

Anatomical variation of the carotid arterial system within the South African population: Implications for the treatment of carotid arterial disease.

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Johannesburg

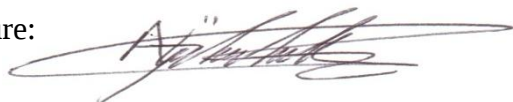
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To my parents for all their support and guidance.

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ABSTRACT

Knowledge of the anatomical variation in the carotid arterial system is important in understanding the pathogenesis and surgical treatment of atheroma. Thus, this study investigated the anatomical variation of the carotid arterial system and the frequency of atheroma within a South African population.

The carotid arterial systems were exposed bilaterally in 77 adult cadavers using standard dissection. The level of the carotid bifurcation, position and curving of the carotid arteries and frequency of common trunks and atheroma were recorded. In addition, the lengths and diameters of the carotid arteries and branches as well as the bifurcation angle were measured. Data was analyzed using descriptive and inferential statistics.

The carotid bifurcation most commonly occurred at the C3-C4 intervertebral disc. White males had longer common carotid arteries than white females. The lengths of the internal and external carotid arteries were longer in white males compared to black males. There was a higher frequency of curving of the carotid arteries in white females compared to white males. The thyro-lingual trunk was the most common trunk within the sample. The internal carotid artery was postero-lateral to the external carotid artery within most individuals. In addition, atheroma was observed at the carotid bifurcation in all individuals.

The level of the carotid bifurcation, positioning, length and diameter of the carotid arteries in the South African population are similar to descriptions in anatomical texts. The differences found within the study may be attributable to the age of the sample as well as the embryological development of the carotid arteries within the South African population. These variations may influence blood flow within the carotid arteries. Thus, knowledge of these variations may aid in understanding the aetiology and the surgical treatment of atheroma.

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LIST OF ABBREVIATIONS

CCA	Common carotid artery
ICA	Internal carotid artery
ECA	External carotid artery
CB	Carotid bifurcation
STA	Superior thyroid artery
LA	Lingual artery
FA	Facial artery
APA	Ascending pharyngeal artery
OA	Occipital artery
PAA	Posterior auricular artery
supTA	Superficial temporal artery
MA	Maxillary artery
H&E	Haematoxylin and eosin
CT	Computer topography
MRI	Magnetic resonance imaging

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1. INTRODUCTION AND LITERATURE REVIEW

Atherosclerosis affects millions of people around the world and may lead to life-threatening complications such as stroke (Salzar *et al.*, 1995). While age, sex, genetic factors, disease and lifestyle factors predispose an individual to atherosclerosis (Stevens *et al.*, 2002), the prevalence of atherosclerosis varies greatly from one region of the arterial system to another (Gnasso *et al.*, 2000; Schulz and Rothwell, 2001b; Thomas *et al.*, 2005). Atherosclerosis commonly occurs around areas of arterial bifurcation such as those reported in the coronary arteries (Dodge *et al.*, 1992; Litovsky *et al.*, 1996; Weydahl and Moore, 2001; Han *et al.*, 2008), abdominal aorta (Hayward *et al.*, 2000), carotid arteries (Schulz and Rothwell, 2001a; Schulz and Rothwell, 2001b; Thomas *et al.*, 2005; Phan *et al.*, 2012) and femoral arteries (Benetos *et al.*, 1993). At bifurcations, disturbances in local blood flow cause changes in wall shear stress resulting in endothelial damage and atherosclerosis (Ku *et al.*, 1985; Perktold *et al.*, 1991; Snow, 2001; Li *et al.*, 2005; Thomas *et al.*, 2005; Bond *et al.*, 2011). The overall vessel length, vessel diameter and area ratios affect blood flow and therefore play a role in plaque formation (Schulz and Rothwell, 2001b). This suggests that certain individuals might have a higher risk of atherosclerosis by virtue of their particular arterial geometry (Thomas *et al.*, 2005; Bond *et al.*, 2011). As atherosclerosis of the carotid arterial system is responsible for 25% of reported stroke cases (Phan *et al.*, 2012), an understanding of the anatomy of the carotid arterial system, particularly the geometry and bifurcation patterns of the arteries, is important (Phan *et al.*, 2012). Furthermore, knowledge of the anatomy of the carotid arterial system is vital in the surgical treatment of atherosclerotic plaques occurring around the carotid bifurcation (Hayashi *et al.*, 2005; Lo *et al.*, 2006).

1.1 Anatomy of the carotid arterial system

The carotid arterial system serves as the main source of oxygenated blood to the head and neck regions (Drake *et al.*, 2005; Sobieszczyk and Beckman, 2006; Standring, 2008). This system comprises three bilateral arteries, namely the common carotid artery, the internal carotid artery and the external carotid artery, all of which are located within the anterior triangle of the neck (Standring, 2008). The common carotid, internal carotid and external carotid arteries lie in a cleft that is bound posteriorly by the transverse processes of the cervical vertebrae, medially by the trachea, thyroid gland, oesophagus, larynx and pharyngeal constrictors and antero-laterally by the sternocleidomastoid muscle and strap muscles of the neck (Drake *et al.*, 2005; Standring, 2008). The common carotid artery and the internal carotid artery are accompanied by the internal jugular vein and vagus nerve within the carotid sheath (Drake *et al.*, 2005).

The common carotid arteries differ on the right and left sides with respect to their origin (Ribeiro *et al.*, 2006). The right common carotid artery arises from the brachiocephalic trunk as it passes behind the sternoclavicular joint, while the left originates directly from the arch of the aorta in the superior mediastinum (Drake *et al.*, 2005; Standring, 2008). Following a similar course on both sides, the common carotid arteries ascend, passing behind the sternoclavicular joint to the superior margin of the thyroid cartilage (C3-C4 intervertebral disc) (Standring, 2008). Subsequently, following the formation of the carotid sinus at the superior border of the thyroid cartilage (Standring, 2008), each common carotid artery bifurcates into two terminal branches: the internal carotid artery, which supplies the brain, and the external carotid artery which supplies structures in the neck and

face through eight named branches (Drake *et al.*, 2005; Anu *et al.*, 2007; Standring, 2008; Avadhani and Chakravarthi, 2012).

A number of variations in the anatomy of the carotid arterial system have been reported with varying frequencies among different populations (Anu *et al.*, 2007; Avadhani and Chakravarthi, 2012). These variations may be related to the complex process of arterial formation during the embryological development of the carotid arterial system (Paulsen *et al.*, 2000; Mahendraker, 2007). In order to understand how these variations transpire, the embryological development of the carotid arterial system must first be addressed.

The carotid arterial system is formed after a complicated process of angiogenesis that includes annexation and regression of blood vessels with remodelling in the vascular system (Murlimanju *et al.*, 2012). The paired dorsal aortae connect to the ventral aortic sac via a series of six pharyngeal arch arteries (Allan and Kramer, 2010). The development of the hypostapedial artery, from the second pharyngeal arch artery, links the neural crest cells involved in arterial development to the aortic arches (Mahendraker, 2007). This is an important event as it initiates the development of the carotid arterial system (Mahendraker, 2007; Allan and Kramer, 2010; Murlimanju *et al.*, 2012; Sadler, 2012). On both sides, the third pharyngeal arch artery persists as the internal carotid artery and utilizes the pre-existing dorsal aorta to extend intracranially (Allan and Kramer, 2010). Each common carotid artery arises from a section of the bilateral horns of the aortic sac, which lie in relation to the third aortic arch arteries (Mahendraker, 2007; Allan and Kramer, 2010; Murlimanju *et al.*, 2012). The external carotid arteries form as a new outgrowth on either side from the root of the internal carotid artery (Allan and Kramer, 2010). Thereafter, the

eight named branches of the external carotid artery arise as *de novo* outgrowths from the external carotid arteries (Mahendraker, 2007; Allan and Kramer, 2010; Murlimanju *et al.*, 2012; Sadler, 2012). However, slight deviation in the normal stages of annexation and regression, as well as straightening of the carotid arteries during embryological development, may result in congenital common trunk formation or incorrect positioning or curving of the carotid arteries in the anterior triangle of the neck (Mahendraker, 2007; Murlimanju *et al.*, 2012). These variations may persist into adulthood (Murlimanju *et al.*, 2012) and may cause complications should surgery of the neck be required (Agrawal and Agrawal, 2011).

During radical neck surgery, the anatomy of the common carotid, internal carotid and external carotid arteries are important as they define the plane of dissection (Ribeiro *et al.*, 2006). Knowledge of the length of the carotid arteries as well as the variation in the location of the carotid bifurcation are also important prior to carotid endarterectomy, as the carotid bifurcation is an important landmark (Hayashi *et al.*, 2005; Ribeiro *et al.*, 2006). The lengths of the left and right common carotid arteries are known to vary due to the asymmetrical origin of these arteries (Drake *et al.*, 2005; Standring, 2008).

The average length of the right common carotid artery was found to be 96 ± 1 mm while the left common carotid artery measured 121 ± 2 mm within a Brazilian cadaveric sample (n=46 males) (Ribeiro *et al.*, 2006). Similarly, the length of the right common carotid artery was reported as 105mm and 102.5mm in a case study of an Indian male cadaver (Chitra, 2008) and a Croatian male cadaver (Gluncic *et al.*, 2000) respectively. However, a case report on an Asian male cadaver (Murlimanju *et al.*, 2012) reported a left common

carotid arterial length of 98mm which was similar to the values for the right common carotid arterial length reported in the Brazilian study (Ribeiro *et al.*, 2006) and Indian (Chitra, 2008) and Croatian (Gluncic *et al.*, 2000) case reports. However, there are no established population specific standards regarding the lengths of the left and right common carotid arteries. In addition, throughout the literature there is no data describing the length of the left and right common carotid arteries within females, as samples in previous studies were comprised predominantly of male cadavers (Gluncic *et al.*, 2000; Ribeiro *et al.*, 2006; Chitra, 2008). Therefore standards for females within specific populations regarding the left and right common carotid arterial lengths are unknown.

Similar to the common carotid artery, few studies have investigated the arterial lengths of the internal and external carotid arteries. Both the internal carotid artery and the external carotid artery have the same origin from the carotid bifurcation (Standring, 2008). However, the termination points differ (Drake *et al.*, 2005) and the arterial lengths may therefore also differ. In Indian cadaveric studies, Shashikant and Sherke (2013) (n=25: 21 males, 4 females) found the lengths of the left ($87 \pm 14.8\text{mm}$) and right ($85 \pm 16.1\text{mm}$) internal carotid arteries were greater than that of the averaged external carotid arterial length (60mm) reported by Sanjeev *et al.* (2010) (n=37: 25 males, 12 females). Furthermore, the external carotid arterial length was shorter in the Indian population (Sanjeev *et al.*, 2010) when compared to the reported $77.8 \pm 9\text{mm}$ in a Japanese cadaveric (n=28: 12 males, 16 females) study (Yonenaga *et al.*, 2011).

Understanding the variation in the length of the carotid arteries is important as it may explain the differences in the level of the carotid bifurcation observed between and within

populations (Hayashi *et al.*, 2005; Lo *et al.*, 2006; Ribeiro *et al.*, 2006; Anangwe *et al.*, 2008; Ozgur *et al.*, 2008; Al-Rafiah *et al.*, 2011; Vatsala *et al.*, 2014). The level at which the carotid bifurcation occurs is conventionally described either in relation to the laryngeal cartilages or to the cervical vertebrae and is widely regarded as symmetrical in nature (Lo *et al.*, 2006). While population differences in the level of the carotid bifurcation are well described (Hayashi *et al.*, 2005; Ribeiro *et al.*, 2006; Anangwe *et al.*, 2008; Ozgur *et al.*, 2008; Al-Rafiah *et al.*, 2011; Vatsala *et al.*, 2014), sex differences have not been well documented.

Relative to the laryngeal cartilages, the most common level of the carotid bifurcation occurs at the superior border of the thyroid cartilage (Standring, 2008). This was reported in 48.3% of Saudi Arabic (n=30) (Al-Rafiah *et al.*, 2011) and in 100% of Indian (n=20) (HimaBindu and Rao, 2012) cadaver populations as well as a number of individual case reports including an Indian female cadaver (Shankar *et al.*, 2008), Turkish male cadaver (Anil *et al.*, 2000) and Asian male cadaver (Murlimanju *et al.*, 2012). Furthermore, the carotid bifurcation occurred at the superior border of the thyroid cartilage in 39% of cadavers from a New Zealand study (n=36: 20 males, 16 females) (Lo *et al.*, 2006). However, the level of the carotid bifurcation has been reported to occur as high as the hyoid bone, as observed within 72.5% of Turkish (n=20: 17 males, 3 females) (Ozgur *et al.*, 2008) and in 55% of New Zealand (Lo *et al.*, 2006) cadavers. This high level of bifurcation has also been reported in eight individual case reports on Indian cadavers (5 males, 3 females) (Vinaiitha *et al.*, 1988; Chitra, 2008; Shankar *et al.*, 2008; Mamatha *et al.*, 2010; Jadhav *et al.*, 2011; Vinnakota *et al.*, 2011; Avadhani and Chakravarthi, 2012; Sugavasi *et al.*, 2012) and was the second most common level of the carotid bifurcation (46.6%) in a Saudi Arabic cadaveric study (Al-Rafiah *et al.*, 2011). Furthermore, the

carotid bifurcation may occur higher than the hyoid bone, as observed in 48.25% of patients in a Turkish computer topography (CT) study (n=100: 50 males, 50 females) (Acar *et al.*, 2013). In contrast to the high bifurcation level, the carotid bifurcation may occur as low as the cricoid cartilage, as observed in 22.5% of cadavers in a Turkish study (Ozgur *et al.*, 2008) and in 5% of cadavers in a Saudi Arabic study (Al-Rafiah *et al.*, 2011).

Similar to the above reported cartilage levels, the vertebral level of the carotid bifurcation is known to vary between populations (Hayashi *et al.*, 2005; Anu *et al.*, 2007; Anangwe *et al.*, 2008; Acar *et al.*, 2013; Vatsala *et al.*, 2014). The most common vertebral level of the carotid bifurcation is between the third and fourth cervical (C3-C4) vertebrae (Drake *et al.*, 2005; Standring, 2008). However, this was the second most common level in Kenyan cadaveric (22.5%; n=40) (Anangwe *et al.*, 2008) and Indian cadaveric (23.7%; n=40) (Vatsala *et al.*, 2014) studies. Furthermore, the carotid bifurcation occurred most frequently at the level of the third cervical vertebra in Indian (Anu *et al.*, 2007; Vatsala *et al.*, 2014), Kenyan (Anangwe *et al.*, 2008), Japanese (n=49: 25 males, 24 females) (Hayashi *et al.*, 2005) adult cadaveric and Turkish fetal (n=20: 9 males, 11 females) (Zumre *et al.*, 2005) studies. However, the frequency at which the carotid bifurcation occurred at the third cervical vertebra varied from 36.7% in the Kenyan population (Anangwe *et al.*, 2008) to 57.5% in the Turkish population (Zumre *et al.*, 2005).

A vertebral carotid bifurcation level inferiorly to the C3-C4 intervertebral disc is rarely reported within the literature. A carotid bifurcation at the level of C5 has been reported in 10% of Turkish fetuses (Zumre *et al.*, 2005) and in 8.04% of Turkish adults (Acar *et al.*, 2013). Furthermore, Anangwe *et al.* (2008) recorded a bifurcation level between C6 and

C7 in 3.75% of individuals within a Kenyan cadaveric population (Anangwe *et al.*, 2008). In contrast, Ribeiro *et al.*, (2006) observed that the level of carotid bifurcation occurred at the second cervical vertebra in 60% of the Brazilian population. This high bifurcation level has also been observed in 12.5% of Kenyan (Anangwe *et al.*, 2008) and 9% of Saudi Arabic (Al-Rafiah *et al.*, 2011) cadavers. In addition, the carotid bifurcation was observed between the C2-C3 vertebrae in 7.03% of Turkish CT patients (Acar *et al.*, 2013) as well as in a Croatian male case report (Gluncic *et al.*, 2000).

A high carotid bifurcation may be associated with a deviation (looping, coiling or curving) in the straight course of the external carotid artery (Vinaitha *et al.*, 1988). This was observed in two individual case reports on Indian female cadavers (Vinaitha *et al.*, 1988; Shankar *et al.*, 2008). However, curving of the carotid arteries may occur irrespective of the level of the carotid bifurcation (Vinaitha *et al.*, 1988; Paulsen *et al.*, 2000; Agrawal and Agrawal, 2011). Yonenaga *et al.*, (2011) found the external carotid artery to be tortuous in 25% of Japanese cadavers. However, coiling, looping or curving is a morphological entity which has most frequently been described in the internal carotid artery in both radiological and cadaveric studies (Vinaitha *et al.*, 1988; Paulsen *et al.*, 2000; Agrawal and Agrawal, 2011; Yonenaga *et al.*, 2011). Furthermore, it is important as it alters blood flow which may aid in the formation of atheroma at the curved points (Vinaitha *et al.*, 1988; Paulsen *et al.*, 2000; Agrawal and Agrawal, 2011).

The internal carotid artery is considered the larger terminal branch of the common carotid artery (Drake *et al.*, 2005; Standring, 2008; Nayak, 2010). It originates at the superior border of the thyroid cartilage and ascends vertically through the carotid canal before

dividing into the anterior and middle cerebral arteries on the inferior surface of the brain (Nayak, 2010). The internal carotid artery supplies intracranial structures which include, the brain, and eyes, therefore, injury to the artery may result in life-threatening complications such as a stroke (Vinnakota *et al.*, 2011).

According to anatomical texts, the cervical part of the internal carotid artery runs a straight course to the base of the skull without branching (Paulsen *et al.*, 2000; Drake *et al.*, 2005; Standring, 2008). However, post-mortem studies and extensive angiographic investigations (Paulsen *et al.*, 2000) report the frequency of deviation from a straight course, resulting in curving or looping of the internal carotid artery, to be between 4% and 66% in adults or 16 and 43% in children in the general population (Vinaitha *et al.*, 1988; Paulsen *et al.*, 2000; Nayak, 2010; Agrawal and Agrawal, 2011). Similarly, curving of the internal carotid artery was observed in 39% of individuals within a New Zealand cadaveric study (Lo *et al.*, 2006). Curving of the internal carotid arteries is somewhat more frequent in females than in males (Paulsen *et al.*, 2000). This was evident in a German body donor study (n=164: 79 males, 85 females), where curving of the internal carotid artery was more common in females (27.3%) when compared to males (25%) (Paulsen *et al.*, 2000).

In the carotid triangle, the internal carotid artery lies postero-lateral to the external carotid artery at the level of the carotid bifurcation (Drake *et al.*, 2005; Standring, 2008). This normal anatomical position has been observed in 98.4% of Saudi Arabic (Al-Rafiah *et al.*, 2011), 95% of Turkish (Ozgur *et al.*, 2008) and 70% of Kenyan (Anangwe *et al.*, 2008) cadavers. However, due to excessive lateral migration of the external carotid artery during embryogenesis (Bailey *et al.*, 2007), the antero-medial position of the internal carotid

artery relative to the external carotid artery at the level of the carotid bifurcation may occur (Bailey *et al.*, 2007; Manupati *et al.*, 2012). An overall frequency between 1.7% and 30% in the reversal of the relationship between the terminal branches of the common carotid artery was recorded in Kenyan (Anangwe *et al.*, 2008), Saudi Arabic (Al-Rafiah *et al.*, 2011) and Turkish (Ozgur *et al.*, 2008) cadaveric studies. In addition, case reports on an Indian male cadaver (Manupati *et al.*, 2012), an Indian female cadaver (Shankar *et al.*, 2008), two European female cadavers (Bailey *et al.*, 2007) and one Japanese male patient (Ueda *et al.*, 1984), reported an antero-medial position of the internal carotid artery relative to the external carotid artery at the level of the carotid bifurcation. The position of the internal and external carotid arteries is important for identification of the arteries during carotid endarterectomy where cross clamping of the carotid arteries is required (Hayashi *et al.*, 2005).

