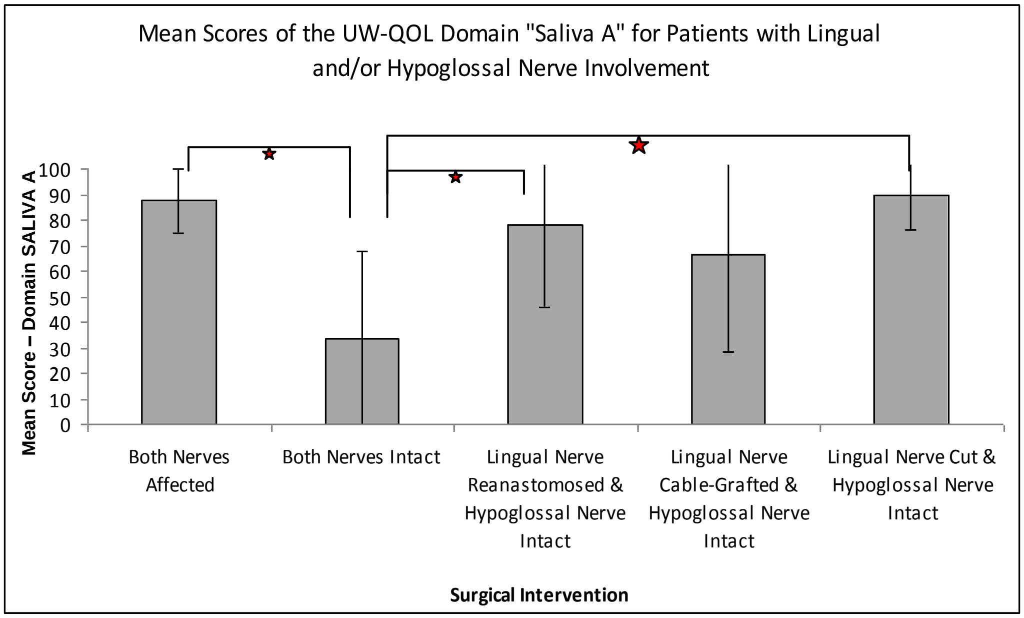


Figure 11. Bar graphs representing the mean score responses for the UW-QOL domain "Saliva A" with significant differences (* $p < .05$) between patient surgical groups based on lingual and/or hypoglossal nerve involvement.

Notes. Higher scores indicate poorer quality of life outcomes

The UW-QOL survey yields an overall "physical function" score for each participant. The results of the one-way ANOVA showed a significant main effect for physical function $F(4, 25) = 2.99$, $p < .05$ between groups. Post hoc comparisons revealed that the patient group with both nerves intact ($M = 33.50$, $SD = 18.38$) performed significantly better ($p < .05$) than the group with both nerves affected ($M = 67.71$, $SD = 10.26$) (Figures 12 and 13).

The mean score responses for the quality of life domains of the UW-QOL questionnaire are presented graphically in Appendix K.

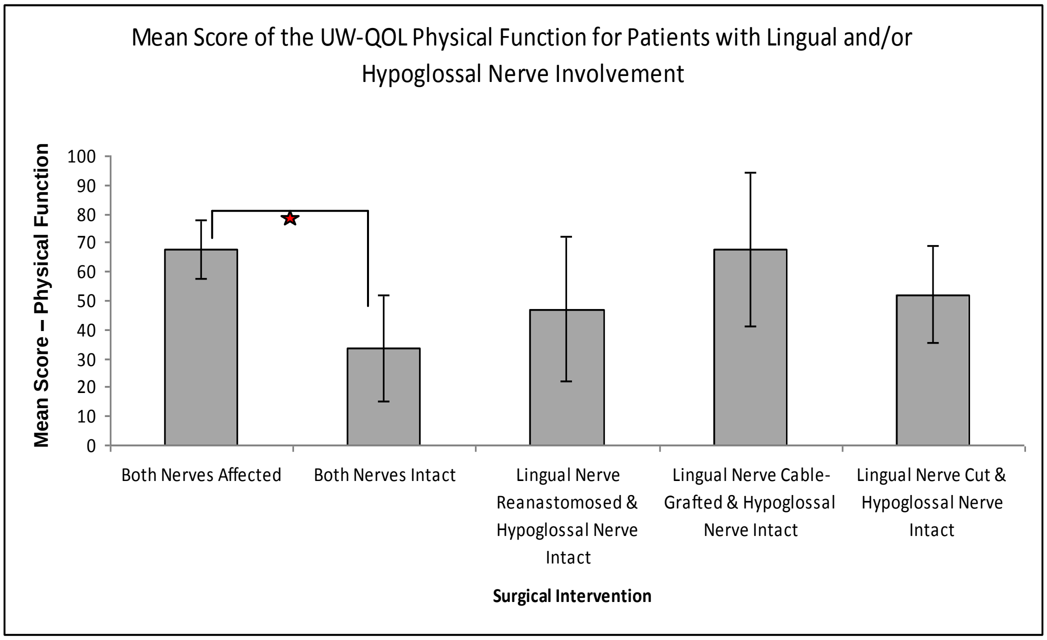


Figure 12. Bar graphs representing significant differences (* $p < .05$) in physical function between patient surgical groups

Notes. Higher scores indicate poorer quality of life outcomes

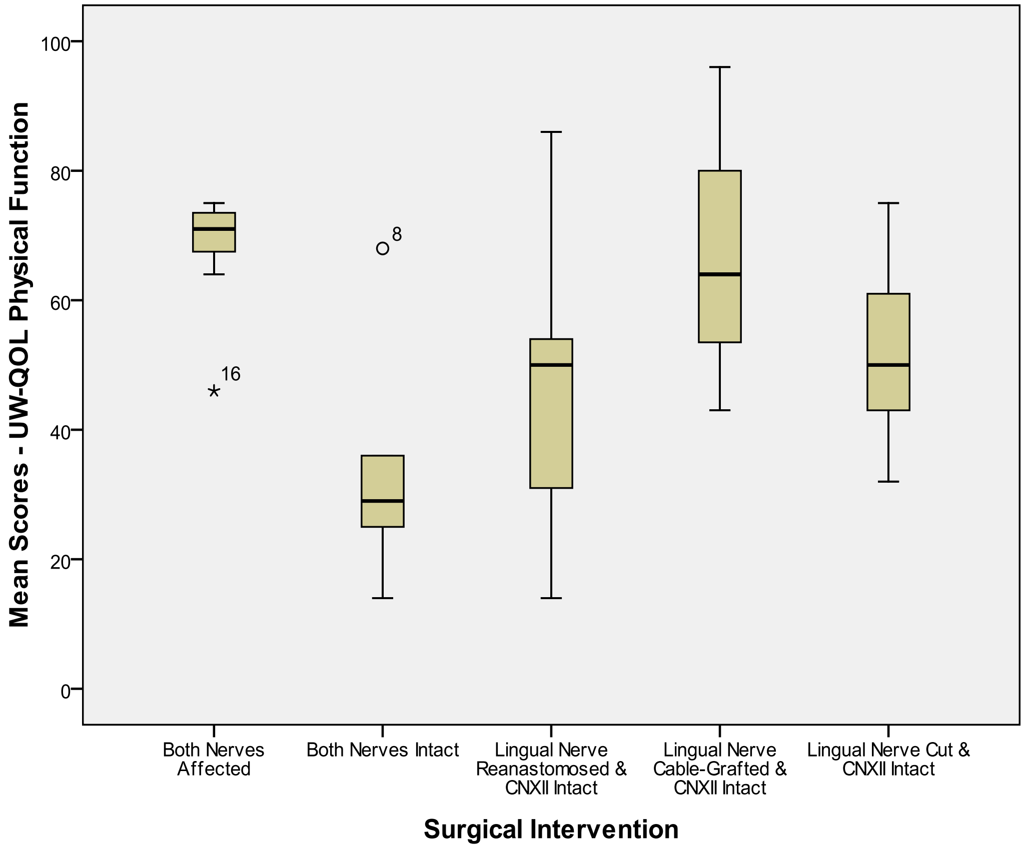


Figure 13. Box plots representing the median, first and third quartiles, minimum and maximum scores, and extreme outliers for physical function scores across patient surgical groups.

Notes. Higher scores indicate poorer quality of life outcomes

Patient Group - Lingual and/or Hypoglossal Nerve Involvement versus EORTC QOL scores

Research question seven was established to determine if there are significant differences between patient surgical groups on quality of life domains from the EORTC questionnaire. Means and SD for the EORTC and UW-QOL surveys for specific quality of life domains are presented in Table 7.

Results showed that for all significant interactions between patient groups, the surgical group with both nerves affected performed significantly worse than the other groups. Specifically, there was a significant main effect for the domain "Swallowing" $F(4, 25) = 6.06$, $p < .001$. Post hoc tests revealed that the patient group with both nerves affected performed significantly worse ($p < .001$) than the group with lingual nerve reanastomosed and the hypoglossal nerve intact, the group with the lingual nerve cut and the hypoglossal nerve intact ($p = .038$), and the group with both nerves intact ($p < .01$) (Figure 14).

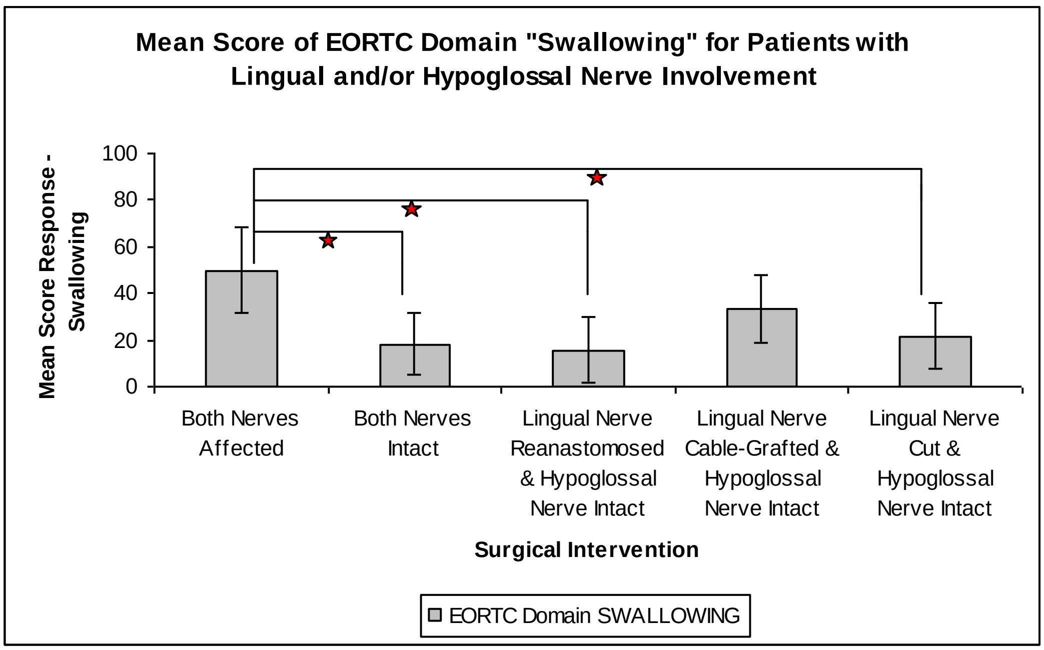


Figure 14. Bar graphs representing the mean score responses for the EORTC domain "Swallowing" with significant differences (* $p < .05$) between patient surgical groups based on lingual and/or hypoglossal nerve involvement.

