ANATOMICAL COURSE, VARIATIONS AND RADIOLOGICAL EVALUATION OF INJURY TO CADAVERIC LINGUAL NERVE

SAMAH MOHAMMED ABDULLA AL-AMERY

FACULTY OF DENTISTRY
UNIVERSITY OF MALAYA
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ABSTRACT

The lingual nerve injury is a serious neurological complication which may interfere with the patient's daily activity, and adversely affect the psychological state of the patient. **Aims:** This study has three aims: (1) To determine the anatomical course and potential variations that may contribute to lingual nerve injury, (2) Assess the effectiveness of the ultrasonography and magnetic resonance imaging (MRI) in detecting bur injury with reference to optical coherence tomography (OCT) images, and (3) Compare the amount of damage of the lingual nerve caused by using two different surgical burs. **Materials and Methods:** This cadaveric research involved the study of 14 hemi-mandibles for: (a) obtaining morphometrical measurements of the lingual nerve position to three landmarks on the alveolar ridge, and (b) determining the number of terminal branches inserting in the ventral surface of the tongue. In the subsequent part of the study, twelve lingual nerves were exposed to injury using two different types of burs (Carbide bur and Dentium bur). The amount of damage caused by the two burs was first measured using OCT. Subsequently, the same lingual nerves were scanned with ultrasound and MRI to assess their capability in detecting the lingual nerve injury. **Result:** The mean distance between the twelve lingual nerves and the alveolar ridge was 12.32 mm, and they were located 11.82 mm from the lower border of the mandible. These distances were varied when near the first molar (M1), second molar (M2) and third molar (M3). The lingual nerve coursed on the floor of the mouth for approximately 25.17 mm before it deviated toward the tongue anywhere between the mesial of M1 and distal of M2. Eleven lingual nerves were found to loop around the submandibular duct for an average distance of 6.91 mm. Their looping occurred anywhere between the M2 and M3. In 72.7% of the cases the loop started around the M3 region while it mostly ended at between M1-M2 (63.6%). The lingual nerve gave out as many as 4 branches at its terminal end to insert in the ventral surface of the tongue, with 2 branches being the most common pattern.

With regards to damage caused by surgical burs, at high speed (1500 rpm), the Dentium bur caused deeper [0.22 (SE 0.04) mm] and wider [1.87 (SE 0.25) mm] laceration than the Carbide bur. Statistically there was no significant different between the OCT recording of damage and the ultrasound reading, while the MRI failed to detect the lingual nerve. **Conclusion:** An awareness of the variations of the lingual nerve is important to prevent any untoward complications or nerve neuropathy. In addition, it appears to be more favorable to use a Carbide bur for surgical procedure (preferably at a low speed) as it minimizes damage to the lingual nerve. The ultrasound scanning capability in detecting the lingual nerve injury would provide an objective evaluation for the amount of nerve damage in-vivo. It is hoped that these findings will be useful for planning surgical procedures in the posterior floor of the oral cavity.

ABSTRAK

Kecederaan pada saraf lingual adalah satu komplikasi neurologi yang serius yang boleh mengganggu aktiviti harian pesakit, dan menjejaskan keadaan psikologi pesakit tersebut. **Tujuan:** Kajian ini mempunyai tiga matlamat: (1) Untuk menentukan perjalanan saraf lingual dan variasinya yang boleh menyumbang kepada kerosakan saraf, (2) Menilai keberkesanan pengimejan ultrasonografi dan Magenetic Resonance Imaging (MRI) untuk mengesan kecederaan bur keatas saraf dengan merujuk kepada imej yang dihasilkan oleh Optical Coherence Tomography (OCT), dan (3) Bandingkan kawasan kerosakan saraf lingual yang disebabkan oleh menggunakan dua bur yang berbeza. **Bahan dan Kaedah:** Ini adalah penyelidikan keatas bahan mayat dengan melibatkan kajian 14 hemi-mandibel untuk: (a) mendapatkan ukuran morphometrikal kedudukan saraf lingual kepada tiga bahagian alveolus, dan (b) menetukan berapa cawangan terminal memasuki kedalam permukaan ventral lidah. Dalam kajaian berikutan, dua belas saraf lingual dekenakan kecederaan menggunakan dua jenis bur (Carbide bur dan Dentium bur). Kerosakan yang disebabkan oleh dua bur ini diukur menggunakan OCT. Akhirnya, saraf lingual yang sama diimbas oleh mesin ultrasound dan MRI untuk menilai keupayaan mengesan kecederaan saraf dan membandingkan penemuan kepada imej OCT. **Keputusan:** Jarak minima di antara dua belas saraf lingual dan alveolus adalah 12.32 mm, dan ia terletak 11.82 mm dari sempadan bawah mandibel. Jarak ini telah ubah apabila berhampiran molar pertama (M1), molar kedua (M2) dan molar ketiga (M3). Perjalanan saraf lingual di lantai mulut adalah selama kira-kira 25.17 mm sebelum ia menyimpang ke arah lidah - di antara mesial M1 dan distal M2. Sebelas saraf lingial didapati bergelung salur kelenjar submandibel untuk jarak sepurata 6.91 mm. Gegelung berlaku di mana-mana antara M2 dan M3. Dalam 72.7% kes, gelung bermula sekitar kawasan M3 dan kebanyakannya berakhir di antara M1-M2 (63.6%). Tambah lagi, terdapat 4 cawangan pada akhir terminal yang memasuki ventral

lidah, dengan 2 cawangan menjadi corak yang paling biasa. Merujuk kepada kerosakkan keatas saraf lingual, pada kelajuan yang tinggi (1500 rpm), bur Dentium yang menyebabkan luka lebih mendalam [0.22 (SE 0.04) mm] dan lebih luas [1.87 (SE 0.25) mm] daripada Carbide bur. Tambah lagi tidak ada perbezaan statitik yang signifikan di antara bacaan kelukaan mengunakan OCT dan bacaan ultrasound, manakala MRI gagal mengesan saraf lingual. **Kesimpulan:** Kesedaran tentang variasi saraf ligual adalah penting untuk mengelakkan sebarang komplikasi yang tidak diingini atau neuropati saraf. Di samping itu, adalah lebih baik menggunakan bur Carbide bagi prosedur pembedahan (sebaik-baiknya pada kelajuan yang rendah) untuk mengurangkan kerosakan pada saraf lingual. Keupayaan ultrasound dan kesahihannya mengesan ukuran kecederaan saraf lingual akan memberi penilaian objektif bagi kecederaan saraf di dalam orang yang masih hidup. Adalah diharapkan dengan kajian ini, prosedur pembedahan di lantai posterior rongga mulut boleh dirancang dengan lebih sempurna.

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I dedicate this project to my parents for persistently keeping me in their prayers. I will always remain indebted to their offerings and sacrifice.

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LIST OF SYMBOLS AND ABBREVIATIONS

LN	:	lingual nerve
OCT	:	Optical coherence tomography
MRI	:	Magnetic resonance imaging
IAN	:	Inferior alveolar nerve
SN	:	Sigmoid notch
OG	:	Otic ganglion
L	:	Lingula
MHN	:	Mylohyoid nerve
N	:	Sample size
M3	:	Third molar
M2	:	Second molar
M1	:	First molar
RM	:	Retromolar
CT	:	Computed tomography
RF	:	Radio frequency
S/N	:	Signal to noise ratio
HR-MRI	:	High resolution magnetic resonance imaging
IBM	:	Inferior border of mandibular border
SMD	:	Submandibular duct
rpm	:	Revolutions per minute

LIST OF APPENDICES

CHAPTER ONE: INTRODUCTION

1.1 Introduction

The oral cavity is a complex region and any procedure performed in this area by various practitioners (including oral and maxillofacial surgeons) is a challenge. The most common dental procedure at the retromolar area is the third molar extraction which causes 0.6% - 2.0% injuries to the lingual nerve (Miloro et al., 1997). Complete care is needed as there is a possibility of damage to the lingual nerve (LN) resulting in serious complications (Bradley, 2014; Gargallo−Albiol et al., 2000; Mendes et al., 2013). Interestingly, although the bone diminishes in the edentulous patient, the lingual nerve does not move inferiorly and this may be the cause of nerve injuries (Benninger et al., 2013). In addition, exposure of the lingual nerve to needle injury due to local anesthesia is possible although this incidence is low. Researchers have reported that the anatomical location and the unpredictable course of the lingual nerve may play an important role in this injury (Queral-Godoy et al., 2006).

The lingual nerve is a branch of the mandibular division of the trigeminal nerve, and is considered the main nerve which provides general sensation to the anterior two third of the tongue and also the lingual tissue (Karakas et al., 2007; Ropper et al., 2014; Snell, 2011). Smith and Lung (2006) reported that recovery of a nerve injury happens within 8 weeks for 85-94 % of cases. It has been further stated that the inferior alveolar nerve injuries may show better prognosis but lingual nerve injuries that do not recover within 8 weeks risk permanent damage (Tara Renton, 2011). It is imperative that after any oral rehabilitation, the patient is expected to experience critical improvement in his oral function. The failure to achieve this has a significant negative psychological effect on the patient (Hillerup & Stoltze, 2007).

Interestingly, the relationship of the lingual nerve to the third molar has been discussed in detail in the literature but the relationship to other posterior teeth is still scarce. The first aim of this study was to determine this relationship. Apart from the pathway being studied, the various anatomical variations were also determined, as this would prevent unwanted surgical complications in this area. The second part of this study looks into various methods to determine a lingual nerve injury should it become in contact with surgical devices. The gross and histomorphological appearance of this injury is quantified.

1.2 Statement of Problem

The lingual nerve is a terminal branch of the mandibular nerve. It is varied in its course and in its relationship to the mandibular alveolar crest, submandibular duct and also the related muscles in the floor of the mouth. This detailed study on the course of the lingual nerve and its relationship to its neighboring structures (including the submandibular duct) will provide a useful reference for surgical procedures in the floor of the mouth, particularly for the Asian population.

1.3 Study Aims

This study consists of 3 main parts. The first part of the study attempts to understand the anatomical course and potential variations that may contribute to injuring the lingual nerve. The second part of this study looks into various imaging modalities to determine a lingual nerve injury while the last part of this study looks into the extent of injury suffered when the lingual nerve comes into contact with a carbide bur or a Dentium® implant bur. The latter bur is designed to be soft tissue friendly.

1.3.1 Understanding the anatomical course and potential variations that may contribute to nerve injury

1.3.1.1 Objectives

a) To determine the location of the lingual nerve in relation to alveolar ridge.

b) To determine the location of lingual nerve in relation to the inferior border of the mandible.

c) To estimate the length of lingual nerve prior to diversion to the tongue

d) To determine the beginning and the end of overlap between the lingual nerve and the submandibular duct

e) To measure the distance of overlap between the lingual nerve and the submandibular duct

f) To identify the location at which the nerve changes its direction toward the tongue.

g) To study the pattern of insertion of the terminal branches of the lingual nerve into the ventral surface of the tongue.

1.3.2 Assess the effectiveness of the ultrasonography and MRI in detecting a lingual nerve bur injury with reference to optical coherence tomography

1.3.2.1 Objectives

a) To compare the observation of a nerve injury by the use of ultrasound and MRI modalities with reference to the Optical coherence tomography (OCT) to determine their validity in detecting a lingual nerve injury.

1.3.3 Compare the measure of damage of the lingual nerve caused by using two difference surgical burs.

1.3.3.1 Objectives

a) To compare the depth and the width of the laceration caused by using a standard carbide bur and a Dentium® implant bur, where the latter is claimed to be soft tissue friendly.

1.4 Null Hypothesis

a) There is no variation in the course of the LN at the third molar region along the floor of the mouth, and during intersection with the submandibular duct.

b) There is no difference in the capability of ultrasound, MRI and optical coherence tomography (OCT) to detect an injury in the lingual nerve.

c) There is no significant difference in the amount of damage of the lingual nerve caused by using a carbide bur and a Dentium® implant bur.

CHAPTER TWO: LITERATURE REVIEW

2.1 Anatomy of the lingual nerve

2.1.1 Gross anatomy and innervation

The role of the tongue and its movements is very critical in speech, mastication, swallowing, taste, respiration and sensation (Hiiemae & Palmer, 2003; Mu & Sanders, 2010; Zur et al., 2004). The tongue is considered as a complex organ innervated by the following cranial nerves:

- The hypoglossal nerve (CN XII), which is carries somatic motor fibers to all the intrinsic and extrinsic muscles of the tongue, except the palatoglossus muscle which is innervated by the accessory nerve (CN XI) via the vagus nerve (CN X) (Binder & Sonne, 2011; Liebgott, 2009).
- The glossopharyngeal nerve (CN IX), which contains motor, sensory, and parasympathetic fibers, and innervates the posterior one-third of the mucosa of the tongue.
- The lingual nerve, a branch that arises from the posterior division of mandibular nerve (CN V3), supplying the anterior two-third of the tongue, mucous membrane of the floor of the mouth and the gingivae related to the lower teeth (Mu & Sanders, 2010; Singh, 2008)
- The chorda tympani, a branch from mastoid segment of the facial nerve (CN VII) which accompanies the lingual nerve and carries gustatory fibers and parasympathetic fibers to supply the submandibular and sublingual salivary gland and anterior two-third of the tongue (Agur & Dalley, 2009; Binder & Sonne, 2011).

- The vagus nerve (CN X), which besides its motor and sensory functions, has a minor role in taste sensation at the posterior part of the tongue. It carries afferent fibres from the root of the tongue (Patestas & Gartner, 2016).

Recently, Saigusa et al. (2006) suggested that a motor fiber originating from the motor root of the CN V, may innervate both the superior and inferior longitudinal muscles of the tongue.

Both, the lingual and chorda tympani nerves travel together as soon as they come out through the pterygotympanic fissure of the glenoid fossa (Girod et al., 1989). The lingual nerve and chorda tympanic descends medially to the lateral pterygoid muscle and inferior alveolar nerve. It continues downward in anterior direction until the nerve reach the ptreygomandibular space, there the lingual nerve continue its way between the medial aspect of the mandibular ramus and the lateral aspect of medial pterygoid muscle. After the nerve passes the anterior edge of the medial pterygoid muscle, it enters the oral cavity. At the oral cavity the lingual nerve runs from the more lateral to medial position as it approaches the mandibular third molar due to the oblique flare in the mandible in this region. Although there is a close relation between the lingual nerve and the mandibular third molar, the position of the lingual nerve in respect to the alveolar bone is variable. This complex relationship has been clarified previously by several studies (Table 2.1) (Behnia et al., 2000; Dias et al., 2015; Hölzle & Wolff, 2001; Karakas et al., 2007; Kiesselbach & Chamberlain, 1984; Miloro et al., 1997; Pogrel et al., 1995).

Table 2.1: Mean horizontal and vertical distances of lingual nerve from the third molar bone crest.

Researchers	Measurements	
	Horizontal distance	Vertical distance
Behnia *et al*. (2000)	2.06 ± 1.10 mm (0.00 to 3.20 mm)	3.01 ± 0.42 mm (1.70 to 4.00 mm)
Bokindo *et al*. (2015)	7.10 ± 2.80 mm (1.30 to 15.60 mm)	10.30 ± 5.20 mm (2.80 to 19.90 mm)
Diaz *et al*. (2015)	0.57 ± 0.56 mm (0.00 to 2.50 mm)	9.15 ± 3.87 mm (2.33 to 17.50 mm)
Erdogmus *et al*. (2008)	9.30 ± 2.10 mm (5.20 to 16.20 mm)	7.06 ± 1.30 mm (5.01 to 8.97 mm)
Hölzle *et al*. (2001)	0.86 ± 1.00 mm (0.00 to 4.00 mm)	7.83 ± 1.65 mm (4.50 to 14.00 mm)
Karakas *et al*. (2007)	4.19 ± 1.99 mm (1.81 to 8.67 mm)	9.50 ± 5.20 mm (1.13 to 17.04 mm)
Kiesselbach & Chamberlain (1984)	0.59 ± 0.90 mm (0.00 to 3.00 mm)	2.28 ± 1.96 mm (2mm above to 7mm below)
Mendes *et al*. (2014)	4.40 ± 2.40 mm (2.00 to 11.00 mm)	16.8 ± 5.70 mm (12.0 to 29.00 mm)
Miloro *et al*. (1997)	2.53 ± 0.67 mm (0.00 to 4.35 mm)	2.75 ± 0.97 mm (1.52 to 4.61 mm)
Pogrel *et al*. (1995)	3.45 ± 1.48 mm (1.00 to 7.00 mm)	8.32 ± 4.05 mm (Range not reported)

During its courses in floor the mouth, the lingual nerve is bounded inferiorly with the mylohyoid muscle. In the region of the mandibular second molar, the submandibular ganglion can be found suspended inferiorly from the LN by autonomic secretory fibres (Garbedian, 2009). The LN then begins to course anteromedially, looping itself under the submandibular (Wharton's) duct. The nerve then passes upward onto the genioglossus muscle to enter the ventral mucosa of the tongue anterior to the circumvallate papillae (Zur et al., 2004).

In the tongue, there are two main branches from the main lingual nerve trunk. The medial branch sends off 2-4 small subdivisions to supply the medial part of the ventrolateral tongue while the lateral branch sends off 3-4 large subdivisions to the anterior tip of the tongue. Each subdivision gives 2-5 distal branches. Both medial and lateral branch have anastomotic connections with the hypoglossal nerve (Fitzgerald & Law, 1958; Zur et al., 2004). This neural interconnection is consistent with the lingua-hypoglossal reflex and is important in the reflex control of tongue movement (Zur et al., 2004).

2.2 Anatomical variations

2.2.1 The course of the lingual nerve in the infratemporal and pterygomandibular regions

Anatomy textbooks describe the lingual nerve as one of three nerves arising from the posterior division of the trigeminal nerve at the level of otic ganglion (Liebgott, 2009). According to Kim et al. (2004) the division of the lingual nerve (LN) from the inferior alveolar nerve (IAN) takes different patterns. They studied 32 cadavers and found that in a majority of specimens (65.6%; n=21) showed that the bifurcation of the LN and IAN was sited between the sigmoid notch (SN) and the otic ganglion (OG) (Figure 2.1.A). In 25.0% of the specimens (n=8), the division patterns was located at the upper half of the ramus (Figure 1.B), while one case showed a bifurcation immediately superior to the lingula (L) (Figure 1.C). Plexiform patterns from CN V_3 were recorded for the remaining of specimens (6.2%; n=2) (Figure 2.1.D).