As the external carotid artery ascends in the neck, it gives off eight named branches which distribute arterial blood to the head and neck regions (Standring, 2008). The superior thyroid, lingual and facial arteries arise from the antero-medial surface of the external carotid artery, while the occipital and posterior auricular arteries arise from the postero-lateral surface (Standring, 2008). The ascending pharyngeal artery arises from the medial surface of the external carotid artery (Standring, 2008; Mamatha *et al.*, 2010; Pick, 2012; Sugavasi *et al.*, 2012). The superficial temporal artery and the maxillary artery are the terminal branches of the external carotid artery (Rao and Shetty, 2011).

Knowledge of the distance of the branches of the external carotid artery from the carotid bifurcation is important during carotid endarterectomy (Hayashi *et al.*, 2005). The overall

distance of the branches of the external carotid artery from the carotid bifurcation increases as the external carotid artery ascends in the neck (Standring, 2008; Sanjeev *et al.*, 2010; Yonenaga *et al.*, 2011). The distance of the branches of the external carotid artery from the carotid bifurcation ranged from 4 to 40mm within an Indian cadaveric study (Sanjeev *et al.*, 2010), with the superior thyroid artery and the lingual artery originating closer to the bifurcation and the posterior auricular artery the greatest distance from the bifurcation (Sanjeev *et al.*, 2010). In contrast, the mean distance of the superior thyroid artery (5.9mm) and the lingual artery (14.9mm) from the carotid bifurcation was greater in New Zealand study (Lo *et al.*, 2006). Furthermore, the mean distance of the lingual artery from the carotid bifurcation was the greatest ($30.8 \pm 11.8\text{mm}$) in a Japanese cadaveric study (Yonenaga *et al.*, 2011). Knowledge of the distances of the branches of the external carotid artery from the carotid bifurcation, especially the superior thyroid artery (Vazquez *et al.*, 2009), is important during carotid endarterectomy where clamping of a branch may result in ischemia of the structure the branch supplies (Hayashi *et al.*, 2005).

The branches of the external carotid artery originate as single entities in 76% to 80% of the general population (Delic *et al.*, 2010). However, due to the complexities of embryological development, common trunks frequently occur (Delic *et al.*, 2010; Vinnakota *et al.*, 2011). The superior thyroid, lingual and facial arteries are involved in common trunk formation more frequently than the remaining external carotid artery branches (Vinnakota *et al.*, 2011). The linguo-facial trunk occurs more frequently (20%) than the thyrolingual trunk (1-3%) within all populations (Delic *et al.*, 2010). However, population specific investigations have indicated a greater frequency of specific trunk formation than previously stated (Zumre *et al.*, 2005; Anangwe *et al.*, 2008; Mata *et al.*, 2012). The most frequent common trunk within Turkish fetal cadavers (Zumre *et al.*, 2005) and Turkish

adult CT studies (Mata *et al.*, 2012) was the linguo-facial trunk (fetuses 20%; adults 19.9%) followed by the occipito-auricular trunk (foetuses 12.5%) (Zumre *et al.*, 2005; Mata *et al.*, 2012). The least frequent trunk formation was the thyro-lingual trunk (fetuses 2.5%; adults 2.8%) and thyro-linguo-facial trunk (fetuses 2.5%) (Zumre *et al.*, 2005; Mata *et al.*, 2012). Similar to the Turkish results (Zumre *et al.*, 2005; Mata *et al.*, 2012), the linguo-facial trunk was the most frequent common trunk observed in 28.6% (Yonenaga *et al.*, 2011) and 18% (Hayashi *et al.*, 2005) of Japanese cadavers as well as in 7% Kenyan (Anangwe *et al.*, 2008) and 1.7% Saudi Arabic (Al-Rafiah *et al.*, 2011) cadavers, with the thyro-lingual trunk reported to be the least frequent (<2%) common trunk (Hayashi *et al.*, 2005; Anangwe *et al.*, 2008; Al-Rafiah *et al.*, 2011; Yonenaga *et al.*, 2011). Understanding the frequency of common trunk formation is clinically significant as it may aid in the understanding of atherogenesis around bifurcating and branching points (Thomas *et al.*, 2005; Bond *et al.*, 2011).

The external diameters of the common carotid, internal carotid and external carotid arteries are important quantitative variables in calculating inflow: outflow ratios which are valuable in assessing blood flow and the extent of atheroma (Williams and Nicolaides, 1987; Samijo *et al.*, 1998). Differences in the external diameters of the carotid arteries are found as early as in newborns and persist into adulthood (Williams and Nicolaides, 1987; Sehirli *et al.*, 2005). The diameters at the origin and termination of the common carotid artery are larger than at the origin of the internal carotid and external carotid arteries as observed within the Brazilian (Ribeiro *et al.*, 2006) and European (n=61: 35 males, 26 females) (Williams and Nicolaides, 1987) cadaveric studies. Furthermore, within these studies, the external diameters of the left and right sides for the common carotid, internal carotid and external carotid artery were similar (Williams and Nicolaides, 1987; Ribeiro *et*

al., 2006). However, in the Brazilian male study (Ribeiro *et al.*, 2006), the external diameters at the termination of the common carotid (left: $13.2 \pm 0.4\text{mm}$, right: $12.9 \pm 0.4\text{mm}$) and the origins of the internal carotid (left: $8.0 \pm 0.2\text{mm}$, right: $8.0 \pm 0.3\text{mm}$) and external carotid (left: $7.1 \pm 0.2\text{mm}$, right: $7.3 \pm 0.2\text{mm}$) arteries were larger than the averaged external diameters at the termination of the common carotid ($8.8 \pm 1.0\text{mm}$) and the origins of the internal carotid ($5.5 \pm 0.6\text{mm}$) and external carotid ($4.9 \pm 0.7\text{mm}$) arteries reported in a European male cadaveric study (Williams and Nicolaides, 1987). Although the Turkish population (Ozgur *et al.*, 2008) had a similar external diameter at the termination of the common carotid artery ($12.8 \pm 2.9\text{mm}$) to the Brazilian population (Ribeiro *et al.*, 2006), the external diameter at the termination of the common carotid artery, within the Turkish population (Ozgur *et al.*, 2008) was larger than the European study (Williams and Nicolaides, 1987). Furthermore, the external diameter at the origin of the internal carotid artery (left: $5.8 \pm 0.9\text{mm}$, right: $5.5 \pm 0.6\text{mm}$) in the Indian population (Shashikant and Sherke, 2013) was similar to the European population (Williams and Nicolaides, 1987), but was smaller than in the Brazilian population (Ribeiro *et al.*, 2006). In addition to these population differences, the external diameters of all the carotid arteries were significantly larger in European males when compared to females (Williams and Nicolaides, 1987).

In contrast to similarities in the diameters of the carotid arteries between the left and right sides, the angle of the carotid bifurcation was found to differ on the left and right sides within individuals (Thomas *et al.*, 2005; Phan *et al.*, 2012). In a Turkish cadaveric study it has been reported that the left angle ($21.7 \pm 20.98^\circ$) is slightly larger than the right angle ($21.35 \pm 20.6^\circ$) (Ozgur *et al.*, 2008). Furthermore, in a cross-sectional MRI study on the

geometry of the carotid bifurcation comparing younger (n=25) and older (n=25) individuals, there was a 15.1° significant difference in the carotid bifurcation angle between younger ($48.5 \pm 6.3^\circ$) and older ($63.6 \pm 15.4^\circ$) individuals (Thomas *et al.*, 2005). Phan *et al.* (2012) supported the theory that the carotid bifurcation angle increases with age. Furthermore, Phan *et al.* (2012) indicated a significant correlation in the angle of the carotid bifurcation and the percentage of stenosis of the internal carotid artery proximal to the carotid bifurcation. A carotid bifurcation angle greater than 43.17° resulted in more than 80% of stenosis of the internal carotid artery cross sectional area (n=178) (Phan *et al.*, 2012). This may affect the blood flow through the carotid bifurcation and increase the potential risk of atheroma formation (Phan *et al.*, 2012).

1.2. Pathophysiology of atheroma

An understanding of the variations in carotid arterial anatomy, including common trunk formation, curving and positioning of the arteries is fundamental in understanding the effect of haemodynamic forces on the arterial wall (Schulz and Rothwell, 2001b; Weydahl and Moore, 2001; Thomas *et al.*, 2005; Bond *et al.*, 2011). The arterial wall is composed of endothelium, smooth muscle, elastin and collagen arranged in three layers (Stevens *et al.*, 2002). The tunica adventitia, the outermost layer, is composed of connective tissue and elastic fibres (Steven *et al.*, 2002; Ross and Pawlina, 2006). The tunica media is composed of smooth muscle and elastic lamellae and the tunica intima, closely associated with the lumen, is composed of endothelium, connective tissue and smooth muscle (Ross and Pawlina, 2006). Together these layers make up a resilient system to maintain vascular tone and resist forces created by blood flow (Stevens *et al.*, 2002).

The arterial wall is not negatively affected by unidirectional and constant blood flow which occurs in regions of the carotid arterial tree with uniform geometry. (Schulz and Rothwell, 2001b; Thomas *et al.*, 2005; Cecchi *et al.*, 2011). However, changes in vessel geometry, such as at arterial bifurcations, arterial stenosis, acute angles, the origins of common trunks and curvatures of arteries (Bressloff, 2007; Cecchi *et al.*, 2011), cause alterations in blood flow which may affect the arterial wall causing endothelial damage and lead to the formation of atheroma (Nazemi *et al.*, 1990; Steinman *et al.*, 2002; Cecchi *et al.*, 2011).

Arteries are constantly subject to mechanical forces in the form of stretch and shear stress created by the pulsatile nature of blood flow (Lehoux and Tedgui, 2003; Papaioannou and Stefanadis, 2005; Cecchi *et al.*, 2011). Blood pressure is the major determinant of arterial stretch (Lehoux and Tedgui, 2003; Papaioannou and Stefanadis, 2005). Blood pressure creates radial and tangential forces which counteract the effects of intraluminal pressure and affect all cell types in the arterial wall (Lehoux and Tedgui, 2003; Papaioannou and Stefanadis, 2005). In addition, fluid shear stress, which acts in parallel to the endothelial surface, results from the friction of blood against the arterial wall (Nazemi *et al.*, 1990; Lehoux and Tedgui, 2003; Cecchi *et al.*, 2011). Alterations in shear stress generate transformations in the arterial wall that aim to accommodate the new conditions and attempt to restore normal levels of shear stress (Nazemi *et al.*, 1990; Lehoux and Tedgui, 2003; Papaioannou and Stefanadis, 2005; Cecchi *et al.*, 2011; Weber and Noels, 2011). However, when shear stress continues over a prolonged period of time, the pressure created causes a loss of elasticity in the arterial wall and leads to endothelial dysfunction (Stevens *et al.*, 2002; Cecchi *et al.*, 2011). This permits sub-endothelial accumulation of naturally occurring low-density lipoprotein molecules (Epstein, 1999; Weissberg, 2000; Stevens *et al.*, 2002; Cecchi *et al.*, 2011).

The infiltration and retention of low-density lipoprotein molecules in the tunica intima initiates an inflammatory response with intimal infiltration of macrophages and T-cells (Weber and Noels, 2011). The accumulation of lipids and macrophages results in the formation of an atheromatous plaque that is known as a fatty streak lesion (Hansson, 2005; Weber, 2005). Over time, successive accumulation of lipids in the intima stimulates the formation of fibrocollagenous tissue which is composed of collagen and smooth muscle cells (Stevens *et al.*, 2002). As fibroatheromatous plaques accumulate in the tunica intima, the underlying muscular tunica media is remodelled (Stevens *et al.*, 2002). This results in reduction of the arterial diameter, reducing blood pressure on the arterial wall and slowing the progression of the fibroatheromatous plaque formation (Lehoux and Tedgui, 2003; Phan *et al.*, 2012).

However, when 50% of the cross-sectional area of the arterial wall consists of fibroatheromatous tissue, the fibroatheromatous plaque compresses the tunica media (Weber, 2005; Phan *et al.*, 2012). This compression causes compression atrophy of the tunica media with the muscle being replaced with collagen (Stevens *et al.*, 2002; Weber, 2005; Phan *et al.*, 2012). At the same time, smooth muscle cells migrate from the tunica media to the tunica intima where they proliferate and deposit extracellular matrix (Stevens *et al.*, 2002; Phan *et al.*, 2012). The increase in extracellular matrix leads to intimal thickening. The fibroatheromatous plaque becomes progressively calcified and forms a necrotic core which extends into the lumen of the artery (Weber, 2005). The extension of the calcified plaque into the lumen decreases the diameter of the lumen and results in stenosis of the artery. This decreases blood flow and is termed complicated necrotic atheroma (Stevens *et al.*, 2002; Weber, 2005). Complicated atheroma are responsible for 25% of stroke cases in the general population (Wong *et al.*, 1993; Phan *et al.*, 2012).

The development of atheromatous plaques within the carotid arterial system are not only caused by changes in blood flow due to variations in anatomical geometry (Thomas *et al.*, 2005; Lee *et al.*, 2008), but may also be induced or accelerated by risk factors such as increased age (Crouse *et al.*, 1987; Vaiktevicius *et al.*, 1993; Joakimsen *et al.*, 1999; Schmidt-Truckass *et al.*, 1999; Stevens *et al.*, 2002; Moreau *et al.*, 2012), sex (Joakimsen *et al.*, 1999; Hayward *et al.*, 2000; Schulz and Rothwell, 2001a; Stevens *et al.*, 2002; Han *et al.*, 2008), genetic factors (Gnasso *et al.*, 2000; Stevens *et al.*, 2002), race (Stevens *et al.*, 2002; Ruan *et al.*, 2009), lifestyle factors, such as smoking (Stevens *et al.*, 2002) and diseases, such as hypertension (Chambless *et al.*, 1997; Stevens *et al.*, 2002) and hyperlipidaemia (Ross and Harker, 1976; Stevens *et al.*, 2002). Age is particularly important (Crouse *et al.*, 1987; Ku *et al.*, 1985). The risk of severe carotid arterial disease increases with each decade up to 85 years of age due to a decrease in elastin fibres within the arterial wall (Ku *et al.*, 1985; Stevens *et al.*, 2002). Thus, the integrity of the arterial wall decreases over time due to the constant stress created by blood flow and pressure (Crouse *et al.*, 1987; Ku *et al.*, 1985; Schmidt-Truckass *et al.*, 1999; Stevens *et al.*, 2002). This is a natural process known as vascular aging, which allows penetration of lipids within the tunica intima (Crouse *et al.*, 1987; Joakimsen *et al.*, 1999; Schmidt-Truckass *et al.*, 1999).

Furthermore, sex differences are evident in the frequency of atheroma (Joakimsen *et al.*, 1999). Studies have shown that, compared to females, males have an increased risk of atheroma up to the age of 75 years due to a decrease in testosterone levels with advanced age (Hayward *et al.*, 2000; Stevens *et al.*, 2002; Brinca *et al.*, 2005; Han *et al.*, 2008). In addition, females have an increased risk of severe atheroma as estrogen levels decrease due to menopause (Hayward *et al.*, 2000; Stevens *et al.*, 2002; Brinca *et al.*, 2005; Moreau *et*

et al., 2012). Although not completely understood, a decrease in testosterone and estrogen is likely to cause structural changes within the arterial wall (Joakimsen *et al.*, 1999; Westendorp *et al.*, 1999). These changes may include increases in collagen or fragmented elastin content, which allows lipids to penetrate the tunica intima and media forming atheromatous plaque (Westendorp *et al.*, 1999; Han *et al.*, 2008; Moreau *et al.*, 2012).

In addition, black African-Caribbean adults in the United Kingdom have an increased carotid intimal-media thickness as a result of a higher prevalence of lifestyle and genetic related hypertension when compared to white Europeans (Whincup *et al.*, 2012). This pattern is also observed in South-Asians, who have an increased risk of developing carotid arterial disease, as a result of hypertension, when compared to white individuals (Bennett *et al.*, 2010). Population based studies have suggested that the increase in the carotid intimal-media wall thickness, associated with atheroma, may be caused by increased hypertension associated with diet (Salonen and Salonen, 1989).

The carotid arterial system is a complex system that is important in supplying oxygenated blood to the head and neck regions (Shankar *et al.*, 2008). Knowledge of the anatomical variation in the carotid arterial system is of vital importance in understanding the pathogenesis of atheroma (Vinaitha *et al.*, 1988; Hayashi *et al.*, 2005; Lo *et al.*, 2006; Phan *et al.*, 2012). Furthermore, lack of knowledge regarding the possible origins, course and relationships of the carotid arteries could lead to serious errors if one artery is mistaken for another (Anu *et al.*, 2007) during surgical or radiological procedures. Previous cadaveric and patient studies have focused on imaging identification and measurements of the common carotid, internal carotid and external carotid arteries within certain populations or

within the sexes, but not both within the same study (Schulz and Rothwell, 2001a; Schulz and Rothwell, 2001b; Phan *et al.*, 2012;). Furthermore, to date, there are no standards of the carotid arteries in the South African population. Thus, this study aimed to investigate the anatomical variations of the carotid arterial system and their potential association with the frequency of atheroma around the carotid bifurcation within the South African cadaveric population.

The following aspects of the carotid arterial system were studied, with regard to the left and right sides in all individuals, between white males and white females as well as between white males and black males:

1. Variations in the level at which the carotid bifurcation occurs in relation to the cervical vertebrae and laryngeal cartilages.
2. The frequency of curvature in the course of the common carotid artery, internal carotid artery and the external carotid artery.
3. The position of the internal carotid artery relative to the external carotid artery at the level of the carotid bifurcation.
4. The positions of the single branches that originated from the external carotid artery.
5. The frequency and positions of common trunks originating from the external carotid artery.
6. The distance of the origin of the single branches or common trunks of the external carotid artery from the carotid bifurcation.
7. The relationship between the level of the carotid bifurcation and the distance of the branches of the external carotid artery from the carotid bifurcation.

8. The lengths of the common carotid artery, the internal carotid artery and the external carotid artery.
9. The external diameters of the common carotid artery, internal carotid artery and external carotid artery as well as the external carotid artery branches at the origins of the arteries.
10. The internal diameters at the origins of the common carotid, internal carotid and external carotid arteries, as well as at the termination of the common carotid artery.
11. The angle of the carotid bifurcation.
12. The presence of macroscopic and microscopic atheroma around the carotid bifurcation.
13. The relationship between the frequency of macroscopic atheroma and variations of the carotid arterial system.

2. MATERIALS AND METHODS

2.1. Materials

One hundred and eleven adult human cadavers were sourced from the School of Anatomical Sciences at the University of the Witwatersrand (n=90) and the Department of Human Anatomy and Physiology at the University of Johannesburg (n=21). The sample included black and white individuals and consisted of 62 males and 49 females who ranged in age from 59 to 100 years and in stature from 1.56 to 1.89 meters. The stature of the cadavers was measured in a straight line from the calcaneus to the occipital protuberance, by the mortuary staff prior to embalming. Ethical clearance for the study was obtained from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (W-CJ-101109-1) (Appendix A1) and the University of Johannesburg Ethics Committee (Appendix A2) prior to dissection of the cadavers.

2.1.1. Inclusion and exclusion criteria

As the study included an assessment of the presence of atheroma in the carotid arteries, individuals presenting with atheroma, stenosis and aneurysms were included in the study. The cause of death for each cadaver was documented and cadavers presenting with other pathologies of the neck region were excluded (n=0). Of the 111 cadavers, the carotid arterial systems of 33 cadavers were damaged during previous dissection by Health Sciences students prior to the study. These cadavers were excluded from the study. In addition one black female was excluded from the study, as this specimen was retained by the Department of Anatomy, University of Johannesburg. Thus, the final sample consisted of 77 cadavers (Table 2.1).

Table 2.1 Demographic data of the sample sourced from the Universities of the Witwatersrand and Johannesburg.