Notes. Higher scores indicate poorer quality of life outcomes

Results also showed a significant main effect for the domain "Less Sexuality" $F(4, 24) = 3.05$, $p < .05$. Post hoc tests revealed that the patient group with both nerves affected performed significantly worse ($p < .05$) than the group with both nerves intact (Figure 15).

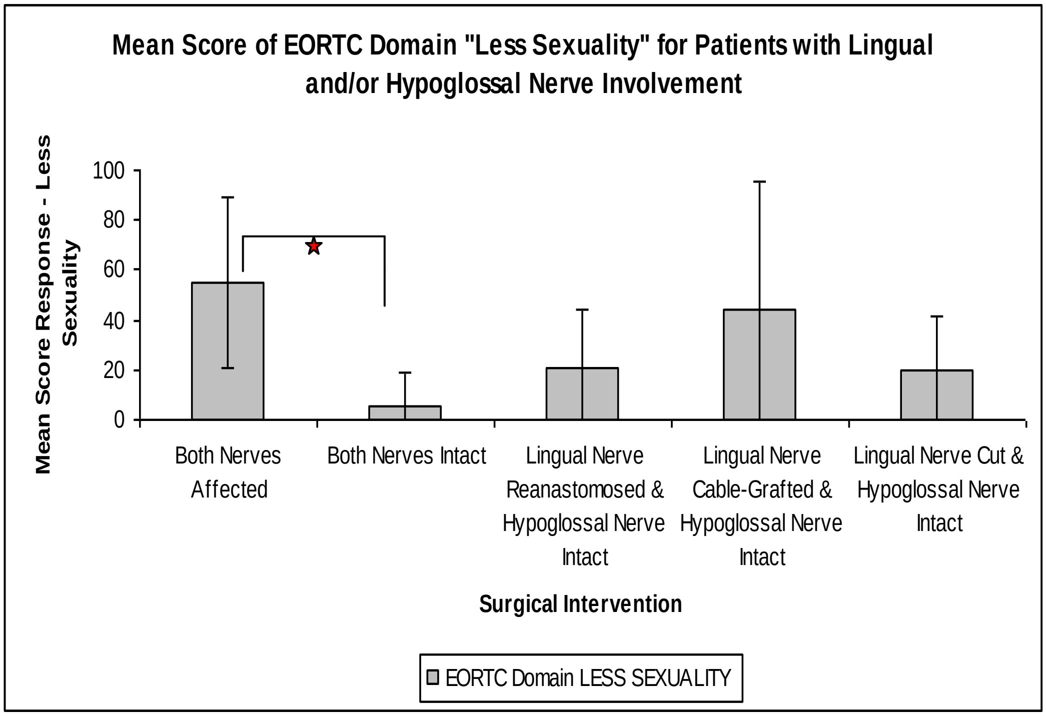


Figure 15. Bar graphs representing the mean score responses for the EORTC domain "Less Sexuality" with significant differences (* $p < .05$) between patient surgical groups based on lingual and/or hypoglossal nerve involvement.

Notes. Higher scores indicate poorer quality of life outcomes.

Results also showed a significant main effect for the domain "Trouble with social eating" $F(4, 25) = 6.45$, $p < .001$. Post hoc tests revealed that the patient group with both nerves affected performed significantly worse ($p < .001$) than the group with lingual nerve reanastomosed and the hypoglossal nerve intact, the group with the lingual nerve cut and the hypoglossal nerve intact (p < .05), and the group with both nerves intact (p < .05) (Figure 16).

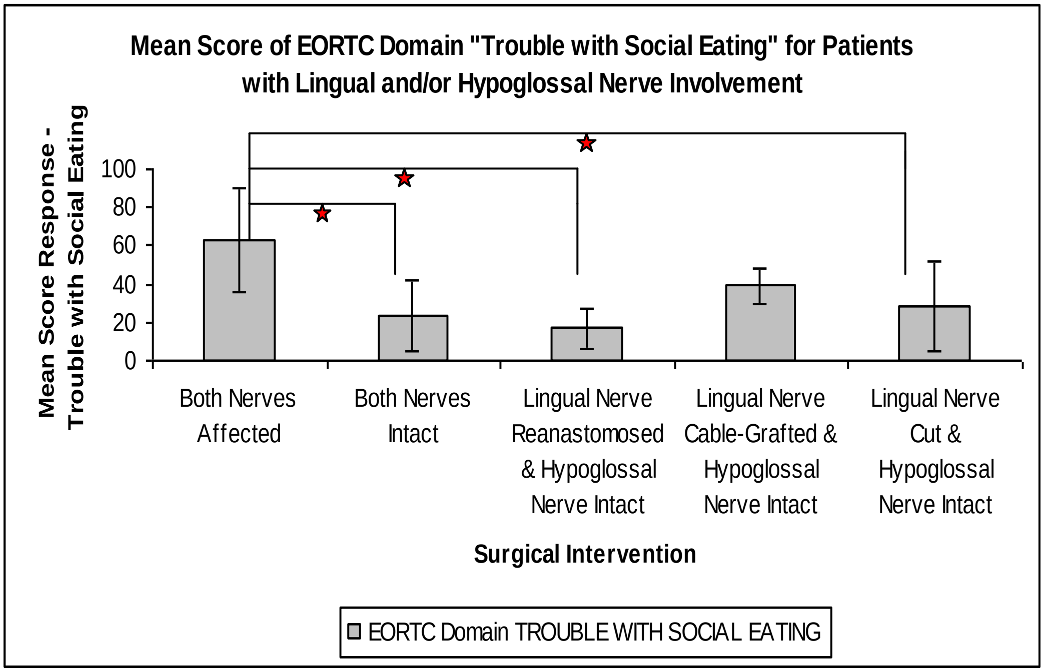


Figure 16. Bar graphs representing the mean score responses for the EORTC domain "Trouble with Social Eating" with significant differences (* *p* < .05) between patient surgical groups based on lingual and/or hypoglossal nerve involvement.

Notes. Higher scores indicate poorer quality of life outcomes.

Results also showed a significant main effect for the domain "Dry Mouth" $F(4, 25) = 3.76$, $p < .05$. Post hoc tests revealed that the patient group with both nerves affected performed significantly worse ($p < .05$) than the group with lingual nerve reanastomosed and the hypoglossal nerve intact (Figure 17).

The mean score responses for each quality of life domain for the EORTC questionnaire are presented graphically in Appendix K.

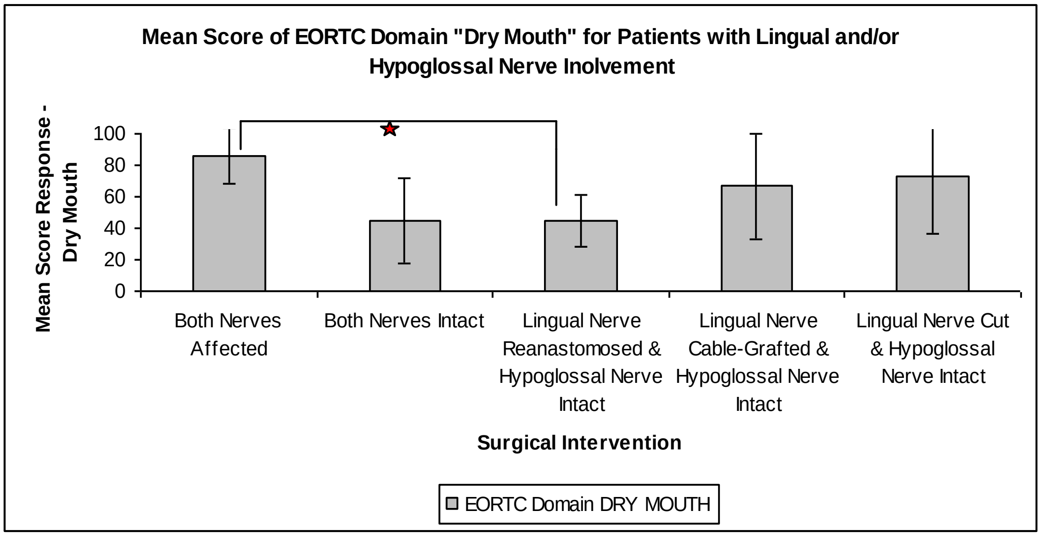


Figure 17. Bar graphs representing the mean score responses for the EORTC domain "Dry Mouth" with significant differences (* $p < .05$) between patient surgical groups based on lingual and/or hypoglossal nerve involvement. *Notes.* Higher scores indicate poorer quality of life outcomes.

Patient Group - Cancer T-stage and % Base of Tongue Resected versus QOL Scores

In head and neck cancer research it is important to examine patient cancer T-stage and the percent of defect resected to patient responses on quality of life. This study examined any correlations with patient cancer T-stage and percent base of tongue resected to the quality of life responses on the EORTC and UW-QOL questionnaires. Pearson correlations and multivariate analysis were performed to explore the question.

For the EORTC questionnaire, cancer T-stage was significantly correlated to the QOL domain Less Sexuality $r = 0.37$, $p = .05$. Multivariate analysis showed a main effect for T-stage and the EORTC domains using Wilks' Lambda $F(34, 2) = 20.91$, $p < .05$, and a trend for the combination of nerve intervention and T-stage with the EORTC QOL domains using Wilks' Lambda $F(85, 9.26) = 2.69$, $p = 0.052$. However, the test of between-subjects effects showed no significant differences for T-stage and QOL domains, with one trend for the combination of nerve involvement and T-stage with the QOL domain Less Sexuality $F(5) = 2.75$, $p = 0.054$. Post hoc multiple comparisons with Bonferroni correction showed one trend for T-stage and the QOL domain Senses Problems $p = .054$ where patients with stage T2 appeared to have better QOL responses in that domain than patients with stage T3 cancer.

There were no significant correlations for percent base of tongue resected and the EORTC QOL domains. Multivariate analysis showed no main effects for percent base of tongue resected and the EORTC domains using Wilks' Lambda. However, tests of between-subjects effects showed significant differences for the combination of nerve intervention and tongue resection with the QOL domains Sticky Saliva $F(5) = 3.04$, $p < .05$ and Nutritional Supplement $F(5) = 3.41$, $p < .05$. Post hoc multiple comparisons with a Bonferroni correction showed no significant differences for percent tongue resected and EORTC QOL domains.