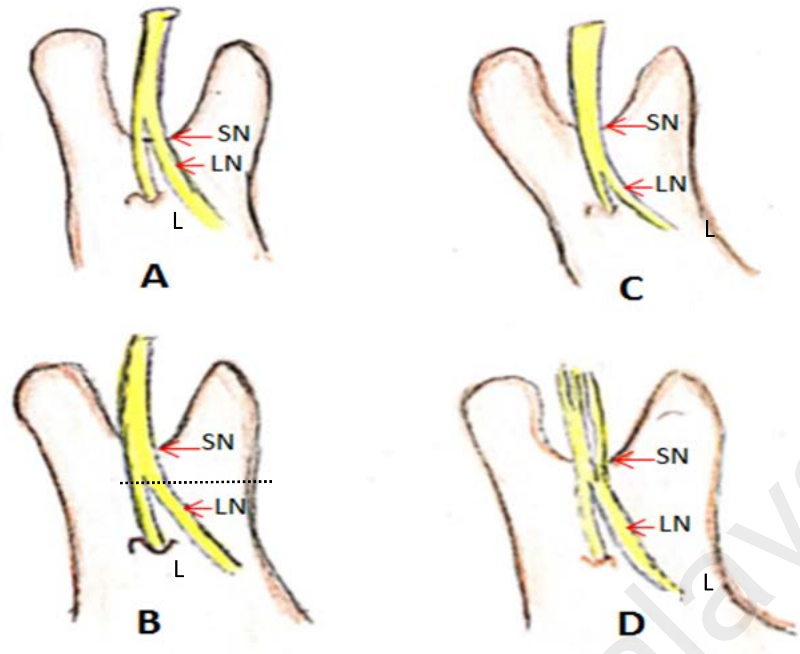

Figure 2.1: Furcation patterns of the lingual nerve (LN) and inferior alveolar nerve (IAN) categorized according to the level of their bifurcation in the medial aspect of the mandibular ramus. A: between the sigmoid notch (SN) and the otic ganglion (OG); B: at the upper half of the ramus; C: immediately superior to the lingula (L); D: Plexiform patterns. Dotted line shows the horizontal reference line which bisected the distance between the mandibular lingual(L) and the sigmoid notch (SN). Figure redrawn based on the original illustration by *Kim, S., Hu, K., Chung, I., Lee, E., & Kim, H. (2004). Topographic anatomy of the lingual nerve and variations in communication pattern of the mandibular nerve branches. Surgical and Radiologic Anatomy, 26(2), 128135.*

This unique plexiform patterns were reported previously by Rácz and Maros (1981) in 8.3% (n=4) of their 48 specimens. Recently, Erdogmus et al.(2008) demonstrated that 66.7% (n=14) of their 21 specimen presented with a branch pattern that was located above the level of the sigmoid notch. The remaining of their cases (n=7) showed a bifurcation between the sigmoid notch and the mandibular lingula. There were 47.61% of specimens (n=10) that recorded 1-3 branches interconnection between LN and IAN; however, no plexiform branching pattern was noted.

Kim et al. (2004), measured the location of bifurcation as a distance from the bifurcation to two stable anatomical landmarks. The bifurcation between LN and IAN occurred at approximately 14.3 mm (range: 7.8 – 24.1 mm) inferior to the foramen ovale and 16.5 mm (range: 4.9 – 24.3) superior to the tip of the hamulus. This variation in the location of nerves bifurcation may significantly contribute to the high failure rate (13-29%) of mandibular nerve block anesthesia in dentistry (Blanton & Jeske, 2003).

2.2.2 The lingual nerve in the retromolar region

In dentistry, several cases of incomplete anaesthesia were recorded following application of local anaesthesia during the mandibular nerve block and long buccal nerve block. This failure to obtain required anaesthesia is explained to be the result of the presence of collateral nerve twigs from the LN supplying the retromolar region (Kim et al., 2004). The presence of these collateral nerve twigs have been reported previously in several studies (Erdogmus et al., 2008; Girod et al., 1989; Kiesselbach & Chamberlain, 1984; Kim et al., 2004). From thirty-two specimens studied by Kim et al. (2004), 81% (n=26) of their specimens showed collateral nerve twigs to the retromolar area innervating the lingual gingiva approximate to the mandibular third molar and retromolar mucosa. An average of one nerve twig was reported with a range of branches from none to three branches. Recently, Erdogmus et al. (2008) reported observing several small nerve branches arising from the LN extending to the paralingual area, but failed to quantify these "variational nerve innervations".

As mentioned earlier, this special branching pattern of the mandibular nerves plays essential role in the failure to obtain adequate anaesthesia (Jablonski et al., 1985; Kim et al., 2004; Krafft & Hickel, 1994). One of these branching is the communication between the mylohyoid nerve (MHN) and lingual nerve where they join together as the LN approaches in the floor of the mouth (Erdogmus et al., 2008; Kim et al., 2004; Rácz & Maros, 1981; Sakamoto & Akita, 2004). Interestingly Kim et al. (2004) studied 32 Korean specimens, and found that in 12.5% (n=4), the communications between MHN and LN was evident. This study was confirmed later by Erdogmus et al. (2008). He noticed 11.9% (n=5) of his 42 cases showed the same communication. This communication between the two nerves would help in the LN function recovery where MHN contributed in the innervation of the tongue (Fazan et al., 2007).

2.2.3 The position of LN in the third molar region

Once the lingual nerve enters the oral cavity at the retromolar area, it becomes in close relationship with the lingual plate of mandible and start following its contours. For several years there was a lack in the quality and the quantity of information regarding the lingual nerve position in this region of the third molar. Only in 1984, Kiesselbach and Chamberlain (1984) decided to evaluate the shape and the position of the lingual nerve in this region (Abbey et al., 1987). Their study included 34 adult cadaver heads plus 256 *in–vivo* observation during the mandibular third molar extraction. Their findings showed variations amongst the specimens in the horizontal distance with an average distance of 0.58 ± 0.9 mm from the lingual plate. The lingual nerve was in contact with lingual plate in 62% (n=21) of the specimens. The vertical relationship of the lingual nerve with alveolar crest recorded a distance of 2.28 ±1.96 mm. The interesting finding was that some 17% of the cadaveric specimens and 4.5% of the *in-vivo* specimens showed the presence of the lingual nerve at level of the alveolar crest or higher (Figure 2.2).

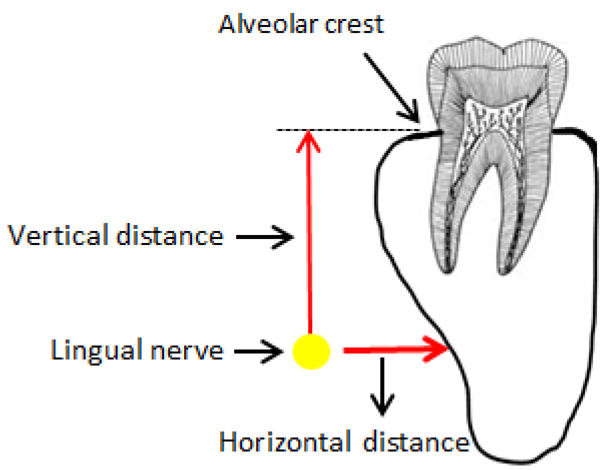

Figure 2.2: Diagrammatic frontal section showing the vertical and the horizontal distance between the lingual nerve and the mandibular lingual plate. Figure redrawn based on the original illustration by *Kiesselbach, J. E., & Chamberlain, J. G. (1984). Clinical and anatomic observations on the relationship of the lingual nerve to the mandibular third molar region. Journal of Oral and Maxillofacial Surgery, 42(9), 565-567.*

Pogrel et al. (1995) used a reproducible osseous landmarks to measure the distance to the lingual nerve irrespective whether there is the presence or the absence of the posterior teeth. In this study, they dissected 20 cadavers (40 sides) and measured the distance from the lingual nerve to the respective osseous points. The results showed variations in the position of the lingual nerve at sagittal and coronal planes, which confirmed the findings of a previous study. At the sagittal plane the mean distance of the lingual nerve before divergence from the lingual plate was 27.7 mm. The mean horizontal distance between the lingual nerve and the lingual plate of the mandible was 3.45 ± 1.48 mm with a range of 1 mm to 7 mm. This was different from the findings recorded by Kiesselbach and Chamberlain (1984). The measurement in the vertical direction revealed that the mean distance between the lingual nerve and the alveolar crest was 8.32 ± 5.69 mm (Figure 2.3).

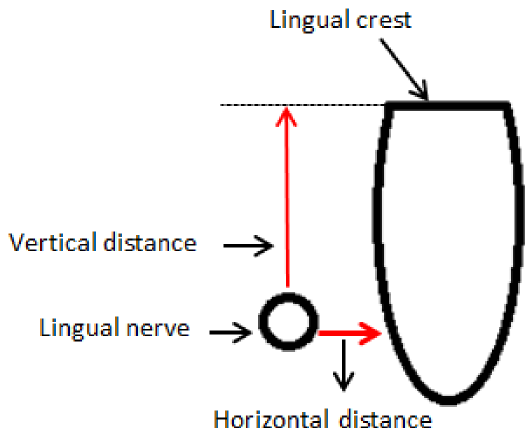

Figure 2.3: Diagram showing the vertical and the horizontal relationship between the lingual nerve and the respective osseous points. Figure redrawn based on the original illustration by *Pogrel, M. A., Renaut, A., Schmidt, B., & Ammar, A. (1995). The relationship of the lingual nerve to the mandibular third molar region: an anatomic study. Journal of Oral and Maxillofacial Surgery, 53(10), 1178-1181.*

In 3 cases (out of 40) the lingual nerve position with regards to the level of the alveolar crest were in agreement with the findings reported by Kiesselbach and Chamberlain (1984). In one case the lingual nerve was located at the level of the alveolar crest and in the anther two cases it was higher than that. Although the third molar was present in 6 sides of the cases, the results did not show any significant statistical differences with regards to the presence and the absence of the third molar (Pogrel et al., 1995).

A potential limitation in the cadaveric studies is iatrogenic displacement of the lingual nerve during the dissection process. To overcome this problem, Behnia et al. (2000), stabilized the location of the lingual nerve by using clips on the lingual surface of the gingiva. Even though this idea may reduce the displacement of the nerve during the dissection procedure, it causes a compression distortion. Behnia’s study was novel with a high number of samples (669 LNs); in addition, it was performed on fresh cadavers within 24 hours of death. Horizontally, the mean distance between the lingual nerve and the lingual plate of the mandible at the third molar region was 2.06 ± 1.10 mm, while the vertical distance with the alveolar crest was 3.01 ± 0.42mm (Figure 2.4).

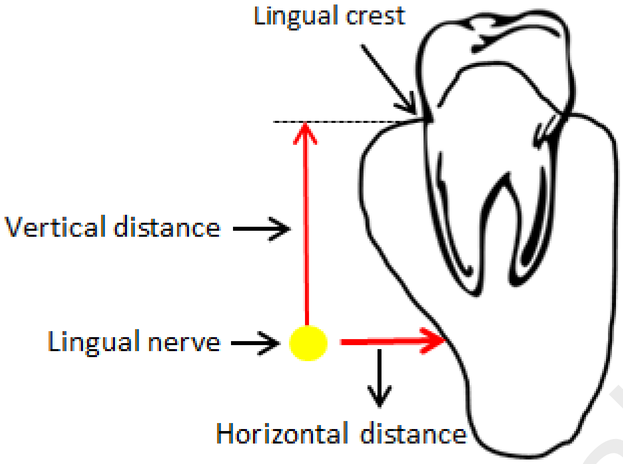

Figure 2.4: Diagram shows a coronal section through the third molar region showing methods of measurement of the vertical distance from lingual crest Horizontal distance from lingual plate used by Behnia (2000). Figure redrawn based on the original illustration by *Behnia, H., Kheradnar, A., & Shahi-okhi, M. (2000). An anatomic study of the lingual nerve in the third molar region. Journal of Oral and Maxillofacial Surgery, 58(6), 649-651.*

A surprising finding of this study was that in one case the lingual nerve was resting on the retromolar pad (Behnia et al., 2000).

In 2001, Hölzle *et al*. studied the position of the lingual nerve in the third molar region in relation to the atrophy of the alveolar crest. The results showed clear correlation, where the distance of the lingual nerve to the crest decrease as the degree of the mandibular atrophy increased (Hölzle & Wolff, 2001). In fact, both the vertical and horizontal distances differed in comparison to previous anatomical studies. The vertical distance between the lingual nerve and the alveolar crest was 7.83 ± 1.65 mm, while the horizontal distance between the two structures was 0.86 ± 1.00 mm (Figure 2.5).

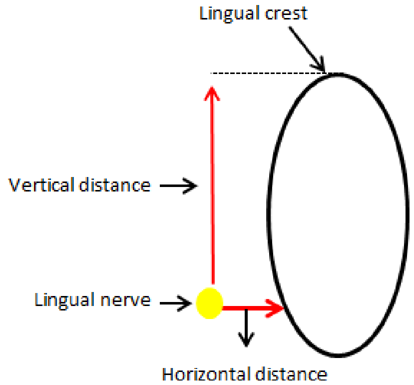

Figure 2.5: Diagram explains the methods of measuring the vertical and the horzontal distance. Figure redrawn based on the original illustration by *Hölzle, F., & Wolff, K.-D. (2001). Anatomic position of the lingual nerve in the mandibular third molar region with special consideration of an atrophied mandibular crest: an anatomical study. International journal of oral and maxillofacial surgery, 30(4), 333-338.*

In all the previous cadaveric studies, the investigators utilized calipers for measuring the vertical and the horizontal distances of the lingual nerve. Karakas et al. (2007) on the other hand, used radiography to evaluate the vertical and the horizontal distances of the lingual nerve with respect to the mandible. He used 21 sagittally sectioned cadaveric heads, where a 3mm wire was positioned along with the lingual nerve. After that a radiographic images were taken in two planes, superior and lateral. Both the vertical and the horizontal distances of the lingual nerve to the mandible were measured on the radiographic image using the digital caliper. The readings obtained in this study were 9.5 ± 5.2 mm and 4.1 ± 1.9 mm Hölzle and Wolff (2001). He stated that the difference in the results might be due to the vertical and the horizontal distances, respectively. Karakas et al. (2007) findings were distinctly greater in comparison to the previous studies by Kiesselbach and Chamberlain (1984) and superior location of the mylohyoid muscle and/or the greater mylohyoid muscle volume.

Recently in 2015, Dias et al. performed a study that included edentulous and dentulous cases. He studied the position of the lingual nerve at two points. The first point was located at the deepest point on the retromolar area (point of the transition from the horizontal to the vertical on the internal oblique line). The second point was located 1 cm anterior to the first point on the alveolar ridge. The vertical distance at the first point was 9.15 (3.87) mm, and the horizontal distance was 0.57 (0.56) mm at the same point. The dentate status affected the measurements at the second point where the lingual nerve was 4.75 mm closer to the lingual crest an edentulous than a dentulous mandible (Dias et al., 2015) (Figure 2.6).

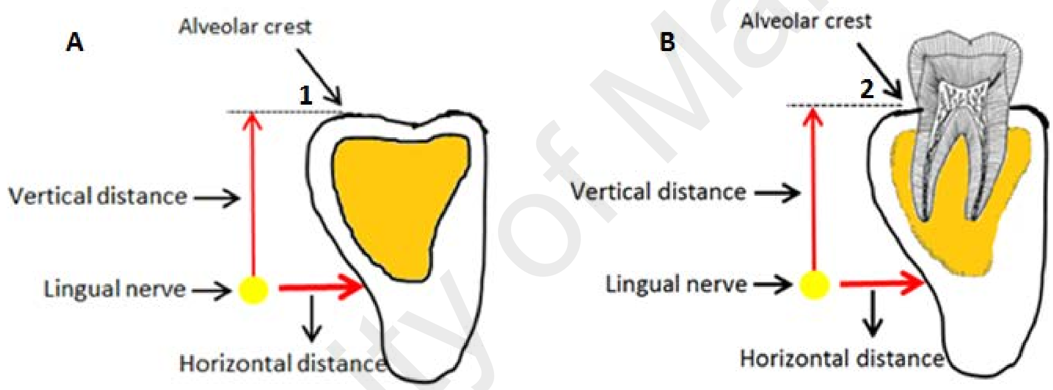

Figure 2.6: Diagram showing the vertical and the horizontal distance between the lingual nerve and the mandible at to reference points.1; at the level of the deepest pinot on the retromolar area,2; 1cm anterior to the first point on the alveolar ridge. Figure redrawn based on the original illustration by *Dias, G., de Silva, R., Shah, T., Sim, E., Song, N., Colombage, S., & Cornwall, J. (2015). Multivariate assessment of site of lingual nerve. British Journal of Oral and Maxillofacial Surgery, 53(4), 347-351.*

2.3 Cross-section morphology

In the literature, the lingual nerve showed cross-section morphological variations along its course in the oral cavity; it was reported to be circular, oval to flat, or ribbon-like (Kiesselbach & Chamberlain, 1984; Kim et al., 2004; Miloro et al., 1997). Table 2.2 summarized the cross-section morphology of the lingual nerve recorded in the literature. In 1984, Kiesselbach & Chamberlain reported that there is no correlation between the nerve morphology and the distance from the medial surface of mandible. In 61% of their cases the nerve took the round shape, oval in 17.6% of the cases while in the remaining 20.5% of the cases it was flat/ribbon like (Kiesselbach & Chamberlain, 1984). In the study by Miloro et al. (1997) 45% of their cases displayed round shape, 30% were elliptical, while the rest 25% were kidney-bean shaped.

Kim et al. (2004) studied the morphology of 32 lingual nerves thoroughly at three areas; retromolar, third molar and second molar region. The most common shape at the retromolar region was of with circular and oval shape, with both sharing a similar incidence of 40% (n=13). At the third and the second molar area, the oval shape predominated with an incidence of 59.4% (n=19), followed by the ribbon-like with an incidence of 62.5% (n=20) at the second molar region and circular shape at the third molar area, with an incidence of 25% (n=8). Interestingly, the ribbon-like shape was not present at the retromolar or third molar region (Kim et al., 2004).