Group	University of the Witwatersrand	University of Johannesburg	Total
Black Male (68± 8 years)	1	11	12
White Male (72±12 years)	25	7	32
White Female (75±12 years)	31	2	33
Total sample (71 ± 10 years)	57	20	77

2.2. Methods

As the study made use of a combination of histological and morphological anatomy techniques, it is important to describe the embalming process. The cadavers were refrigerated within 24 hours of death, embalmed in 10% formaldehyde solution and wrapped in formalin soaked sheets before the study commenced. As a result of embalming occurring immediately after death and the percentage of formaldehyde used, tissue shrinkage is not likely to affect the observations or measurements included in this study (Gupta and Gauba, 2011).

Additionally, the arteries and veins of the cadavers that were sourced from the University of Johannesburg (n=20) were injected with latex to distinguish between the blood vessels in the head and neck regions. The cadavers sourced from the University of the Witwatersrand (n=57) were not injected with latex. Furthermore, it was noted that the latex did not expand upon hardening and as such no measureable effect was expected from the latex hardening.

2.2.1. Dissection

In each cadaver, the left and right carotid arterial systems were exposed by dissection of the head, neck and thoracic regions using a standardised dissection kit. The bilateral dissection included exposing the origins of the common carotid arteries within the thorax as well as the termination of the external carotid arteries within the neck and the internal carotid arteries as they entered the base of the skull. Of the 77 bodies, 57 were previously dissected by Health Sciences students from the respective universities and therefore only removal of fascia around the left and right carotid arterial systems was required.

In order to expose the carotid arterial system bilaterally, in each cadaver a skin incision was made anteriorly from the jugular notch to the mental protuberance. Additional incisions were made bilaterally along the inferior border of the mandible, from the mental protuberance to the bigonial angles of the mandible and from the jugular notch along the clavicles to the acromioclavicular joints. These incisions allowed lateral reflection of the skin, fascia, platysma muscles and external jugular veins. Thereafter, the sternocleidomastoid muscles were reflected superiorly through incisions at their sternal and clavicular attachments. The strap muscles of the neck, namely the sternohyoid, sternothyroid, thyrohyoid and omohyoid muscles were reflected to reveal the hyoid bone, the thyroid gland, the tracheal cartilages, the larynx and the left and right carotid sheaths. The common carotid arteries, the carotid bifurcations, the internal carotid arteries and the external carotid arteries were exposed bilaterally by reflecting the carotid sheaths and removing the internal jugular vein.

In addition, dissection of the fascia and adipose tissue associated with the right and left external carotid arteries allowed for exposure of the branches of each external carotid artery. The branches of each external carotid artery were identified using the criteria listed in Table 2.2, which included the position of the branch on the external carotid artery and the structure supplied by each branch. Thereafter, bilateral dissection of the face and reflection of the mandible, as described below, exposed the posterior auricular artery and the superficial temporal and the maxillary arteries.

Bilateral vertical skin incisions were made from the gonial angle of the mandible to the vertex of the skull and extended posteriorly to the external occipital protuberance. The skin and fascia were reflected laterally and the underlying muscles of mastication were exposed. The mandible of each cadaver was reflected superiorly by bilateral incisions through the mandibular attachments of the temporalis, buccinator, mylohyoid, geniohyoid and medial and lateral pterygoid muscles. The maxillary artery was identified as the medial artery extending deep toward the maxilla, while the superficial temporal artery was identified as the lateral artery supplying the temporalis muscle.

Table 2.2 Criteria used to identify the branches of the left and right external carotid arteries.

External carotid artery branch	Position/location on the external carotid artery	Structure it supplies	Other features
Superior thyroid artery	First branch – anterior surface	Thyroid gland	Arises below greater cornu of the hyoid bone
Lingual artery	Second branch – anterior surface	Tongue	Arises opposite greater cornu of the hyoid bone
Facial artery	Third branch – anterior surface	Face and submandibular gland	Deep to the hypoglossal nerve at its origin
Ascending pharyngeal artery	Medial surface, close to the carotid bifurcation	Constrictor muscles of the pharynx	Ascends vertically between the internal carotid artery and pharynx
Occipital artery	Posterior surface	Sternocleidomastoid muscle	Crossed by the hypoglossal nerve at its origin
Posterior auricular artery	Posterolateral surface	Digastric muscle	Arises above the digastric and stylohyoid muscles
Superficial temporal artery	Lateral terminal branch of the external carotid artery	Temporalis muscle	Arises in the parotid gland
Maxillary artery	Medial/ deep terminal branch of the external carotid artery	Buccinator muscle	Third part located in the pterygopalatine fossa of the maxilla

Adapted from Standring (2008).

Reflection of the thoracic cage allowed the left and right common carotid arteries to be traced back to their respective origins in the thorax. Bilateral incisions were made through the respective sternoclavicular joints, the subclavius muscles and the costal shafts along the midaxillary line. The anterior thoracic wall was reflected inferiorly to expose the underlying structures of the mediastinum, where the heart and the arch of the aorta were identified. The three branches arising from the aortic arch were identified from right to left as the brachiocephalic trunk, left common carotid artery and left subclavian artery. Originating from the brachiocephalic trunk, the right common carotid artery was identified as the artery ascending into the neck superiorly, while the right subclavian artery was identified as the artery extending laterally towards the axilla.

Following the dissection of the head, neck and thoracic regions, to expose the carotid arterial system, a protractor, a Vernier sliding calliper (0.02mm), a metric ruler and cotton were used to take measurements of the carotid arteries and their corresponding branches. The measurements from the Vernier sliding calliper and metric ruler was rounded off to the nearest 10th of a mm, while the measurements from the protractor was rounded off to the nearest 10th of a degree. In addition, a NIKON D90 camera (18 -105 mm VR lens) was used to document all specimens.

2.2.2. Morphological assessment

The level of the carotid bifurcation was classified in relation to the cervical vertebrae and the laryngeal cartilages. To determine the relationship with the cervical vertebrae, cotton was extended in a straight line from the carotid bifurcation to the cervical vertebrae posteriorly. Palpation and counting of the transverse processes of the cervical vertebrae up to the location of the cotton, allowed for accurate recording of the level of the carotid bifurcation with respect to the vertebrae or intervertebral discs. To determine the relationship to the laryngeal cartilages, cotton was extended in a straight line anteriorly from the carotid bifurcation to the adjacent laryngeal cartilage. The level of the carotid bifurcation was then recorded as follows: at the level of the hyoid bone, thyro-hyoid membrane, superior or inferior borders of the thyroid cartilage or the cricoid cartilage (Anangwe *et al.*, 2008).

The courses of the common carotid artery, the internal carotid artery and the external carotid artery were classified as straight or curved. For each category the straight line plane, from the midpoint of the carotid bifurcation to the midpoint of the mandibular notch

was the point of reference. A straight course was recorded if the artery ascended straight in the neck, without any curving relative to the reference plane during its course. If deviation from the reference plane occurred medially, laterally, anteriorly or posteriorly along the artery's course, the artery was classified as curved (Fig. 2.1). Looping of the common carotid, the internal carotid and the external carotid arteries was not included in the classification as the arteries were observed in situ and therefore looping could not be accurately identified.

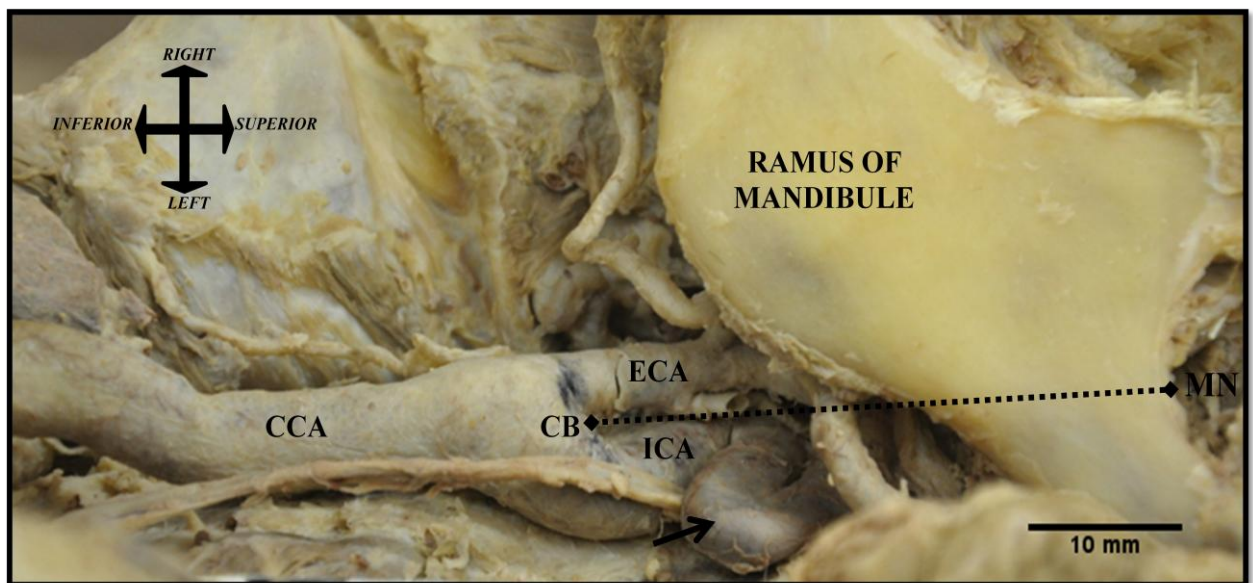


Figure 2.1 A photograph of a 74 year old white female cadaver sourced from the University of the Witwatersrand, illustrating the curvature (arrow) in the course of the internal carotid artery (ICA) using the reference plane from the midpoint of the carotid bifurcation (CB) to the mandibular notch (MN), indicated by the dotted line. CCA: common carotid artery, ECA: external carotid artery.

Following observation of the course of the carotid arteries, the position of the internal carotid artery relative to the external carotid artery at the carotid bifurcation was recorded as either postero-lateral or postero-medial. Thereafter, the positions of the origins of the branches of the external carotid artery were recorded as anterior, posterior, medial or lateral relative to the external carotid artery. Common trunks were classified as two or more branches of the external carotid artery sharing a common origin (Sugavasi *et al.*,

2012). The common trunks were named according to the arteries involved in the formation of the common trunk as described by Sugavasi *et al.* (2012) (Table 2.3). Thereafter, the positions of the origins of the common trunks were recorded as anterior, posterior, medial or lateral relative to the external carotid artery.

Table 2.3 Classification of the common trunks formed by the branches of the external carotid artery.

Common trunk	Arteries involved
Thyro-lingual trunk	Superior thyroid artery and lingual artery
Linguo-facial trunk	Lingual artery and facial artery
Linguo-pharyngeal trunk	Lingual artery and ascending pharyngeal artery
Thyro-linguo-facial trunk	Superior thyroid artery, lingual artery and facial artery
Occipito-pharyngeal trunk	Ascending pharyngeal artery and occipital artery
Occipito-auricular trunk	Occipital artery and posterior auricular artery
Pharyngeal-Occipito-auricular trunk	Ascending pharyngeal artery, occipital artery and posterior auricular artery
Auriculo-temporal trunk	Posterior auricular artery and superficial temporal artery

Adapted from Sugavasi *et al.* (2012).

Once the positions of the carotid arteries were recorded, the lengths of the common carotid, the internal carotid and the external carotid arteries were measured bilaterally along the anterior border of each artery following the curvature of the respective artery (Fig 2.2). The length of the right common carotid artery was measured from the midpoint of the artery at the level of the bifurcation of the brachiocephalic trunk to the midpoint of the artery at the level of the carotid bifurcation. The length of the left common carotid artery was measured from the midpoint of the artery at its origin from the arch of the aorta to the midpoint of the artery at the level of the carotid bifurcation. The lengths of the external carotid and the internal carotid arteries were measured bilaterally from the midpoint of the respective arteries at their origins to the midpoint of their respective termination points, the bifurcation into the maxillary and superficial temporal arteries for the external carotid artery and the carotid canal opening at the base of the skull for the internal carotid artery (Fig. 2.2).

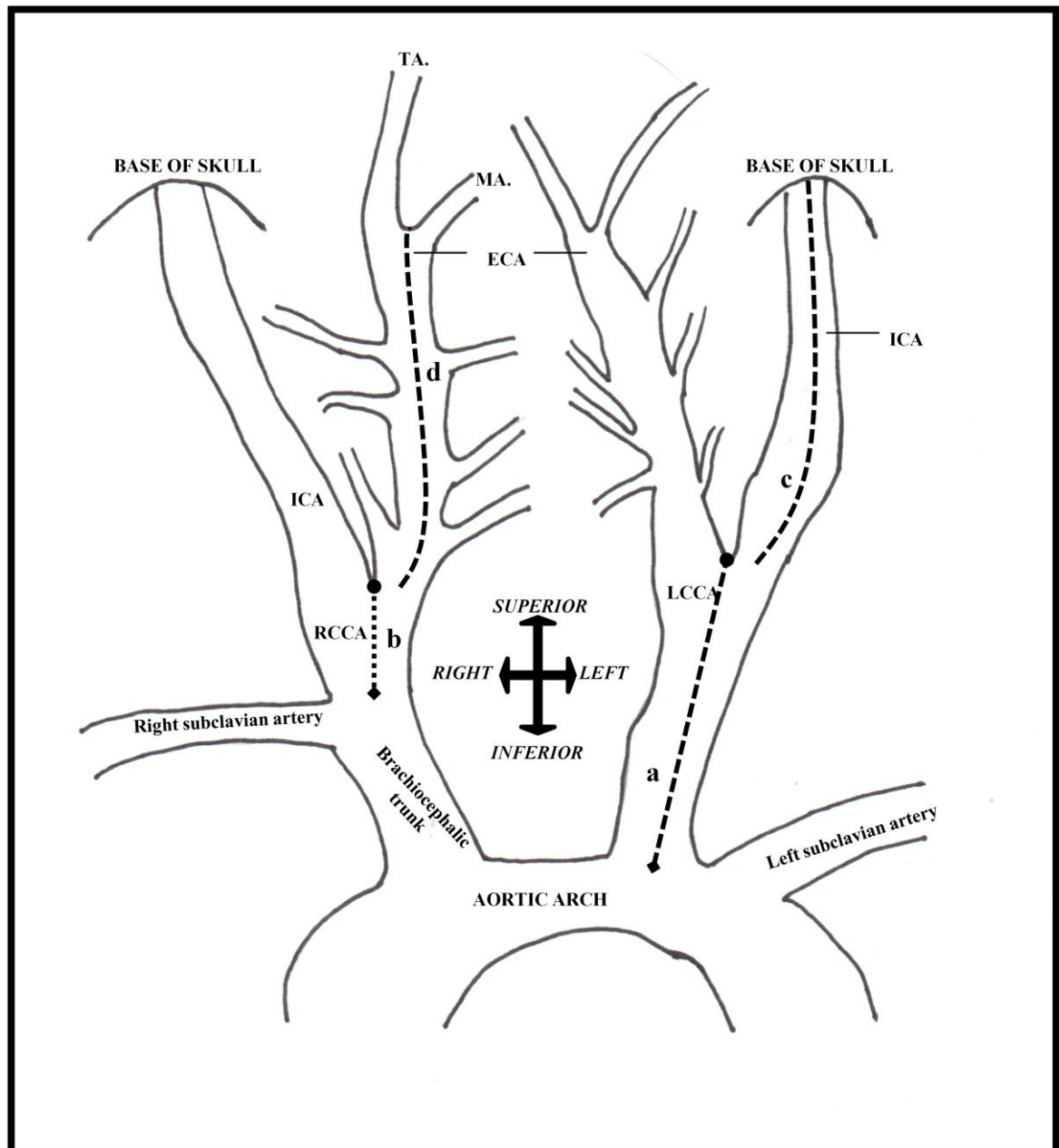


Figure 2.2 A schematic diagram representing the measurement of the carotid arterial lengths. a. the length of the left common carotid artery (LCCA) from the midpoint of the artery at its origin to the carotid bifurcation. b. the length of the right common carotid artery (RCCA) from the midpoint of the artery at its origin to the carotid bifurcation c. the length of the left internal carotid artery (ICA) from the midpoint of the artery at its origin to the midpoint of the artery as it enters into the base of the skull. d. the length of the right external carotid artery (ECA) from the midpoint of the artery at its origin to the bifurcation of the external carotid artery into the maxillary artery (MA) and superficial temporal artery (TA).

In addition, the distance from the carotid bifurcation to the origin of each branch of the external carotid artery was measured bilaterally. Using a permanent marker, horizontal lines were drawn on the external carotid artery at the level of the carotid bifurcation as well as through the midpoints of the origins of the branches of the external carotid artery. The straight line distance between the two lines was measured along the anterior surface of the external carotid artery using cotton and a metric ruler. The measurement of the distance of the facial artery from the carotid bifurcation using this method is illustrated in Figure 2.3.

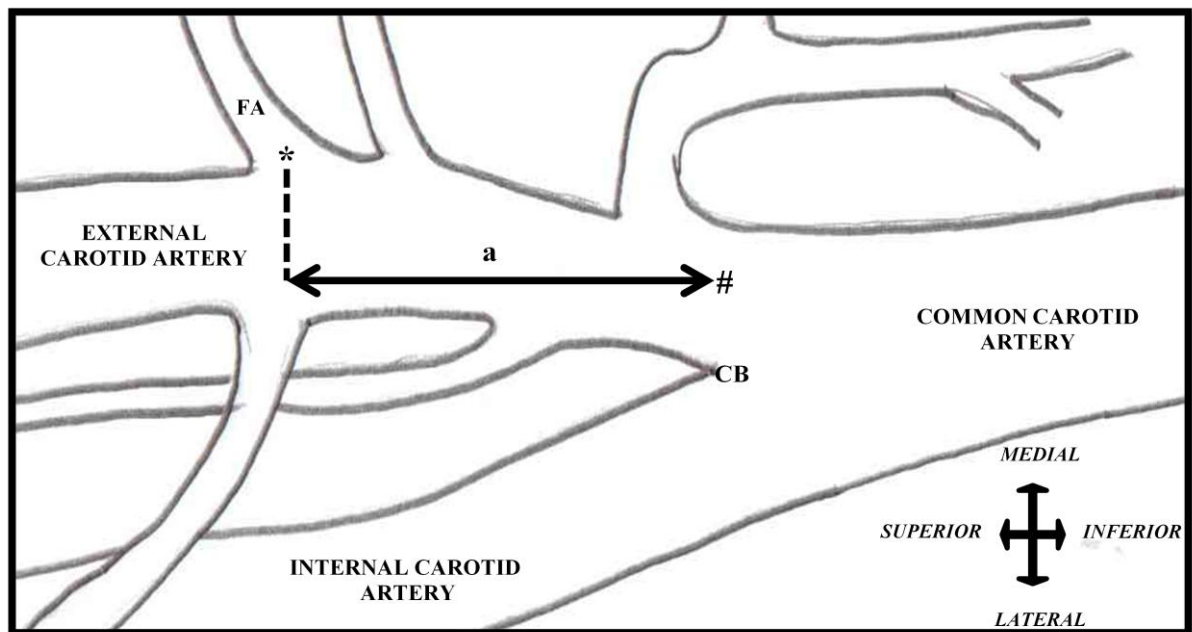


Figure 2.3 A schematic diagram representing the measurement of the distance of the origin of the facial artery (FA) from the carotid bifurcation (CB). a. The straight line distance from the midpoint (#) of the external carotid artery at the level of the carotid bifurcation on the anterior surface of the external carotid artery to the line through the midpoint of the origin of the facial artery (*).

Once the distances of the branches of the external carotid artery from the carotid bifurcation were measured, the angle of the carotid bifurcation was measured using a protractor. The angle was measured between the lateral wall of the external carotid artery and the medial wall of the internal carotid artery (Fig. 2.4).