For the UW-QOL questionnaire, cancer T-stage was significantly correlated to the QOL domains Physical Function $r = 0.45$, $p < .05$, Eating A $r = 0.41$, $p < .05$ and Eating B $r = 0.48$, $p < .01$. Multivariate analysis revealed no significant main effects for cancer T-stage and QOL domains using Wilks' Lambda, and no significant main effect for the combination of cancer T-stage and nerve involvement for QOL domains using Wilks' Lambda. Tests of between-subjects effects found no significant differences between cancer T-stage and the

QOL domains and with the combination of cancer T-stage and nerve involvement for the QOL domains. Post hoc multiple comparisons with a Bonferroni correction revealed significant differences for cancer T-stage and QOL domains for Activity $p < .05$ between cancer stages T2 and T3, and for Eating B $p < .05$ between cancer stages T2 and T3, where patients with stage T2 appeared to have better QOL responses than patients with stage T3 cancer.

For percent base of tongue resected and the UW-QOL domains there were no significant correlations found. Multivariate analysis also revealed no significant main effect between percent resection and QOL domains, and none for the combination of percent resection and nerve involvement for the QOL domains. Tests for between-subjects effects revealed significant differences for percent resection and the QOL domain Recreation $F(3) = 3.71$, $p < 0.05$, and for the combination of percent resection and nerve involvement for the QOL domain Eating B $F(5) = 5.39$, $p < .01$. Post hoc multiple comparisons with a Bonferroni correction found significant differences for percent resection and the QOL domain Recreation between 50% and 100% BOT resection $p < .05$, and between 75% and 100% BOT resection $p < .05$, where patients with 100% BOT resection appeared to have poorer QOL responses than patients with 50% and 75% resection.

Patient Group - Qualitative Semi-Structured Interviews on Quality of Life

Quality of life interviews were semi-structured and consisted of open-ended questions about patients' concerns and experiences after their surgery. Each transcribed interview was examined separately by two different raters, and analyzed for negative and/or positive coping strategies, patients' overall attitudes and behaviours, and underlying themes. The negative coping strategies identified were social withdrawal and avoidance, denial, anger and externalization. The positive coping strategies identified were the forming of support groups, engaging in physical activities, and engaging in new hobbies. Many patients presented characteristics suggesting passive or passive aggressive strategies for coping with stress. Overall themes included: depression, frustration, social isolation, and social and livelihood limitations.

Discussion

This study examined sensation and motor outcomes of the anterior tongue in patients who had radial forearm free flap surgery for base of tongue cancer. The six sensory functions tested were temperature, two-point discrimination and light touch (fine touch discrimination), taste, stereognosis (form) and texture. The motor functions that were examined included muscle atrophy, fasciculations, and tongue deviation upon protrusion. The results of this study provided insight about focal and whole mouth sensations, basic tongue motor function and quality of life in this patient group. The major finding was that type of surgical nerve intervention significantly influenced sensory, motor and quality of life outcomes. More specific interpretations of results are presented in the context of each research question.

Question #1: Within the patient group, are there significant differences in sensation based on lingual nerve involvement?

When transected lingual nerves have undergone microsurgical repair during base of tongue reconstruction, there is the possibility of the recovery of taste and some neurosensory function to the anterior two-thirds of the tongue (Rutner, Ziccardi, & Janal, 2005). However, the return of sensory function is often limited, and outcomes vary with surgical procedures used and other clinical factors, for example the nerves resected, post-operative radiotherapy or chemoradiation (Dvali & Mackinnon, 2007). In addition to reconstruction, the type of surgical nerve repair (e.g., direct anastomosis or grafting) may impact functional outcomes. For this reason, direct anastomosis of a severed/resected nerve is preferable to an interpositional graft, unless the nerve is under tension (Pogrel & Maghen, 2001; Dvali & Mackinnon., 2007; Shindo, 1999). Thus, in the present study, it was hypothesized that patients with direct anastomosis of the lingual nerve would have superior sensory outcomes to patients who had the lingual nerve repaired with a cable-graft. Previous research also shows that for sensory recovery to occur in the anterior two-thirds of the tongue, microsurgical repair is necessary to re-appose the cut ends of the lingual nerve. Patients with the lingual nerve left severed or transected, will likely experience limited spontaneous recovery due to the poor opportunity sprouting axons have of extending down their original connective tissue sheaths (Holland, 1996). Thus, it was hypothesized in the present study, that the patients with the lingual nerve resected and unrepaired, would have the worst sensory outcomes after reconstructive surgery. Overall, it was expected that the patients with the lingual nerve left intact would have the greatest functional sensory outcomes, given the continuity of sensory innervation.

Results from the current study showed that there were no differences between groups for taste, light touch, form and texture. However, significant differences were found between surgical groups for temperature and two-point discrimination on the affected tongue side.

Thermal sensations in the tongue are divided into two categories, warm and cold, which are perceived by specific receptors in the mucosa, called thermoreceptors (Jacobs et al., 2002). Thermoreceptors (temperature) and nociceptive (pain) sensory fibres dominate sensory innervation of much of the oral cavity including the tongue, faucial pillars, and palate (Miller, 2002). The results of this study indicated differences in patient perception of temperature based on type of surgical repair. As expected, when the lingual nerve was left intact after surgery, patients performed significantly better on measures of temperature at the affected tongue tip than those who had the lingual nerve severed and unrepaired, and from those who had the nerve repaired with a cable-graft. There were no differences in temperature sensation for patients with the lingual nerve reanastomosed, suggesting superior sensory outcomes to other types of nerve repair. These findings are congruent with literature on microsurgical nerve repair, which suggests that direct end-to-end anastomosis (reanastomosis) will generally provide superior sensory results over an interpositional graft (Shindo, 1999) as well as over spontaneous recovery of a severed nerve.

Two-point discrimination involves pressure receptors of the tongue (mechanoreceptors). However, two-point discrimination also requires higher level processes that lead to the perception of two points instead of one. The ability of our sensory system to distinguish between two points of stimulation occurs through a mechanism called lateral inhibition (Kuriakose, Loree, Spies, Meyers, & Hicks, 2001) where sensory information is processed in a series of complicated relay nuclei within the brain. In the current study, patients with the lingual nerve intact had better outcomes for two-point discrimination at the affected tongue tip and body as compared to all other patients with or without nerve repair. As expected, these results highlighted that continuity of the lingual nerve provides superior sensory results over lingual nerve repair. Regardless of lingual nerve damage or repair, patients in this population could expect decreased levels of fine touch discrimination, possibly affecting oral perception of bolus size in relation to mastication and swallowing. However, a study by Engelen, van der Bilt and Bosman (2004) suggests that two-point discrimination only stimulates the superficial receptors of the tongue involving fine touch, and that the oral perception of bolus or sphere size excites more deeply-set receptors which appear to be critical in masticatory performance and swallowing.

The perception of thermal sensations requires a lesser degree of acuity than two-point discrimination, where the latter requires a greater distribution and number of receptors in the oral mucosa for discrimination, as well as higher level processes to determine a stimulus through lateral inhibition. These sensory differences may help explain why all patients with nerve repair have poorer outcomes for two-point discrimination (tongue tip and body) than for temperature (only tongue tip). When lower levels of acuity are required to detect a stimulus (as with temperature), surgical repair with direct anastomosis may be able to provide superior results to a cable-grafted or severed nerve. However, changes in two-point discrimination at the tongue tip and body may also be due to changes in the networks that underlie lateral inhibition, as well as a reduction in receptor density. Thus, all nerve repairs may be inadequate in providing appropriate sensory recovery from nerve regeneration alone. As well, when the lingual nerve is left severed and unrepaired, sensory recovery for two-point discrimination would be inadequate due to the limitations of spontaneous nerve regeneration and the physiological effects of synaptic stripping from neural degeneration. When synaptic stripping occurs in a severed nerve, recovery of sensory function is impaired and synaptic function is depressed, leading to insufficient sensory outcomes.

The clinical significance of sensory outcomes as assessed in the present question are two-fold. First, one type of surgical repair over another may not have a significant impact on overall sensory outcomes for taste, light touch, form and texture. However, temperature detection may be impacted by the surgical repair selected, where direct anastomosis may provide superior results to cable-grafting. Second, patients left with an intact lingual nerve have superior sensory outcomes over all other surgical groups for two-point discrimination and thermal sensation.

Question #2: Within the patient group, does the surgically affected side of tongue perform significantly worse than the unaffected side of tongue on sensation measures?

The removal of tissue surrounding a tumour is necessary in tongue resection and varies from patient to patient depending on tumour size. During reconstructive surgery of the base of tongue, the hypoglossal and/or lingual nerves can be damaged on one side, affecting the motor innervation of the extrinsic and intrinsic lingual muscles, and/or the sensory relay of information from the anterior two-thirds of the tongue. Thus, side of tongue for patients in the present study was classified as either affected or unaffected based on the side in which the majority of the surgical resection occurred. If the nerves were left intact but surgical resection occurred predominantly on one side, that side of resection was still classified as affected. In this study, it was important to investigate the differences between the affected and unaffected sides of a patient's tongue in an effort to appreciate the impact of surgery. It was hypothesized that the affected side of the tongue in the patient group would have some return of sensory function, although below normal levels. Thus, the affected side of the tongue would measure significantly worse than the unaffected side of the tongue due to surgical resection and possible nerve disruption or repair. Additionally, it was important to examine the possibility of asymmetrical sensory function in the tongue. By comparing both the affected and unaffected tongue sides after surgical repair, it was possible to gain a better understanding of the tongue relative to perturbed versus relatively unperturbed dynamics. While it was not possible to measure sensory compensation in this current paradigm, the possibility of the unaffected side of the tongue compensating for sensory loss on the contralateral side is supported by the nature of lingual nerve distribution. In the anatomical literature of the tongue, Rusu, Nimigean, Podoleanu, Ivaşcu, and Niculescu (2008) found that 1 of 6 adult cadaver tongues exhibited lingual fibres crossing midline on the ventral surface of the tongue tip, essentially heightening the distribution of sensory fibres contralaterally.

Results of the present study showed that there were significant differences between sides of the tongue on all focal sensation measures. In this patient group, the affected side of the tongue (tip and body) showed significantly worse outcomes for temperature, light touch, two-point discrimination and taste than the unaffected side of the tongue. Clinically, these results highlight the limitations of sensory recovery in the anterior tongue after reconstructive surgery, even with lingual nerve repair. One side of the tongue remains defected on varying levels of sensation as compared to the untouched, unaffected tongue side. These results are consistent with previous findings, indicating that intraoral sensation (light brush, pin prick, temperature, light touch) had deteriorated 6 months after radiotherapy and surgery for oral or pharyngeal cancer in patients, and had persisted 1 year after treatment for the operated side of tongue (affected side) as compared to healthy controls (Bodin, Jäghagen & Isberg, 2004). Bodin et al. (2004) also found an association between postoperative sensory deterioration and resection of the lingual nerve.