Table 2.2: Literature summary of cross- sectional morphology of lingual nerve

Study	**N**	**Location**	**Cross Sectional Morphology**			
			Circular	**Oval**	**Flat**	**Ribbon-like**
Kiesselbach & Chamberlain	34	M3	31.7%	17.6%	20.5%	_
Kim et al	32	RM	40.6%	40.6%	18.8%	0
		M3	25%	59.4%	15.6%	0
		M2	3.1%	18.8%	15.6%	62.5%
Miloro et al	20	M3	45%	30% (elliptical)	25% (kidney-like)	–

N= Sample size; M3= Third molar; M2= second molar; RM= Retromolar

2.4 Microanatomy

The microanatomy of the lingual nerve looks similar to other peripheral nerves. Like other nerves, the lingual nerve has a polyfasicular pattern, which consists of several fascicles different in size but without fascicular grouping (Abbey et al., 1987; Svane et al., 1986). At the third molar area, the number of the fascicles range from 8.5 to 10 ± 4.0 (Girod et al., 1989). The reduction in the number of the fascicles with progress of the lingual nerve in the oral cavity was reported by (Abbey et al., 1987). The number of the fascicles in the third molar region ranged between 15 -18 fascicles before it decreased to 9 fascicles at the tongue, starting its insertion in this structure. The cross section area of the lingual nerve fascicles was evaluated by Girod et al. (1989) who reported an average area of 1.87 mm ± 0.38 mm^2. The careful evaluation of the number and the size of the fascicles is a critical factor to the success of the microsurgery, where the repair of a nerve requires correlation between the donor and host nerve.

2.5 The relationship between the lingual nerve and the submandibular duct

The lingual nerve enters the submandibular region after passing forward and medially, inferior to the lower border of the superior constrictor muscle of the pharynx after which it is in close relationship to the lower third molar (Drake et al., 2012; Snell, 2011). As the lingual nerve progresses through the hypoglossus, it passes above the submandibular duct (Wharton's duct). Continuing forward, the lingual nerve crosses superficially and then hooks around the submandibular duct until it reaches the medial side (Drake et al., 2014; Singh, 2008).

The submandibular duct on the other hand, emerges from the medial side of the deep lobe of the submandibular gland, inferior to the mylohyoid muscle in the oral cavity and opens in a small sublingual papilla beside the base of the frenulum of the tongue (Drake et al., 2014; Fischer et al., 2006). In the study done by (Hölzle & Wolff, 2001), they reported that the submandibular duct passed above the lingual nerve in most of the cases (30 samples) while in only 4 cases the submandibular duct was running deeply in the floor of the mouth and did not show a relationship with lingual nerve. In 2013, Mendes *et al*. studied 24 human half heads; in 15 samples which represented 62.5% of his cases the submandibular duct passed above the lingual nerve (Figure 2.7 a); while in 9 of the samples which represented 37.5% of the cases the duct crossed below the nerve (Figure 2.7 b) (Mendes et al., 2013).

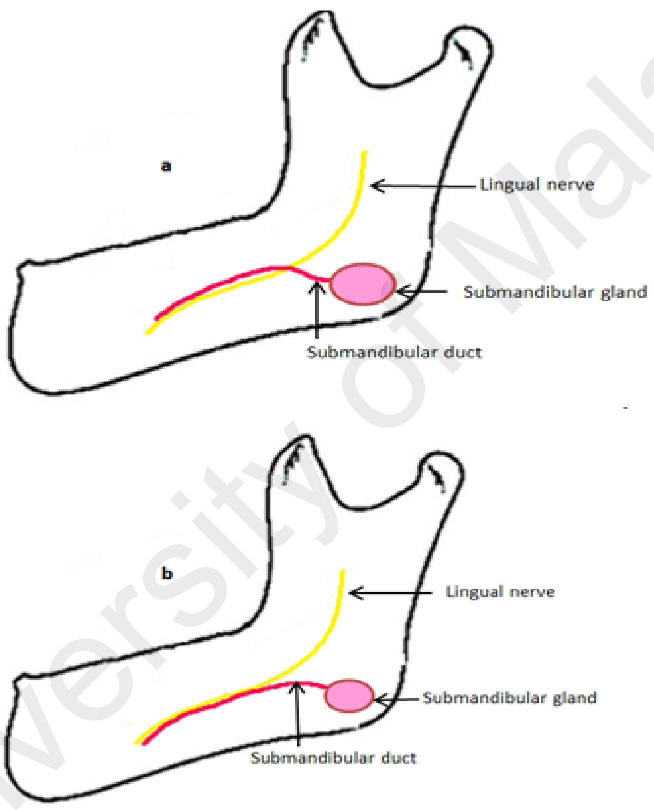

Figure 2.7: Diagram showing the relationship between the lingual nerve and the submandibular duct. a; submandibular duct passed above the lingual nerve, b; the submandibular duct crossed below the lingual nerve. Figure redrawn based on the original illustration by Mozsary *PG, Middleton RA (1984) Microsurgical reconstruction of the lingual nerve. Journal of Oral and Maxillofacial Surgery 42: 415-420.*

Therefore, the submandibular duct contacts the lingual nerve, which presents the risk of lingual nerve injury during surgical interventions such as ductoplasty and removal of sialotiths. Likewise, surgical procedures to the lingual nerve in this region will increase the possibility of submandibular duct injury, which may then cause a ranula. Ranula in the floor of the mouth will interfere with normal daily activity of the patient, especially when eating and speaking (Chi et al., 2008; Chung et al., 2012).

2.6 Imaging studies of the lingual nerve

2.6.1 Introduction

In the literature, imaging studies performed to evaluate the position of the lingual nerve are limited (Karakas et al., 2007; Miloro et al., 1997; Olsen et al., 2007). As mentioned before, Karakas et al. (2007) utilized a plain film radiograph to study the position of the lingual nerve by fitting a metal wire along the LN in cadaveric specimens. This technique is not practical and provides no diagnostic merit. The study done by Miloro et al. (1997) was the first study in-vivo employing magnetic resonance imaging (MRI) in the investigation of the lingual nerve at the third molar region. Later on, Olsen et al. (2007) used the ultrasonography to determine the location of the lingual nerve in cadaveric pigs.

2.6.2 Magnetic resonance imaging (MRI)

MRI is a complex but effective imaging system that has a variety of clinical indications directly related to the diagnosis and treatment of oral and maxillofacial abnormalities (Katti et al., 2011). Like all other radiographic methods, MRI has advantages and disadvantages. Pekar (2006) summarized the advantages and the disadvantages of MRI as following:

Advantages of MRI:

1. No ionizing radiation can be used in child bearing women and children. Where the radio frequency, RF pulses used in MRI do not cause ionization and have no harmful effects of ionizing radiation.
2. Non-invasive technic.
3. Contrast resolution: It is the principle advantage of MRI, i.e. ability of an image process to distinguish adjacent soft tissue from one another.
4. Multiplanar image: With MRI, we can obtain direct, sagittal, coronal and oblique image which is impossible with radiography.
5. It could differentiate between acute and chronic transit and fibrous phases parallel with histopathological changes.
6. Absence of significant artifact associated with dental filling.
7. No adverse effect has yet been demonstrated.
8. Image manipulation can be done.
9. Useful in determining intramedullary spread.

Disadvantages of MRI:

1. MRI equipment is expensive to purchase, maintain, and operate. Hardware and software are still being developed.
2. Because of the strong magnetic field used in patient electrically, magnetically or mechanically activated implants such as cardiac pacemakers, implantable defibrillators and some artificial heart valves may not be able to withstand MRI safely.
3. The MRI image becomes distorted by metal, so the image is distorted in patients with surgical clips or stents.

4. Bone does not give MR signal, a signal is obtained only from the bone marrow. The scanning time is long and requires patient' co-operation.
5. The very powerful magnets can pose problems with siting of equipment although shielding is now becoming more sophisticated.
6. MRI scanners are noisy.
7. Patient could develop an allergic reaction to the contrasting agent, or that a skin infection could develop at the site of injection.
8. MRI cannot always distinguish between malignant tumors or benign disease, which could lead to a false positive result.
9. Bone, teeth, air and metallic objects all appear black, making differentiation difficult.

Previously the MRI was unable to recognize the course of nerves due to distortion (signal to noise ratio [S/N]) (Miloro et al., 1997). Because of this, some improved protocols were applied to the LN by Miloro et al. (1997), such as the use of high resolution (HR-MRI) and specific imaging tools including the phase encode time reduction acquisition (PETRA). A bilateral, axial and coronal HR-MRI PETRA of mandible was done for 10 healthy volunteers with intact third molar in their study. The mandible was scanned and 1.5 mm slices were reconstructed for the area between the lingual nerve the mental foramen. The horizontal distance between the lateral side of the LN and the lingual plate of the mandible was measured and showed a mean distance of 2.53 (±0.67) mm, while the vertical distance between the superior edge of the nerve and the lingual crest was 2.75 (±0.97) mm. The diameter of the lingual nerve was 2.54 mm. In this study there was no bilateral correlation regarding the position of the lingual nerve, where the nerve was located above the alveolar crest in 10% of the cases (2 cases), and in 255 of the cases the nerve was contact to the lingual plate. One further investigation was performed by

Miloro et al., (1997) where they studied the relationship between the position of the tongue and the position of the lingual nerve, but found no correlation.

Despite the possibility to use the HIR-MIR to imaging the LN, its use in the clinical applications is limited primarily due to its high cost and availability.

Furthermore, documenting in situ LN injuries would be limited to complete transections, as subtle injuries would be indiscernible (Miloro et al., 1997).

2.6.3 Ultrasonography

Ultrasound is one of the most common clinical imaging modality. It has wide range of applications such as imaging of internal organ systems, transluminal endoscopic imaging, and catheter-based intravascular imaging. The function of ultrasound is based on a high-frequency sound wave, which launched by the ultrasonic probe to the organ or tissue being imaged. The quality of the image depends on the frequency of the sound wave (Kremkau, 2001).

In 2007, a new technique was used to identify the lingual nerve. Olson et al. used ultrasonography in visualizing the LN in cadaver pigs (Olsen et al., 2007). Several attempts were made before the three investigators could accurately identify the LN. The mean distance between the lingual nerve and the lingual cortex was 1 mm. This application of ultrasonography proves promising in humans, as the pig's LN is approximately 1/4 the size of the human lingual nerve. Moreover, when they become familiar with the ultrasonographic appearance of the lingual nerve all evaluators could correctly identify an intact, partially transected or fully transected nerve injury 63% of the time.

2.6.4 The optical coherence tomography

In the study of injuries of nerve in vitro, a new scanning machine, optical coherence tomography (OCT) has become a very useful machine. The OCT was introduced to the market as a non-invasive, non-radiative optical imaging modality in 1991 capable to perform high-resolution cross-sectional imaging using light. Unlike ultrasound, OCT used light instead of sound; it allows the imaging of the internal microstructure in materials and biologic system through the measuring backscattered light. An imaging resolution of 1 to 15 µm can be achieved at one to two orders of magnitude (Fujimoto et al., 2000; Hsieh et al., 2013; Huang et al., 1991). This high resolution approximates that of histopathology and allows architectural morphology and some cellular feature to be resolved (Fujimoto et al., 2000). The ability of OCT to provide cross-sectional images of tissue structure on the micron scale in situ and in the real time, made it a helpful imaging technology for medical diagnostic compared to conventional histopathology which requires removing and processing of a tissue specimen before the microscopic examination can be performed (Fujimoto et al., 2000).

Over the past few years, several functional optical coherence tomography systems were developed, such as Doppler OCT (DOCT) (Zvyagin et al., 2000), polarization sensitive OCT (PS-OCT) (Pircher et al., 2004), endoscopic OCT (Herz et al., 2004) and acoustic OCT (Lesaffre et al., 2011). These different systems were used during a variety of biomedical researches activities, not only because of their ability to produce structure images, but also for providing specific optical characteristics, including blood flow velocity and tissue orientation. Moreover, deeper transmission depth is achieved with combination of fluorescence (Iftimia et al., 2012; Park et al., 2010).

Recently, the application of OCT in dentistry has become more popular. In 1998, Colston used the OCT for the first time in vitro to image the dental hard and soft tissue in a porcine model (Colston et al., 1998). Later, the in vivo imaging of human dental tissue was presented (Fujimoto et al., 2000). In the dental clinic, the diagnosis of the dental caries and the soft tissue diseases in the oral cavity is based on the examination using dental exploration and radiographs (Xiang et al., 2010). The poor sensitivity of the routine dental instruments makes it difficult for dental practitioner to monitor the progression of periodontal destruction and the treatment outcome. At the present time, the radiograph is considered as the most popular diagnostic tool. However, it has a limitation of providing two-dimensional images. This limitation makes the detection of the caries or bone structure on the buccal and lingual sides of the teeth quite difficult, where it may superimposed by other tooth structures or normal anatomic structures (Hsieh et al., 2013).

The OCT overcomes this limitation where it analyses and detects the qualitative and the quantitative morphological changes of dental hard and soft tissue in vivo. The high spatial resolution of the OCT makes early prediction of diseases more possible. Early detection of the dental diseases can increase the survival rates of the teeth (Hsieh et al., 2013) and also detections of mechanical injuries to nerves.

2.7 Lingual nerve injury

2.7.1 Introduction

The lingual nerve provides sensory-discriminative-secretomotor function. This nerve is responsible for the sensation of the anterior two third of the tongue and the floor of the mouth (Benninger et al., 2013). The position of the lingual nerve increases the chance of the nerve injury during the various surgical procedures (Jacob, 2007). Injury to the lingual nerve may cause permanent or transitional changeable degree of anaesthesia, paraesthesia, dysaesthesia or hypoaesthesia. Symptoms of burning sensation, pain, speech changes, loss of taste to the anterior two-third of the tongue, drooling and tongue biting may occur because of nerve injury (Fielding et al., 1997; Graff‐Radford & Evans, 2003; Pichler & Beirne, 2001; Renton & McGurk, 2001).

2.7.2 Incidence of lingual nerve injury

Although some iatrogenic injury to the lingual nerve is inevitable especially during the removal of the malignant mass, a high percentage of the nerve damages are the result of elective or unfortunate iatrogenic procedures (Lam & Holmes, 2002; Robinson, Loescher, et al., 2004). Several dental and surgical procedures that may cause damage to the lingual nerve are the insertion of dental implant (Berberi et al., 1992), inattentive instrumentation during mandibular osteotomies (Becelli et al., 2004; Jacks et al., 1998; Zuniga et al., 1997), and the administration of local anaesthetic agent (Fagin et al., 2012). Surgical intervention of the submandinular gland (Dias et al., 2015) and the removal of impacted third molars are considered the common causes of lingual nerve injury (Boffano et al., 2012).

The removal of impacted third molar has been reported to be responsible for 75% of the lingual nerve injury (Lam & Holmes, 2002). This is not surprising because this procedure is one of the most commonly performed procedure in the dental clinic (Lam & Holmes, 2002). In 2001,150,000 case of impacted third molars per year were reported in Britain and their removal happens to be the eighth common surgical procedure (Renton & McGurk, 2001). The relationship of surgical removal of the third molar to the lingual nerve injury in the literature is conflicting. In most of the previous studies, lingual nerve injury was reported to happen in 0.6% - 2.0% of the surgeries performed (Bataineh, 2001; Behnia et al., 2000; Brann et al., 1999; Chossegros et al., 2002; Hölzle & Wolff, 2001; Karakas et al., 2007; Pogrel et al., 1995; Renton & McGurk, 2001). However, in a contrasting report, the prevalence has been reported to be as high as 23% (Middlehurst et al., 1988). The sensory disturbance, which came as a result of the nerve injury may be often temporary and recovery occurs in 8 weeks, with only 0.5 – 1.0 % of the cases reported lingual nerve dysfunction that was permanent (Blackburn & Bramley, 1989; Jerjes et al., 2006).

2.7.3 Factors influencing lingual nerve injuries

Many factors may play a role in causing nerve injuries and contribute to the lingual nerve paraesthesia during the third molar surgery. This includes the surgical techniques adopted, which included the use of the lingual retractor during procedure. This association is well documented in the literature (Brann et al., 1999; Mason, 1988; Obiechina, 1990; P. Robinson & Smith, 1996b; Rood, 1983, 1992; Schultze-Mosgau & Reich, 1993; Wofford & Miller, 1987). Avoidance of the lingual retractor reduces the frequency of temporary lingual nerve injury and reduces the possibility of permanent nerve damage (Bataineh, 2001; Chossegros et al., 2002; Robinson & Smith, 1996b). However, in 2001, Pichler and Beirne reported that there was no significant difference in the presence of permanent nerve damage whether when the lingual retractor was used or not (Pichler & Beirne, 2001). Greenwood et al. (1994) argued in support of a broad retractor to protect the LN rather than a Howarth periosteal elevator since it produces less paraesthesia at one month. In contrast, Appiah-Anane and Appiah-Anane (1997) reported reduction in the rate of lingual nerve injury to 0.2% by avoiding the use of the lingual flap and maintaining the lingual plate of the mandible.

In 1993, Peterson showed an interesting finding that relates lingual nerve injury to the angulation of the impacted third molar. According to his study 43% of lingual nerve paraesthesia was associated with mesioangular impacted third molar, while only 6% associated with distoangular impaction (Peterson, 2003). On the other hand, Bataineh (2001) failed to record any relationship between the angulation of the tooth and the rate of lingual nerve paraesthesia. The effect of age on the nerve paraesthesia is conflicting. Both Lyons et al. (1980) and Chiapasco et al. (1995) reported a positive association between aging and the increase in the incidence of lingual nerve damage. Lyons et al. (1980) recorded a incidence of 1.8% of lingual nerve damage in patients with a mean age of 46.5 years, while patients with a mean age of 20 years showed only 0.6% of lingual nerve injury. However, many other studies failed to recognize a relationship between nerve damage and the age of the patient (Bataineh, 2001; Brann et al., 1999; Jerjes et al., 2006).