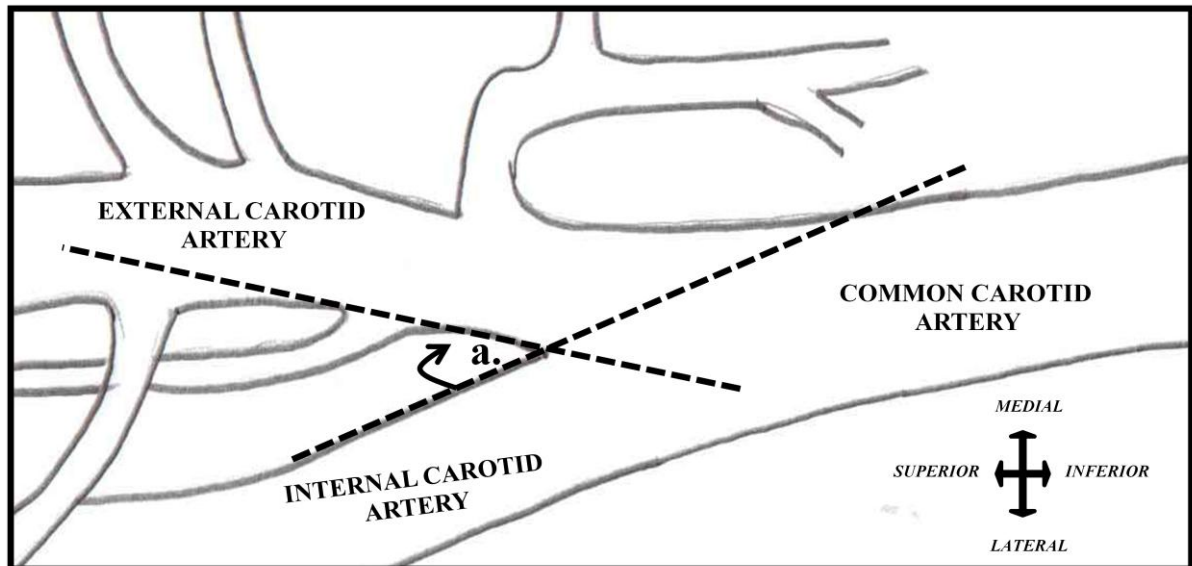


Figure 2.4 A schematic diagram representing the measurement of the angle of the carotid bifurcation (a.) which is created by the medial wall of the internal carotid artery and the lateral wall of the external carotid artery.

Thereafter, the external diameters of the left and right common carotid, internal carotid and external carotid arteries were measured at the origin and the termination of each artery. The external diameters of the branches of the external carotid artery were measured at their origin. The external diameters were measured using manual sliding callipers from the external aspect of the medial wall of the artery to the external aspect of the lateral wall of the artery.

Furthermore, the internal circumferences at the origin and termination of the left and right common carotid, internal carotid and external carotid arteries were measured bilaterally. A “Y” incision was made through the anterior wall of the common carotid artery and extended into the internal and external carotid arteries. The arterial wall was opened and using manual sliding callipers, the internal circumference of the wall was measured in a straight line from the medial wall to the lateral wall at the respective origin and termination points of the carotid arteries. Thereafter, a mathematical equation ($c = 2\pi r$) (Bradley *et al.*, 2014) was used to calculate the internal diameter from the internal circumference so that the external and internal diameters could be compared.

Following the “Y” incision in the carotid arteries, the internal aspect of the arterial wall was assessed for the presence of macroscopic atheroma around the carotid bifurcation. The arterial wall was observed for the presence (score = 1) or absence (score = 0) of atheroma around the carotid bifurcation. The criteria as described by Stevens *et al.* (2002) were used to identify the presence of macroscopic atheroma of the left and right common carotid, internal carotid and external carotid arteries around the carotid bifurcation (Table 2.4).

Table 2.4 Criteria used to identify macroscopic atheroma in the carotid arteries around the carotid bifurcation.

Type of macroscopic atheroma	Features
Fatty streak	Pale yellow colouring when compared to the rest of the arterial wall.
Expansion of arterial wall with narrowing of the lumen	Bulge, extending into the lumen, of the arterial wall, but not hard when felt.
Calcification of plaque	Nodular appearance and rough when felt.

Adapted from Stevens *et al.* (2002).

2.2.3. Histological assessment

As the Department of Anatomy and Physiology at the University of Johannesburg retained the body of the only black female for specimens, histological analysis could not be done on this cadaver. Therefore, the left and right carotid bifurcations from 77 individuals (154 carotid bifurcations) were assessed histologically. Following the morphological assessment, a 10mm region around the carotid bifurcation was excised bilaterally. The excised tissue included a portion of the common carotid artery, the internal carotid artery and the external carotid artery.

The 10mm tissue surrounding the carotid bifurcation was placed in 10% buffered formalin (Appendix B1) for 24 hours. Thereafter, it was processed according to the protocols of the School of Anatomical Sciences at the University of the Witwatersrand. Each 10mm length of tissue surrounding the carotid bifurcation was dehydrated by passing the tissue through a series of graded alcohols and cleared in chloroform before being embedded in paraffin wax. Serial sections (5µm thick) were cut from the paraffin embedded tissue of each artery and mounted on Sta-on[®] tissue section adhesive (Leica, USA) coated glass slides. Three non-adjacent 5µm sections, including sections proximal to the carotid bifurcation, at the carotid bifurcation and distal to the carotid bifurcation, from the left and right carotid bifurcation of each individual included in the histological analyses (n=462 sections) were selected for routine haematoxylin and eosin (H&E) staining (Appendix B2). The sections were 100µm apart. H&E staining was used as attempts to stain using the Van Gieson stain (Appendix B3) were not successful. This may be due to the tissue not being processed immediately after embalming and drying of the cadavers due to the length of time the cadavers were in the dissection halls (Gupta and Gauba, 2011).

The 462 H&E stained sections were assessed using the 40x objective of a Zeiss microscope for the presence of atheroma and to measure the intima-media thickness (Ruan *et al.*, 2009) in the region of the carotid bifurcation. However, in the majority of sections, the layers of the arterial wall had degraded and separated. The separation may have occurred over time, as the tissues were not processed immediately after embalming (Gupta and Gauba, 2011). Therefore, the intima-media thickness measurement could not be standardised and was excluded.

The presence of atheroma was scored histologically according to three categories based upon the description by Stevens *et al.* (2002). A score of “0” indicated no atheroma within the arterial wall (Fig. 2.5a). “Early” stages of atheroma, indicated by proliferation of cells and collagen bundles within the tunica intima (Fig. 2.5b), were scored as “1”. A score of “2” indicated “late” atheroma, with cholesterol clefts or areas of necrosis or calcification within the tunica intima (Fig. 2.5c). The 462 sections were assessed and scored according to the three categories. Thereafter, for each individual, the overall atheroma score in the left and right carotid bifurcations was classified according to the highest score the individual received for the left and right sides respectively. The highest score was chosen as it indicated the clinical severity of the atheroma (Hellings *et al.*, 2010).

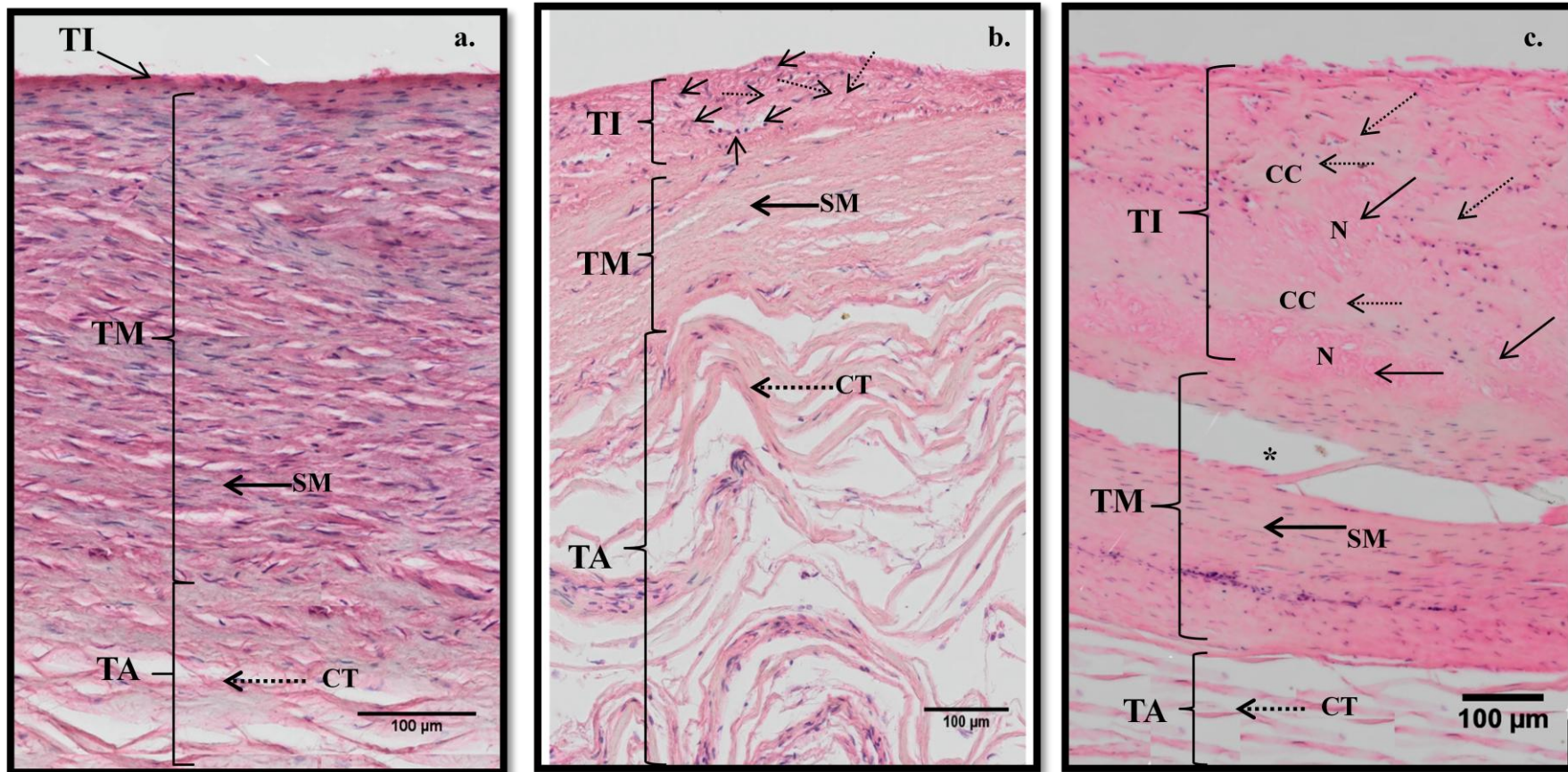


Figure 2.5 Representative photographs indicating the stages of atheroma surrounding the carotid bifurcations. a. No atheroma (score=0) present within the tunica intima (TI) or tunica media (TM). Organised layers of smooth muscle (SM) cells were used to mark the start of the tunica media and connective tissue fibres (CT) was used to identify the tunica adventitia (TA) b. “Early” atheroma (score=1): Cell nuclei (solid arrows) and connective tissue (dotted arrows) in the thickened tunica intima indicating fibroproliferation. c. “Late” atheroma (score=2): Solid arrows indicating areas of necrosis (N) and dotted arrows indicating areas of cholesterol clefts (CC) within the tunica intima. * indicates the separation of the tunica media layer possibly due to drying of the cadaveric tissue. Source: University of the Witwatersrand.

2.3. Statistical analysis

The data was analysed using Microsoft excel, PAST v2.17c and STATISTICA v12. The quantitative variables, including the length and external diameters of the carotid arteries and the distance of the branches of the external carotid artery from the carotid bifurcation as well as the carotid bifurcation angle, were measured three times and the mean calculated for each individual. The mean was used for further analysis.

2.3.1. Observer errors

For the categorical variables, the inter- and intra-observer errors were performed on repeated measurements collected by the primary observer and a secondary observer on the entire sample. Intra- and inter-observer errors were assessed using Cohen's kappa coefficient (Cohen, 1960). Co-efficients of 0.9 or greater were obtained (Appendix C1) and considered evidence of acceptably low levels of observer error for the categorical variables (Blackman and Koval, 2000).

For the quantitative variables, the relevant measurement was repeated on 10% of the sample by the primary observer as well as a second independent observer. Intra- and inter-observer error was calculated using Lin's Concordance correlation (Allan, 1982). Co-efficients of 0.9 or greater were obtained (Appendix C2) and considered evidence of high repeatability and a low level of observer error (Allan, 1982).

2.3.2. Descriptive statistics

The distribution of the quantitative variables was assessed using a Shapiro-Wilk normality test in which a p-value greater than 0.05 indicated that the data was normally distributed (Ghasemi and Zahediasl, 2012). The majority of the data was found to be nonparametric (Appendix D). Therefore, the median and inter-quartile ranges were chosen to describe the data (Whitley and Ball, 2002a).

2.3.3. Inferential statistics

There was no significant difference between the internal and external diameters of the origin and termination of the common carotid, internal carotid and external carotid arteries (Appendix E). Therefore, the external diameters were chosen for further statistical analysis as they are the most frequently reported in cadaveric studies (Williams and Nicolaides, 1987; Sehirli *et al.*, 2005; Ribeiro *et al.*, 2006; Shashikant and Sherke, 2013).

A Wilcoxon sign rank test, was used to determine whether there was a significant difference ($p < 0.05$) between measurements of the left and right sides within the same individual (Whitley and Ball, 2002b). Measurements in which the left side and right sides were statistically different were not averaged (Table 2.5). However, measurements of the left and right sides that were not statistically different ($p > 0.05$) were averaged and the average value of each individual was used for further statistical analysis. Table 2.5 indicates which variables were averaged and which not.

Due to the small sample of black male cadavers ($n=12$), analyses for sex and racial affinity were conducted as follows. Analyses to assess sex differences were conducted using the white males ($n=33$) and white females ($n=32$) groups. Subsequently the racial affinity

analysis was conducted on white males (n=33) and black males (n=12). This was done to prevent sex confounding the racial affinity analysis or the racial affinity confounding the sex analysis. A Kruskal Wallis one-way analysis of variance was used to determine whether there was a significant difference ($p < 0.05$) between the sexes and between the racial affinity for the quantitative variables (Zar, 1999; McDonald, 2014).

Frequency tables were used to analyse the categorical variables (Bewick *et al.*, 2004). Contingency tables as well as M-L Chi-square test were performed to assess whether there was a statistical difference in the observed frequencies for the left and right sides between white females and white males, as well as between white males and black males (Bewick *et al.*, 2004). A p-value less than 0.05 was considered statistically significant (McDonald, 2014).

To investigate the associations between the variables, the entire sample (n=77) was used. This was done to increase the sample size. To assess relationships between the quantitative variables within the entire sample, a Spearman's correlation was used. A p-value less than 0.05 was considered significant and a r-value greater the 0.70 was considered a strong relationship (Zar, 1999). Furthermore, to assess if significant differences existed for the quantitative variables between the categories of the categorical variables, a Kruskal Wallis one-way analysis of variance was used (McDonald, 2014).

Table 2.5 The variables for which measurements of the left and right sides were averaged as well as the variables which were not averaged for statistical analyses.

Averaged measurements	Non-averaged measurements
Length of the ICA	Length of the left CCA
Length of the ECA	Length of the right CCA
External diameter at the origin of the CCA	Left CB angle
External diameter at the origin of the ICA	Right CB angle
External diameter at the origin of the ECA	Distance of the origin of the left FA from the CB
External diameter at the termination of the CCA	Distance of the origin of the right FA from the CB
External diameter at the termination of the ICA	External diameter of the origin of the left PAA
External diameter at the termination of the ECA	External diameter of the origin of the right PAA
External diameter at the origin of the STA	Distance of the origin of the left PAA from the CB
Distance of the origin of the STA from the CB	Distance of the origin of the right PAA from the CB
External diameter at the origin of the LA	Distance of the origin of the left supTA from the CB
Distance of the origin of the LA from the CB	Distance of the origin of the right supTA from the CB
External diameter of the origin of the FA	Distance of the origin of the left MA from the CB
External diameter of the origin of the APA	Distance of the origin of the right MA from the CB
Distance of the origin of the APA from the CB	
External diameter of the origin of the OA	
Distance of the origin of the OA from the CB	
External diameter of the origin of the supTA	
External diameter of the origin of the MA	

CCA=common carotid artery; ICA=internal carotid artery; ECA=external carotid artery; CB=carotid bifurcation; STA=superior thyroid artery; LA=lingual artery; FA=facial artery; APA=ascending pharyngeal artery; OA=occipital artery; PAA=posterior auricular artery; supTA=superficial temporal artery; MA=maxillary artery.

3. RESULTS

Few significant differences were found in the investigated variables between the respective sexes or racial affinity groups. In addition, no significant differences were found in stature or age between the assessed groups (Table 3.1). However, curving of the common carotid, internal carotid and external carotid arteries occurred more frequently in white females when compared to white males. Moreover, it was observed that curving of the internal carotid artery had a higher frequency in longer internal carotid arteries. Significant differences were also found in the length of the common carotid artery between white males and white females. In addition, significant differences were found in the lengths of the internal carotid and external carotid arteries between white males and black males. Within the entire sample, an interesting correlation was found between the external diameters of the common carotid, internal carotid and external carotid arteries and the angle of the carotid bifurcation. Furthermore, macroscopic atheroma, which was found in the majority of individuals, was associated with a smaller external diameter at the origin of the external carotid artery.

In the assessment of the level of the carotid bifurcation, no significant differences were found in the vertebral or cartilage levels of the carotid bifurcation between the sexes or the racial affinity groups (Table 3.2 and Table 3.3). The C3-C4 intervertebral disc or superior border of the thyroid cartilage were the most common levels reported for white females and black males on both the left and right sides (Table 3.2 and Table 3.3). Although the C3-C4 intervertebral disc was the most common vertebral level in white males, the carotid bifurcation occurred at the hyoid bone and superior border of the thyroid cartilage with identical frequencies (Table 3.2 and Table 3.3). The most superior vertebral bifurcation

level was recorded at the level of C2 for white and black males and at C2-C3 intervertebral disc for white females. However, the lowest reported vertebral bifurcation level occurred at C4 for both white females and white males (Table 3.2).

In contrast to the bifurcation level, significant differences were noted between the sexes in the frequency of curving of the carotid arteries (Table 3.4). In the majority of cases, the course of the carotid arteries was straight. However, white females had a significantly higher frequency of curving of the left and right common carotid ($p=0.03$; $p=0.01$), internal carotid ($p=0.03$; $p=0.04$) and external carotid ($p=0.04$; $p=0.01$) arteries when compared to white males (Table 3.4). In contrast, there was no significant difference in the frequency of curvature of the left and right common carotid ($p=0.16$; $p=0.87$), the internal carotid ($p=0.33$; $p=0.25$) or the external carotid ($p=0.54$; $p=0.54$) arteries between white males and black males (Table 3.4).

Furthermore, there was no significant difference in the position of the internal carotid artery relative to the external carotid artery in curved or straight carotid arteries ($p<0.05$ for all arteries) (Table 3.5). The internal carotid artery was most commonly positioned postero-lateral to the external carotid artery within the sexes and racial affinity groups (Table 3.6). There was no statistically significant difference between the sexes or between the racial affinity groups in the position of the left ($p=0.09$; $p=0.54$), right ($p=0.22$; $p=0.20$) or the combined sides ($p=0.60$; $p=0.41$) of the internal carotid arteries relative to the external carotid arteries at the carotid bifurcation (Table 3.6). Although not statistically significant, 19.70% of internal carotid arteries in white females were postero-medial to the external carotid artery at the level of the carotid bifurcation. This contrasts with white

males where the relationship was found in 7.81% of internal carotid arteries (Table 3.6). Furthermore, associations were found between the postero-lateral position of the internal carotid artery relative to the external carotid artery at the level of the carotid bifurcation and antero-medial positions of the origins of the superior thyroid artery ($p=0.01$), the lingual artery ($p=0.02$) and the facial artery ($p=0.02$) (Table 3.7). However, the antero-medial position of the origin of the superior thyroid artery, lingual artery and facial artery was the most frequent position observed within the sexes and racial affinity groups (Table 3.8). In addition, the origin of the ascending pharyngeal artery was most frequently found to be postero-medial and the occipital artery origin postero-lateral on the external carotid artery within the sexes and racial affinity groups (Table 3.8). There was no statistical significant difference between white males and white females or between white males and black males in the positioning of the origin of the external carotid artery branches on the left or right sides (Table 3.8).