Whereas patients may suffer from a loss of taste sensation (gustation) on one side of the tongue, taste is more realistically perceived as a whole mouth sensation involving receptors on the whole tongue, soft palate and epiglottis. Saliva also plays an important role in taste sensation, as specialized gustatory receptors in the oropharyngeal mucosa are stimulated by chemicals dissolved in the saliva (Scrivani, Moses, Donoff & Kaban, 2000). The stimulation of these receptor cells must occur before a taste sensory signal can be sent to the lingual nerve. The majority of patients in the current study (28 of 30) had radiation therapy post-surgery, which can cause xerostomia. This decrease in saliva production in the oral cavity could also severely impact the patients' sense of taste. However, while patients in this study had objective sensory differences in taste sensations between tongue sides, they would most likely be unable to isolate taste dysfunction to a specific area or side of the tongue when eating or drinking. This is due largely to the fact that taste sensations (gustation) only play a small part of the overall perception of flavour that we experience when eating and drinking. Flavour of food and beverages is perceived by various inputs from multiple sensory systems (Veldhuizen, Shepard, Wang & Marks, 2010). The inputs come from olfaction (smell), gustation (produces sweet, sour, salty, bitter and savory taste sensations) and somatosensations such as texture and temperature (Veldhuizen et al., 2010). Thus, patients' decreased sense of taste sensation (gustation) on the affected side of the tongue would only play a small part of their overall perception of the flavour of food and drinks.

The perception of taste and flavour also plays an important role in patient functional outcomes. In a retrospective study by Scrivani et al. (2000) the authors examined patient perception of whole mouth taste sensation after lingual nerve repair. They found that the majority of patients perceived whole mouth taste as abnormal, and while 82% of patients had objective improvements in sensory function after nerve repair, only 35% of the patients reported an improvement in whole mouth taste sensation. Thus, patients may perceive and report overall taste function as deteriorated or abnormal following surgery, even though somatosensory function may have actually improved. Again, this could be explained by the combination of factors that play a role in taste perception e.g. saliva, sensory input, and flavour perception e.g. taste, temperature, texture, smell.

In the present study, 93% of the patients also were treated with postoperative chemotherapy and/or radiotherapy, which could play a part in their deteriorated sensory function for taste, two-point discrimination, light touch and temperature on the surgically affected side of the tongue. Radiotherapy can cause fibrosis in the oral cavity, essentially altering sensory function through the stretching of tissues (Bodin, et al., 2004). Bilateral radiotherapy could also affect sensation for both sides of the tongue, whereas unilateral radiotherapy restricted to the side of the tumor may not affect sensation on the non-tumor side (Bodin et al., 2004). Overall, the combination of surgical resection/repair of the lingual nerve and radiotherapy could negatively affect the outcomes of sensory function in the tongue (Bodin et al., 2004), and lingual nerve involvement may not singly explain the observed sensory loss in this patient population.

This study provides insight into surgical nerve repair in this patient population, emphasizing the limitations of surgical intervention for sensory functions such as taste, temperature, two-point discrimination and light touch on the affected side of the tongue. However, these results do not address the issue of sensory differences between the affected and unaffected sides of the tongue based on type of nerve repair, or having the lingual nerve left intact or resected. As well, to further examine the impact of surgery and the possibility of asymmetrical sensory function, we would need to compare sensation between the unaffected tongue side and the control group. While the data from the current study cannot address compensatory sensory function by the unaffected side of the tongue, it does provide evidence that the unaffected side maintains or preserves sensory function similar to that exhibited by controls. These issues are addressed in the following question.

Question #3: Between the patient group and age-matched control group, do the control participants perform significantly better on focal sensation measures than the patients (divided by type of lingual nerve intervention) on the affected and unaffected sides of the tongue?

Results of the current study indicated that the matched control participants performed significantly better than patients with lingual nerve involvement for the affected tongue side, tip and/or body, depending on the sensation measured. Thus, regardless of type of lingual nerve repair/resection, decreased levels of sensory function were observed in the patient group when compared to healthy controls. Previous literature also has shown decreased sensory function of the anterior tongue after surgical reconstruction with nerve repair. A study by Bodin et al. (2004) examined intraoral sensations pre- and post-surgical treatment and radiotherapy for oral and pharyngeal cancers. The authors compared pre-treatment measures of patients to reference individuals, which showed no significant differences for side of tongue, between patient and control groups, or between oral and pharyngeal cancer groups. Overall, they found that light brush, pin-prick, heat and cold sensations were significantly decreased on the affected tongue side post radiotherapy and surgery with lingual nerve resection as compared to pre-treatment measures. However, the authors did not account for type of nerve resection or repair, and the sample included both oral and pharyngeal cancers, though there were no significant differences in sensation between cancer groups.

As expected, patients with the lingual nerve intact did not perform significantly different from the control group or the unaffected side of the tongue on measures of light touch, taste, two-point discrimination and temperature. There is no known literature on base of tongue reconstruction that has examined specifically the results of lingual nerve continuity on the surgically affected side of the tongue for the anterior native tissue, nor has any study compared these patients to a healthy control population. Further research is required to confirm and explore the sensory outcomes of preservation of the lingual nerve in this patient population for the native tissue of the anterior tongue.

Currently, research has not fully investigated type of lingual nerve intervention in oropharyngeal reconstruction and its effects on the anterior tongue tissue for sensory outcomes. However, the results from the present study showed that there were differences between patients and controls according to how the lingual nerve was repaired, with varying outcomes for the affected tongue tip versus the affected tongue body. Patients with the lingual nerve reanastomosed performed significantly worse than matched control subjects on measures of temperature at the tongue body, light touch and two-point discrimination for the tongue tip and body, and taste on the affected tongue side. Patients with the lingual nerve cable-grafted performed significantly worse than matched control subjects only at the affected tongue tip for temperature and two-point discrimination. Patients with the lingual nerve cut performed significantly worse than matched control subjects only on light touch and two-point discrimination (both fine touch sensations) at the affected tongue tip. Statistical analysis indicated that patients with the lingual nerve cut performed better than the other surgical subgroups, when compared to the control group, and that the lingual reanastomosed patient group performed the worst in comparison to matched controls. These results were unexpected, given that direct anastomosis of peripheral nerves can provide superior sensory outcomes in microsurgical nerve repair to interpositional grafts (Pogrel & Maghen, 2001; Dvali & Mackinnon., 2007; Shindo, 1999), and also evidence indicating that the spontaneous recovery of a transected lingual nerve is limited (Holland, 1996). However, as presented in question 1, when comparing patients according to type of lingual nerve involvement, there is statistical evidence that direct anastomosis of the lingual nerve does provide superior sensory outcomes to other types of lingual nerve repair and resection. The large differences in sensation when compared to matched controls may be directly related to differences in sample size and statistical power. Patients with the lingual nerve reanastomosed comprise the largest group (n=12) from the patient sample, approximately double the size of the cable-graft (n=7) and severed lingual nerve (n=5) groups. The smaller sample sizes of the cable-graft and severed nerve groups, as well as the large variability within groups, decreases the statistical power of the analysis so that it is more difficult to find statistically significant differences. However, when examining the mean scores for the patient groups, it is apparent that the reanastomosis group performed better than the cable-graft group, and better than the cut group when compared to matched controls. With increased sample sizes for lingual nerve intervention involving cable-grafting and resection, we would expect similar trends in the data, such that each group would show significantly worse measures of focal sensation when compared to matched controls. Future research could address these limitations by increasing the sample sizes for type of nerve intervention after reconstructive surgery and comparing intraoral sensation to a control population.

As expected, there were no differences in tongue sensation between matched control subjects and patient groups for the unaffected side of the tongue on any measures of focal sensation. In contrast to our results, a study by Loewen, et al. (2010) reported that the unaffected tongue side in hemiglossectomy patients did have decreased levels of two-point discrimination at the tongue tip as compared to a healthy control population. However, it is not surprising that decreased levels of sensation were found in their patient group on the unaffected tongue side, as the surgical reconstruction occurred more closely to the native tongue tissue, likely disturbing the nerve branches in the tongue. Presently, there are few known studies that have examined the specific effects of base of tongue reconstruction on the unaffected tongue side, nor have many compared the unaffected side to a healthy control group. Current studies in surgical reconstruction for head and neck cancer often use the unaffected side of the tongue as a control to compare to the affected tongue side (Kuriakose et al., 2001; Sabesan et al., 2008). According to the results of this study, it could be deemed appropriate within this patient population to use the unaffected tongue side as a control, given that there are no differences in focal sensory function from a healthy control group.

This study has shown that continuity of the lingual nerve in base of tongue reconstruction will provide patients with the best sensory outcomes for the anterior tongue for taste, temperature, two-point discrimination and light touch. With the lingual nerve intact, patients could expect that both sides of the tongue may be comparable to a healthy control population. For patients with lingual nerve intervention on the affected tongue side, they may expect decreased levels of sensory function compared to healthy controls. However, regardless of the type of lingual nerve intervention, the unaffected tongue side will remain normal on measures of taste, light touch, two-point discrimination and temperature.

Question #4: Between the matched control group and patient surgical groups, does the control group perform significantly better for whole-mouth sensations form (stereognosis) and texture?

In this study, form (stereognosis) and texture were used to analyze whole-mouth sensations. Stereognosis involves oral manipulation and palpation of shapes within the oral cavity, and requires cortical evaluation of the sensory input to help differentiate and compare the shapes to previously stored images (Dahan, Lelong, Celant, & Leysen, 2000). Stereognosis is a psychophysical measure of perception that is applicable to the oral cavity (Dahan et al., 2000), even though it also involves sensory receptors in nearby structures such as the muscles, tendons and temporomandibular joints (Jacobs, Bou Serhal, & van Steenberghe, 1998). Texture is detected by the mechanoreceptors in the oral mucosa, and involves friction across the surface of the tongue to stimulate the underlying receptors (Engelen & Van der bilt, 2008). The sensory discrimination of texture was only applied to the surface of the tongue, whereas stereognosis allowed for the use of the tongue and hard palate. It was hypothesized that patients with lingual nerve intervention would show decreases in sensory function for form and texture when compared to the matched control subjects. Patients with the lingual nerve left intact would be expected to be comparable to the control group, with no significant differences in sensory function for form and texture. However, the present results showed that the patients with the lingual nerve intact performed significantly worse than its matched controls for form. One possible explanation is the higher mean score for the lingual intact matched control group (M = 16.67) in comparison to the other control groups (*M* = 13.17, 14.00, 14.29), although there were no significant differences noted. Another explanation is the confounding variables affecting oral stereognosis. Whereas patients with the lingual nerve intact and their matched controls were the youngest overall group (mean age = 55), with only one patient reporting severe problems with his/her teeth, the learning effect, memory and cultural factors may have played a role in these unexpected results.