The contribution of the general anaesthesia in increasing the rate of the lingual nerve injury during the surgical procedure in comparison to the local anesthesia was evident (Brann et al., 1999; Lyons et al., 1980). Brann et al. (1999) demonstrated a 5-times increase in the rate of lingual nerve paraesthesia under general anesthesia in comparison to local anaesthesia. He related this association with several factors during the procedures, such as the patient supine position, greater surgical force, high amount of bone removal, and the extent of flap exposure. The experience of the surgeon is also considerated an important factor in the incidence of the lingual nerve injury (Bataineh, 2001; Gülicher & Gerlach, 2001; Jerjes et al., 2006; Sisk et al., 1986). Jerjes et al. (2006) in his prospective study estimated several predictors of tongue paraesthesia. Their finding showed that the seniority of the surgeon to be a significant predictor (P=0.022) in determining whether a permanent LN paresthesia will occur. The permanent lingual nerve damage was reported to be 4-fold more in the trainees group. This high percentage may due to the lack of experience, inappropriate use of force and improper instrumentation.

2.7.4 Classification of LN injuries

Several classifications for the sensory disturbance following peripheral nerve damage include histopathologic, anatomic, physiologic, symptomatic and pathophysiologic (McGuire, 2005). Seddon (1943) and Sunderland (1951) classifications are the most used where they correlate with the severity with prognosis.

2.7.4.1 Seddon's classification

This classification is based on the degree of damage to the three main fibers of the nerve; epineurium, perineurium and endoneurium. The first type of injury in this classification is considered less severe and was termed neurapraxia. It completely recovers within hours to several days where the axon remains intact and the damage is restricted to the myelin and this interrupts the conduction of impulse. Most of the injuries that occur as a result of using lingual retractor during the surgical procedures are classified as neurapaxia. The second type in his classification is axonotmesis, and this type is considered more severe than neurapraxia. Although the epineurium is intact, some fibers show degeneration. Incomplete recovery may occur in the duration range from weeks to years, with a possibility of neuroma formation. The last type of injury is termed neurotmesis and denotes a more serious injury. Due to the loss of continuity in the connective tissue layers, the axon is poorly regenerated and no recovery will take place (Seddon, 1943).

2.7.4.2 Sunderland's classification

In 1951, Sunderland based his classification on Seddon's classification, but he included the mechanism of injury and the way to manage such injuries. Sunderland classified the degree of nerve injury into five levels. The first level were sub-classified into three types, all the three were equivalent to Seddon's neurapraxia. At this level, although the axon and the connective tissue are intact, the conduction is temporarily blocked. First level type I injuries occur as a result of mild traction or compression leading to transient ischaemia. Recovery occurs within twenty-four hours without surgical intervention. First level type II injuries are the result of more severe traction or compression, leading to decreased blood flow, intrafascicular oedema and a conduction blockade (Graff - Radford & Evans, 2003). The recovery takes from days to weeks and the sensation returns after oedema has decreased. First level type III injuries are considered more serious than the other two, where the traction and the compression caused a localized mechanical disruption of myelin sheaths and demyelinization. The disturbance in sensation will take place from one to two months before the normal sensation returned. In this classification the second, third and fourth level belong Seddon's classification of axonotmesis. In second level injuries, despite the three main layers of the nerve fiber (epineurium, perineurium and endoneurium) being intact, Wallerian degeneration of the axon takes place. Sensory recovery will occur within 2-3 month but it may extend to one year for full recovery. In contrast, Wallerian degeneration of the axon in the third level which occurs as a result of moderate to severe crush or traction insult causes a disruption to the endoneurium layer. The affected endoneurium will prevent the regeneration of the axon and lead to a degree of loss of sensation. At the fourth level injuries which come as a result of a severe trauma, both endoneurium and perineurium layer will be involved and the loss of sensation will take place with a possibility of neuroma formation or intraneural fibrosis. The fifth level injuries correlate with Seddon's neurotmesis classification. These types of serious injuries are occurring due to transection, avulsion or laceration of the nerve and leading to the disruption of the three connect tissue layers. A complete anaesthesia will take place with a potential for several sensory disorders such as allodynia, hyperalgesia or hyperpathia (Fonseca, 2005). In 1990, MacKinnon and Dellon, added the sixth level of injury to Sunderland's classification in which different level of injury that may co–exist within a signal nerve (Mackinnon & Dellon, 1990).

2.7.5 The outcomes following lingual nerve injury

The lingual nerves can be severed, stretched or crushed during surgery or trauma (Cheung et al., 2010). The LN can be damaged during many diverse interventions such as dentoalveolar, implant, orthognathic and benign and malignant tumour surgeries, endodontic therapy, facial trauma repair and local anaesthetic injection. The outcomes following such injury may vary according to the different causative factors of injury, times until repair and reconstruction types. Yamauchi et al. (2006) (Yamauchi et al., 2006) evaluated three LN-injury patients injured during third-molar extraction and treated with tension-free anastomosis. In his study, all the patients had some improvement, although some were still considered sensory impaired. Rutner et al. (2005) (Rutner et al., 2005) studied the long-term outcome of LN-injury repair. In his study, 90% of patients reported subjective improvement, with 50% rating the improvement as moderate or significant, and 85% showed neurosensory improvement. Farole and Jamal (2008) performed a study on third-molar extraction LN and IAN injuries repaired with a NeuraGen bioabsorbable collagen nerve cuff. In that study, they showed some success, with eight of nine patients showing some to good improvement. Hillerup (2008) studied IAN injuries, including those from third-molar extractions. Interestingly, of the patients who opted out of surgery, only those with third-molar injuries spontaneously recovered, whereas injuries from local anaesthetic injections, implant surgery and endodontic therapy did not (Hillerup, 2008). One study focused on the lingual nerve injuries resulting from maxillofacial trauma. In that study, the functional sensory recovery (FSR) was achieved in 86% of the 30 patients.

The time to repair following IAN and LN injury is a controversial issue. It played a significant role in overall surgical outcome, although the exact timing is still variable. Susarla et al. (2007) stated that patients with LN repair within 90 days of injury had FSR within 1 year after repair in 93% of cases. Pogrel et al., stated that microsurgical repair within 10 weeks of injury showed better results for FSR of both the IAN and LN (Pogrel, 2002; Pogrel & Maghen, 2001; Pogrel et al., 1998). Jones (2010) stated that 3 months after injury is the optimal time for nerve repair unless it is known that the injury has occurred at the time of surgery, in which case immediate nerve reconstruction provides better recovery results (Jones, 2010). Ziccardi et al. (2009) observed improved treatment of diverse iatrogenic IAN and LN injury if intervention began within 6 months of damage (Ziccardi et al., 2009). Two of the larger studies calculated that the odds of FSR decreased between 5.8 and 11% for each month of delay (Bagheri et al., 2012; Bagheri et al., 2010). When reviewing repair methods, the literature supports using external decompression or direct suturing of injured nerve ends whenever possible (Mozsary & Syers, 1985; Robinson et al., 2000). In cases with neuroma excision followed by direct suturing, FSR was slightly decreased or delayed, but this is still the best method overall (Mozsary & Syers, 1985; Susarla et al., 2007). Where direct suturing without tension is not possible, nerve grafting should be considered (Lam et al., 2003; Strauss et al., 2006; Susarla et al., 2005).

CHAPTER THREE: A STUDY ON THE VARIATION OF THE LINGUAL NERVE IN CADAVERS

3.1 Introduction

To recapitulate, LN is one of the two terminal branches of the posterior division of the mandibular nerve. It supplies the general sensation to the mucosa of the anterior two-thirds of the tongue, the sublingual mucosa, the mandibular lingual gingiva and the floor of the mouth (Chao et al., 2013; K. W. Chung & Chung, 2008; Snell, 2011; Weaker, 2013). The chorda tympani nerve, a branch of the facial nerve joins this nerve carrying taste fibers from the anterior two third of the tongue and parasympathetic fibers to the submandibular ganglion (Drake et al., 2012; Weaker, 2013)

This nerve occasionally communicates with the inferior alveolar, auriculotemporal or the mylohyoid nerves, and then passes between the lateral and medial pterygoid muscles in the infratemporal fossa before proceeding anteriorly and inferiorly on the surface of the medial pterygoid muscle. It has been found to have variable relationships with the medial surface of the medial pterygoid muscle during its course (Erdogmus et al., 2008; Mendes et al., 2013). The LN courses closer to the medial surface of the mandibular ramus until it is just a few millimeters below and behind the junction of the vertical and horizontal rami of the mandible (McGeachie, 2002). It enters the submandibular region after passing forward and medially, inferior to the lower border of the superior constrictor muscle of the pharynx and then becomes in close relationship to the lower third molar (Snell, 2011).

It then courses along the periosteum on the medial surface of the mandible to lie opposite the posterior root of the lower third molar. Here, it is covered only by the gingival mucoperiosteum, which is closely bound to the lingual plate of the mandible for a distance of 28.17 mm (Dias et al., 2015; Mendes et al., 2013; Piagkou et al., 2011). It has been reported that in 20 – 62% of the time, the LN is in contact with the lingual cortical plate (Behnia et al., 2000; Dias et al., 2015; Hölzle & Wolff, 2001; Kiesselbach & Chamberlain, 1984; Miloro et al., 1997). Furthermore, in between 4.6% and 21.0% of the cases, the LN may be situated at/or above the crest of bone (Behnia et al., 2000; Benninger et al., 2013; Dias et al., 2015; Hölzle & Wolff, 2001; Kiesselbach & Chamberlain, 1984; Pogrel et al., 1995). Interestingly the less common site is at the retromolar pad region, which was noticed in 0.15 and 1.5% of the cases (Behnia et al., 2000; Kiesselbach & Chamberlain, 1984). When not in contact with the lingual plate, the LN usually lies within 2.28 – 16.8 mm below the alveolar crest and 0.57 – 7.10 mm medial from the lingual plate (Behnia et al., 2000; Bokindo et al., 2015; Mendes et al., 2013). Trost *et al*. found that the LN can be very close to the periosteum with a mean horizontal distance of only 1.9 mm but did not report the vertical relationship (Trost et al., 2009). The average shortest distance between the LN and the retromolar region was 4.45 – 8.62 mm (Benninger et al., 2013; Erdogmus et al., 2008; Hölzle & Wolff, 2001; Kim et al., 2004; Mendes et al., 2013; Pogrel et al., 1995). The average distance from the mesial and the distal portion of the mandibular third molar area to the LN has been reported to be 9.5 mm and 15.5 mm, respectively (Kim et al., 2004). The variations in mean distances of lingual nerve to the mandible as reported by several researchers are summarized in Table 1.1 in Chapter 2 (*Literature review*).

The LN may give off a branch to the lingual gingival tissue, extending horizontally from the medial mandibular cortex at the level of the retromolar pad to mesial of the lower first molars-second premolars to supply the lingual periosteum, gingiva, and mucosa that are overlying the medial alveolar process (Bokindo et al., 2015; Erdogmus et al., 2008; Kim et al., 2004; Kocabiyik et al., 2009). Kim et al. called it "collateral nerve twigs" while Kocabiyik et al. proposed that it should be named "the gingival branch of the lingual nerve" (Kim et al., 2004; Kocabiyik et al., 2009).

From the third molar region, the LN leaves the lingual plate and courses towards the tongue. The mean sagittal distance of the nerve from retromolar area up to its medial bend toward the tongue has been reported to be 21.47 mm (Hölzle & Wolff, 2001). Chan et al. reported that 75% of LNs turned toward the tongue at the first and second molar region. The vertical distance from the LN to the mid-lingual cemento-enamel junctions of mandibular molars and premolars has been reported to be 9.6 mm, 13 mm, and 14.8 mm at the second molar, first molar, and second premolar, respectively (Chan et al., 2010). The LN then runs anteriorly and medially on the upper surface of the mylohyoid muscle to travel on the external surface of the hyoglossus muscle deep to the submandibular gland. At the anterior border of the hyoglossus the LN turns around the outer side of the submandibular duct (Wharton's duct) to ascend into the body of the tongue medial to the duct (Rusu et al., 2008).

The LN usually passes lateral to the submandibular duct, winds below it and then passes upwards and forwards on its medial side on its way to the surface of hyoglossus (Erdogmus et al., 2008; Hölzle & Wolff, 2001). This relationship has been reported to be the norm in 62.5% side cadaver heads, with the remaining 37.5% cases showing the LN crossing above the duct (Mendes et al., 2013). No constant position has been found to relate the point of intersection as it can happen anywhere from the distal part of the second premolar tooth to the retromolar trigone. One study reported that this intersection often happens around the premolar region (Mendes et al., 2013) while another reported that

55% of the intersection occurred at the level of the third molar tooth or behind it (Castelli et al., 1969). The length of this intersection has never been reported. The distance between the alveolar plate, at the level of the third molar region, and the sublingual region of intersection was reported to be 22.6 mm (Mendes et al., 2013). Occasionally, the submandibular duct runs deep in the floor of the mouth, with no relationship with the LN. This accounted for 11.8% of samples in one cadaveric study (Hölzle & Wolff, 2001).

The LN may give out branches that communicate with the mylohyoid nerve, sometimes termed as the "mylohyoid or sublingual curl" (Fazan et al., 2007; Kim et al., 2004; Rácz & Maros, 1981). The prevalence of such communication has been reported to range between 12.5% and 33.3% (Kim et al., 2004; Rácz & Maros, 1981). The average length of this communicating nerve ranged from 14.2 mm to 20.1 mm, with an average of 17.2 mm (Fazan et al., 2007; Kim et al., 2004; Sato et al., 2004; Thotakura et al., 2013). In addition, the LN may also communicate with the hypoglossal nerve on the anterior border of the hyoglossus muscle (Păduraru & Rusu, 2013; Piagkou et al., 2011; Rusu et al., 2008; Saigusa et al., 2006; Touré et al., 2005). The prevalence of such communication has been reported to be 40% in a cadaveric study (Fitzgerald & Law, 1958).

The submandibular duct on the other hand, emerges from the medial side of the deep lobe of the submandibular gland, inferior to the mylohyoid muscle in the oral cavity and opens in a small sublingual papilla beside the base of the frenulum of the tongue (Drake et al., 2014; Fischer et al., 2006).

Lingual nerve neuropathy can results from the presence of pathology or following surgical procedures performed to structures adjacent to the vicinity of the LN.

As a consequence, patients may suffer from neurosensory disturbance or impaired taste sensation (Fielding & Reck, 1986; Klasser et al., 2008; Tan et al., 2014). Due to its course and location, the medial aspect of the mandible adjacent to the third molar and the lateral edge of the tongue base are the areas where the LN is most susceptible to surgical or procedural trauma (McGeachie, 2002; Windfuhr et al., 2009) The cause for LN injury in the former site is third molar surgery (Blackburn & Bramley, 1989; Fielding & Reck, 1986; Gülicher & Gerlach, 2001; Loescher et al., 2003; Mason, 1988; McGeachie, 2002; Mozsary & Middleton, 1984; Queral-Godoy et al., 2006; T Renton & McGurk, 2001; Valmaseda-Castellón et al., 2000; Walters, 1996), orthognathic surgery (Al-Bishri et al., 2004; Guernsey & DeChamplain, 1971; Jacks et al., 1998; Meyer, 1990), and occasionally periodontal (Hunt, 1976; Reinhart, 1990) or pre-prosthetic surgery (Mozsary & Middleton, 1984). LN injury at the lateral edge of the tongue base has occasionally been reported to occur in association with the provision of general anaesthesia via submental endotracheal intubation (Toledo et al., 2013) or following trauma that results from endolaryngeal microsurgery (suspended laryngoscopy) (Gaut & Williams, 2000; Mohamad & Mohamad, 2012). As the LN intersects with the submandibular duct in the floor of the mouth, there is a risk of lingual nerve injury during surgical interventions in this region, such as ductoplasty and removal of sialoliths. Likewise, surgical procedures to the lingual nerve in this region will increase the possibility of submandibular duct injury, which may then cause a ranula to develop (Chi et al., 2008; Chung et al., 2012).

3.2 Summary

As shown by the review above, there is a wide variation in the course of the LN at the third molar region up to its intersection with the submandibular duct. Therefore, appreciating variations in the course of the LN is important for achieving successful outcomes in various dental, oncological and reconstructive procedures by minimizing the risk of injuring this nerve. This part of the research aimed to describe and relate in detail the course of the LN in cadavers, in relation to its adjacent structures, beginning at the molar region in relation to the third molar and the alveolar ridge and lower border of the mandible, along the floor of the mouth, and when intersecting with the submandibular duct. Tracking of the terminal branches of LN in the ventral surface of the tongue was also performed.

3.3 Materials and Methods

This study received the relevant Institutional Board of Study approval of the Faculty of Medicine [968.35] and the Faculty of Dentistry [DF DP 1305/0023(P)], University of Malaya. For the human cadavers, consent was obtained following a protocol set by the University of Malaya when the bodies were donated for teaching/research purposes.

3.3.1 Methods

Seven human cadavers (all elderly Asian males) who were stored in 10% formalin were obtained from the Department of Anatomy, Faculty of Medicine, University of Malaya. The mandibles were checked to be free of lesion and had not undergone any surgery or reconstructive procedure at the area of investigation. The presence or absence of the mandibular molar teeth was recorded. In all, these cadavers had altogether 30 missing molars (average ~ 4 molars per cadaver). Therefore in total we had fourteen lingual nerves for our study.

This study consisted of two parts: (a) obtaining morphometrical measurements of the lingual nerve, and (b) obtaining non-metrical or morphological appearance of its terminal branches. The exploration of the LN was achieved through an incision made in the retromolar region, extending until the point where it adopted a horizontal pathway away from the lingual plate, towards the point where it crosses the submandibular duct.

As there was difficulty to insert a standard pair of calipers into the narrow exposed retromolar region and in order to avoid over retracting the soft tissue (which may change the anatomical relation of the lingual nerve), a customized ruler was fabricated to ensure good access and standardization in measuring all the anatomical sites in this study (Figure 3.1).

Figure 3.1: Image showing the custom-made ruler fabricated for this study.

The vertical distances from the lingual nerve to two anatomical landmarks, namely the alveolar ridge and the lower border of the mandible, was measured using this measuring device. The dentition on the mandible was used as a position landmark because all mandibles came in different sizes, and it was difficult to standardize the sites for measurement. In cases where posterior teeth were missing, reconstruction of the lost teeth was done by placing average sizes of the molar teeth onto the alveolar ridge. The width or length of each molar was determined using Woelfel's dental anatomy guideline (Scheid, 2012) and this position was marked on the alveolar ridge using a permanent marker. The approximate positions of the occlusal surface landmarks (cusps and developmental groove) were marked accordingly.