Although there was no statistically significant difference in the frequency of the formation of the common trunks between the sexes ($p=0.47$) or racial affinity groups ($p=0.21$), common trunk formation was found in 50.00% of white females, 43.75% white males and in 75.00% of black males (Table 3.9). While the linguo-facial trunk was the most frequently observed trunk within all groups (Table 3.9), the second most frequent trunk in white females and black males was formed from the ascending pharyngeal artery and occipital artery. However, in white males the thyro-lingual trunk was the second most frequently observed (Table 3.9). In addition, the frequency of common trunk formation was not different in curved or straight common carotid ($p=0.14$), internal carotid ($p=0.20$) or external carotid ($p=0.66$) arteries within the sample. Furthermore, the length of the

external carotid artery was not related to the frequency of common trunk formation as a whole (left: $p=0.87$, right: $p=0.62$) (Table 3.10).

In the assessment of the quantitative data, white males were observed to have significantly longer left ($p=0.0004$) and right ($p=0.001$) common carotid arteries when compared to white females (Table 3.11). In contrast, the length of the internal carotid artery appeared to be longer in white females when compared to white males, although this difference did not reach the level of significance (Table 3.11). Furthermore, white males were observed to have significantly longer internal carotid ($p=0.0003$) and external carotid ($p=0.001$) arterial lengths when compared to black males (Table 3.11). Similarly, the superficial temporal and the maxillary arteries in white males were significantly further from the carotid bifurcation when compared to black males ($p=0.01$; $p=0.004$) (Table 3.11).

Throughout the sample, there was no correlation ($p>0.05$; $r<0.05$) between the length of the common carotid artery and the distance of the branches of the external carotid artery from the carotid bifurcation (Table 3.12). However, the length of the external carotid artery was correlated with the distance of the branches of the external carotid artery from the carotid bifurcation (Table 3.12). The strongest correlations were in the distance from the carotid bifurcation of the superficial temporal and maxillary arteries ($r=0.97$) while the weakest correlation was the superior thyroid artery ($r=0.23$). Furthermore, while a high carotid bifurcation level seemed to occur with a longer common carotid artery length, the length of the common carotid (left: $p=0.34$; right: $p=0.36$), internal carotid (left: $p=0.58$; right: $p=0.24$) and external carotid arteries (left: $p=0.42$; right: $p=0.06$) did not differ

significantly between the vertebral or cartilage bifurcation levels (Table 3.13 and Table 3.14).

In addition, there was no correlation found between the length of the common carotid artery and the stature of the cadavers (left: $p=0.06$, $r=0.31$; right: $p=0.07$; $r=0.43$). Furthermore, there was no association between stature and the level of the carotid bifurcation within an individual (left: $p=0.09$; right: $p=0.11$). However, an association was found in which a longer internal carotid artery was associated with curving of the left ($p=0.01$) and right ($p=0.04$) internal carotid arteries (Table 3.15).

Additionally, an association was found in which larger external diameters at the origins of the internal ($p=0.001$; $r=0.37$) and external ($p=0.007$; $r=0.53$) carotid arteries as well as at the termination of the common ($p=0.002$; $r=0.35$) carotid artery were associated with a more obtuse angle (Table 3.16). However, there was no significant difference in the left and right carotid bifurcation angles between the sexes ($p=0.57$; $p=0.41$) or the racial affinity groups ($p=0.43$; $p=0.49$) (Table 3.17).

Similarly, no significant differences between the sexes or racial affinity groups were found in the external diameters of the carotid arteries or the branches of the external carotid artery (Table 3.18). However, it was observed that as the external diameter at the origin of the common carotid ($p=0.001$; $r=0.56$), internal carotid ($p=0.001$; $r=0.52$) and external carotid ($p=0.001$; $r=0.46$) arteries increased, so did the diameter at the termination of the respective arteries. Additionally, it was observed that as the length of the common carotid artery increased so did the diameter at the origin of the common carotid artery ($p=0.007$,

$r=0.30$) which was not found with the internal carotid ($p=0.84$, $r=-0.02$) or the external carotid ($p=0.52$, $r=-0.07$) arteries.

Macroscopic atheroma and microscopic atheroma was found in the majority of cadavers with no significant difference between the sexes and racial affinity groups (Table 3.19 and Table 3.20). However, when macroscopic atheroma was present at the carotid bifurcation, the external diameters at the origin of the external carotid artery was significantly smaller than when macroscopic atheroma was absent (left: $p=0.02$, right: $p=0.01$) (Table 3.21). In addition, further analysis revealed no difference in the length or curving of the carotid arteries or in the angle of the carotid bifurcation ($p>0.05$) as well as common trunk formation as a whole ($p=0.41$) or position of the external carotid artery branches ($p>0.05$) between individuals with and without macroscopic atheroma around the carotid bifurcation (Table 3.22, Table 3.23 and Table 3.24).

In summary, the following differences were found in the measured variables of the carotid arterial system.

- White males had significantly longer common carotid arteries when compared to white females.
- White males had significantly longer internal and external carotid arteries when compared to black males.
- White females had a significantly higher frequency of curving of the common carotid, the internal carotid and external carotid arteries when compared to white males.
- Curving of the internal carotid artery was associated with a significantly longer internal carotid artery.

- Throughout the sample, the length of the external carotid artery and the distance of the branches of the external carotid artery from the carotid bifurcation were correlated.
- An increase in the length of the common carotid artery was associated with a larger external diameter of the common carotid artery at its origin.
- An increase in the external diameter at the origins of the internal and the external carotid arteries as well as the termination of the common carotid arteries was associated with a more obtuse carotid bifurcation angle.
- A smaller external diameter at the origin of the external carotid artery was associated with macroscopic atheroma around the carotid bifurcation.

Furthermore, the level of the carotid bifurcation most commonly occurred at the C3-C4 intervertebral disc and at the superior border of the thyroid cartilage. There was no relationship between the length of the common carotid artery and the level of the carotid bifurcation. Additionally, there was no correlation between stature and the length of the common carotid arteries or the level of the carotid bifurcation within an individual. The internal carotid artery originated postero-lateral to the external carotid artery at the level of the carotid bifurcation. In addition, there was a high frequency of common trunk formation within the sample. There was a high frequency of atheroma around the carotid bifurcation within all assessed groups. Despite the above listed anatomical variations, there was no difference in the angle of the carotid bifurcation, length of the carotid arteries or curvature of the carotid arteries between the cadavers with and without macroscopic atheroma around the carotid bifurcation. However, an interesting correlation between the external diameter of the external carotid artery and the presence of atheroma as well as sex differences in the length and curving of the carotid arteries were found within the sample.

Table 3.1 Descriptive statistics for the age and stature within white females, white males and black males.

Measurement	White females (n=33)	White Males (n=32)	Black Males (n=12)	p-value ¹	p-value ^{2 *}
	<i>Median ± quartile range</i>	<i>Median ± quartile range</i>	<i>Median ± quartile range</i>	<i>Mann-Whitney u-test</i>	<i>Mann-Whitney u-test</i>
Age	75 ± 12 years	72 ± 12 years	68 ± 8 years	p=0.11	p=0.24
Stature	1.72 ± 0.08m	1.76 ± 0.07m	1.79 ± 0.07m	p=0.16	p=0.32

¹ Comparing white females to white males; ² Comparing white males to black males.

*p-value<0.05 was considered statistically significant.

Table 3.2 Frequencies of the cervical vertebral levels of the carotid bifurcation for white females, white males and black males.

Vertebral level	White Females (n=33)			White Males (n=32)			Black Males (n=12)		
	Left ¹ (n=33)	Right ³ (n=33)	Left & right ⁵ (n=66)	Left ^{1 2} (n=32)	Right ^{3 4} (n=32)	Left & right ^{5 6} (n=64)	Left ² (n=12)	Right ⁴ (n=12)	Left & right ⁶ (n=24)
C2	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (15.63%)	5 (15.63%)	10 (15.63%)	1 (8.33%)	1 (8.33%)	2 (8.33%)
C2-C3	9 (27.27%)	7 (21.21%)	16 (24.24%)	5 (15.63%)	6 (18.75%)	11 (17.19%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
C3	3 (9.09%)	2 (6.06%)	5 (7.58%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
C3-C4	20 (60.61%)	22 (66.67%)	42 (63.64%)	19 (59.38%)	18 (56.25%)	37 (57.81%)	11 (91.67%)	11 (91.67%)	22 (91.67%)
C4	1 (3.03%)	2 (6.06%)	3 (4.55%)	3 (9.38%)	3 (9.38%)	6 (9.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Left: ¹White females vs. white males p=0.40; ²White males vs. black males p=0.19.

Right: ³White females vs. white males p=0.10; ⁴White males vs. black males p=0.15.

Left & right: ⁵White females vs. white males p=0.89; ⁶White males vs. black males p=0.96.

*p<0.05 was considered statistically significant.

Table 3.3 Frequencies of the laryngeal cartilage levels of the carotid bifurcation for white females, white males and black males.

Cartilage level	White Females (n=33)			White Males (n=32)			Black Males (n=12)		
	Left ¹ (n=33)	Right ³ (n=33)	Left & right ⁵ (n=66)	Left ^{1 2} (n=32)	Right ^{3 4} (n=32)	Left & right ^{5 6} (n=64)	Left ² (n=12)	Right ⁴ (n=12)	Left & right ⁶ (n=24)
Hyoid bone	13 (39.39%)	13 (39.39%)	26 (39.39%)	14 (43.75%)	15 (46.88%)	29 (43.31%)	5 (41.67%)	4 (33.33%)	9 (37.50%)
Thyro-hyo membrane	3 (9.09%)	1 (3.03%)	4 (6.06%)	1 (3.13%)	1 (3.13%)	2 (3.13%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Superior thyroid cartilage	16 (48.48%)	18 (54.55%)	34 (51.52%)	15 (46.88%)	14 (43.75%)	29 (43.31%)	7 (58.33%)	8 (66.67%)	15 (62.50%)
Inferior thyroid cartilage	1 (3.03%)	1 (3.03%)	2 (3.03%)	2 (6.25%)	2 (6.25%)	4 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Left: ¹White females vs. white males p=0.71; ²White males vs. black males p=0.71.

Right: ³White females vs. white males p=0.81; ⁴White males vs. black males p=0.49.

Left & right: ⁵White females vs. white males p=0.45; ⁶White males vs. black males p=0.34.

*p<0.05 was considered statistically significant.

Table 3.4 Frequencies of the course of the common carotid, internal carotid and external carotid arteries for white females, white males and black males.

Course	White Females (n=33)			White Males (n=32)			Black Males (n=12)		
	Left (n=33)	Right (n=33)	Left & right (n=66)	Left (n=32)	Right (n=32)	Left & right (n=64)	Left (n=12)	Right (n=12)	Left & right (n=24)
Straight CCA	19 (57.58%)	16 (48.48%)	35 (53.03%)	23 (71.88%)	26 (81.25%)	49 (76.56%)	11 (91.67%)	10 (83.33%)	21 (87.5%)
Curved CCA	14 (42.42%) ¹	17 (51.52%) ⁷	31 (46.97%) ¹³	9 (28.13%) ^{1,4}	6 (18.75%) ^{7,10}	15 (23.44%) ^{13,16}	1 (8.33%) ⁴	2 (16.67%) ¹⁰	3 (12.5%) ¹⁶
Straight ICA	14 (42.42%)	14 (42.42%)	28 (42.42%)	22 (68.75%)	21 (34.38%)	43 (67.19%)	10 (83.33%)	10 (83.33%)	20 (83.33%)
Curved ICA	19 (57.58%) ²	19 (57.58%) ⁸	38 (57.58%) ¹⁴	10 (31.25%) ^{2,5}	11 (34.38%) ^{8,11}	21 (32.81%) ^{14,17}	2 (16.67%) ⁵	2 (16.67%) ¹¹	4 (16.67%) ¹⁷
Straight ECA	27 (81.82%)	25 (75.76%)	52 (78.79%)	31 (96.88%)	31 (96.88%)	62 (96.88%)	12 (100.00%)	12 (100.00%)	24 (100.00%)
Curved ECA	6 (18.18%) ³	8 (24.24%) ⁹	14 (21.21%) ¹⁵	1 (3.13%) ^{3,6}	1 (3.13%) ^{9,12}	2 (3.12%) ^{15,18}	0 (0.00%) ⁶	0 (0.00%) ¹²	0 (0.00%) ¹⁸

Left: ¹White females CCA vs. white males CCA p=0.03; ²White females ICA vs. white males ICA p=0.03; ³White females ECA vs. white males ECA p=0.04

⁴White males CCA vs. black males CCA p=0.16; ⁵White males ICA vs. black males ICA p=0.33; ⁶White males ECA vs. black males ECA p=0.54.

Right: ⁷White females CCA vs. white males CCA p=0.01; ⁸White females ICA vs. white males ICA p=0.04; ⁹White females ECA vs. white males ECA p=0.01.

¹⁰White males CCA vs. black males CCA p=0.87; ¹¹White males ICA vs. black males ICA p=0.25; ¹²White males ECA vs. black males ECA p=0.54.

Left & right: ¹³ White females CCA vs. white males CCA p=0.02; ¹⁴White females ICA vs. white males ICA p=0.01; ¹⁵White females ECA vs. white males ECA p=0.04; ¹⁶White males CCA vs. black males CCA p=0.19; ¹⁷White males ICA vs. black males ICA p=0.43; ¹⁸White males ECA vs. black males ECA p=0.29.

CCA=common carotid artery; ICA=internal carotid artery; ECA=external carotid artery.

*p<0.05 was considered statistically significant.

Table 3.5 Frequencies of the course of the carotid arteries according to the position of the internal carotid artery relative to the external carotid artery at the level of the carotid bifurcation within the entire sample.

ICA position	Side	Straight CCA	Curved CCA	Straight ICA	Curved ICA	Straight ECA	Curved ECA
Postero-lateral	Left	67 (85.89%) ¹	5 (6.41%) ¹	45 (57.69%) ²	27 (34.62%) ²	69 (88.46%) ³	3 (3.85%) ³
	Right	65 (83.33%) ⁴	7 (8.97%) ⁴	40 (51.28%) ⁵	26 (33.3%) ⁵	63 (80.77%) ⁶	3 (3.85%) ⁶
Postero-medial	Left	3 (3.85%) ¹	3 (3.85%) ¹	2 (2.56%) ²	4 (5.13%) ²	2 (2.56%) ³	4 (5.13%) ³
	Right	2 (2.56%) ⁴	4 (5.13%) ⁴	6 (7.69%) ⁵	6 (7.69%) ⁵	6 (7.69%) ⁶	6 (7.69%) ⁶

Left: ¹Position vs. CCA p=0.21; ²Position vs. ICA p=0.14; ³Position vs. ECA p=0.16.

Right: ⁴Position vs. CCA p=0.13; ⁵Position vs. ICA p=0.16; ⁶Position vs. ECA p=0.49.

CCA=common carotid artery; ICA=internal carotid artery; ECA=external carotid artery.

*p<0.05 was considered statistically significant.

Table 3.6 Frequencies of the position of the internal carotid artery relative to the external carotid artery at the level of the carotid bifurcation for white females, white males and black males.

Position	White Females (n=33)			White Males (n=32)			Black Males (n=12)		
	Left ¹ (n=33)	Right ³ (n=33)	Left & right ⁵ (n=66)	Left ^{1,2} (n=32)	Right ^{3,4} (n=32)	Left & right ^{5,6} (n=64)	Left ² (n=12)	Right ⁴ (n=12)	Left & right ⁶ (n=24)
Postero-medial	5 (15.15%)	8 (24.24%)	13 (19.70%)	1 (3.13%)	4 (12.50%)	5 (7.81%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Postero-lateral	28 (84.85%)	25 (75.76%)	53 (80.30%)	31 (96.88%)	28 (87.50%)	59 (92.19%)	12 (100.00%)	12 (100.00%)	24 (100.00%)

Left: ¹White females vs. white males p=0.09; ²White males vs. black males p=0.54.

Right: ³White females vs. white males p=0.22; ⁴White males vs. black males p=0.20.

Left and right: ⁵White females vs. white males p=0.60; ⁶White males vs. black males p=0.41.

*p<0.05 was considered statistically significant.

Table 3.7 Frequencies of the position of the origins of the branches of the external carotid artery according to the position of the internal carotid artery relative to the external carotid artery at the level of the carotid bifurcation within the entire sample.

ICA position	Side	STA		LA		FA		APA		OA		
		Antero-medial	Postero-lateral	Antero-medial	Postero-lateral	Antero-medial	Postero-lateral	Postero-medial	Postero-lateral	Postero-lateral	Postero-medial	Antero-medial
Postero-lateral	Left	72 (92.31%) ¹	0 (0.00%) ¹	72 (92.31%) ²	0 (0.00%) ²	72 (92.31%) ³	0 (0.00%) ³	62 (79.49%) ⁴	10 (12.82%) ⁴	69 (88.46%) ⁵	2 (2.56%) ⁵	1 (1.28%) ⁵
	Right	66 (84.62%) ⁶	0 (0.00%) ⁶	66 (84.62%) ⁷	0 (0.00%) ⁷	66 (84.62%) ⁸	0 (0.00%) ⁸	62 (79.49%) ⁹	4 (5.13%) ⁹	62 (79.49%) ¹⁰	4 (5.13%) ¹⁰	0 (0.00%) ¹⁰
Postero-medial	Left	3 (3.85%) ¹	3 (3.85%) ¹	4 (5.13%) ²	2 (2.56%) ²	4 (5.13%) ³	2 (2.56%) ³	5 (6.41%) ⁴	1 (1.28%) ⁴	6 (7.69%) ⁵	0 (0.00%) ⁵	0 (0.00%) ⁵
	Right	5 (6.41%) ⁶	7 (8.97%) ⁶	11 (14.10%) ⁷	1 (1.28%) ⁷	11 (14.10%) ⁸	1 (1.28%) ⁸	12 (15.38%) ⁹	0 (0.00%) ⁹	12 (15.38%) ¹⁰	0 (0.00%) ¹⁰	0 (0.00%) ¹⁰

Left: ¹Position vs. STA p=0.001; ²Position vs. LA p=0.001; ³Position vs. FA p=0.001; ⁴Position vs. APA p=0.85; ⁵Position vs. OA p=0.88.

Right: ⁶Position vs. STA p=0.001; ⁷Position vs. LA p=0.02; ⁸Position vs. FA p=0.02; ⁹Position vs. APA p=0.38; ¹⁰Position vs. OA p=0.38.

ICA=internal carotid artery; STA=superior thyroid artery; LA=lingual artery; FA=facial artery; APA=ascending pharyngeal artery; OA=occipital artery.

*p<0.05 was considered statistically significant.

Table 3.8 Frequencies of the position of the origins of the branches of the external carotid artery for white females, white males and black males.