The patients with the lingual nerve reanastomosed were comparable to the matched control subjects, with no significant differences in form or texture. However, patients with the lingual nerve cable-grafted showed significantly worse scores for form than matched control subjects. Based on the literature, these results confirmed that direct anastomosis of a nerve can provide superior sensory results to using a cable-graft (Shindo, 1999; Pogrel & Maghen, 2001; Dvali & Mackinnon., 2007) in relation to form recognition or stereognosis. However, stereognosis can be enhanced with training, and there is evidence that performance can be affected by age, culture, and dental factors, as well as the orthodontic state of the oral cavity (Dahan et al., 2000). Many of the patients in this study were dealing with dentures, prosthetic implantations, loss of teeth, decreased range of motion for jaw opening, and/or difficulties with chewing food. The differences in form recognition when comparing to a control population may be due more to these dental and orthodontic factors than to the presence of lingual nerve repair/resection, although dentition and orthodontic factors were not grouping variables within the current study.

Patients with the lingual nerve cut had significantly worse scores for texture than matched controls. Texture recognition is of great importance for the appreciation of food (Szczesniak, 1963a; Matsumoto & Matsumoto, 1977; Lucas et al., 2004; Nishinari, 2004; Engelen & Van der bilt, 2008) and for the recognition of food. Taste provides only a part of the ability to recognize and appreciate food products. Previous work showed that taking away texture cues by blending food products resulted in correctly identifying only 40% of the products based on their flavour alone (Schiffman, 1977; Engelen & Van der bilt, 2008). The addition of a deficit in texture recognition may influence taste sensation negatively, although it may only play a small role in the overall perception of taste and flavour.

The results of the present study showed that type of nerve repair plays a role in whole-mouth sensations, where reanastomosis of the lingual nerve provides the best sensory outcomes for texture and stereognosis. Clinically, patients who have the lingual nerve cable-grafted or severed may have difficulty with the recognition and location of a bolus in the oral cavity, leading to problems with swallowing and mastication.

Question #5: Does lingual nerve intervention affect motor function in the patient group as compared to the control group?

In the present study, motor function was defined as the absence or presence of tongue deviation, fasciculations, and/or muscle atrophy. Currently, there is no standardized objective protocol to measure motor function of the tongue. Tongue mobility can be affected by both the quantity and degree of postoperative and/or postradiotherapy fibrosis (Urken et al., 1991; Cicconetti et al., 2000), affecting tongue protrusion and retrusion, as well as creating deviation upon protrusion. Tongue mobility also can be affected by the presence of motor innervation. Motor nerve repair of the hypoglossal nerve may result in the return of some motor function of the tongue, although full functional recovery after peripheral nerve injury is rarely achieved. The majority of patients in this study had post-surgical chemotherapy and/or radiotherapy, which are known to negatively affect motor innervation and tongue mobility due to fibrosis. Thus, motor function outcomes based on surgical intervention alone cannot be addressed within this studies' paradigm. However, it would be expected that patients with hypoglossal nerve involvement would have decreased levels of motor function due to the primary motor innervation of the tongue through cranial nerve XII.

Recently, studies have examined the role of the lingual nerve in motor control of the extrinsic lingual muscles. Anatomically, there are different areas of anastomoses between the hypoglossal and lingual nerve within the muscles of the tongue, indicating areas of sensorimotor reflex loops, and possible effects of the sensory nerve for motor function. In an article by Saigusa, Tanuma, Yamashita, Saigusa and Niimi (2006), the researchers performed nerve fiber analysis and histological study for the lingual nerve in adults, which linked the lingual nerve to neuromotor control of the tongue in conjunction with the hypoglossal nerve.

The present results advance our understanding related to the consequences of lingual nerve intervention on motor function in patients who have had reconstructive surgery affecting the base of tongue. For example, the current results showed that there were no differences in motor function between patient groups based on sensory nerve repair alone. Regardless of type of lingual nerve repair (reanastomosis or cable-graft) or damage (severed), motor function remained unaffected. Not surprising, when both the lingual and hypoglossal nerves were affected, motor function was significantly worse than when both nerves were left intact. Unfortunately, there were no patients in the present sample that had the lingual nerve intact and only the hypoglossal nerve affected, making it impossible to isolate the effects of hypoglossal nerve damage on motor function. However, these results highlight the importance of motor and sensory nerve repair in surgical reconstruction. Whereas damage to the lingual nerve alone does not appear to affect motor function based on deviation, fasciculations, and muscle atrophy, the combination of hypoglossal and lingual nerve damage does have negative effects.

Motor function also involves far more than dysfunctions in tongue protrusion (deviation), muscle atrophy, and fasciculations. Clinical evaluation of tongue motor skills often includes tongue lateralization, protrusion and retrusion, up/down movements, and observations for accuracy, speed, signs of deviation, atrophy, tremors, and/or fasciculations. Further clinical evaluation would include measurements for speech production, and examining the affects of tongue motor skill defects on overall speech intelligibility. A study by Koshino, Hirai, Ishijima, and Ikeda (1997) also examined tongue motor skills through ultrasound analysis in relationship to mastication. Videofluoroscopic swallowing studies (VFSS) attempt to measure tongue motor skills indirectly, by examining swallowing function. A study by O'Connell et al. (2009) examined the oral residue, bolus oral transit time, and aspiration scores of patients after hypoglossal and lingual nerve reconstruction in head and neck cancer. The present study included a limited definition of motor function of the tongue, and therefore would require further clinical examination in order to provide a better understanding of motor outcomes and type of surgical intervention applied. The present data do not allow for the separation of the effects of sensory nerve damage, motor nerve damage, or radiotherapy fibrosis on tongue motor function.

Question #6: Within the patient group, are there significant differences between type of lingual nerve intervention and quality of life responses for the UW-QOL survey (University of Washington Quality of Life) and the EORTC QLQ-H&N35 survey (European Organisation for Research and Treatment of Cancer, Quality of Life – Head and Neck)?

The functional outcomes of reconstructive surgery can directly or indirectly affect a patient's social, psychological, and emotional well-being, consequently influencing their quality of life. In the current study, quality of life analysis found that two specific domains for the UW-QOL survey were significantly different among surgical groups including: mouth pain and amount of saliva production. The other survey used in this study was the EORTC QLQ-H&N35 survey, which showed significant differences between surgical groups for four different domains: Swallowing, dry mouth, trouble with social eating, and less sexuality. Previous literature on health-related quality of life has compared patients with oropharyngeal reconstruction to other head and neck cancer patients, examining overall trends in QOL (quality of life) for standardized questionnaires and attempting to correlate QOL to functional outcomes. For example, Pepjin et al. (2007) found that patients who have undergone oral or oropharyngeal reconstruction often have to deal with three major factors affecting their quality of life: speech, the ability to eat, and physical appearance. However, previous literature has not examined the effects of type of nerve repair, e.g. direct anastomosis versus cable-grafting, on health-related QOL outcomes in patients who have undergone oropharyngeal reconstruction.

The results for the UW-QOL questionnaire showed that patients with both nerves intact had significantly better QOL responses than the patients with lingual and/or hypoglossal nerve involvement. Clinically, this highlights the importance of lingual and hypoglossal nerve preservation in base of tongue reconstruction, and the effects of tongue sensorimotor function on QOL outcomes for mouth pain and saliva. For pain in the mouth, the results of this study show that reanastomosis of the lingual nerve and lingual nerve continuity provided superior QOL outcomes to having the lingual nerve cable-grafted.

The results for the EORTC questionnaire showed that patients with both nerves affected had significantly worse QOL responses than the other patient groups, most often worse than patients with the both nerves intact and/or the lingual nerve reanastomosed. For the QOL domains swallowing and trouble with social eating, patients with both nerves affected had significantly worse QOL responses than patients with both nerves intact, the lingual nerve reanastomosed, and the lingual nerve cut. There were no significant differences for these QOL domains between patients with both nerves affected and with the lingual nerve cable-grafted, also suggesting poorer quality of life outcomes for patients with a cable-graft nerve repair. However, most prominent is the implication that patients who have experienced both sensory and motor nerve repairs appear to have poorer QOL outcomes related to swallowing, dry mouth, social eating and sexuality, indicating an association between tongue sensorimotor function and QOL.

The UW-QOL survey also calculates a physical function score, based on the average domain scores for saliva, speech, chewing, swallowing, taste, and physical appearance (Lowe & Rogers, 2008). The questionnaire used in this study included saliva A (amount) and B (consistency), thus the physical function score was calculated based on the average of 7 different domains. Results showed that patients with both nerves affected scored significantly worse in physical function than patients with both nerves intact. Clinically, this also highlights the impact of tongue sensorimotor function on health-related QOL for patients with base of tongue reconstruction.

In this study, the two standardized QOL questionnaires did not yield consistent findings. Most notable was that the EORTC QLQ-H&N35 questionnaire identified swallowing as an issue between patient groups, whereas the UW-QOL survey did not. Conversely, the UW-QOL survey identified pain in the mouth as an area of concern for patients, although the EORTC survey only examines pain as a general question (including pain and soreness in the mouth, and pain in the throat and jaw) which was not significantly different between patient groups. The EORTC also found differences between patient groups for less sexuality and trouble with social eating, which are issues that are not addressed in the UW-QOL survey. There is some overlap between surveys in identifying amount of saliva (UW-QOL) and dry mouth (EORTC) as significant domains between patient groups, as these questions refer to the same issue but are simply worded differently. The current results have implications for research using QOL questionnaires as a functional outcomes measure, given the dissimilar results observed between the two standardized questionnaires in this study. In the literature, researchers may misuse QOL questionnaires as a way to measure functional outcomes in patient populations, and will blur the lines between "quality of life", "functional status" and "functional outcomes". Functional status can be defined as the patients' ability to perform typical daily activity, eating, and swallowing (D'Antonio, Zimmerman, Cella, & Long, 1996; Netscher, Meade, Goodman, Alford, & Stewart, 2000), whereas quality of life is a more global concept that is subjective and multidimensional, including emotional, mental and physical status (Cella & Bonomi, 1995; Netscher et al., 2000). Functional outcomes are objective measures of treatment, such as sensory function, swallowing function or speech intelligibility. Often researchers will use the terms functional status and quality of life interchangeably, although it is recognized that they mean two separate things. However, a study by Brown, Rogers and Lowe (2006) suggests that a QOL questionnaire such as the UW-QOL can be used as an accurate measure of function as well as health-related QOL according to support from previous studies. The studies that Brown et al. (2006) refer to compared objective functional measures to UW-QOL questions and found equivalent results within the same patient sample e.g. a soft palate functional study where speech intelligibility and a video swallow were used with UW-QOL swallowing and speech questions, finding similar results (Brown, Zuydam, Jones, Rogers & Vaughan, 1997). However, the results of this study would suggest that it would not be appropriate to assume functional outcomes based on QOL responses, given varying results within the same population on two standardized questionnaires widely used in head and neck cancer populations. Additionally, the patients in this study exhibited decreased levels of sensory function on the affected side of their tongue involving taste, two-point discrimination, light touch and temperature, although the two QOL questionnaires did not show equivalent results for taste or senses.