3.3.1.1 The distance of lingual nerve to alveolar ridge.

After the three sites of each molar tooth was determined and marked on the alveolar ridge, the horizontal bar of the ruler was placed onto the alveolar ridge and the vertical ruler, which was attached to the horizontal bar of the device, was slid by using the adjacent part until it contacted the lingual nerve. This distance was recorded from the alveolar ridge (Figure 3.2).

3.3.1.2 The distance of lingual nerve to the inferior mandibular border

The process of obtaining this measurement was made following exposure of the inferior border of the mandible. This measurement was determined as the distance between the lingual nerve and the inferior border of mandibular border (IBM) at the previously determined three points of reference sites marked on the alveolar ridge (Figure 3.2).

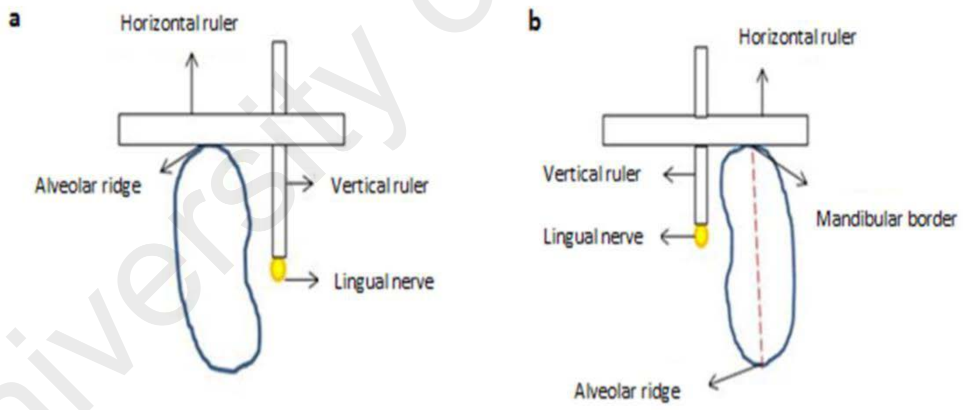

Figure 3.2: Illustration showing the ruler in use for measuring the distance of the lingual nerve to (a) the alveolar ridge and (b) the lower border of the mandible.

3.3.1.3 The length of lingual nerve prior to diversion to the tongue

One other measurement performed was the length of the lingual nerve at the floor of the mouth prior to diversion towards the tongue. This extension of the lingual nerve was measured as a distance from the deepest point at the angle of the ramus and body of the mandible to the point at which it changes its direction toward the tongue (Figure 3.3).

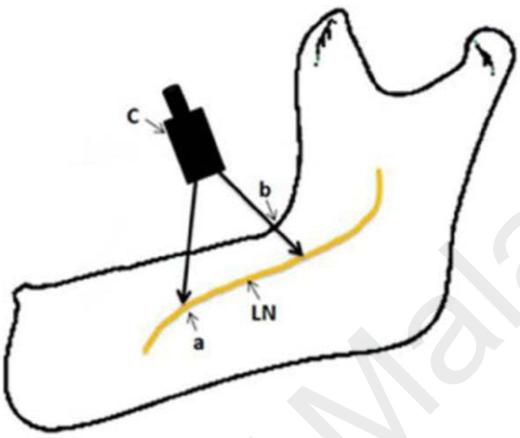

Figure 3.3: The length of the lingual nerve at the floor of the mouth; a) the point at which the lingual nerve changes direction towards the tongue, b) the deepest point at the angle of the mandible, c) the caliper used to measure the length of lingual nerve.

As the nerve extends anteriorly, it bends and changes its direction to reach the tongue. The location at which the nerve changes its direction varies. These locations were observed in all the 14 cases, and their exact sites were recorded.

The deep incision described above was extended from the point at which the lingual nerve changes its direction toward the tongue. Then, the soft tissue was dissected carefully until the submandibular duct was found, while maintaining its anatomical relationship with the lingual nerve. The presence of the lingual nerve looping around the submandibular duct was first determined.

3.3.1.4 Determining the beginning and the end of overlap between the lingual nerve and submandibular duct

When present, the custom-made vertical ruler was slid down until it touched the starting point of the overlap of the lingual nerve and the submandibular duct. The horizontal ruler was supported on the alveolar ridge as in Method (3.2.1.1). The position at which the horizontal bar rested on the alveolar ridge in relation to the dentition was recorded (Figure 3.4). These positions were reported as being any of the followings:

i) At the lingual developmental groove of first molar
ii) Between first & second molars
iii) At the lingual developmental groove of second molar
iv) Between second & third molars
v) At the lingual developmental groove of third molar
vi) At the distal surface of third molar

The same steps were followed to determine dental relationship at the end of this overlap.

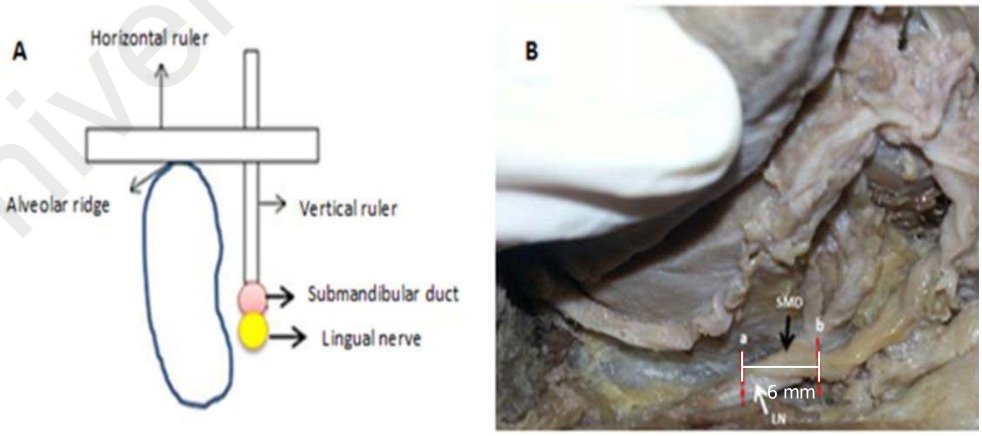

Figure 3.4: (A) The diagram illustrates the way to determine the start and the end point of overlap between the submandibular duct and the lingual nerve. (B) The start of the overlap (a); the end of overlap (b); LN: lingual nerve; SMD: submandibular duct.

3.3.1.5 Measuring the distance of overlap between the lingual nerve and the submandibular duct

Using the landmarks identified in Method (3.2.1.1), the extent of overlap between the lingual nerve and the submandibular duct was measured from the start to the end of the overlap between the two structures using a pair of manual calipers (Figure 3.5).

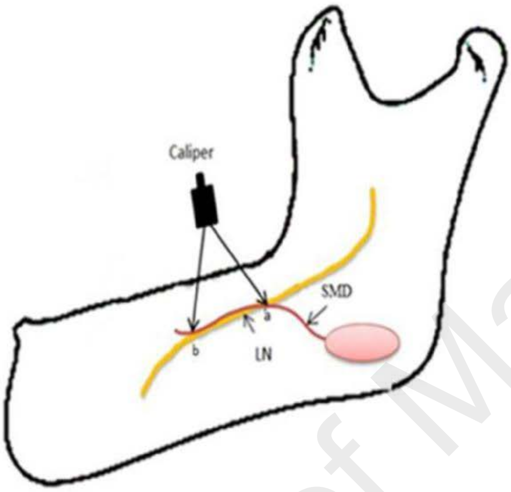

Figure 3.5: The diagram illustrates the measuring of the extent of overlap between the lingual nerve and the submandibular duct (distance a-b).

3.3.1.6 Non-metrical or morphological considerations prior to insertion into the tongue

As the nerve extends anteriorly, it inserts into the tongue. The location at which the nerve changes its direction to insert into the tongue varies, and all their exact sites were recorded. Furthermore, a detailed study was done on the pattern of the lingual nerve endings at the ventral surface of the tongue (Figure 3.6). This pattern is described as the followings:

Pattern 1: Only one lingual nerve at the terminal end

Pattern 2: Two branches were found at the terminal end

Pattern 3: Three branches were found at the terminal end

Pattern 4: Four branches or more were found at the terminal end.

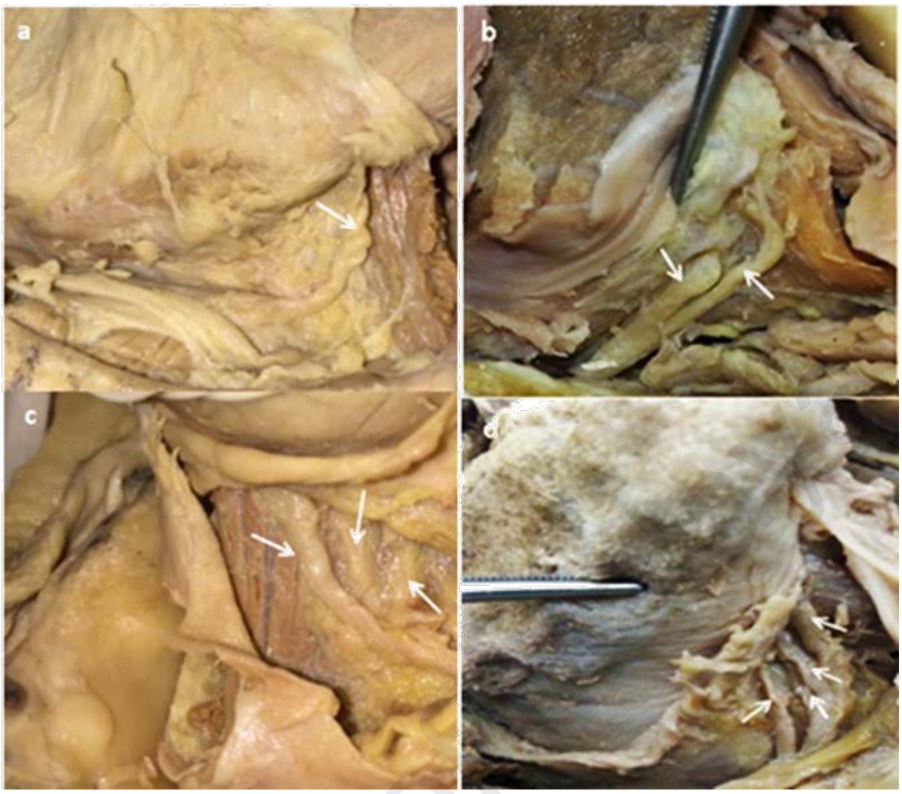

Figure 3.6: The four different patterns of the lingual nerve endings at the ventral surface of the tongue (a) Only one lingual nerve at the terminal end; (b) Two branches were found at the terminal end; (c) Three branches were found at the terminal end; (d) Four branches or more were found at the terminal end.

3.4 Reliability of measurements

Intra-examiner reliability was assessed by re-evaluating of all the samples thrice with a one week interval and without the knowledge of the previous measurements. All the data obtained were by using the same methods described earlier. Data collected was analyzed statistically. The reliability test (Tables 3.1, 3.2) shows that there was correlation between the first, second and third measurements. The variations between the measurements were negligible. Therefore, reproducibility of the evaluation method was acceptable.

Table 3.1: Reliability test (Intraclass Correlation)

Intraclass Correlation Coefficient

	Intraclass Correlation[b]	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.997[a]	.995	.998	919.024	84	168	.000
Average Measures	.999[c]	.998	.999	919.024	84	168	.000

Table 3.2: Reliability test (Kappa test)

Symmetric Measures

		Value	Asymp. Std. Error[a]	Approx. T[b]	Approx. Sig.
Measure of Agreement	Kappa	1.000	.000	15.248	.000
N of Valid Cases		40			

3.5 Statistical analysis

All collection of measurements were performed by the same examiner and descriptive analyses reporting on the mean and standard deviations was performed using SPSS 20 program.

3.6 Results

In the present study, the mean distance between the LN and the alveolar ridge was 12.36 mm (SD 3.37) [Table 2]. This distance varies between sites, measuring at the third molar region at an average of 12.61 (SD 3.40) mm. At the second molar region, this distance became shorter at 11.46 (SD 2.98) mm before increasing again at the first molar area to 14.38 (SD 4.35) mm.

In comparison, the distance between the lingual nerve and the inferior mandibular border increased gradually from the third molar region to the first molar region. At the third molar region, this distance was 10.79 (SD 3.49) mm, 12.46 (SD 3.97) mm at the second molar, and 15.00 (SD 2.16) mm at the first molar region. In general, the LN was located 12.03 mm from the lower border of the mandible. Table 3.3 provides the mean distance as well as 95% confidence interval of all the measurements obtained.

Table 3.3: The mean distance between the lingual nerve and the 2 anatomical landmarks

Site	**Distance in mm (mean ± SD; 95% CI)**	
	Alveolar ridge	**Lower border of mandible**
First molar	14.38 (4.35) CI: 7.46 to 21.29	15.00 (2.16) CI: 11.56 to 18.44
Second molar	11.46 (2.98) CI: 9.66 to 13.26	12.46 (3.97) CI: 10.06 to 14.86
Third molar	12.61 (3.40) CI: 10.64 to 14.57	10.79 (3.49) CI: 8.77 to 12.80
Overall	12.36 (3.37) CI: 11.12 to 13.59	12.03 (3.75) CI: 10.66 to 13.41

Table 3.4 outlined the detailed measurements obtained from each cadaver, together with the extent of the lingual nerve on the floor of the mouth prior to diversion towards the tongue. It also provides the number of terminal branches of the lingual nerve.

Table 3.4: Detailed morphometric measurements of each cadaver when tracing the course of the lingual nerve. The number of terminal branches is shown at the far right of the table

	Distance between LN & alveolar ridge (mm)*		**Distance between LN & IBM (mm)$^{\varphi}$**		**Length of LN on the floor of mouth (mm)**		**No. of Terminal branches**	
No. 1	right	left	right	left	right	left	right	left
M3	17	17.5	12	16	41	38	2	2
M2	17.5	16	17	15				
M1	19	16.5	16	17				
No. 2								
M3	11.5	14	7	10	23	28	2	3
M2	11.5	13	9	13				
M1	-	-	-	-				
No. 3								
M3	10	13	12	14	31	24	3	4
M2	12	13	10	16				
M1	13	-	12					
No. 4				-				
M3	15	8	8	12	20	17	2	1
M2	8	8	10	13				
M1	-	-	-	-				
No. 5								
M3	15	10	15	10	22	22	2	3
M2	12	8	15	13				
M1	-	9	-	15				
No. 6								
M3	7	7	6	4	17	19	4	3
M2	9	-	2	-				
M1	-	-	-	-				
No. 7								
M3	15	14.5	12	13	25	29	2	2
M2	10	11	15	14				
M1	-	-	-	-				

IBM: inferior border of mandible; LN: lingual nerve
*No significant difference noticeable between sides (P>0.05) φ No significant difference noticeable between sides (P>0.05)

We are mindful that the LN passes besides the lingual plate in the oral cavity, then lies of the floor of the mouth before it changes direction and deviates toward the tongue. The point at which the lingual nerve changed direction (deviated) varied from one cadaver to another. The mean distance of the LN lying on the floor of the mouth before it curved and deviated toward the tongue was 25.43 (SD 7.31) mm (Table 3.4). This distance ranged from 17 mm to 41 mm. The 95% confidence interval was 21.21 to 29.65 mm. The five different locations where deviation occurred are summarized in Figure 3.7.

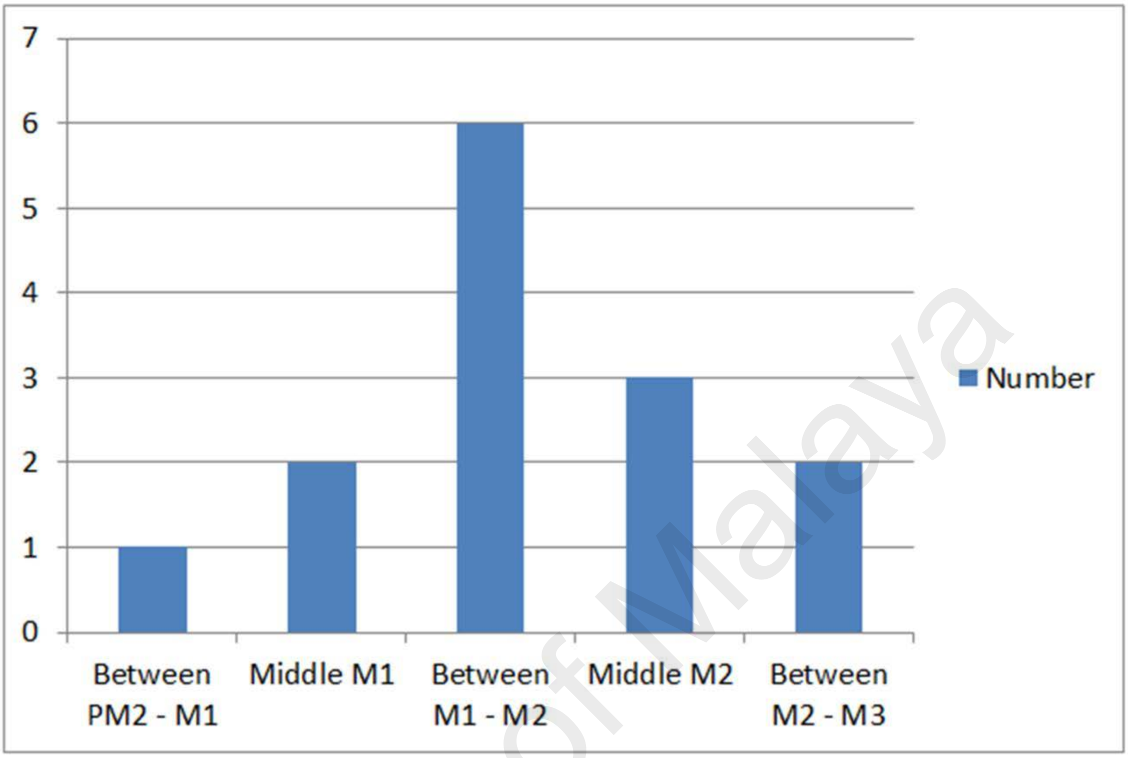

Figure 3.7: The location at which the lingual nerve made a sudden deviation toward the floor of the mouth.

In all cases, the LN was found to make a sudden deviation towards the floor of the mouth between the mesial of the first molar (M1) and distal of the second molar (M2) teeth regions (Fig 7). In most cases (42.9%), the deviation occurred at between the proximal surfaces of the first and second molar (M1-M2). The most mesial location of deviation was noticed a single case, occurring at the mesial aspect of the first molar.