Branch	Position	White Females (n=33)			White Males (n=32)			Black Males (n=12)		
		Left ¹ (n=33)	Right ³ (n=33)	Left & right ⁵ (n=66)	Left ^{1,2} (n=32)	Right ^{3,4} (n=32)	Left & right ^{5,6} (n=64)	Left ² (n=12)	Right ⁴ (n=12)	Left & right ⁶ (n=24)
STA	Antero-medial	30 (90.91%)	29 (87.88%)	59 (89.39)	32 (100.00%)	29 (90.63%)	61 (95.31%)	12 (100.00%)	12 (100.00%)	24 (100.00%)
	Antero-lateral	3 (9.09%)	4 (12.12%)	7 (10.61%)	0 (0.00%)	3 (9.38%)	3 (4.69%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
LA	Antero-medial	31 (93.94%)	32 (96.97%)	63 (95.45%)	32 (100.00%)	32 (100.00%)	64 (100.00%)	12 (100.00%)	12 (100.00%)	24 (100.00%)
	Antero-lateral	2 (6.06%)	1 (3.03%)	3 (4.55%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
FA	Antero-medial	31 (93.94%)	32 (96.97%)	63 (95.45%)	32 (100.00%)	32 (100.00%)	64 (100.00%)	12 (100.00%)	12 (100.00%)	24 (100.00%)
	Antero-lateral	2 (6.06%)	1 (3.03%)	3 (4.55%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
APA	Postero-medial	28 (84.85%)	31 (93.94%)	59 (89.39)	29 (90.63%)	30 (93.75%)	59 (92.19%)	9 (75.00%)	12 (100.00%)	21 (87.50%)
	Postero-lateral	5 (15.15%)	2 (6.06%)	7 (10.61%)	3 (9.38%)	2 (6.25%)	5 (7.81%)	3 (25.00%)	0 (0.00%)	3 (12.5%)
OA	Postero-medial	1 (3.03%)	2 (6.06%)	3 (4.55%)	1 (3.13%)	2 (6.25%)	3 (4.69%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
	Postero-lateral	31 (93.94%)	31 (93.94%)	62 (93.94%)	31 (96.88%)	30 (93.75%)	61 (95.31%)	12 (100.00%)	12 (100.00%)	24 (100.00%)
	Antero-medial	1 (3.03%)	0 (0.00%)	1 (1.51)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Left: ¹White females vs. white males STA: p=0.18; LA: p=0.16; FA: p=0.16; APA: p=0.48; OA: p=0.61; ²White males vs. black males STA: p=0.81; LA: p=0.26; FA: p=0.42; APA: p=0.18; OA: p=0.54.

Right: ³White females vs. white males STA: p=0.72; LA: p=0.32; FA: p=0.32; APA: p=0.97; OA: p=0.97; ⁴White males vs. black males STA: p=0.79; LA: p=0.34; FA: p=0.32; APA: p=0.38; OA: p=0.38.

Left & right: ⁵White females vs. white males p=0.87; ⁶White males vs. black males p=0.63.

STA=superior thyroid artery; LA=lingual artery; FA=facial artery; APA=ascending pharyngeal artery; OA=occipital artery.

*p<0.05 was considered statistically significant.

Table 3.9 Frequencies of the different types of common trunks originating on the external carotid artery for white females, white males and black males.

Trunks	White Females (n=33)			White Males (n=32)			Black Males (n=12)		
	Left ¹ (n=33)	Right ³ (n=33)	Left & right ⁵ (n=66)	Left ^{1 2} (n=32)	Right ^{3 4} (n=32)	Left & right ^{5 6} (n=64)	Left ² (n=12)	Right ⁴ (n=12)	Left & right ⁶ (n=24)
No trunks	18 (54.55%)	15 (45.45%)	33 (50.00%)	16 (50.00%)	20 (62.50%)	36 (56.25%)	2 (16.67%)	4 (33.33%)	6 (25.00%)
APA & OA	3 (9.09%)	6 (18.18%)	9 (13.64%)	2 (6.25%)	1 (3.13%)	3 (4.69%)	3 (25.00%)	0 (0.00%)	3 (12.50%)
LA & FA	10 (30.30%)	10 (30.30%)	20 (30.03%)	13 (40.63%)	7 (21.88%)	20 (31.25%)	7 (58.33%)	8 (66.67%)	15 (62.50%)
STA & LA	1 (3.03%)	0 (0.00%)	1 (1.52%)	1 (3.13%)	3 (9.38%)	4 (6.25%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
OA & PAA	0 (0.00%)	1 (3.03%)	1 (1.52%)	0 (0.00%)	1 (3.13%)	1 (1.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
LA & APA	1 (3.03%)	1 (3.03%)	2 (3.03%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Left: ¹White females vs. white males p=0.79; ²White males vs. black males p=0.20.

Right: ³White females vs. white males p=0.12; ⁴White males vs. black males p=0.19.

Left and right: ⁵White females vs. white males p=0.47; ⁶White males vs. black males p=0.21.

STA=superior thyroid artery; LA=lingual artery; FA=facial artery; APA=ascending pharyngeal artery; OA=occipital artery.

*p<0.05 was considered statistically significant.

Table 3.10 The length of the external carotid artery in individuals with and without common trunks within the entire sample.

External carotid arterial length	Side	No trunks	Common trunks	p-value*
	Left	65.0 ± 11.0mm	62.0 ± 18.9mm	p=0.87
	Right	70.0 ± 14.0mm	66.9 ± 18.6mm	p=0.62

*p<0.05 was considered statistically significant.

Table 3.11 Descriptive statistics of the length of the common carotid artery, the internal carotid artery, the external carotid artery and the distance of the external carotid artery branches from the carotid bifurcation for white females, white males and black males.

Measurement	White females (n=33)	White males (n=32)	Black males (n=12)	p-value ¹	p-value ²
	<i>Median ± quartile range (mm)</i>	<i>Median ± quartile range (mm)</i>	<i>Median ± quartile range (mm)</i>	<i>Mann-Whitney u-test*</i>	<i>Mann-Whitney u-test*</i>
Left CCA length	117.0 ± 19.0	130.5 ± 27.0	121.0 ± 20.0	p=0.0004	p=0.18
Right CCA length	93.0 ± 15.0	100.5 ± 15.5	96.0 ± 15.0	p=0.0012	p=0.33
Average ICA length	71.5 ± 15.0	63.5 ± 16.8	54.5 ± 7.0	p=0.06	p=0.0003
Average ECA length	68.0 ± 9.5	65.3 ± 15.5	56.5 ± 7.5	p=0.69	p=0.001
Average distance STA from CB	3.0 ± 5.0	1.5 ± 4.1	2.4 ± 4.0	p=0.29	p=0.44
Average distance LA from CB	12.3 ± 6.6	11.0 ± 8.6	11.3 ± 5.0	p=0.41	p=0.85
Left FA distance from CB	15.5 ± 9.8	14.8 ± 9.5	12.0 ± 6.0	p=0.77	p=0.21
Right FA distance from CB	18.3 ± 14.3	17.5 ± 14.0	11.0 ± 4.5	p=0.21	p=0.22
Average distance APA from CB	13.5 ± 14.9	11.8 ± 13.5	12.0 ± 13.0	p=0.55	p=0.79
Left PAA distance from CB	46.9 ± 13.0	44.0 ± 11.3	43.0 ± 7.0	p=0.47	p=0.53
Right PAA distance from CB	49.0 ± 13.9	46.3 ± 13.4	42.5 ± 11.0	p=0.96	p=0.05
Average distance OA from CB	16.8 ± 15.8	19.5 ± 12.0	19.0 ± 7.0	p=0.52	p=0.57
Left supTA distance from CB	68.5 ± 11.0	63.0 ± 17.0	55.0 ± 3.0	p=0.64	p=0.004
Right supTa distance from CB	72.5 ± 15.0	67.5 ± 16.0	60.0 ± 11.0	p=0.32	p=0.01
Left MA distance from CB	68.5 ± 11.0	63.0 ± 17.0	55.0 ± 3.0	p=0.64	p=0.004
Right MA distance from CB	72.5 ± 15.0	67.5 ± 16.0	60.0 ± 11.0	p=0.32	p=0.01

¹ Comparing white females and white males; ² Comparing white males and black males.

*p<0.05 was considered statistically significant.

CCA=common carotid artery; ICA=internal carotid artery; ECA=external carotid artery; CB=carotid bifurcation; STA=superior thyroid artery; LA=lingual artery; FA=facial artery; APA=ascending pharyngeal artery; OA=occipital artery; PAA=posterior auricular artery; supTA=superficial temporal artery; MA=maxillary artery.

Table 3.12 Relationship between the distance of the origins of the external carotid artery branches from the carotid bifurcation and the lengths of the common carotid and external carotid arteries within the entire sample.

External carotid artery branch	Spearman's correlation with the length of the common carotid artery*		Spearman's correlation with the length of the external carotid artery*	
	p-value	r-value	p-value	r-value
Superior thyroid artery	p=0.48	r=-0.08	p=0.04	r=0.23
Lingual artery	p=0.22	r=-0.26	p=0.01	r=0.29
Facial artery	p=0.06	r=-0.22	p=0.003	r=0.40
Ascending pharyngeal artery	p=0.24	r=-0.14	p=0.007	r=0.30
Occipital artery	p=0.62	r=-0.06	p=0.008	r=0.37
Posterior auricular artery	p=0.36	r=-0.10	p=0.003	r=0.54
Superficial temporal artery	p=0.58	r=-0.06	p=0.001	r=0.97
Maxillary artery	p=0.58	r=-0.06	p=0.001	r=0.97

* p<0.05 was considered statistically significant, r<0.5 was considered a weak relationship; 0.5<r<0.6 was considered a moderate relationship; r>0.7 was considered a strong relationship.

Table 3.13 The length of the carotid arteries according to the vertebral level of the carotid bifurcation within the entire sample.

Arterial length	Side	C2	C2-C3	C3	C3-C4	C4	p-value*
Common carotid artery	Left	141.0 ± 21.0mm	120.0 ± 27.3mm	120.0 ± 13.0mm	123.0 ± 22.0mm	127.5 ± 76.5mm	p=0.34
	Right	106.5 ± 22.0mm	100.0 ± 15.5mm	103.5 ± 29.8mm	98.0 ± 15.0mm	92.0 ± 44.5mm	p=0.36
Internal carotid artery	Left	63.0 ± 20.3mm	66.5 ± 12.0mm	73.0 ± 19.0mm	66.0 ± 22.0mm	76.5 ± 28.0mm	p=0.58
	Right	60.0 ± 20.3mm	67.0 ± 14.0mm	81.5 ± 21.0mm	66.5 ± 23.8mm	75.0 ± 26.5mm	p=0.24
External carotid artery	Left	60.5 ± 12.3mm	68.0 ± 8.8mm	60.0 ± 21.0mm	67.0 ± 17.0mm	71.5 ± 27.3mm	p=0.42
	Right	56.5 ± 12.5mm	70.0 ± 9.0mm	70.0 ± 32.0mm	69.0 ± 14.5mm	74.0 ± 22.0mm	p=0.60

*p<0.05 was considered statistically significant.

Table 3.14 The length of the carotid arteries according to the cartilage level of the carotid bifurcation within the entire sample.

Arterial length	Side	Hyoid bone	Thyro-hyo membrane	Superior thyroid cartilage	Inferior thyroid cartilage	p-value*
Common carotid artery	Left	129.0 ± 21.0mm	119.5 ± 28.0mm	123.0 ± 23.0mm	105.0 ± 87.0mm	p=0.47
	Right	100.0 ± 13.0mm	112.0 ± 35.8mm	96.0 ± 15.0mm	78.0 ± 51.0mm	p=0.16
Internal carotid artery	Left	63.0 ± 16.0mm	71.5 ± 15.0mm	69.0 ± 22.0mm	80.0 ± 36.0mm	p=0.30
	Right	64.5 ± 18.8mm	76.5 ± 34.5mm	69.0 ± 24.5mm	75.0 ± 36.0mm	p=0.21
External carotid artery	Left	65.5 ± 12.8mm	72.0 ± 24.0mm	67.0 ± 13.0mm	68.0 ± 34.0mm	p=0.81
	Right	65.0 ± 12.5mm	76.5 ± 25.5mm	72.0 ± 16.0mm	73.0 ± 27.0mm	p=0.71

*p<0.05 was considered statistically significant.

Table 3.15 The length of the carotid arteries according to their course within the entire sample.

Arterial length	Side	Straight	Curved	p-value*
Common carotid artery	Left	124.0 ± 21.5mm	127.0 ± 24.3mm	p=0.08
	Right	97.0 ± 13.5mm	100.0 ± 16.5mm	p=0.06
Internal carotid artery	Left	65.0 ± 18.0mm	71.0 ± 25.0mm	p=0.01
	Right	65.0 ± 18.0mm	71.5 ± 25.1mm	p=0.04
External carotid artery	Left	68.0 ± 15.6mm	70.0 ± 16.0mm	p=0.51
	Right	69.0 ± 15.8mm	71.0 ± 16.2mm	p=0.51

*p<0.05 was considered statistically significant.

Table 3.16 Relationship between the external diameters of the carotid arteries and the carotid bifurcation angle within the entire sample.

External diameter	Spearman's correlation with the carotid bifurcation angle*	
	p-value	r-value
Termination of Common carotid artery	p=0.002	r=0.348
Origin of internal carotid artery	p=0.001	r=0.366
Origin of external carotid artery	p=0.007	r=0.526

* p<0.05 was considered statistically significant, r<0.5 was considered a weak relationship; 0.5<r>0.6 was considered a moderate relationship; r>0.7 was considered a strong relationship.

Table 3.17 Descriptive statistics of the angle of the carotid bifurcation for white females, white males and black males.

Measurements	White females (n=33)	White males (n=32)	Black males (n=12)	p-value ¹	p-value ²
	<i>Median ± quartile range (°)</i>	<i>Median ± quartile range (°)</i>	<i>Median ± quartile range (°)</i>	<i>Mann-Whitney u-test*</i>	<i>Mann-Whitney u-test*</i>
Left carotid bifurcation angle	3.5 ± 1.56°	3.61 ± 1.91°	3.5 ± 1.78°	p=0.57	p=0.43
Right carotid bifurcation angle	3.6 ± 1.58°	3.64 ± 1.92°	3.52 ± 1.78°	p=0.41	p=0.49

¹ Comparing white females and white males; ² Comparing white males and black males.

*p<0.05 was considered statistically significant.

Table 3.18 Descriptive statistics of the diameters at the origin and termination points of the common carotid artery, the internal carotid artery and the external carotid artery and the diameters of the origins of the branches of the external carotid artery for white females, white males and black males.

Measurements	White females (n=33)	White males (n=32)	Black males (n=12)	p-value ¹	p-value ²
	<i>Median ± quartile range (mm)</i>	<i>Median ± quartile range (mm)</i>	<i>Median ± quartile range (mm)</i>	<i>Mann-Whitney u-test*</i>	<i>Mann-Whitney u-test*</i>
Average external diameter origin CCA	9.3 ± 1.9	9.8 ± 2.5	9.5 ± 2.0	p=0.11	p=0.27
Average external diameter origin ICA	7.8 ± 2.0	8.3 ± 1.9	8.3 ± 2.1	p=0.09	p=0.87
Average external diameter origin ECA	5.8 ± 1.5	6.3 ± 1.5	7.0 ± 1.6	p=0.07	p=0.09
Average external diameter termination CCA	12.7 ± 2.1	13.1 ± 2.9	13.0 ± 4.1	p=0.20	p=0.83
Average external diameter termination ICA	5.7 ± 1.8	5.8 ± 0.9	5.9 ± 0.9	p=0.59	p=0.77
Average external diameter termination ECA	4.9 ± 0.6	5.2 ± 0.5	5.3 ± 0.4	p=0.30	p=0.21
Average diameter origin STA	2.4 ± 0.6	2.5 ± 0.8	2.5 ± 0.6	p=0.26	p=0.11
Average diameter origin LA	3.1 ± 1.2	3.2 ± 1.1	3.6 ± 1.2	p=0.58	p=0.31
Average diameter origin FA	3.4 ± 0.9	3.7 ± 0.9	3.8 ± 0.9	p=0.21	p=0.28
Average diameter origin APA	1.9 ± 0.4	2.0 ± 0.5	2.1 ± 0.9	p=0.89	p=0.30
Left diameter origin PAA	1.8 ± 0.5	2.0 ± 0.5	2.1 ± 0.8	p=0.07	p=0.91
Right diameter origin PAA	1.9 ± 0.4	2.0 ± 0.5	2.1 ± 0.6	p=0.09	p=0.43
Average diameter origin OA	2.5 ± 0.6	2.8 ± 0.6	3.0 ± 0.9	p=0.12	p=0.10
Average diameter origin supTA	3.1 ± 0.5	3.5 ± 0.6	3.5 ± 0.8	p=0.30	p=0.15
Average diameter origin MA	4.0 ± 0.6	4.4 ± 0.6	4.5 ± 0.6	p=0.10	p=0.30

¹ Comparing white females and white males; ² Comparing white males and black males.

*p<0.05 was considered statistically significant.

CCA=common carotid artery; ICA=internal carotid artery; ECA=external carotid artery; STA=superior thyroid artery; LA=lingual artery; FA=facial artery; APA=ascending pharyngeal artery; OA=occipital artery; PAA=posterior auricular artery; supTA=superficial temporal artery; MA=maxillary artery.

Table 3.19 Frequencies of macroscopic atheroma at the left and right carotid bifurcations for white females, white males and black males.

Macroscopic atheroma	White Females (n=33)			White Males (n=32)			Black Males (n=12)		
	Left ¹ (n=33)	Right ³ (n=33)	Left & right ⁵ (n=66)	Left ^{1 2} (n=32)	Right ^{3 4} (n=32)	Left & right ^{5 6} (n=64)	Left ² (n=12)	Right ⁴ (n=12)	Left & right ⁶ (n=24)
Present	26 (78.79%)	28 (84.85%)	54 (81.82%)	29 (90.63%)	29 (90.63%)	58 (90.63%)	11 (91.67%)	11 (91.67%)	22 (91.67%)
Absent	7 (21.21%)	5 (15.15%)	12 (18.18%)	3 (9.38%)	3 (9.38%)	6 (9.37%)	1 (8.33%)	1 (8.33%)	2 (8.33%)

Left: ¹White females vs. white males p=0.19; ²White males vs. black males p=0.91.

Right: ³White females vs. white males p=0.48; ⁴White males vs. black males p=0.91.

Left and right: ⁵White females vs. white males p=0.34; ⁶White males vs. black males p=0.86.

*p<0.05 was considered statistically significant.

Table 3.20 Frequencies of microscopic atheroma at the left and right carotid bifurcations for white females, white males and black males.

Microscopic atheroma	White Females (n=33)			White Males (n=32)			Black Males (n=12)		
	Left ¹ (n=33)	Right ³ (n=33)	Left & right ⁵ (n=66)	Left ^{1 2} (n=32)	Right ^{3 4} (n=32)	Left & right ^{5 6} (n=64)	Left ² (n=12)	Right ⁴ (n=12)	Left & right ⁶ (n=24)
Early atheroma	1 (3.03%)	0 (0.00%)	1 (1.52%)	0 (0.00%)	2 (6.25%)	2 (3.13%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Late atheroma	32 (96.97%)	33 (100.00%)	65 (98.48%)	32 (100.00%)	30 (93.75%)	62 (96.87%)	12 (100.00%)	12 (100.00%)	24 (100.00%)

Left: ¹White females vs. white males p=0.32; ²White males vs. black males p=0.67.

Right: ³White females vs. white males p=0.15; ⁴White males vs. black males p=0.54.

Left and right: ⁵White females vs. white males p=0.24; ⁶White males vs. black males p=0.61.

*p<0.05 was considered statistically significant.

Table 3.21 The external diameter of the carotid arteries according to the frequency of macroscopic atheroma around the carotid bifurcation within the entire sample.

Arterial diameter	Side	Macroscopic atheroma		
		Atheroma present	Atheroma absent	p-value*
Termination of Common carotid artery	Left	12.0 ± 3.0mm	13.0 ± 4.0mm	p=0.84
	Right	12.0 ± 4.5mm	12.0 ± 2.2mm	p=0.51
Origin of internal carotid artery	Left	8.5 ± 2.5mm	8.8 ± 2.2mm	p=0.75
	Right	8.0 ± 2.0mm	7.6 ± 2.3mm	p=0.34
Origin of external carotid artery	Left	6.0 ± 1.6mm	5.0 ± 1.0mm	p=0.02
	Right	6.0 ± 1.6mm	5.0 ± 1.0mm	p=0.01

*p<0.05 was considered statistically significant.

Table 3.22 The length of the carotid arteries according to the frequency of macroscopic atheroma within the entire sample.