In the current study, an older version of the UW-QOL was used for quality of life analysis. Differences between the version used and the newest UW-QOL (version 4) are the addition of mood, anxiety and shoulder to version 4, as well as global health-related quality of life questions with rating scales. If the UW-QOL version 4 was used, it was not expected that results would have been changed. Saliva may still have been significant, as the newest version gets rid of Saliva B but maintains responses most similar to Saliva A. Mouth pain would not have shown up with the newest version, as all three pain domains were amalgamated into one domain for general pain. The newest domains mood, anxiety and shoulder may or may not have been significant. However, interviews were conducted to provide further insight and depth into the patient's health-related quality of life, also pertaining to their social, emotional, and psychological well-being. The qualitative analysis of interviews with patients can help supplement the limitations of the QOL questionnaires, and provide further information about patient's concerns following reconstructive surgery for the base of tongue.

T-stage Cancer and % Base of Tongue Resection

Prior research has shown that the percentage of the base of tongue resected in oropharyngeal cancer can have an effect on speech and swallowing outcomes (Rieger et al., 2007). The T-stages in cancer refer to the size of the tumor, and correspond to the amount of tissue that will be resected from the region. When relating nerve intervention to quality of life, it is also important to investigate the possible effects of T-stage and percent of base of tongue resection on patient outcomes. The results of this study revealed that only one QOL domain on the EORTC scale (sexuality) was related to T-stage. The percentage of base of tongue resected did not appear to influence the results of the EORTC. Results related to the UW-QOL questionnaire appear to be influenced to a greater degree by T-stage, having an effect on Physical Function, Chewing and Swallowing outcomes. As with the EORTC, the percentage of base of tongue resected did not appear to be influential. Although the results related to T-stage were statistically significant, their clinical significance must be questioned. While T-stage is related to the amount of tissue resected, the greatest impact on function is the actual amount of tissue resected. Being that the percentage of resection did not influence the results on either QOL scale, the differences in QOL outcomes reported in the present study appear to be a consequence of type of nerve repair.

Qualitative Analysis: Quality of Life Patient Interviews

The quality of life interviews consisted of open-ended questions about patients' concerns and experiences after their surgery. The questions offered patients the opportunity to comment and expand upon quality of life issues that affected them in their daily life and social activities. The results of the qualitative analysis of patient interviews provided a dimension of quality of life not currently realized by standardized tools. The main themes emphasized throughout the patient interviews were: depression, frustration, social isolation, and social and livelihood limitations. However, the most resounding issues were around eating. Many participants were putting themselves at physical risk in order to eat during social situations, such as out with friends or family, eating at a restaurant or partaking in a celebration or event. For example, many patients stated that they would eat food more quickly or take larger bites in order to keep pace with others, despite knowing it could lead to a choking episode or get them into trouble when swallowing. Many patients also routinely ate alone when at home, isolating themselves from their families. Some important coping strategies also emerged from the interviews, such as social withdrawal and avoidance, denial, anger and externalization. Many patients had become passive or passive aggressive in their behaviours and attitudes. However, a few patients had succeeded in acquiring more positive coping strategies, such as forming support groups, engaging in physical activities, and engaging in new hobbies. Overall, the patient group appeared to be doing only marginally well, with 2 or 3 participants exhibiting extreme emotional vulnerability from a psychological standpoint. The composite of psychological stressors and coping strategies provided further insight and depth of understanding about the quality of life of this patient group, emphasizing the limitations of using standardized questionnaires to examine quality of life issues in this population. However, qualitative analysis and extended patient interviews on QOL are not clinically appropriate in most settings, as the collection and analysis of data can be time-consuming and costly.

Overall, the patients in this study had decreased levels of quality of life as exhibited through patient interviews and standardized questionnaires. Appendix K presents graphical information about the overall mean score responses for the UW-QOL and EORTC QLQ-H&N35 questionnaires within the patient group.

Study Limitations

Patient selection was limited by the inclusion criteria for participation in this study, as patients were taken from a convenience sample of 80 patients who had undergone reconstructive surgery for the base of tongue. In order to answer the research questions, statistical power was limited by the varying sample sizes for surgical nerve involvement, ranging from 5 to 12 participants per group. Parametric statistics were used to analyze the data, despite uneven distributions in our populations. However, Shoukri and Pause (1999) state the following:

> It has been reported (Miller, 1986, p.80) that lack of normality has very little effect on the significance level of the F-test. The robustness of the F-test improves with increasing the number of groups being compared, together with an increase in the group size. (p. 1)

Conversely, heterogeneity of variances can be more serious for unbalanced populations, particularly if a large standard error is associated with a small sample size. Statistical research recommends balancing the experiment whenever possible in order for unequal variances to have the least effect (Shoukri & Pause, 1999).

This study uses objective sensation testing and a standardized protocol to examine the sensory outcomes of patients after reconstructive surgery of the base of tongue. However, the testing protocol requires the use of hand-held instruments, increasing potential for experimental error and variance. With hand-held instruments, the experimenter is unable to keep constant the contact duration, force levels and rate of application for light touch, two-point discrimination and temperature. The measurement of taste also is limited by experimental conditions, due to variability in the area of the tongue that is swabbed by the experimenter, rate of application and contact duration. The taste map for each participant is not absolute, with dominant taste receptors varying in each individual for placement and area. The patient population also had increased functional barriers to reliable testing, such as limited jaw opening creating difficulty in accurate testing, decreased saliva production possibly affecting taste sensations, and increased levels of fatigue with prolonged testing times.

Conclusion

For all focal sensation measures (temperature, two-point discrimination, light touch, and taste) the sides of the tongue with lingual nerve repair or resection had significantly worse perception as compared to the unaffected sides of the tongue and to matched control subjects. However, surgical reconstruction that involves preservation of the lingual nerve provides the best sensory outcomes for patients, and surgical nerve repair with direct anastomosis appears to provide the best option for sensory recovery. Motor function was not affected by damage or repair to the lingual nerve, although showed decreased levels of function when both hypoglossal and lingual nerves were affected as compared to both nerves preserved. The standardized quality of life questionnaires provided insight into domains that were significantly different between surgical groups, such as swallowing, dry mouth/saliva, trouble with social eating, less sexuality, and pain in the mouth. Differences between patient groups were based on lingual and/or hypoglossal nerve intervention, where patients with both nerves affected generally showed poorer QOL responses than patients with both nerves intact or with the hypoglossal nerve intact and the lingual nerve reanastomosed. However, there were differences between the domains identified by each questionnaire, emphasizing the importance of using the UW-QOL and EORTC questionnaires as simple measures of quality of life versus functional outcome measures. Attempts to compare the questionnaires were limited by the varying responses, scales, and domains on each. Qualitative analysis of patient interviews uncovered many more areas of concern for patients than documented with standardized questionnaires. Some of the major themes for QOL issues were depression, frustration, social isolation, and social and livelihood limitations. Resounding problems around eating were identified. Patients reported putting themselves at physical risk in order to eat during social situations, and routinely found themselves eating alone when at home. Some important coping themes also surfaced from the interviews, including social withdrawal and avoidance, denial, anger and externalization. Many patients also had become passive or passive aggressive in their behaviours and attitudes. Positive coping strategies for some patients were also identified, including forming support groups, engaging in physical activities, and picking up new hobbies. Future research could expand upon the quality of life issues that affect this patient population as surgical interventions continue to improve. The functional outcomes of this population also could be explored following surgery and nerve repair, such as speech, swallowing and taste and their effects on quality of life.

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Appendix A

Patient Recruitment Letter

Date

Patient Name
Patient Address

Dear *Patient Name,*

A Master's student at the University of Alberta is doing a research study for her thesis. We would like your help. The study is looking at tongue sensation and quality of life after reconstruction of the tongue. If you decide to participate, we would need about 45 minutes of your time. The study will take place at IRSM (previously known as COMPRU) in the Misericordia Community Hospital, where you have been seen before to assess your speech and swallowing function after your surgery. You will be compensated for your parking up to a cost of $10.00.

We will assess the sensation of parts of your tongue using simple tests. We will test your tongue function by having you move the tongue in different ways. We will ask you a number of questions about your tongue sensation and about your quality of life. We will also ask you to fill out a brief survey about your quality of life.

By participating you will add to scientific knowledge about the relationship between tongue sensation and quality of life. The information you provide could help ensure the best treatment procedures for future head and neck cancer patients. You may refuse to participate or choose to withdraw from the study at any time. Information will be kept strictly confidential. There are no known risks to participating in this study.

We will be contacting you by phone in about two weeks. You will be able to ask any questions about the study at that time. You can say "no" at the time we contact you with no consequences to your treatment. If you do **not** want to be contacted, please call Sandie Pouliot at 780-735-2575. There will be no consequences to your treatment. Thank you for your time and consideration.

Sincerely,

Jana Rieger, PhD
Program Director, Functional Outcomes
Institute for Reconstructive
Sciences in Medicine (iRSM)

Tracy Gaertner, BSc.
Masters Student
University of Alberta

Appendix B

Patient Group - Information Letter

Project Title: Perceptual and physical sensation of native tongue tissue after radial forearm free-flap surgery of the base of tongue: Functional outcomes and quality of life

Investigators: Tracy Gaertner, BSc.
Co-supervisors: Jana Rieger, PhD and Carol Boliek, PhD

Affiliation: Institute for Reconstructive Science in Medicine (iRSM), Misericordia Community Hospital; Department of Speech-Language Pathology and Audiology, University of Alberta

Purpose of Study: You are being asked to participate in this research study because we want to understand the relationship between tongue sensation, tongue function, speech and quality of life for patients following tongue reconstruction. We would like to test your tongue sensation and tongue function.

Procedure: We will test the sensation of the front of your tongue. We will see how you can sense light touch, temperature, the distance between two points, taste, texture, and form. Some sensation tasks will be tested near the front of your tongue, on the left and right sides. Other sensation tasks will use your whole mouth, such as taste, form, and texture. You will be asked to wear a blindfold during the sensation testing. None of the items will cause discomfort. The sensation being tested will be obvious.

- To test temperature, we will place a dental mirror on your tongue and ask you whether it feels warm or cold.
- To test light touch, we will place a thin piece of thread near the front of your tongue. You will be asked if you felt it or not.
- When testing the distance between two points, we will place two blunt points against your tongue. This is another test of touch. You will be asked to respond if you felt two points or one point.
- Form will be tested with small plastic shapes attached to rods. You will be asked to place a shape in your mouth while holding onto the rod. You will be able to move the shape around in your mouth. You will be asked to look at a picture of 12 different shapes and point to the shape that you felt with your tongue.
- When testing your taste sense, we will use 5 flavours. Using a cotton swab, bitter, sour, salty, sweet, or regular water will be swabbed on different areas of your tongue. You will be asked to identify the taste.

- In order to test texture, you will be asked to place a small plastic ball-shaped object attached to a rod on your tongue. You will be asked if the shape feels rougher or smoother compared to another ball-shaped object.