Thirteen lingual nerves were found to overlap or loop around the submandibular duct, i.e. they coursed from the superior to the beneath the submandibular duct. In one case the submandibular duct was surprisingly not traceable. These looping began somewhere between the second and third molars (Table 3.5). It is evident that the majority of them occurred between the lingual developmental grooves of the second and third molars

(92.4%). In 10 out of the 13 cases, the loop started around the third molar region but only in one case this loop began at the distal surface of the third molar.

Table 3.5: The location where the looping of the lingual nerve over the submandibular duct began

Location		Number (percent)
At the lingual developmental groove of second molar		3 (23.1%)
Between second & third molars		4 (30.8%)
At the lingual developmental groove of third molar		5 (38.5%)
At the distal surface of third molar		1 (7.6%)
	Total	13 (100%)

The looping of the LN over the submandibular ended somewhere between the first and the third molars region. The majority (69.2%) of these looping ended at between the M1-M2 and at the lingual developmental groove of the second molar. In the remaining 4 cases, 2 of the overlaps terminated at the level of the lingual developmental groove of the first molar, while the remaining two ended this relationship between the second and third molar (Table 3.6).

Table 3.6: The location where the looping of the lingual nerve over the submandibular duct ended

Location		Number (percent)
At the lingual developmental groove of first molar		2 (15.4%)
Between first & second molars		5 (38.5%)
At the lingual developmental groove of second molar		4 (30.8%)
Between second & third molar		2 (15.4%)
	Total	13 (100%)

In summary, it can be observed that in 76.9% of the cases the loop started around the M3 region but all looping ended at around the first and second molar teeth region, with none of them occurring beyond the lingual groove of M1.

The exact distance of the overlap was measured for each of the 13 cases and a mean distance of 6.92 (SD 2.78) mm was found. This distance measured as little as 1.50 mm to as much as 13.00 mm.

At the ventral surface of the tongue, the lingual nerves gave out more than one terminal branch in 13 hemi-mandibles. This study recorded 4 different patterns of nerve endings, as shown in Figure 3.8.

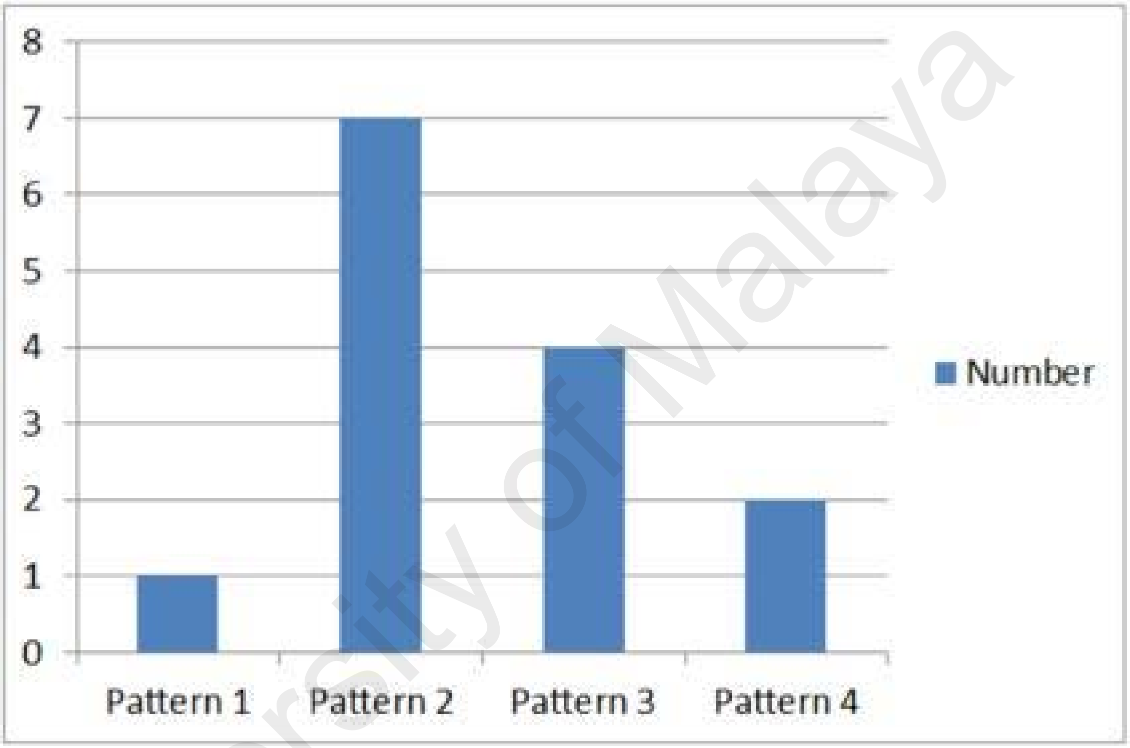

Figure 3.8: The pattern of terminal branching of the lingual nerve.

The most common pattern was the presence of 2 terminal branches at the ventral surface of the tongue, accounting for half of the pattern of branching. The presence of 3 and 4 terminal branches were also evident (28.6% and 14.3% respectively). The least common was the presence of a single terminal branch in one case. Interestingly the findings showed variations within each cadaver (between the right and left side), with only two cadavers showing similar pattern of terminal branching at both sides (Table 3.4).

3.7 Discussion

The most commonly reported neuropathy of the LN is associated with surgical trauma that results from removal of the impacted lower third molars (Hillerup & Stoltze, 2007; Robinson & Smith, 1996a), followed by needle-related injury associated with the provision of inferior alveolar nerve blocks (Harn & Durham, 1990; Pogrel et al., 2003; Pogrel & Thamby, 2000). Other less common causes include periodontal and pre-prosthetic surgery that is performed at the vicinity of the lingual nerve at the retromolar region (Mozsary & Middleton, 1984), resection of tumour at the retromolar trigone (Goldie et al., 2006), neural invasion of cancer (Lee et al., 2015) and orthognathic surgery (Jacks et al., 1998). Most of these cases of injury or tumor invasion have been reported to happen at the medial aspect of the mandible adjacent to the third molar and the lateral edge of the tongue base (McGeachie, 2002; Windfuhr et al., 2009). One other site where lingual nerve injury has been reported is at the floor of the mouth, as a result of submental endotracheal intubation (Toledo et al., 2013).

As the main cause of LN injures involves third molar surgeries, the initial objective of this study was to determine the relationship of the LN to the third molar tooth, as shown in Table 2.1. In this study, the average vertical distance was greater than the distance recorded by all other authors, apart from Mendes et al. (2013) (Table 2.1). There was no difference between the measurements obtained from the right and left sides of the hemi-mandibles, so all results shown were those of pooled data. No attempt was made to measure the distance of the lingual nerve to the lingual bone plate as it was found that dissecting cadavers fixed in formalin cause distortion to the horizontal relationship between the two structures. This in turn could affect the vertical measurement of the lingual nerve. The relationship of this nerve to the other posterior teeth was not given prominence as there is just one study that reported the vertical distance of the LN adjacent to the first, second and third molars (Chan et al., 2010). However, this dental relationship may be important clinically as incidences of lingual nerve injury have been reported in relation to vestibuloplasty (Koomen, 1977) and implant surgery performed anterior to the third molars (Ellies, 1992). The current study attempts to address this shortcoming and provide additional information on a group of population that has not been examined before consisting of Asian subjects, (Chan et al., 2010).

Chan et al. (2010) determined the vertical relationship between the LN and the adjacent dentition and found that it extended to as far anteriorly as the premolar region, before diverting towards the tongue. They noticed that the distance between the LN and the adjacent dentition increase as the nerve travelled toward the anterior region. They reported that at the second molar, the vertical distance from the cement-enamel junction to the LN was 9.6 (SD 3.4) mm and this increased gradually to become 12.95 (SD 4.0) mm at the first molar region and 15 (SD 2.55) mm at the second premolar region; at the left side the nerve extends up to the first premolar region and a distance of 13.2 mm had been recorded. Their measurements differ from those recorded in this study, where the mean distances were 11.65 (SD 3.2) mm and 14.4 (SD 4.3) mm at the second and the first molar region respectively. No LN was found to be closely related to the premolars in the current study. This variation in findings may arise as a result in the selections of the sample, namely racial origin of the cadaver studied. It was noted that the LN was closer to the alveolar ridge around the second molar region (at 11.64 mm) as opposed to the first (14.37 mm) or third molars (12.25 mm). This relationship may occur as a result of the presence of the submandibular gland beneath the floor of the mouth that may have displaced the nerve along with the floor, superiorly.

Unlike other studies, the current research also studied the distance of the LN to the inferior border of the mandible. The LN was located progressively away from the inferior border of the mandible beginning from the third molar anteriorly. It was located at 10.5 (SD 3.71) mm from the mandibular inferior border at the third molar, at 12.0 (SD 4.2) mm at the second molar and 15.0 (SD 2.16) mm at the first molar. The LN then runs anteriorly and medially on the upper surface of the mylohyoid muscle, crosses the styloglossus to travel on the external surface of the hyoglossus muscle deep to the submandibular gland. The distance travelled by the nerve before reaching the point at which it deviated sharply toward the tongue was 25.16 (SD 7.8) mm with a range of 17 – 41 mm. This distance is only slightly higher than the 21.47 mm reported by Hölzle and Wolff (2001) (Hölzle & Wolff, 2001). This information shall become useful for any surgeon who explores the submandibular region from an extra oral approach. In addition, this information is important for cosmetic surgeons who plan to shave off the lower border of the mandible to sharpen the shape of the mandible. They will have a mental map of the course of the LN in relationship to the lower border of the mandible, and hence avoid causing any unnecessary iatrogenic injury along its course of 25 mm.

The site where the LN diverts toward the tongue is the site where the submandibular gland is situated. Chan et al. (2010) recorded different locations where the LN made a diversion toward the tongue. In their study, most cases showed a sudden change in the direction of the LN at the level of the first molar on both sides of the jaw. In this study, an attempt was made to be more precise when identifying the turning point by describing in detail the site of the molar teeth concerned, namely the mesial-distal contact points and the developmental groove of the relevant teeth. Chan et al. reported that the LN deviated toward the tongue anywhere between distal surface of the second premolar and the mesial surface of the third molar (Chan et al., 2010). In this current study, it was noticed that the proximal area between the first and second molars was the most common site of deviation. It is believed that such difference occurred due to difference in the size of the jaw and floor of the mouth of the cadavers. The cadavers used in this study were Asians, hence they have smaller oral cavity, which may cause the lingual nerve to divert to the tongue earlier (more distally) than in Caucasians.

Most studies simplified the relationship between the LN and the submandibular duct by describing a loop configuration of the nerve around the duct (Garbedian, 2009; Halim, 2008; Parker, 2013). In more detail, the LN passes lateral to the submandibular duct, winds below it and then passes upwards and forwards on its medial side on its way to the surface of hyoglossus (Erdogmus et al., 2008; Hölzle & Wolff, 2001). However, Mendes *et al.* reported that this norm only occurred in 62.5% side of cadaver heads. In the remaining 37.5% of cases, the LN crossed above the duct (Mendes et al., 2013). In 12 out of the 13 cases in this study, the lingual nerve passed below the submandibular duct before rising again toward the ventral surface of the tongue; this follows the normal pattern described by Mendes et al. Occasionally, the submandibular duct runs deep in the floor of the mouth, with no relationship with the lingual nerve. This accounted for 11.8% of samples in a different cadaveric study (Hölzle & Wolff, 2001). One such position out of the 14 sites dissected was discovered to present with this relationship.

Mendes et al. reported no constant position was found to relate the point where the LN intersects the submandibular duct although this often happens around the premolar region (Mendes et al., 2013). In contrast, Klepácek and Skulec (1993) observed a constant beginning of this association between the two structures in the vicinity of the upper surface of the posterior portion of the mylohyoid muscle close to the inner surface of the apex of the third lower molar socket (Klepácek & Skulec, 1993). The finding of the current study is similar to their finding. The distance of overlap (loop) between these 2 structures was found to be 6.92 (SD 2.78) mm. In a majority (69.62%) of loops, they ended at between M1-M2, and at the lingual developmental groove of M2. It is reported that the high amount of viscous mucuos secretion of the submandibular gland increases the chance of the gland to be affected by the formation of small sialoliths, thus increasing the need for surgical intervention in this area (Gupta et al., 2013; Vishram, 2006). Such surgical procedures if performed without enough appreciation of this complex relationship will increase the possibility of injury to the lingual nerve as it is intertwined with the submandibular duct.

The LN gives out terminal branches when it reaches the ventral surface of the tongue (Rusu et al., 2008; Touré et al., 2005). Two patterns were recorded by Rusu et al. (Rusu et al., 2008) with 50% of the cases reporting presence of a single primary trunk while the rest showed two primary trunks. Although both the current study and Rusu et al.'s had the same sample size, there was a difference between these two studies in the pattern of insertion of the terminal branches into the ventral surface of the tongue. Four different type of patterns were recorded for the terminal branches in this study. The presence of two terminal branches was the most common pattern and accounted for 50.0% of the cases. In 28.6% of cases, the LN terminated with 3 terminal branches, and in 14.3%, it had four terminal endings.

This different in the patterns at which the nerve ends at the ventral surface of the tongue may be the result of variation in racial ancestry of the sample studied. The anatomical variations were not only restricted between the different cadavers, but also noted within the same cadaver. Beside variations in the metrical measurement, as shown in Table 3.4, the numbers of the terminal branches of the lingual nerve on the ventral surface of the tongue were different on both sides of cadaver. This difference in pattern, with more branching in Asians may affect the way we use the tongue as a donor site of regional flap.

Lastly, in between 4.6% and 21.0% of cases, the LN was reported to be the situated at/or above the crest of bone (Behnia et al., 2000; Benninger et al., 2013; Dias et al., 2015; Hölzle & Wolff, 2001; Kiesselbach & Chamberlain, 1984; Pogrel et al., 1995) or at the retromolar pad region in another 0.15-1.5% of cases (Behnia et al., 2000; Kiesselbach & Chamberlain, 1984). So far, these variations had only been observed in Caucasian cadavers (Kim et al., 2004), and rightly so, none was observed in the current Asian cadavers. The LN has been reported to give off a branch to the lingual gingival extending horizontally from the medial mandibular cortex at the level of the retromolar pad to mesial of the lower first molars-second premolars, giving rise to the so called "collateral nerve twigs" (Kim et al., 2004) or "the gingival branch of the lingual nerve" (Kocabiyik et al., 2009). It has also been reported to communicate with either the medial or lateral trunk of the hypoglossal nerve on the anterior border of the hyoglossus muscle (Păduraru & Rusu, 2013; Piagkou et al., 2011; Rusu et al., 2008; Saigusa et al., 2006; Touré et al., 2005). Both of these variations were not observed in the current study.

Given the facts that all these hemi-mandibles came in different sizes, it was difficult to standardize the sites to obtain reliable measurements. Hence dentition on the mandible was used as a position landmark as the researcher thinks that this is a practical approach with possible clinical application. However, the other limitation of this study is the fact that some of these cadavers presented with missing mandibular molar teeth (30 altogether in 7 cadavers). The researcher is aware that this may affect the reliability of some measurements; hence as outlined in the Methodology section, attempt was made to standardize the landmarks by reconstructing the missing teeth by placing average sizes for molar teeth onto the alveolar ridge. The width or length of each molar was determined using Woelfel's dental anatomy guideline (Scheid, 2012).

3.8 Conclusion

The course of the LN at the molar region and its pattern of insertion at the ventral surface of the tongue showed great variations - not only between the different cadavers but also between the two opposing sides of the same cadaver. These anatomical variations are assumed to be the possible causes of complications or reasons for injury after injecting local anaesthesia or even following normal third molar extraction. This detailed study on the course of the lingual nerve and its relationship to neighboring structures (including the submandibular duct) will provide a useful reference for preparation of clinical applications and surgical procedures in the floor of the mouth, particularly in the Asian population.

CHAPTER FOUR: RADIOLOGICAL EVALUATION OF INJURY TO CADAVERIC LINGUAL NERVE CAUSED BY TWO DIFFERENT BURS

4.1 Introduction

As described in the literature review in Chapter 2, LN injury is a serious neurological complication and several factors have been deemed to contribute to its incidence. These include anatomical variations (which have been studied and presented in Chapter 3), surgical technique and surgeons' skills. The most common dental procedure which causes 0.6% - 2.0% of the lingual nerve injuries is the third molar extraction (Miloro et al., 1997).

Although temporary disturbances in the sensation are more common, the incidence of the permanent disturbances was recorded in 2% of the cases (Middlehurst et al., 1988). The "Lingual Split-Bone Technique" has been reported to result in a higher frequency of lingual nerve disturbances following third molar removal than the "Buccal Approach." The first comparison between these two techniques was reported by Rud (1970). Rud used the split-bone technique in 718 cases of impacted third molars, and he found that this technique was faster than the buccal approach for deep horizontal or distoverted impactions. Temporary impairment of lingual sensation was reported in 1% of the cases using split-bone technique and there was also one case of permanent lingual paraesthesia (0.1%). However, the buccal approach appeared to be safer, where there was no reported lingual nerve damage in 162 mandibular third molars extracted using this technique. Mason (1988) reported that there were no significant effects of nerve injury that was related to the retention or removal of the plate after the lingual split, nor operator skill level on lingual nerve impairment. The incidence of lingual nerve dysfunction, however, was significantly related to lingual flap elevation, overhanging distal bone removal, and lingual plate-splitting.

In the same year, Middlehurst et al. (1988) used lingual flap retraction and possibly distal bone removal with their buccal approach and they reported favorable outcome, in contrast to the findings reported by Blackburn and Bramley (1989) where all their cases showed a permanent damage to the lingual nerve when a bur was used to remove distal bone. They referred this complication to the difficult position where the third molars obscured vision during surgical procedure and also the false faith placed on the retractor to protect the nerve. Several years later, Rood (1992) compared the removal of 790 impacted third molar using two different techniques, lingual split technique with chisels and the buccal approach with a drill to remove buccal and distal bone. In both surgical procedures the lingual retraction with the Howarth's periosteal elevator was used. The findings of this study showed significantly more permanent lingual nerve damage with bur, and more temporary damage with lingual split technique. This finding was similar to the finding recorded by Blackburn and Bramley (1989). Since the lingual retractor was used in all cases, there must be another factor in the surgical technique that explained the higher incidence of permanent damage with the bur. The most likely explanation is the removal of distal bone with the bur and perforation through it, and inadequate lingual nerve protection by the Howarth periosteal elevators (Rood, 1992).