Length of artery	Side	Macroscopic atheroma		
		Present	Absent	p-value*
Common carotid artery	Left	126.0 ± 25.0mm	126.0 ± 25.0mm	p=0.74
	Right	100.0 ± 17.0mm	100.0 ± 17.0mm	p=0.81
Internal carotid artery	Left	67.0 ± 22.0mm	67.0 ± 22.0mm	p=0.51
	Right	69.0 ± 20.5mm	69.0 ± 20.5mm	p=0.35
External carotid artery	Left	66.0 ± 16.0mm	66.0 ± 16.0mm	p=0.63
	Right	70.0 ± 15.0mm	70.0 ± 15.0mm	p=0.36

*p<0.05 was considered statistically significant.

Table 3.23 The course of the carotid arteries related to the frequency of macroscopic atheroma around the carotid bifurcation within the entire sample.

Course	Side	Macroscopic atheroma		
		Present	Absent	p-value*
Common carotid artery: straight	Left	44 (56.41%)	10 (12.82%)	p=0.09
	Right	45 (57.69%)	8 (10.26%)	p=0.15
Common carotid artery: curved	Left	23 (29.49%)	1 (1.28%)	p=0.09
	Right	24 (30.77%)	1 (1.28%)	p=0.15
Internal carotid artery: straight	Left	41 (52.56%)	6 (7.69%)	p=0.68
	Right	41 (52.56%)	5 (6.41%)	p=0.83
Internal carotid artery: curved	Left	26 (33.3%)	5 (6.41%)	p=0.68
	Right	28 (35.90%)	4 (5.13%)	p=0.83
External carotid artery: straight	Left	60 (76.92%)	11 (14.10%)	p=0.26
	Right	6 (76.92%)	9 (11.54%)	p=0.25
External carotid artery: curved	Left	7 (8.97%)	0 (0.00%)	p=0.26
	Right	9 (11.54%)	0 (0.00%)	p=0.25

*p<0.05 was considered statistically significant.

Table 3.24 The angle of the carotid bifurcation according to the frequency of macroscopic atheroma around the carotid bifurcation within the entire sample.

Carotid bifurcation angle	Side	Macroscopic atheroma		
		Present	Absent	p-value*
	Left	3.0 ± 2.1°	3.0 ± 1.5°	p=0.38
	Right	3.2 ± 2.1°	3.3 ± 2.0°	p=0.77

*p<0.05 was considered statistically significant.

4. DISCUSSION

The variations within the carotid arterial system highlighted by this study, including the high frequency of common trunk formation as well as sex differences in the frequency of curvature of the carotid arteries, may contribute to the understanding of the pathogenesis of atheroma. Furthermore, knowledge of the anatomy of the carotid arterial system within the South African population, including the level of the carotid bifurcation and the position of the internal carotid artery relative to the external carotid artery, may aid in the surgical treatment of atherosclerotic lesions around the carotid bifurcation in this population.

The level of the carotid bifurcation is fundamental in defining the plane of dissection during carotid endarterectomy (Ribeiro *et al.*, 2006). Similar to descriptions in anatomical texts (Drake *et al.*, 2005; Standring, 2008), within the current study the carotid bifurcation occurred at the level of the C3-C4 intervertebral disc and at the superior border of the thyroid cartilage. However, these levels of the carotid bifurcation differed from those reported in the Turkish (Zumre *et al.*, 2005; Ozgur *et al.*, 2008), Kenyan (Anangwe *et al.*, 2008), Japanese (Hayashi *et al.*, 2005), New Zealand (Lo *et al.*, 2006) and Indian (Anu *et al.*, 2007) populations. In these latter studies the C3 vertebra and the hyoid bone were the most common levels reported.

The differences in the level of the carotid bifurcation may be a result of differences in stature between the populations. It has been suggested there is a correlation between torso height, a measure for stature estimation, and aortic length in which aortic length increases as torso height increases (Morrisen *et al.*, 2014). This regional correlation of arterial length and stature may occur in other regions of the body, such as the neck (Hassel and Farman,

1995; Ellyeus *et al.*, 2011). Therefore, there may be correlations between stature, common carotid arterial length and the level of the carotid bifurcation.

However, within the Turkish (Zumre *et al.*, 2005; Ozgur *et al.*, 2008; Acar *et al.*, 2013), Kenyan (Anangwe *et al.*, 2008), Japanese (Hayashi *et al.*, 2005), New Zealand (Lo *et al.*, 2006) and Indian (Anu *et al.*, 2007; Chitra, 2008) populations, the carotid bifurcation commonly occurred at the C3 vertebral level and at the hyoid bone, even though stature variations, due to geographical distribution, are evident in these populations (Ruff, 2002). Within the current study, the common carotid arterial lengths were longer than the Brazilian population (Ribeiro *et al.*, 2006) as well as the Indian (Chitra, 2008) and Croatian (Gluncic *et al.*, 2000) case reports. Furthermore, longer left and right common carotid arteries and a lower carotid bifurcation level was observed in the current study when compared to the Brazilian population (Ribeiro *et al.*, 2006). In addition, a longer right common carotid artery and a lower right carotid bifurcation level was observed in the current study when compared to Indian (Chitra, 2008) and Croatian (Gluncic *et al.*, 2000) case reports. This was unexpected if stature, the common carotid arterial length and the level of the carotid bifurcation level, are proportionally related. Furthermore, no associations were found between stature, the length of the common carotid artery and the level of the carotid bifurcation within the current study. Thus, the common carotid arterial length and stature of the individual does not seem to influence the level of the carotid bifurcation.

Curving of the common carotid arteries observed within the current study has not previously been reported in literature (Vinaitha *et al.*, 1988; Paulsen *et al.*, 2000; Lo *et al.*,

2006; Shankar *et al.*, 2008; Agrawal and Agrawal, 2011; Yonenaga *et al.*, 2011) and may explain the length differences in the common carotid arteries between the current study and other populations (Gluncic *et al.*, 2000; Ribeiro *et al.*, 2006; Chitra, 2008; Yonenaga *et al.*, 2011). Within the current study, the length measurement followed the curvature of the carotid arteries. Furthermore it was observed that a longer internal carotid artery was associated with curving of the internal carotid artery. However, no association was found between curving and the length of the common carotid and external carotid arteries which may be due to less frequent curving of these arteries within the study. Thus there may be methodological differences which could explain the differences in the common carotid arterial lengths between the current study and the Brazilian (Ribeiro *et al.*, 2006) and Japanese (Yonenaga *et al.*, 2011) populations as well as Indian (Chitra, 2008) and Croatian (Gluncic *et al.*, 2000) case reports which did not investigate common carotid artery curvature.

Previous studies within the Japanese (Yonenaga *et al.*, 2011), New Zealand (Lo *et al.*, 2006) and German (Paulsen *et al.*, 2000) populations and three Indian case reports (Vinaitha *et al.*, 1988; Shankar *et al.*, 2008; Agrawal and Agrawal, 2011), focused on the course of the internal or external carotid arteries. However, the frequency of curvature of the external carotid artery within the current study appeared to be less frequent than the Japanese population (Yonenaga *et al.*, 2011). Furthermore, there are similarities in the frequency in the curvature of the internal carotid artery between the current study, German (Paulsen *et al.*, 2000) and New Zealand (Lo *et al.*, 2006) populations all of which fell within the normal range of variation (4-66%) reported within the general population (Paulsen *et al.*, 2000, Nayak, 2010).

Curvature of the carotid arteries, particularly the internal carotid artery, is thought to be the result of a congenital abnormality occurring during embryonic development, which may persist into adulthood (Vinaitha *et al.*, 1988; Paulsen *et al.*, 2000; Lo *et al.*, 2006; Agrawal and Agrawal, 2011). However, similar to the Japanese (Yonenaga *et al.*, 2011), German (Paulsen *et al.*, 2000) and New Zealand (Lo *et al.*, 2006) cadaveric studies, the current study was comprised of an elderly sample. Therefore the high frequency of curvature within the current study is more likely due to a loss of elastin within the arterial wall (Paulsen *et al.*, 2000; Stevens *et al.*, 2002) which increases with age (Stevens *et al.*, 2002) and may be due to decreases in sex hormones associated with aging (Stevens *et al.*, 2002; Brincat *et al.*, 2005). The decrease in elasticity may make the arteries more susceptible to curving due to blood flow patterns and gravity (Paulsen *et al.*, 2000).

In addition, within the current study, curving of the common, internal and external carotid arteries were significantly more common in white females when compared to white males. These results are similar to the high frequency of curvature in the internal carotid artery of German females when compared to German males (Paulsen *et al.*, 2000). The most likely explanation for the increase in curvature in females within both studies is a decrease in sex hormones (Natoli *et al.*, 2005) due to an increase in age (Paulsen *et al.*, 2000). A decrease in estrogen has been suggested to result in a greater reduction of elastin within the arterial wall when compared to a decrease in testosterone (Natoli *et al.*, 2005). This may account for the sex differences observed between the white females and white males in the curvature of the common, internal and external carotid arteries within the current study. In addition, this sexual dimorphism may explain the longer common carotid arteries in white males compared to white females, despite white females having a higher frequency of common carotid curvature. Furthermore, as no significant differences in stature or carotid

bifurcation level were found between white males and white females, the longer common carotid arteries observed in white males may indicate a sexually dimorphic characteristic (Krejza *et al.*, 2006). This is similar to what Krejza *et al.* (2006) reported in which females are generally smaller than males even when differences in stature are accounted for. As the racial affinity analysis in the current study was comprised solely of males within no significant differences in age, similar decreases in testosterone levels would be expected (Natoli *et al.*, 2005). Thus, no differences in the curvature of the common, internal and external carotid arteries between white and black males were expected.

However, curvature of the internal and external carotid arteries within the current study does not explain the difference in the internal carotid and external carotid arterial length between white males and black males. Furthermore, there was no significant difference in curving between white males and black males within the current study. White males had longer internal and external carotid arteries when compared to black males. Population differences are evident, as both white and black males within the current study had shorter internal carotid arteries when compared to the Indian population (Shashikant and Sherke, 2013). Although, the white and black males had longer external carotid arteries when compared to the Indian population (Sanjeev *et al.*, 2010), they were shorter when compared to the Japanese population (Yonenaga *et al.*, 2011). These differences may be a racial affinity characteristic.

Generally, populations are known to differ from each other due to the differences in ancestry (Patriquin *et al.*, 2002; Oettle *et al.*, 2009). Furthermore, it is known that there are measurable differences in the size and proportions throughout the skeleton between

populations (Patriquin *et al.*, 2002). This is especially prevalent in the craniofacial bones which are used in racial affinity determination (Oettle *et al.*, 2009). In addition, racial affinity differences in the skeleton have been found between white and black South Africans (Patriquin *et al.*, 2002; Oettle *et al.*, 2009). Therefore, as certain skeletal structures are different between populations due to their racial affinities and ancestry (Patriquin *et al.*, 2002; Oettle *et al.*, 2009), one may hypothesise that same may be true for differences in arterial anatomy. Therefore, diversity in the racial affinities and ancestry may account for the differences in length of the carotid arteries, between white and black males within the current study as well as with the other populations (Gluncic *et al.*, 2000; Ribeiro *et al.*, 2006; Chitra, 2008). Furthermore, the geographic variation in body size can be attributed to adaptations to environmental factors such as climate and altitude which differ between populations (Ruff, 2002). An increase in altitude is known to affect the morphology of the cardiovascular system causing hypertrophy of the right ventricle (Recavarren and Arias-Stella, 1962). Thus, environmental factors such as climate and altitude may affect the morphology of the carotid arterial system including the carotid bifurcation level or the lengths of the carotid arteries. This may account for the differences found between populations.

Understanding the lengths of the carotid arteries as well as knowledge of the distance of the branches from the carotid bifurcation is of surgical importance when cross clamping of the carotid arteries is required during endarterectomy (Hayashi *et al.*, 2005). Similar to what is described in literature (Drake *et al.*, 2005; Lo *et al.*, 2006; Standring, 2008; Vazquez *et al.*, 2009; Sanjeev *et al.*, 2010; Yonenaga *et al.*, 2011), the superior thyroid artery was closest to the carotid bifurcation followed by the lingual, facial, ascending pharyngeal, occipital and posterior auricular arteries. Furthermore, the position of the

internal carotid artery relative to the external carotid artery and the positions of the origins of the branches of the external carotid artery conformed to the normally described anatomy (Drake *et al.*, 2005; Standring, 2008).

In addition, the length of the external carotid artery and the distance of the branches of the external carotid artery from the carotid bifurcation were significantly correlated. This was expected as the branches of the external carotid artery arise as *de novo* outgrowths during embryological development (Mahendraker, 2007; Allan and Kramer, 2010; Sadler, 2012). Furthermore, these arteries supply structures that are sequentially further from the carotid bifurcation (Mahendraker, 2007; Standring, 2008; Murlimanju *et al.*, 2012). Thus, it is expected that those arteries supplying the most distal structures in the head and neck would arise at the greatest distance from the carotid bifurcation.

However, further studies exploring the correlation between the length of the external carotid artery and distance of the branches may assist in the development of a formula to predict the distance of the branches from the carotid bifurcation within the South African population. Ultimately, this may be of benefit to vascular surgeons to estimate the distance of smaller branches of the external carotid artery, which may not appear on MRI scans (Heiken *et al.*, 1989), from the carotid bifurcation. This knowledge is of particular importance to vascular surgeons during endarterectomy, when the clamp must be placed beyond the distal extent of the plaque of the internal carotid artery and proximal to the branches of the external carotid artery to create a bloodless working field (Billerm *et al.*, 1998; Hayashi *et al.*, 2005). Correct placement is essential to prevent back bleeding and loss of blood to essential structures in the neck (Hayashi *et al.*, 2005).

Additional variations that are of interest during radial neck surgery include the position of the carotid arteries and their respective branches (Hayashi *et al.*, 2005). Similar to descriptions in anatomical texts (Drake *et al.*, 2005; Standring, 2008) as well as the Kenyan (Anangwe *et al.*, 2008), Saudi Arabic (Al-Rafiah *et al.*, 2011) and Turkish (Ozgur *et al.*, 2008) populations, in the majority of individuals within the current study, the internal carotid artery was found postero-lateral to the external carotid artery at the level of the carotid bifurcation.

Interestingly, the current study provides evidence of population variation in the frequency of common trunk formation. Within the current study, common trunk formation was found within 50% of white females, 43.8% of white males and in 75% of black males which is greater than previously reported (Hayashi *et al.*, 2005; Anangwe *et al.*, 2008; Al-Rafiah *et al.*, 2011; Delic *et al.*, 2012; Mata *et al.*, 2012). In addition, the frequency of the linguo-facial trunk within the current study was higher than reported in the Turkish (Mata *et al.*, 2012), Kenyan (Anangwe *et al.*, 2008), Japanese (Hayashi *et al.*, 2005) and Saudi Arabia (Al-Rafiah *et al.*, 2011) populations. However, the frequency of the thyro-lingual trunk was similar to that reported in the Kenyan (Anangwe *et al.*, 2008), Japanese (Hayashi *et al.*, 2005), Saudi Arabic (Al-Rafiah *et al.*, 2011), Turkish adult (Mata *et al.*, 2012) and Turkish foetus (Zumre *et al.*, 2005) populations. Similar to the previous studies (Hayashi *et al.*, 2005; Zumre *et al.*, 2005; Anangwe *et al.*, 2008; Al-Rafiah *et al.*, 2011), no differences were found between the sexes in the frequency of common trunk formation. Of note, there was a higher frequency of the formation of the trunk consisting of the ascending pharyngeal artery and occipital artery within the current study which has not been reported in the Kenyan (Anangwe *et al.*, 2008), Japanese (Hayashi *et al.*, 2005), Saudi Arabic (Al-Rafiah *et al.*, 2011) and Turkish (Zumre *et al.*, 2005) populations. The reason for these

similarities and differences in common trunk formation may be a result of different genes expressed during embryological development (Mahendraker, 2007; Murlimanju *et al.*, 2012; Sadler, 2012).

Cytokines and growth factors, such as vascular endothelial growth factor, are known to control arterial development (Sadler, 2012). One can hypothesize that changes in the expression of these cytokines and growth factors, may result in changes in the annexation of arteries causing common trunks (Mahendraker, 2007). The frequency of arterial variations may be higher in the South African population when compared to other populations, as seen in the frequency of the median artery of the upper limb (Henneberg and George, 1992). This may suggest that the expression of the factors regulating arterial development, such as vascular endothelial growth factor, may be different in the South African population. This may result in the formation of common trunks which persist into adulthood (Zumre *et al.*, 2005; Mahendraker, 2007; Sadler, 2012). Therefore, differences during embryological development may account for the high frequency of common trunks observed within the study.

Knowledge of the external diameters of the carotid arterial system is important to surgeons in order to prevent puncture of the carotid arteries during cauterisation of the arteries when carotid endarterectomy is performed (Hayashi *et al.*, 2005; Ozgur *et al.*, 2008). Furthermore, the awareness of the external diameters of the carotid arteries, particularly around the carotid bifurcation, may be used to calculate the inflow: outflow ratios to assess blood flow through the carotid bifurcation (Williams and Nicolaides, 1987; Samijo *et al.*, 1998). While no differences were found in the external diameters of the carotid arteries or

the respective branches between the assessed groups, the external diameters of all the carotid arteries within the current study were smaller than the external diameters of the carotid arteries reported in the Brazilian population (Ribeiro *et al.*, 2006). However, the external diameters of the internal carotid and external carotid arteries were similar to the European (Williams and Nicoladies, 1987) and Indian (Shashikant and Sherke, 2013) populations. It is accepted that arterial diameters decrease with advancing age (Bell and Ball, 1986). Therefore, as the current study and the European (Williams and Nicoladies, 1987) and Indian (Shashikant and Sherke, 2013) populations were comprised of older individuals compared to the younger individuals with the Brazilian population (Ribeiro *et al.*, 2006) this may account for the differences and similarities in the arterial diameters found between the current study and these latter populations. Furthermore, similar to the carotid bifurcation, environmental factors such as climate and altitude may affect the morphology of the external diameters of the carotid arterial system. This may account for the differences found between populations.

In addition, due to the high frequency of atheroma observed around the carotid bifurcation remodelling of the tunica media may have occurred (Stevens *et al.*, 2002). This remodelling of the tunica media may have resulted in a reduction in the arterial diameter of the carotid arteries (Stevens *et al.*, 2002), which may account for the lack of significant differences between the sex or racial affinity groups within the current study.

Furthermore, within the current study, an increase in the external diameters at the termination of the common carotid artery as well as at the origins of the internal and external carotid arteries resulted in a larger carotid bifurcation angle. Clinically, this is an

important relationship to note, as not to damage the arterial wall while feeding a catheter from the common carotid artery into the internal carotid artery during endovascular atherosclerotic intervention (Thompson *et al.*, 1997). Within the current study, the carotid bifurcation angle was smaller than that reported in the Turkish population (Ozgur *et al.*, 2008). This was not expected as the external diameter at the termination of the common carotid artery was larger when compared to the Turkish population (Ozgur *et al.*, 2008). However, Ozgur *et al.* (2008) did not report on the external diameters at the origins of the internal carotid and external carotid arteries. In addition, the Turkish sample (Ozgur *et al.*, 2008) was comprised of younger individuals and therefore would be expected to have smaller bifurcation angles as reported by Thomas *et al.* (2005). In addition, the differences in the angle between the current study and the Turkish population (Ozgur *et al.*, 2008) may be due to differences in measuring techniques. Within the current study, the angle of the carotid bifurcation was measured from the medial wall of the internal carotid artery to the lateral wall of the external carotid artery. However, Ozgur *et al.* (2008) measured the angle from the midpoint of the internal carotid artery to the midpoint of the external carotid artery in their cadaveric study. Therefore, this included the space between the two external walls as well as a portion of either artery and may account for differences found in the angle.

Furthermore, the current study recorded a high frequency of atheroma around the carotid bifurcation most likely due to the advanced age of the cadavers (Stevens *et al.*, 2002). As most individuals were observed to have the late stages of atheroma, the fibroatheromatous plaque may have projected into the tunica media (Stevens *et al.*, 2002; Weber, 2005; Phan *et al.*, 2012). This projection into the tunica media (Stevens *et al.*, 2002) may decrease the

distance between the internal carotid and external carotid arteries, thus accounting for the small carotid bifurcation angle compared to the Turkish population (Ozgur *et al.*, 2008).