After sensation testing, we will be testing your tongue movement. We will ask you to stick your tongue out as far as you can go, and then move it back into your mouth. After testing your tongue movement, we will ask some questions about your tongue sensation and tongue movement and how they are related to your quality of life. These questions will be audio-recorded so we can note your responses later. We will also record a short sample of your speech. We will ask you to read a short paragraph, 2 lists of 6 sentences, and 25 nonsense words. These will also be recorded for later analysis. Lastly you will be asked to fill out a brief written questionnaire about your quality of life.

The total time you will spend with us will be approximately 50 minutes, and all tasks will be done at iRSM. This time includes 15 minutes of discussing the study and answering any of your questions throughout the tasks. There are no known risks to participating in this study. Your participation in this study will help ensure that future patients with head and neck cancer receive the best possible treatment procedures.

You will be compensated $10 for parking when you arrive, and may withdraw or refuse to participate in this study at any time. You will not need to give a reason. We will need access to your medical records at iRSM regarding your tongue reconstruction, surgery details, and date of birth. The information that we collect from you will be strictly confidential. Your name will not be attached to the data you provide. Your name or identifying information will not be used in any conference presentations or published documents. All information that you provide will be kept for at least 5 years after the study is completed. The researcher will store the information in a locked filing cabinet.

Contact: If you have any further questions about this study, you can contact Dr. Jana Rieger at 780-735-2223 or Dr. Carol Boliek at 780-492-0841

If you have any questions or concerns with the study or the way in which it is carried out, please call: Dr. Glen Griener, Chair, Health Research Ethic Board – Health Panel, 780-492-0302.

Appendix C

Patient Group - Consent Form

Part 1

Title of Project: Perceptual and physical sensation of native tongue tissue after radial forearm free-flap surgery of the base of tongue: Functional outcomes and quality of life
Principal Investigators:
Tracy Gaertner, BSc.
Jana Rieger, PhD and Carol Boliek, PhD (Co-supervisors)
Phone Number: 780-735-2223

Part 2

Do you understand that you have been asked to be in a research study?

Yes☐ No☐

Have you read and received a copy of the attached Information Sheet?

Yes☐ No☐

Do you understand the benefits and risks involved in taking part in this research study?

Yes☐ No☐

Have you had an opportunity to ask questions and discuss this study?

Yes☐ No☐

Do you understand that you are free to withdraw from the study or refuse to participate at any time? You will not have to give a reason.

Yes☐ No☐

Has confidentiality been explained to you?

Yes☐ No☐

Do you understand who will have access to your records, including personally identifiable health information, in order to gain information about your tongue surgery?

Yes☐ No☐

Do you understand that secondary analysis of your data may occur but only after approval is obtained from the Health Research Ethics Board?

Yes☐ No☐

This study was explained to me by: ________________________________

I agree to take part in this study: Yes☐ No☐

By signing the consent form you give permission to the study staff to access any personally identifiable health information which is under the custody of other health care professionals as deemed necessary for the conduct of the research.

Signature of Research Participant: ____________________________________

Printed Name: _________________________________ Date: ___________

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

Signature of Investigator _________________________ Date: __________

If you have any questions or concerns with the study or the way in which it is carried out, please call: Dr. Glen Griener, Chair, Health Research Ethic Board – Health Panel, 780-492-0302.

Appendix D

Control Group - Information Letter

Project Title: Perceptual and physical sensation of native tongue tissue after radial forearm free-flap surgery of the base of tongue: Functional outcomes and quality of life

Investigators: Tracy Gaertner, BSc.
Co-supervisors: Jana Rieger, PhD and Carol Boliek, PhD

Affiliation: Institute for Reconstructive Science in Medicine (iRSM), Misericordia Community Hospital; Department of Speech-Language Pathology and Audiology, University of Alberta

Purpose of Study: You are being asked to participate in this research study because we want to compare your tongue sensation and tongue function to patients with head and neck cancer who have had tongue reconstruction. We will assess your tongue sensation and tongue function, and your speech.

Procedure: We will test the sensation of the front of your tongue. We will see how you can sense light touch, temperature, the distance between two points, taste, texture, and form. Some sensation tasks will be tested near the front of your tongue, on the left and right sides. Other sensation tasks will use your whole mouth, such as taste, form, and texture. You will be asked to wear a blindfold during the sensation testing. None of the items will cause discomfort. The sensation being tested will be obvious.

- To test temperature, we will place a dental mirror on your tongue and ask you whether it feels warm or cold.
- To test light touch, we will place a thin piece of thread near the front of your tongue. You will be asked if you felt it or not.
- When testing the distance between two points, we will place two blunt points against your tongue. This is another test of touch. You will be asked to respond if you felt two points or one point.
- Form will be tested with small plastic shapes attached to rods. You will be asked to place a shape in your mouth while holding onto the rod. You will be able to move the shape around in your mouth. You will be asked to look at a picture of 12 different shapes and point to the shape that you felt with your tongue.

- When testing your taste sense, we will use 5 flavours. Using a cotton swab, bitter, sour, salty, sweet, or regular water will be swabbed on different areas of your tongue. You will be asked to identify the taste.
- In order to test texture, you will be asked to place a small plastic ball-shaped object attached to a rod on your tongue. You will be asked if the shape feels rougher or smoother compared to another ball-shaped object.

After sensation testing, we will be testing your tongue movement. We will ask you to stick your tongue out as far as you can go, and then move it back into your mouth. We will also record a short sample of your speech. We will ask you to read a short paragraph, 2 lists of 6 sentences, and 25 nonsense words. These will also be recorded for later analysis.

The total time you will spend with us will be approximately 50 minutes, and all tasks will be done at iRSM. This time includes 15 minutes of discussing the study and answering any of your questions throughout the tasks. There are no known risks to participating in this study. Your participation in this study will help ensure that future patients with head and neck cancer receive the best possible treatment procedures.

You will be compensated $10 for parking when you arrive, and may withdraw or refuse to participate in this study at any time. You will not need to give a reason. The information that we collect from you will be strictly confidential. Your name will not be attached to the data you provide. Your name will not be used in any conference presentations or published documents. All information that you provide will be kept for at least 5 years after the study is completed. The researcher will store the information in a locked filing cabinet.

Contact: If you have any further questions about this study, you can contact Dr. Jana Rieger at 780-735-2223 or Dr. Carol Boliek at 780-492-0841
If you have any questions or concerns with the study or the way in which it is carried out, please call: Dr. Glen Griener, Chair, Health Research Ethic Board – Health Panel, 780-492-0302.

Appendix E

Control Group - Consent Form

Part 1

Title of Project: Perceptual and physical sensation of native tongue tissue after radial forearm free-flap surgery of the base of tongue: Functional outcomes and quality of life.

Principal Investigators:
Tracy Gaertner, BSc.
Jana Rieger, PhD and Carol Boliek, PhD (Co-supervisors)

Phone Number: 780-735-2223

Part 2

Do you understand that you have been asked to be in a research study?
Yes ☐ No ☐

Have you read and received a copy of the attached Information Sheet?
Yes ☐ No ☐

Do you understand the benefits and risks involved in taking part in this research study?
Yes ☐ No ☐

Have you had an opportunity to ask questions and discuss this study?
Yes ☐ No ☐

Do you understand that you are free to withdraw from the study or refuse to participate at any time? You will not have to give a reason.
Yes ☐ No ☐

Has confidentiality been explained to you?
Yes ☐ No ☐

Do you understand who will have access to your study information?
Yes ☐ No ☐

This study was explained to me by: ________________________________

I agree to take part in this study: Yes ☐ No ☐

Signature of Research Participant: ____________________________________

Printed Name: __________________________________ Date: ___________

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

Signature of Investigator _________________________ Date: __________

If you have any questions or concerns with the study or the way in which it is carried out, please call: Dr. Glen Griener, Chair, Health Research Ethic Board – Health Panel, 780-492-0302.

Appendix F

Table F.1.

Two-point discrimination coding system with code numbers, testing combinations and possible correct responses, and number of correct responses out of 3 possible attempts.

Code #	Two-point discrimination Testing combinations and possible correct responses	# Correct out of 3
0 (all incorrect)	2 two-point, 1 one-point = 0 correct	0
	1 two-point, 2 one-point = 0 correct	0
1 (missed all two-point touches)	2 two-point, 1 one-point = 1 one-point correct	1
	1 two-point, 2 one-point = 1 one-point correct	1
	1 two-point, 2 one-point = 2 one-point correct	2
2 (at least 1 two-point touch felt)	2 two-point, 1 one-point = 1 two-point correct	1
	1 two-point, 2 one-point = 1 two-point correct	1
	2 two-point, 1 one-point = 1 two-point & 1 one-point correct	2
	1 two-point, 2 one-point = 1 two-point & 1 one-point correct	2
*No coding	1 two-point, 2 one-point = 2 two-point correct	2
3 (all correct)	1 two-point, 2 one-point = 1 two-point & 2 one-point correct	3
	2 two-point, 1 one-point = 2 two-point & 1 one-point correct	3

Note. *Responses were not coded for this combination due to low frequency in the population and difficulty in placing the combination into the coding system.

Appendix G

Table G.1.

Light touch coding system with code numbers, testing combinations and possible correct responses, and number of correct responses out of 3 possible attempts.

Code #	Light touch Testing combinations and possible correct responses	# Correct out of 3
0 (all incorrect)	2 touches, 1 sham = 0 correct	0
	1 touch, 2 shams = 0 correct	0
1 (no touches felt)	2 touches, 1 sham = 1 sham correct	1
	1 touch, 2 shams = 1 sham correct	1
	1 touch, 2 shams = 2 shams correct	2
2 (at least one touch felt)	2 touches, 1 sham = 1 touch correct	1
	1 touch, 2 shams = 1 touch correct	1
	2 touches, 1 sham = 1 touch & 1 sham correct	2
	1 touch, 2 shams = 1 touch & 1 sham correct	2
*No coding	1 touch, 2 shams = 2 touches correct	2
3 (all correct)	1 touch, 2 shams = 1 touch & 2 shams correct	3
	2 touches, 1 sham = 2 touches & 1 sham correct	3

Note. *Responses were not coded for this combination due to low frequency in the population and difficulty in placing the combination into the coding system.

Appendix H

EORTC QLQ - H&N35 Questionnaire

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by circling the number that best applies to you.