In comparison to the use of chisel and mallet, the availability of electric drill (micromotor and handpiece) have significantly reduced the time required for bone removal and tooth sectioning. The use of a fissure or round carbide surgical bur mounted on an electric drill is considered the instrument of choice in the present day impaction surgery. It has the advantage of rapid bone cutting with minimal discomfort to the patient. At the same time the possibility of the development of emphysema associated with an air driven hand-piece is avoided. However, the use of drill comes with a risk of perforating the lingual plate and cutting through the lingual nerve behind it. Because of this concern, the second aim of the study looks into the use of 2 different types of burs to remove bone in the vicinity of lingual nerve in the hope to minimize injury when there is a need to encroach into this site. The second aim of this part of the study was to assess the effectiveness of different imaging modality, namely the ultrasound and magnetic resonance imaging in detecting lingual nerve injuries that may happened during such procedures.

4.2 Materials and Methods

Twelve lingual nerves were removed from the right and left sides of 6 mandibles and fixed between two flexible, transparent strips after opening four windows on one of these strips to provide access to the nerve. The strip with the nerve fixed on a special mobile holder is a part of a module fabricated to hold a constant force device (Figure 4.1).

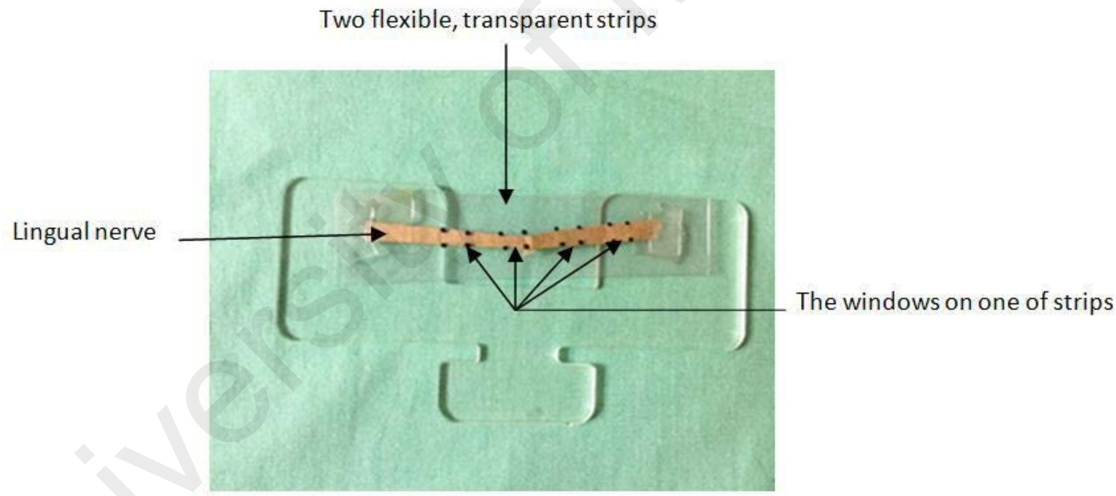

Figure 4.1: The lingual nerve with flexible strips fixed on a holder**.**

The device was held by a mobile plastic plate, which has two opening, one for the constant force device and the other to hold the dental hand piece, to ensure a constant movement of the hand piece during all the steps of the procedure (Figure 4.2).

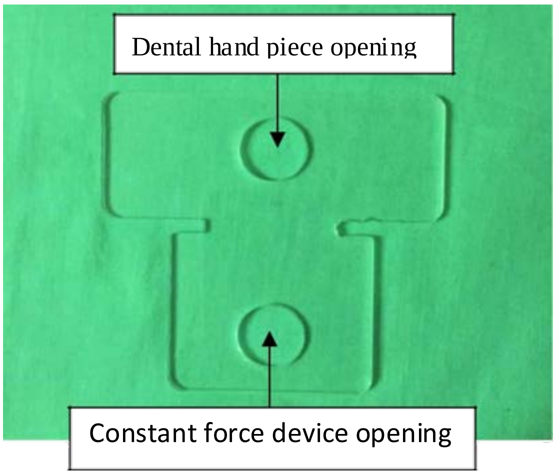

Figure 4.2: A mobile plastic plate with two opening.

Two type of surgical dental burs were used in this study; the DSA (Dentium® Advanced Sinus) round bur (size 3.3 Ø), was chosen as the test subject because of the claim that it has favourable effect on the soft tissue, namely on Sneiderian membrane in the maxillary sinus (Lozada et al., 2011). It is hope that this bur will also work favourably when being in contact with the lingual nerve by accident. The positive control used is a similar Ø 3.3 mm carbide bur that is routinely used for the removal of mandibular third molar in this centre (Figure 4.3).

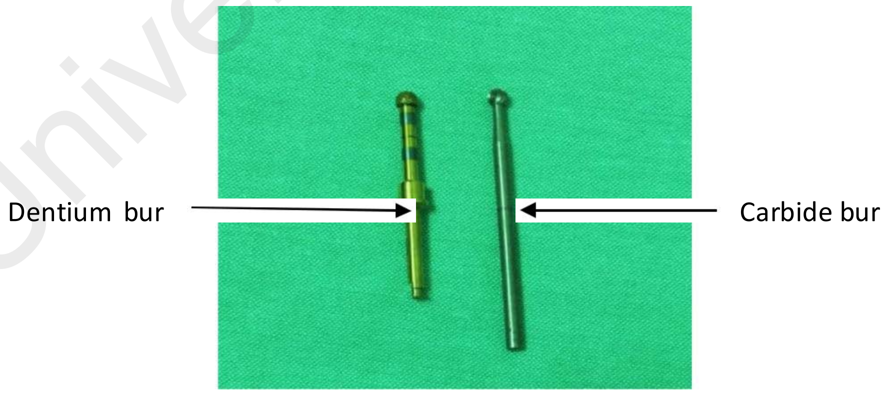

Figure 4.3: The two different surgical burs used in this study.

As for the speed chosen, the use of normal surgical motor speed of 35,000 rpm used for third molar surgery was deemed too high and too risky if one were to remove bone around the distolingual site. In 1999, Toews et al. looked into the effect of feed rate and drill speed on temperatures employing two different speeds, a low speed of 317rpm and a high speed of 1,242 rpm (Toews et al., 1999). Based on their study, we employed 1500 rpm as the maximum speed, as this speed is the maximum recommended for implant osteotomy that can also remove bone of Type I hardness (Recommendation by Implantium, Korea, the manufacturer of Dentium®). The lowest speed advocated for bony ostetomy for implant is 50 rpm (Recommendation by Bicon® USA), which were deemed as too low, and a low speed close to the 317 rpm used by Toews et al. was chosen. A speed of 420 rpm was chosen as this was the best constant speed which could be obtained by using the KaVo® Surgical motor.

For performing the experiment, the constant force device would start moving and pushed the plastic plate holding the hand piece until the tip of the bur touched the nerve through the window on the plastic strip (Figure 4.4). This process was repeated four times - two times with each bur with different speeds.

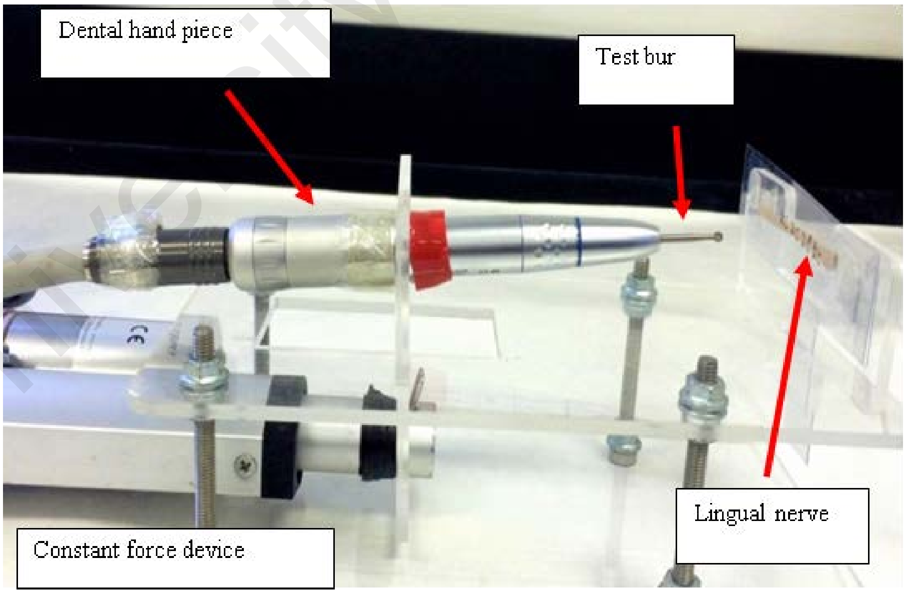

Figure 4.4: The set-up of both the dental hand piece and the constant force device fixed on special mobile holder.

Next, the strip with the nerve were removed from the holder and transferred to the optical coherence tomography scanning machine (OCT, Thorlabs, Santec Corporation, Japan) device (Figure 4.5) for assessment.

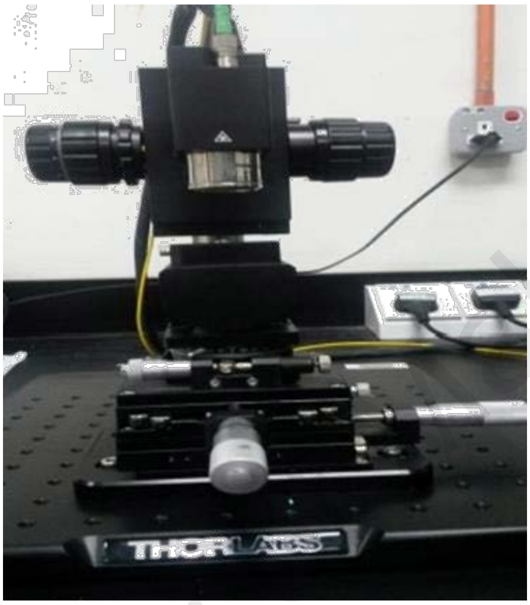

Figure 4.5: The optical coherence tomography scanning machine.

In this study the nerve samples were fixed on the imaging stage to determine the amount of damage inflicted after calibrating the control panel. The X pixels were set on 1024 while X width set on 5 mm. The depth of the sample to be imaged was 3 mm. After OCT data was acquired and the images captured, the line measure was activated to measure the depth and the width of the damage. Four cursors appeared on the screen, two vertical to measure the width of the damage and two horizontal to measure the depth of the damage.

To measure the depth of the damage, the horizontal cursors were set in two positions. The upper cursor was set at the upper border of the nerve body. The position of the imaging stage was moved to get a complete image of the damaged site. At that time the lower cursor was set at the lowest point of the damage. Whereas, the width of the damage was measured using the two vertical cursors (Figure 4.6).

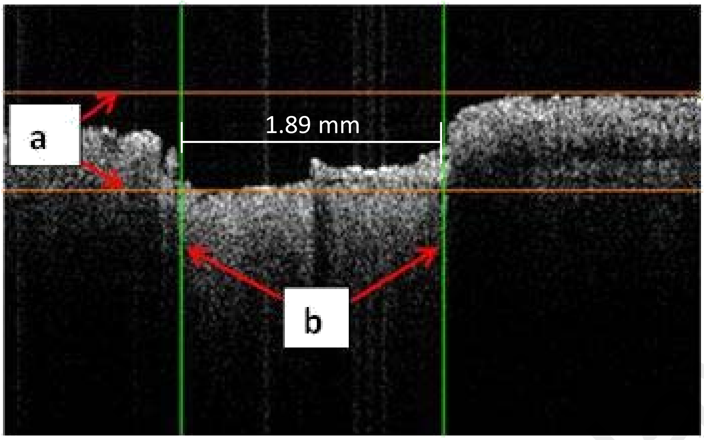

Figure 4.6: show the OCT cursors (a) horizontal cursors (brown); (b) vertical cursors.

After that the twelve lingual nerves that were subjected to two different bur tests were returned to the floor of the mouth (in the cadaver) and sutured securely in its original place with 5/0 sutures. A Philips IU22 ultrasound machine (USA) with L15-7io probe (Broadband liner array, Philips, USA) was used to obtain the images of these 12 nerves (Figure 4.7; a & b).

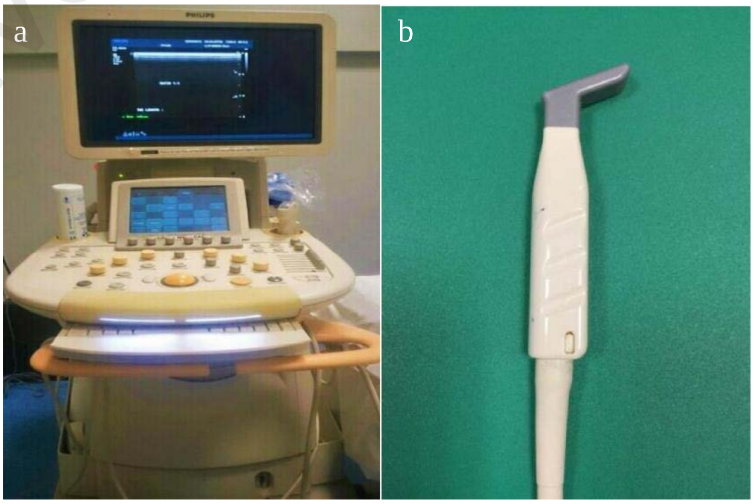

Figure 4.7: (a) A Philips IU22 ultrasound machine and; (b) L15-7io probe.

The handle of the probe was held parallel to the residual ridge of the mandible, with the flat surface of the probe presses firmly against the soft tissue covering the nerve. Positional adjustments of the probe were made to assess variations in the course of the nerve. Both the depth and width of the damaged lingual nerve sites were measured.

Another investigation performed was done to study the capability of MRI in detecting injury to the lingual nerve, as proposed by Miloro et al. Two mandibles were scanned using 3T MRI Prisma, Siemens, after embedding them in a gelatin to ensure stability during this procedure. The cadaver hemi-mandibles were protected by a plastic wrap to prevent contact between the gelation and the sample (Figure 4.8, a & b).

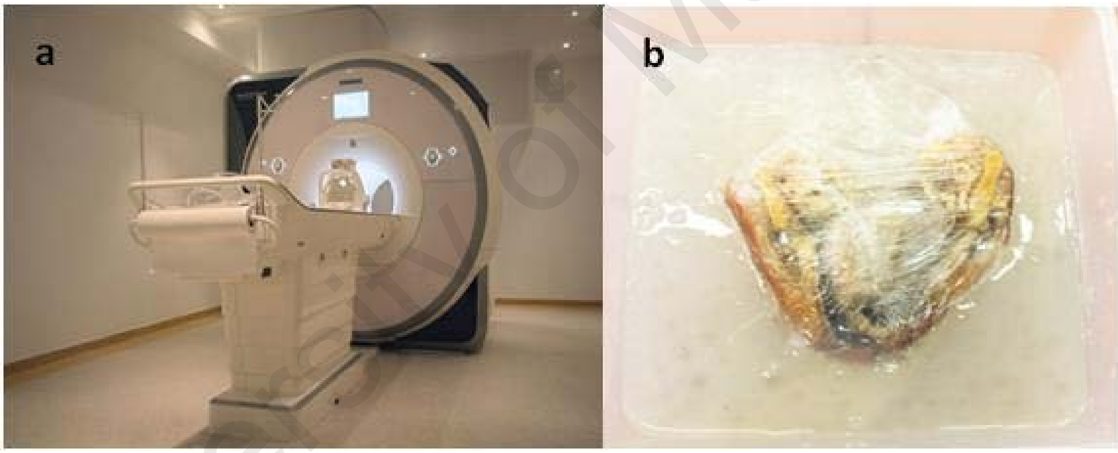

Figure 4.8: (a) The 3T MRI Prisma, Siemens device; and (b) the mandible embedded in a gelatin.

A specific HR-MRI imaging protocol was used for this study, where the images were produced using a thin-section, three-dimensional Fournier transformation MRI 0.50 mm slice thickness. The sequence use a gradient-echo technique with a TR 8.50, TE 3.91, and field of view 156, base resolution 320 and flip angle 50. All the images were interpreted by a medical radiologist.

4.3 Statistical analysis

The data analysis was done using SPSS. The non-parametric Mann-Whitney U test was performed to comparing the depth and width of laceration caused by Carbide and Dentium® bur at different speeds and to comparing the amount of nerve damage observed using OCT and ultrasound.

4.4 Result

The first part of this experiment revealed that both surgical burs caused damage to the epineurium and part of the lingual nerve (Table 4.1). Depth-wise, carbide bur caused a shallower damage than the Dentium® diamond coated bur (thereafter named "Dentium® bur") at both low and high speed. The depth of damage caused by the carbide bur was 0.16 mm at 410 rpm, which increased slightly to 0.18 mm at 1500 rpm. In contrast, the Dentium® bur caused a 0.24 mm and 0.22 mm depth damage at 410 rpm and 1500 rpm respectively. The carbide bur also appeared to cause a slightly narrower laceration than the Dentium® bur at both low and high speed.

At low speed, the depths and widths caused by both burs were not significantly different. At high speed, however, the widths caused by both burs increased significantly (Carbide bur, P=0.035; Dentium® bur P=0.001). Worse, the depth and width caused by the Dentium® diamond coated bur were significantly more than the respective sizes caused by the carbide bur.

Table 4.1: OCT readings that compare the laceration depth and widths caused by Carbide and Dentium® bur at different speeds

Laceration	Carbide 410	Carbide 1500	Dentium 410	Dentium 1500
Depth	0.16 (SE 0.02)	0.18 (SE 0.02)[a]	0.24 (SE 0.03)	0.22 (SE 0.04)[a]
Width	0.95 (SE 0.2)[c]	1.27 (SE 0.12)[b c]	1.00 (SE 0.13)[d]	1.87 (SE 0.25)[b d]

[a] Mann Whitney U test; P= 0.009
[b] Mann Whitney U test; P= 0.02
Mann Whitney U test; P= 0.035
[c] Mann Whitney U test; P= 0.006

On the other hand, the ultrasound readings confirmed the lesser amount of damage inflicted by the carbide bur in comparison to the Dentium® bur, where it created a shallower and a narrower damage. Table 4.2 summarized the reading obtained by the ultrasound device.

Table 4.2: Ultrasound readings that compare the laceration depth and widths caused by Carbide and Dentium bur set at different speed

Laceration	Carbide 410	Carbide 1500	Dentium 410	Dentium 1500
Depth	0.15 (SE 0.03)	0.17 (SE 0.02)[a]	0.24 (SE 0.03)	0.23 (SE 0.06)[a]
Width	0.92 (SE 0.19)[c]	1.31 (SE 0.13)[b,c]	1.01 (SE0.13)[d]	1.89 (SE 0.25)[b,d]

[a] Mann Whitney U test; P= 0.009
[b] Mann Whitney U test; P= 0.001
[c] Mann Whitney U test; P= 0.022
[d] Mann Whitney U test; P= 0.006

The depth of the laceration caused by the carbide bur was 0.15 mm at 410rmp and when the speed was increased to 1500rmp, it became 0.17mm deep. Although there was no significant difference in depth at low and high speeds, the laceration width was significantly different (P=0.022), being 0.92mm and 1.31mm at 410 rmp and 1500rmp, respectively. The Dentium® bur showed no significant difference in the damage depth at both low and high speed, however, it recorded wider laceration area at a high speed of 1500rmp than at low speed of 410rmp (P=0.006), measuring at 1.8 9mm and 1.01 mm respectively.

At low speed, the depths and widths caused by both bur were not significantly different. At high speed, the Dentium® bur caused significantly deeper and wider damage than the carbide bur (depth; P=0.009, widths; P=0.001). The investigations showed that there is no significant difference between the ultrasound reading and the OCT reading (Table 4.3).

All readings recorded that the Dentium® bur caused deeper damage than the carbide bur at both low and high speed. On another hand, the MRI scan failed to detect the presence of the lingual nerve in both samples, in comparison to OCT and the ultrasound scan.

Table 4.3: Comparison between the amount of nerve damage observed using OCT and ultrasound

Type of bur; speed; depth/width	OCT Median (SE)	Ultrasound Median (SE)	*P*-value*
Carbide bur 410rmp depth	0.16 (SE 0.02)	0.15 (SE 0.03)	0.69
Carbide bur 410rmp width	0.95 (SE 0.2)	0.92 (SE 0.19)	0.82
Carbide bur 1500rmp depth	0.18 (SE 0.02)	0.17 (SE 0.02)	0.89
Carbide bur 1500rmp width	1.27 (SE 0.12)	1.31 (SE 0.13)	0.76
Dentium bur 410rmp depth	0.24 (SE 0.03)	0.24 (SE 0.03)	0.91
Dentium bur 410rmp width	1.00 (SE 0.13)	1.01 (SE0.13)	0.69
Dentium bur 1500rmp depth	0.22 (SE 0.04)	0.23 (SE 0.06)	0.95
Dentium bur 1500rmp width	1.87 (SE 0.25)	1.89 (SE 0.25)	0.91

P >0.05 in all comparison

4.5 Discussion

The morbidity and the disturbances in sensation secondary to the lingual nerve injury is considered a serious complication which may occur after several different surgical procedures. Some of the unfortunate consequence of life, such as malignancy and tumor removal, may necessitate the sacrifice of the LN. Otherwise, damage to the lingual nerve comes as a direct result of elective and iatrogenic procedure (Holmes HI & DK., 2002; P. Robinson et al., 2000; P. P. Robinson, Boissonade, et al., 2004) , such as administration of local anaesthesia (Hillerup & Jensen, 2006), the inadvertent instrumentation of the floor of the mouth, mandibular osteotomies (Becelli et al., 2004;

Jacks et al., 1998) and the removal of the mandibular third molars (Queral-Godoy et al.,2006; Vora et al., 2005). It has been reported that 75% of annual incidence of the lingual nerve injury occurred after surgical removal of the mandibular third molars (Holmes HI & DK., 2002). There is a broad range in incidence reported, ranging from 0.2% (Van Gool et al., 1977) to 23% (Mason, 1988), depending on the surgical technique used.

In 1996, Robinson and Smith found temporary lingual sensory disturbance in 6.9% of the patients and requiring lingual nerve repair in 0.8% of the 385 patients who underwent lingual flap retraction for third molar removal. Surgery without lingual flap retraction in 386 patients resulted in lingual nerve injury in 0.8% of the patients requiring lingual nerve repair in a lower percentage (0.3%) of patients (P. Robinson & Smith, 1996a). Blackburn and Bramley (1989) determined the incidence of lingual nerve damage to be 11% in a study of 1,117 surgical procedures of lower third molar removal. Of these cases, 0.5% (n=6) cases failed to make full recovery.

In 2011, Lozada et al., used a specially designed surgical drills and curettes (DASK Advanced Sinus Kit; Dentium®, Seoul, Korea) which was then introduced to the market as the best choice to perform lateral and crestal windows for the purpose of the grafting of the maxillary sinus floor, as these surgical drills are more soft tissue friendly, hence will reduce the possibility of membrane perforation. It is this feature in the the Dentium® bur that spurred the current researcher to investigate if this drill would be safe to use at the distolingual site of the mandible. But unlike its effect on the Sneiderian membrane, this Dentium® bur was found to damage to the epineurium and part of the lingual nerve. In fact, the finding of this current part of the study suggested that Dentium® bur causes more damage at high speed than a carbide bur. The Dentium® bur appeared to cause a deeper and wider laceration than carbide bur, and a reason for this may be caused by the fact that the diamond particles are very sharp, in comparison to the blades of the carbide bur.

The lingual nerve is located within the soft tissue of the lingual retromolar region. It may be accidentally injured during third molar surgery, but this injury may not be visible to the attending surgeon, especially when no flap is raised. In such case, when a lingual nerve injury is suspected to happen, an imaging modality capable of visualizing the lingual nerve would provide an objective evaluation of the extent of injury and therefore aid in the decision process of surgical intervention. Figure 4.9 showed the ability of the OCT in detecting the damage inflicted on the lingual nerve and measured accurately the extent of this injury. Hence it was used as a method to compare the extent of damage caused by 2 different surgical burs. As has been described in Table 4.1 of the *Result* section, OCT was able to accurately define the depth and width of lingual nerve damage.

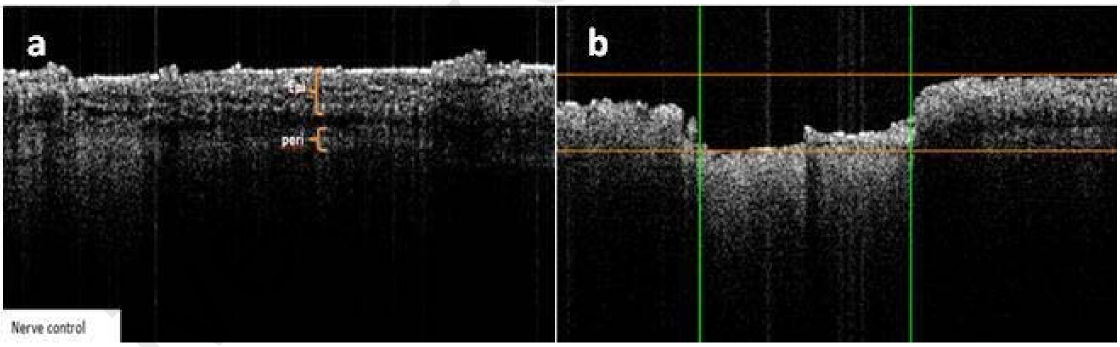

Figure 4.9: OCT images showed (a) The lingual nerve before injure; (b) The same nerve after being in contact with a surgical drill.

However, it is not possible to utilize OCT in a clinical situation due to the difficulty to reach the lingual region. In addition, when a flap is raised and the lingual nerve is explored, the surgeon shall be able to evaluate the condition of the nerve with the use of a pair of surgical microscope. Hence, there is still a need to have a non-invasive imaging system than can clinically scan the structure of the lingual nerve. Ultrasound and magnetic resonance imaging appear to fit the bill.

Olson *et al*. first used ultrasonography to visualize the LN in cadaver pigs in 2007 (Olsen et al., 2007). Due to a steep learning curve, several attempts were made before the three investigators could accurately identify the LN. However, once they become familiar with the ultrasonographic appearance of the lingual nerve, all evaluators could correctly identify an intact, partially transected or fully transected nerve injury 63% of the time. As the pig's LN is approximately $^{1}/_{4}$ the size of the human lingual nerve, it is enticing to try to use this scanning modality in human. The current experiment shows that it is possible to view the intact and damaged lingual nerve by an OCT scan. This has great advantage clinically as the inexpensive ultrasound machine is widely available at most hospital, and can be utilized to scan suspected damaged nerve without the need to raise a flap. The validity of ultrasound to detect the nerve injury as shown in Figure 4.10 will increase the demand for serial ultrasonographic studies as it is an inexpensive technique that can be accomplished quickly without risks from radiation (Olsen et al., 2007). Hence it can also be used to evaluate recovery following nerve injury where only abrasion of the nerve bundle is observed. Its limitation is the steep learning curve. It is therefore recommended that this mode of investigation be introduced in routine clinical practice where peripheral nerve injury is suspected.

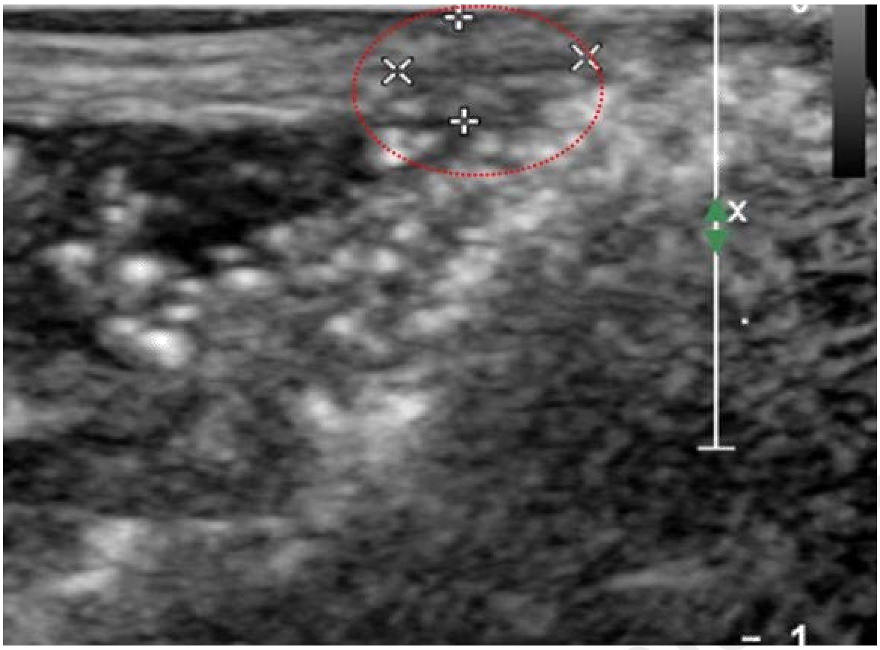

Figure 4.10: Damage the lingual nerve injury as detected by ultrasound.

Magnetic resonance imaging (MRI) has been shown to be capable of imaging the lingual nerve, but it is not commonly used in practice because of expense and difficulty in interpreting whether nerve injury exists (Miloro et al., 1997). Furthermore, Miloro et al. reported that documenting in situ LN injuries would be limited to complete transections, as subtle injuries would be indiscernible.

This current study however, echoed Miloro et al.'s finding whereby MRI imaging was not able to detect lingual nerve injury when it is not transected. In this study failure of the MRI in detecting such injury (Figure 4.11) may come as a result of the tissue dehydration which may take place during the cadaver preservation process. It has however been reported that the MRI is capable of producing clear images of well-hydrated tissue (Shin et al., 2010).

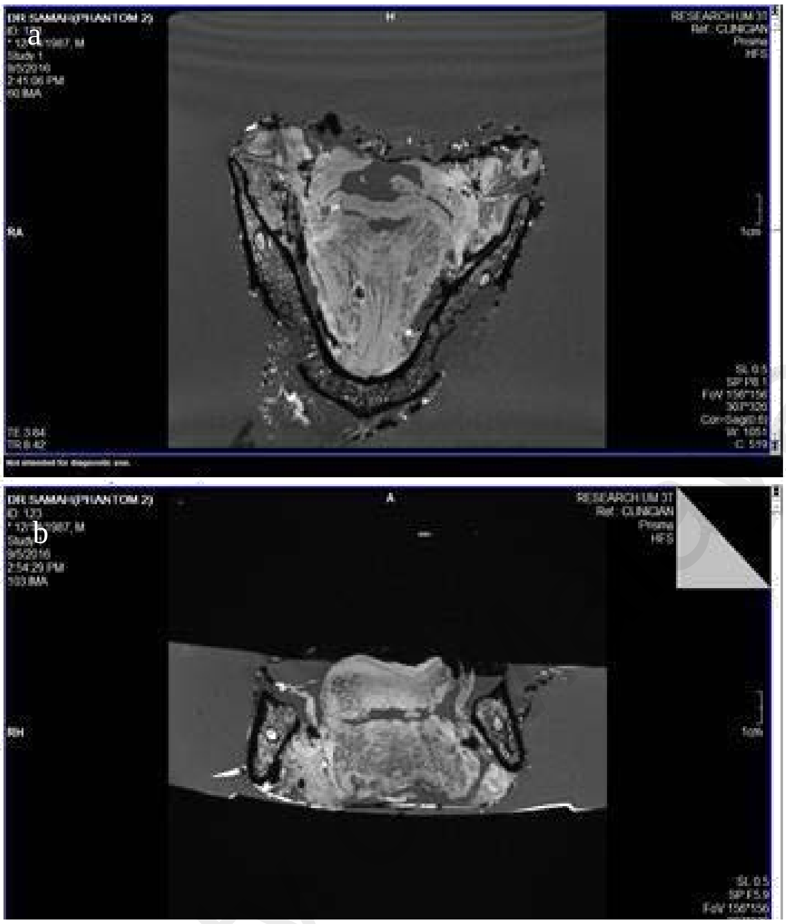

Figure 4.11: MRI images show the failure of MRI in detecting the lingual nerve (a) axil view, (b) coronal view.

CHAPTER FIVE: CONCLUSION

5.1 Introduction

A study of the course of the lingual nerve and its relation to the adjacent anatomical structures, a comparison of the amount of lingual nerve damage caused by using two different surgical burs, and assessment of the validity of the ultrasound and MRI images in detection the lingual nerve injury when compared to OCT images were the goals of this study.

5.2 Summary of findings

This research was aimed to study nine objectives from which the following results were obtained:

Anatomical variations of the lingual nerve course:

1. Great variations were shown in the course of the lingual nerve at the molar region, and in its pattern of insertion at the ventral surface of the tongue.
2. These anatomical variations occurred not only between the different cadavers but also between different sides of the same cadaver.
3. In the Malaysian Mongoloid population, the anterior extension of the lingual nerve (adjacent to the mandibular dentition) was not observed anterior to the premolar region.
4. According to the distance recorded between the lingual nerve and the upper border of the mandible (alveolar ridge) and the lower border of the mandible, the first molar region appears to be the safest area for the dental procedures.
5. Almost in all the cases the lingual nerve overlapped with the submandibular duct.

6. In the majority of the cases, the overlapping between the lingual nerve and the submandibular duct occurred between the lingual developmental grooves of the second and third molars and ended at between the first and second molars and at the lingual developmental groove of the second molar.

Lingual nerve damage caused by using two different types of dental burs (Dentium® bur and Carbide bur):

1. Both surgical burs caused damage to the epineurium and part of the lingual nerve.
2. The carbide bur causes a shallower and narrower damage than the Dentium® bur when used at high and low speed.
3. The Dentium® bur cause wider and deeper damage than the carbide bur, and this may be because of the sharpness of the diamond particles.
4. The increase in the speed increased the damages caused by the two different burs.
5. The effect of the Dentium® bur on the lingual nerve may be different than its effect on the Sneiderian membrane. This may be caused as a result in the difference in the tissue nature of both structures.

Validity of using ultrasound and MRI in detecting lingual nerve injury

1. The ultrasound showed high effectiveness in detecting the lingual nerve injuries.
2. Magnetic resonance imaging was not able to detect lingual nerve injury.

5.3 Implications of the study

This study clearly showed a lot of variations in the course of the lingual nerve and its relation to the adjacent anatomical structures, especially the submandibular duct and the mandibular borders. This anatomical variability in the path of the lingual nerve may be clinically important when performing surgical procedures such as the third molar removal and implant placement, etc. When dealing with the Asian population, the lingual nerve will be in close contact to the lingual plate at the third molar region which may increase the chance of sustaining nerve injury while dental surgical procedures at the first molar area will be safer. Another challenge is the need for surgical intervention at the area of overlap between the submandibular duct and the lingual nerve, where a lack of understanding of this complex relationship between these two structures may cause undesirable complication. The current study hopefully provided the first take on this much needed information.

Thus, it is highly recommended that the surgeons familiarize themselves with the variations in the course of the lingual nerve and its relationship to the adjacent anatomical structures prior to performing any surgical procedures in order to avoid unnecessary neurosensory disturbances and other potential complications. This study provides evidence for the validity of ultrasound in detecting the lingual nerve or its injuries which will help in reducing the time to make a decision on the need of surgical intervention.

5.4 Recommendation for future research

The variations in the lingual nerve course may be affected by several factors such as; race, age, gender and the present or absent of teeth. So, it is recommended that future studies assess the relationship between these factors and the course of the lingual nerve. Moreover, studies should be performed on living persons employing MRI to determine if the lingual nerve pathway can be ascertained.

5.5 Limitations of the study

1. There were a limited number of cadavers available at the Department of Anatomy, which caused a low sample size and makes the extrapolation of the findings to the general population not possible.

2. Some of these cadavers presented with missing mandibular molar teeth (30 altogether in 7 cadavers), leading to a need to reconstruct their dentition using teeth sizes available from the literatures.

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List of Publications and Papers Presented

1. Al-Amery SM, Nambiar P, Naidu M, Ngeow WC (2016) Variation in Lingual Nerve Course: A HumanCadaveric Study. PLoS ONE 11 (9): e0162773.doi:10.1371/journal.pone.0162773.