During the past week:	**Not at all**	**A little**	**Quite a bit**	**Very much**
31. Have you had pain in your mouth?	1	2	3	4
32. Have you had pain in your jaw?	1	2	3	4
33. Have you had soreness in your mouth?	1	2	3	4
34. Have you had a painful throat?	1	2	3	4
35. Have you had problems swallowing liquids?	1	2	3	4
36. Have you had problems swallowing pureed food?	1	2	3	4
37. Have you had problems swallowing solid food?	1	2	3	4
38. Have you choked when swallowing?	1	2	3	4
39. Have you had problems with your teeth?	1	2	3	4
40. Have you had problems opening your mouth wide?	1	2	3	4
41. Have you had a dry mouth?	1	2	3	4
42. Have you had sticky saliva?	1	2	3	4
43. Have you had problems with your sense of smell?	1	2	3	4
44. Have you had problems with your sense of taste?	1	2	3	4
45. Have you coughed?	1	2	3	4
46. Have you been hoarse?	1	2	3	4
47. Have you felt ill?	1	2	3	4
48. Has your appearance bothered you?	1	2	3	4

During the past week:	Not at all	A little	Quite a bit	Very much
49. Have you had trouble eating?	1	2	3	4
50. Have you had trouble eating in front of your family?	1	2	3	4
51. Have you had trouble eating in front of other people?	1	2	3	4
52. Have you had trouble enjoying your meals?	1	2	3	4
53. Have you had trouble talking to other people?	1	2	3	4
54. Have you had trouble talking on the telephone?	1	2	3	4
55. Have you had trouble having social contact with your family?	1	2	3	4
56. Have you had trouble having social contact with friends?	1	2	3	4
57. Have you had trouble going out in public?	1	2	3	4
58. Have you had trouble having physical contact with family or friends?	1	2	3	4
59. Have you felt less interest in sex?	1	2	3	4
60. Have you felt less sexual enjoyment?	1	2	3	4

During the past week:	No	Yes
61. Have you used pain-killers?	1	2
62. Have you taken any nutritional supplements (excluding vitamins)?	1	2
63. Have you used a feeding tube?	1	2
64. Have you lost weight?	1	2
65. Have you gained weight?	1	2

Appendix I

UW-QOL Questionnaire

Each of the following items lists different numbered statements. Think about what each statement says, then place a circle around the one statement that most closely describes how you have been feeling during the <u>past</u> week, including today. Please circle only <u>one</u> statement for each item.

Example: *In the past week and today, if you have not experienced any pain from your cancer or treatment, you would circle sentence 0 for item 1 (I have no pain).*

I PAIN (General)

A General
0 I have no pain.
25 There is mild pain not needing medication.
50 I have moderate pain - requires regular medication (codeine or non-narcotic)
75 I have severe pain controlled only by narcotics.
100 I have severe pain not controlled by narcotics.

B Mouth
0 I have no pain in my mouth.
25 I have mild pain but it is not affecting my eating.
50 I have moderate pain which is affecting my eating.
75 I have severe pain and need medication in order to eat.
100 I have severe pain and cannot eat even with the medication.

C Throat
0 I have no pain in my throat
25 I have mild pain but it is not affecting my eating.
50 I have moderate pain which is affecting my eating.
75 I have severe pain and need medication in order to eat.
100 I have severe pain and cannot eat even with the medication.

II DISFIGUREMENT

0 There is no change in my appearance.
25 The change in my appearance is minor.
50 My appearance bothers me but I remain active.
75 I feel significantly disfigured and limit my activities due to my appearance.
100 I cannot be with people due to my appearance.

III ACTIVITY

0 I am as active as I have ever been.
25 There are times when I can't keep up with my old pace, but not often.
50 I am often tired and I have slowed down my activities although I still get out.
75 I don't go out because I don't have the strength.
100 I am usually in a bed or chair and don't leave home.

IV RECREATION/ENTERTAINMENT

0 There are no limitations to recreation at home or away from home.
25 There are a few things I can't do but I still get out and enjoy life.
50 There are many times when I wish I could get out more, but I'm not up to it.
75 There are severe limitations to what I can do, mostly I stay at home and watch T.V.
100 I can't do anything enjoyable.

V EMPLOYMENT

0 I work full time.
25 I have a part time but permanent job.
50 I only have occasional employment.
75 I am unemployed.
100 I am retired (circle one below)
  51 not related to cancer treatment
  52 due to cancer treatment

VI EATING

A Chewing
0 I can chew as well as ever.
25 I have slight difficulty chewing solid foods.
50 I have moderate difficulty chewing solid foods.
75 I can only chew soft foods.
100 I cannot chew soft foods.

B Swallowing
0 I swallow normally.
25 I cannot swallow certain solid foods.
50 I can only swallow soft foods.
75 I can only swallow liquid foods.
100 I cannot swallow because.

VII SALIVA

A Amount
0 I have a normal amount of saliva.
25 I have a mild loss of saliva.
50 I have a moderate loss of saliva.
75 I have a severe loss of saliva.
100 I have no saliva.

B Consistency
0 My saliva has normal consistency.
25 My saliva is slightly thicker.
50 My saliva is moderately thicker.
75 My saliva is extremely thicker.
100 I have saliva that dries in my mouth and/or on my lips.

VIII TASTE
0 I can taste food normally.
25 I can taste most foods normally.
50 I can taste some foods normally.
75 I can taste few foods normally.
100 I cannot taste any foods normally.

IX SPEECH
0 My speech is the same as always.
25 I have difficulty with saying some words but can be understood over the phone.
50 I have moderate difficulty saying some words, and cannot use the phone.
75 Only my family and/or friends can understand me.
100 I cannot be understood.

X MUCUS OR PHLEGM
A Amount
0 I have a normal amount of mucus.
25 I have a mild amount of mucus.
50 I have a moderate amount of mucus.
75 I have a severe amount of mucus.
100 I have no mucus.

B Consistency
0 My mucus has normal consistency
25 My mucus is slightly thicker.
50 My mucus is moderately thicker.
75 My mucus is extremely thicker.
100 I have no mucus.

Appendix J

Patient Group - Open-ended Interview Questions

1. Describe three things in your life that have changed the most since your surgery.

2. Some patients find certain foods taste differently since their surgery. Other patients taste no difference in what they eat. Do you find some foods taste differently because of your surgery? Does this affect what types of food you eat?

3. Some people find eating and mealtimes to be less enjoyable since their surgery. Others do not find this. How do you feel about eating and mealtimes? Why?

4. Some patients feel worse about eating out because of their surgery. Other patients feel the same or better about eating out. Do you feel differently about eating out since your surgery (e.g. worse, better, the same)? Explain.

5. Have any of your usual leisure activities or work changed because of your surgery? How?

6. Some people find social gatherings (e.g. holidays or get-togethers) to be less enjoyable since their surgery. Others feel social gatherings are still enjoyable. Do you feel that social gatherings are less enjoyable because of your surgery? Why?

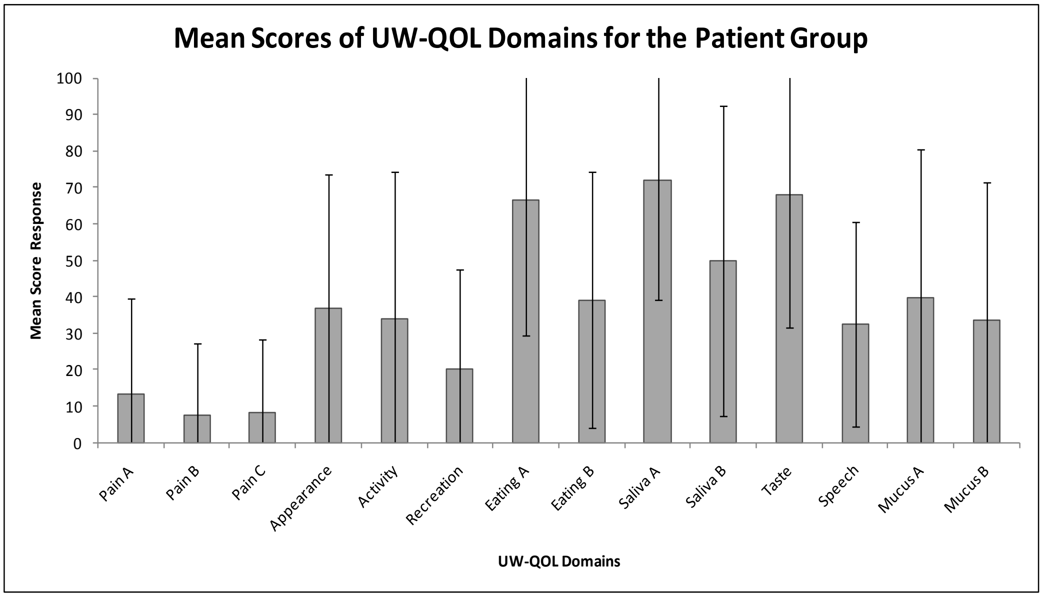
7. Since your surgery, do you find it more challenging to say certain words or sounds?

8. Have you experienced any depression since your surgery? Describe these experiences.

9. Provide one example of when you became frustrated because of your surgery.

Appendix K

a



b

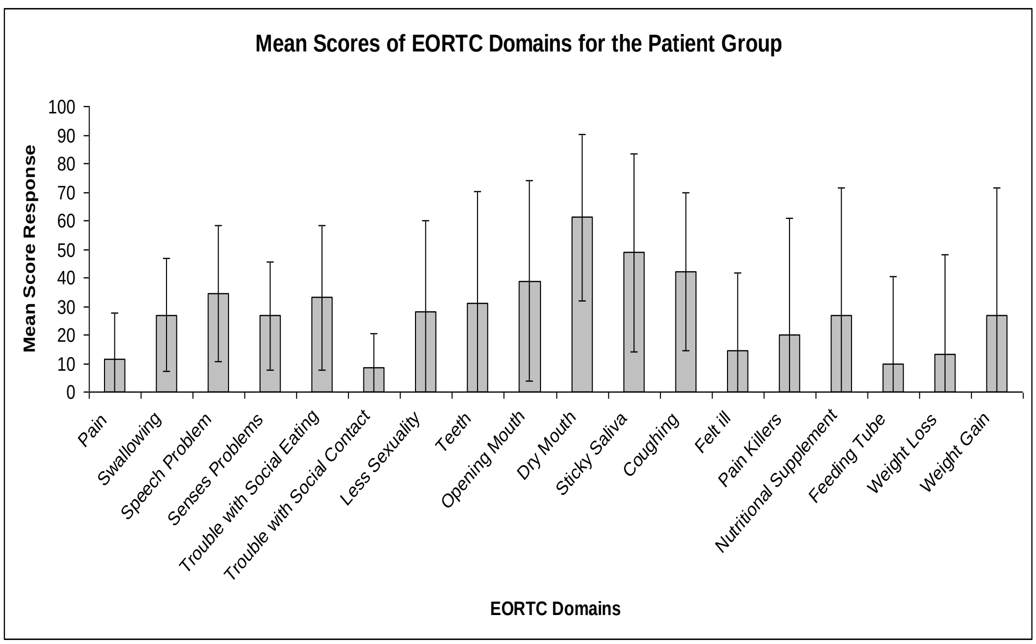


Figure K.1. Mean scores for each quality of life domain within the patient group a. UW-QOL scores b. EORTC scores

Notes. Higher scores indicate poorer quality of life outcomes

a. UW-QOL: Pain A=general, Pain B=mouth, Pain C=throat, Eating A=chewing, Eating B=swallowing, Saliva/Mucus A=amount, Saliva/Mucus B=consistency; missing Employment A and B.