The correlation between the external diameters of the origins and termination points of the carotid arteries was expected, as it allows laminar blood flow to be maintained to the structures within the head and neck regions (Standring, 2008; Phan *et al.*, 2012). Additionally, with a larger external diameter at the origin of an artery, the length of the artery would be expected to increase to ensure maintenance of a homeostatic pressure and blood flow to the surrounding structures (Phan *et al.*, 2012). However, within the current study, the relationship between the external diameter at the origin and length of the artery was only observed in the common carotid artery. The common carotid artery may have this relationship because of exposure to variations in blood pressure due to its proximity to the heart whereas the internal and external carotid arteries originate higher in the neck where the pressure is more constant (Phan *et al.*, 2012). As pressure affects blood flow (Phan *et al.*, 2012), which in turn affects the endothelial layer within the arterial wall (Schulz and Rothwell, 2001a; Thomas *et al.*, 2005; Bond *et al.*, 2011), the common carotid artery may increase its length to prevent non-uniform blood flow around its origin, thus preventing endothelial damage and atherogenesis (Ku *et al.*, 1985; Perktold *et al.*, 1991; Snow, 2001; Stevens *et al.*, 2002; Li *et al.*, 2005; Phan *et al.*, 2012).

As atheromatous plaques tend to develop near bifurcations (Nazemi *et al.*, 1990; Schulz and Rothwell, 2001a; Zhao *et al.*, 2002; Bressloff, 2007; Lee *et al.*, 2008; Phan *et al.*, 2012), regions of arterial narrowing (Schulz and Rothwell, 2001a; Schulz and Rothwell, 2001b; Ruan *et al.*, 2009; Cecchi *et al.*, 2011), common trunk formations (Nazemi *et al.*,

1990; Zhao *et al.*, 2002) and curvature (Weydahl and Moore, 2001; Thomas *et al.*, 2005), the high frequency of atheroma at the carotid bifurcation, noted in this study, was expected. Interestingly, of the variables measured within the current study, a smaller diameter at the origin of the external carotid artery was associated with macroscopic atheroma around the carotid bifurcation. This was expected, as a smaller diameter at the origin of the external carotid artery may result in turbulent blood flow around the carotid bifurcation (Nazemi *et al.*, 1990; Schulz and Rothwell, 2001b; Zhao *et al.*, 2000; Lehoux and Tedgui, 2003; Resnick *et al.*, 2003; Bressloff, 2007; Lee *et al.*, 2008; Ruan *et al.*, 2009; Phan *et al.*, 2012).

However, the high frequency of common trunk formation and curvature of the carotid arteries was expected to be associated with macroscopic atheroma around the carotid bifurcation (Schulz and Rothwell, 2001b; Zhao *et al.*, 2002; Lee *et al.*, 2008; Phan *et al.*, 2012). The lack of association may be a result of the high frequency of atheroma due to the median age of the sample (71 ± 10 years). Thus, geometry may have played a role in the formation of atheroma but was not associated with the presence of atheroma as all individuals had atheroma. Considering the median age of the current study, the frequency of atheroma is most likely due to vascular aging of the carotid arteries (Crouse *et al.*, 1987; Schmidt-Truckass *et al.*, 1999) aiding in plaque formation (Crouse *et al.*, 1987; Benetos *et al.*, 1993; Vaiktevicius *et al.*, 1993; Schmidt-Truckass *et al.*, 1999; Stevens *et al.*, 2002; Zhao *et al.*, 2002; Thomas *et al.*, 2005).

Considering the increased frequency of atheroma in the world's male population up to the age of 75 years (Joakimsen *et al.*, 1999; Stevens *et al.*, 2002), the similar frequencies of

atheroma between the males and females in this study was unexpected. However, the advanced age of the sample may again be playing a role (Crouse *et al.*, 1987). The decrease in sex hormone levels and associated changes in collagen and elastin within the arterial wall that occur with aging (Moreau *et al.*, 2012) results in a similar frequency of atheroma between males and females above 75 years of age (Joakimsen *et al.*, 1999; Westendorp *et al.*, 1999; Stevens *et al.*, 2002; Han *et al.*, 2008). These findings are supported by a Norwegian study which reported a similar frequency of atheroma between males and females in a study sample of advanced age (Joakimsen *et al.*, 1999).

Although the advanced age of the sample may have been the reason for the high frequency of atheroma within the study (Crouse *et al.*, 1987; Schmidt-Truckass *et al.*, 1999), the lack of a significant difference between white males and black males was expected due to the uneven sample sizes of black and white males. In addition, the high frequency of atheroma in black males may be explained by the advanced age of the sample as well as diseases such as hypertension (Crouse *et al.*, 1987; Seftel, 1978; Lopes, 2002; Stevens *et al.*, 2002; Thomas *et al.*, 2005). It has been suggested that interactions between biological and behavioural factors and mechanisms initiated during fetal life (which are not necessarily genetic) may potentially increase the salt sensitivity of South African black males (Salonen and Salonen, 1989, Lopes, 2002; Thomas *et al.*, 2005). Dietary salt modulates renal production of transforming growth factor and has been linked to hypertensive-related cardio-renal complications in black males when compared to white males (Salonen and Salonen, 1989, Lopes, 2002; Bennett *et al.*, 2010). This suggests that South African black males may be genetically predisposed to hypertension and therefore at increased risk of atherogenesis (Seftel, 1978; Stevens *et al.*, 2002). While white South African males may not be genetically predisposed to hypertension (Seftel, 1978), they are genetically

predisposed to hyperlipidaemia (Jenkins *et al.*, 1980; Brink *et al.*, 1987). In conjunction with age (Crouse *et al.*, 1987), this may account for the frequency of atheroma in white males within the current study (Ku *et al.*, 1985; Stevens *et al.*, 2002).

Vascular aging (Crouse *et al.*, 1987; Schmidt-Truckass *et al.*, 1999) is most likely to be the greatest contributing factor to the high frequency of atheroma found within the current study's males. However, the current study could not control for the advanced age of the cadavers, disease or lifestyle factors. Therefore, additional studies should be conducted in younger males in order to assess of the effect of genetic hypertension and hyperlipidaemia and the role of arterial geometry on atherogenesis in the South African population. These results may assist in the prevention of atherosclerosis within the South African population.

5. CONCLUSION

Atherosclerosis is a problem that affects millions of people around the world (Salzar *et al.*, 1995; Phan *et al.*, 2012). The results from this study have supported previous studies (Perktold *et al.*, 1991; Schulz and Rothwell, 2001b; Thomas *et al.*, 2005; Phan *et al.*, 2012) that atheroma tends to occur around the carotid bifurcation. Furthermore, the present study found similarities to the normal reported anatomical texts (Drake *et al.*, 2005; Standring, 2008) with regards to the level of the carotid bifurcation and position of the carotid arteries which are important during radical neck surgery (Hayashi *et al.*, 2005). However, the present study also highlighted a higher frequency of common trunk formation than previously reported in cadaveric studies (Hayashi *et al.*, 2005; Zumre *et al.*, 2005; Anangwe *et al.*, 2008; Al-Rafiah *et al.*, 2011). White females had a higher frequency of common carotid, internal carotid and external artery curvature when compared to white males. Although these results could be expected due to the age of the sample (Stevens *et al.*, 2002), these variations are important to note as they may influence the dynamics of blood flow within the arteries (Schulz and Rothwell, 2001b; Thomas *et al.*, 2005) and are therefore important in understanding the aetiology and treatment of atheroma (Schulz and Rothwell, 2001b; Hayashi *et al.*, 2005). Furthermore, there was a relationship between the external diameter at the origin of the external carotid artery and the presence of macroscopic atheroma around the carotid bifurcation. This may suggest that the arterial geometry, particularly arterial diameter, around the carotid bifurcation could possibly be a potential risk factor of atherogenesis (Schulz and Rothwell, 2001b). In addition, a correlation between the distances of the branches of the external carotid artery from the carotid bifurcation may assist in surgical treatment of atherosclerosis around the carotid bifurcation within the South African population.

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7. APPENDICES

A. CLEARANCE CERTIFICATES

A1. Ethical clearance waiver from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand.

Human Research Ethics Committee (Medical) (formerly Committee for Research on Human Subjects (Medical))		University of the Witwatersrand, Johannesburg	
Secretariat: Research Office, Room SH10005, 10th floor, Senate House • Telephone: +27 11 717-1234 • Fax: +27 11 339-5708 Private Bag 3, Wits 2050, South Africa			
Ref: W-CJ-130327-1		27/03/2013	
TO WHOM IT MAY CONCERN:			
Waiver:	This certifies that the following research does not require clearance from the Human Research Ethics Committee (Medical).		
Investigator:	Andrea Kolkenbeck-Ruh (student no 3614678)		
Project title:	Anatomical variation of the carotid arterial system within the South African population: Implications for treatment of carotid arterial disease. (To be done on anatomical department cadavers at the Universities of the Witwatersrand, Johannesburg and KwaZulu-Natal with the permissions of the heads of these departments).		
Reason:	In terms of Chapter 8, sections 62-64 of the National Health Act No 61 of 2003 donated bodies and their tissues may be used for, among other purposes, health research. Use of such material is subject only to permission from the responsible person in the School of Anatomical Sciences - the Head or person designated by the Head. A waiver to this effect W-CJ-101109-1 was issued to the School of Anatomical Sciences.		
			
Professor Peter Cleaton-Jones Chair: Human Research Ethics Committee (Medical)			
copy: Anisa Keshav, Research Office, Senate House, Wits			

A2. Ethical clearance certificate from the Academic Ethics Committee from the University of Johannesburg.



**FACULTY OF HEALTH SCIENCES
ACADEMIC ETHICS COMMITTEE**

24 May 2013

Dear Dr Eagleton

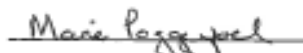
APPROVAL TO USE THE DISSECTION FACILITIES

At the AEC Meeting which was held on **20 May 2013** the following research proposal were proposed for **Kolkenbeck-Ruh, A (361468)** for the degree MSc. She is a student of the University of Witwatersrand.

Anatomical variation of the carotid arterial system within the South African population: Implications for the treatment of carotid arterial disease

Ms Kolkenbeck-Ruh's research was approved by the Academic Ethics Committee.

Yours sincerely,


Prof M Poggenpoel

Academic Ethics Committee: Faculty of Health Sciences

B. REAGENTS AND BUFFERS USED FOR HISTOLOGY

B1. 10% buffered (neutral) formalin

100ml 40% formaldehyde

900ml Distilled water

4g sodium dihydrogen phosphate monoxide

6,5g di-sodium hydrogen orthophosphate anhydrous

B2. Mayer's Haematoxylin and Eosin stain

Haematoxylin: Haematoxylin 4g

Distilled water 1000ml

Sodium iodate 0,3g

Potassium Alum 50g

Citric acid 1,5g

Chloral hydrate 75g

Eosin: 1% Eosin 500ml

1% Phloxine 250ml

Distilled water 750ml

Process according to the protocols of the School of Anatomical Sciences:

1. Incubate slides in xylene for 5 minutes before passing through a graded series of alcohols.
2. Wash in running tap water for 5 minutes.
3. Stain in haematoxylin for 5 minutes.
4. Wash in tap water until excess stain removed.
5. Dip in 1% Acid alcohol.
6. Wash in running tap water for 5 minutes.
7. Counter stain in Eosin for 1 minute.
8. Wash briefly in running tap water and pass sections through alcohol and xylene.
9. Mount with a cover slip coated with Sta-on[®] tissue section adhesive (Leica, USA).

B3. Van Gieson Stain

Verhoeff's Working Solution:

5% alcoholic hematoxylin 20 ml

10% ferric chloride 8 ml

Weigert's iodine solution 8 ml

2% aqueous ferric chloride:

10% ferric chloride from above 10 ml

Distilled water 50 ml

Van Gieson's counterstain:

1% aqueous acid fuchsin 5 ml

Saturated aqueous picric acid 100 ml

Process according to the protocols of the School of Anatomical Sciences:

1. Incubate slides in xylene for 5 minutes before passing through a graded series of alcohols and washing in running tap water for 5 minutes.
2. Stain in Verhoeff's working solution for 60 minutes.
3. Rinse in running tap water (2-3 changes) until excess stain is removed.
4. Differentiate in 2% aqueous ferric chloride for 1 minute.
5. Dip in running water and check microscopically for black elastic fibre staining. Differentiate again if need.
6. Wash in running tap water for 5 minutes.
7. Counterstain in Van Gieson's solution for 5 minutes.
8. Rinse in running tap water (2-3 changes) until excess stain is removed.
9. Wash briefly in running tap water and pass sections through alcohol and xylene.
10. Mount with a cover slip coated with Sta-on[®] tissue section adhesive (Leica, USA).

C. OBSERVER ERRORS FOR THE CATEGORICAL AND QUANTITATIVE VARIABLES

C1. Inter-observer and intra-observer error results of the categorical variables from Cohen's Kappa.

Measurements	Inter-observer error (left/right)	Intra-observer error (left/right)
Position of the superior thyroid artery on the external carotid artery.	1/1	0.99/1
Position of the lingual artery on the external carotid artery.	1/1	0.99/0.99
Position of the facial artery on the external carotid artery.	1/1	1/1
Position of the ascending pharyngeal artery on the external carotid artery.	0.97/0.98	0.98/0.98
Position of the occipital artery on the external carotid artery.	0.99/1	0.99/1
Position of the posterior auricular artery on the external carotid artery.	0.99/0.99	0.99/1
Position of the superficial temporal artery on the external carotid artery.	1/1	1/1
Position of the maxillary artery on the external carotid artery.	1/1	1/1
Thyro-lingual trunk	1/1	0.98/0.99
Linguo-facial trunk	1/1	1/0.99
Linguo-pharyngeal trunk	1/1	0.97/0.98
Thyro-linguo-facial trunk	1/1	1/1
Occipito-pharyngeal trunk	1/1	1/1
Occipito-auricular trunk	1/1	1/1
Pharyngeal-Occipito-auricular trunk	1/1	1/1
Auricular-temporal trunk	1/1	1/1
Vertebral level of the carotid bifurcation	0.97/0.96	0.98/0.98
Cartilage level of the carotid bifurcation	0.91/0.93	0.93/0.94
Position of the internal carotid artery relative to the external carotid artery.	1/1	1/1
Course of the common carotid artery.	0.97/0.97	0.99/0.99
Course of the internal carotid artery.	0.99/0.99	1/1
Course of the external carotid artery.	0.98/0.97	0.98/0.98
Macroscopic atheroma around the carotid bifurcation.	1/1	1/1
Microscopic atheroma at the level of the carotid bifurcation	0.97/0.99	0.98/0.98

C2. Inter-observer and intra-observer error results of the quantitative variables from Lins Concordance correlation.

Measurements	Inter-observer error (left/right)	Intra-observer error (left/right)
The length of the common carotid artery	0.92/0.91	0.97/0.98
The length of the internal carotid artery.	0.94/0.95	0.95/0.95
The length of the external carotid artery.	0.96/0.96	0.97/0.98
The diameter at the origin of the common carotid artery.	0.98/0.97	0.95/0.95
The diameter at the origin of the internal carotid artery.	0.91/0.92	0.93/0.93
The diameter at the origin of the external carotid artery.	0.94/0.96	0.91/0.92
The diameter at the termination of the common carotid artery.	0.99/0.99	0.98/0.99
The diameter at the termination of the internal carotid artery.	0.90/0.91	0.91/0.92
The diameter at the termination of the external carotid artery.	0.93/0.92	0.97/0.98
The left angle of the carotid bifurcation.	0.95/0.95	0.95/0.96
The distance of the origin of the superior thyroid artery from the carotid bifurcation.	0.91/0.91	0.92/0.93
The distance of the origin of the lingual artery from the carotid bifurcation.	0.93/0.94	0.94/0.93
The distance of the origin of the facial artery from the carotid bifurcation.	0.96/0.96	0.97/0.98
The distance of the origin of the ascending pharyngeal artery from the carotid bifurcation.	0.90/0.91	0.91/0.90
The distance of the origin of the occipital artery from the carotid bifurcation.	0.96/0.95	0.96/0.96
The distance of the origin of the posterior auricular artery from the carotid bifurcation.	0.93/0.92	0.92/0.91
The distance of the origin of the superficial temporal artery from the carotid bifurcation.	0.96/0.98	0.97/0.98
The distance of the origin of the maxillary artery from the carotid bifurcation.	0.96/0.98	0.97/0.98
The diameter of the origin of the superior thyroid artery.	0.93/0.92	0.97/0.96
The diameter of the origin of the lingual artery.	0.98/0.96	0.97/0.98
The diameter of the origin of the facial artery.	0.97/0.97	0.97/0.97
The diameter of the origin of the ascending pharyngeal artery.	0.92/0.91	0.91/0.90
The diameter of the origin of the occipital.	0.93/0.93	0.97/0.96
The diameter of the origin of the posterior auricular artery.	0.96/0.94	0.93/0.92
The diameter of the origin of the superficial temporal artery.	0.93/0.92	0.97/0.98
The diameter of the origin of the maxillary artery.	0.93/0.92	0.97/0.98

D. NORMALITY RESULTS

D1. Normality results for each quantitative measurement within white females, white males and black males.

Measurements	p-values* for white males (left/right)	p-values* for white females (left/right)	p-values* for black males (left/right)
Common carotid artery length	p=0.11/p=0.77	p=0.12/p=0.78	p=0.12/p=0.78
Internal carotid artery length	p=0.27/p=0.34	p=0.26/p=0.37	p=0.26/p=0.37
External carotid artery length	p=0.46/p=0.41	p=0.46/p=0.44	p=0.46/p=0.44
Diameter: origin of the common carotid artery	p=0.03/p=0.01	p=0.03/p=0.02	p=0.03/p=0.02
Diameter: origin of the internal carotid artery	p=0.19/p=0.30	p=0.16/p=0.25	p=0.16/p=0.25
Diameter: origin of the external carotid artery	p=0.01/p=0.03	p=0.01/p=0.02	p=0.01/p=0.02
Diameter: termination of the common carotid artery	p=0.45/p=0.02	p=0.35/p=0.04	p=0.35/p=0.04
Diameter: termination of the internal carotid artery	p=0.34/p=0.12	p=0.43/p=0.21	p=0.43/p=0.21
Diameter: termination of the external carotid artery	p=0.01/p=0.01	p=0.02/p=0.01	p=0.02/p=0.01
Carotid bifurcation angle	p=0.02/p=0.02	p=0.03/p=0.01	p=0.01/p=0.01
Superior thyroid artery diameter	p=0.01/p=0.04	p=0.02/p=0.01	p=0.01/p=0.01
Superior thyroid artery distance from the carotid bifurcation	p=0.01/p=0.02	p=0.01/p=0.01	p=0.01/p=0.01
Lingual artery diameter	p=0.04/p=0.03	p=0.05/p=0.03	p=0.05/p=0.03
Lingual artery distance from the carotid bifurcation	p=0.07/p=0.06	p=0.08/p=0.06	p=0.08/p=0.06
Facial artery diameter	p=0.01/p=0.05	p=0.11/p=0.15	p=0.01/p=0.15
Facial artery distance from the carotid bifurcation	p=0.03/p=0.02	p=0.04/p=0.03	p=0.03/p=0.03
Ascending pharyngeal artery diameter	p=0.01/p=0.01	p=0.02/p=0.03	p=0.01/p=0.03
Ascending pharyngeal artery distance from the carotid bifurcation	p=0.02/p=0.01	p=0.02/p=0.03	p=0.02/p=0.01
Occipital artery diameter	p=0.01/p=0.03	p=0.02/p=0.01	p=0.01/p=0.01
Occipital artery distance from the carotid bifurcation	p=0.41/p=0.04	p=0.14/p=0.06	p=0.14/p=0.05
Posterior auricular artery diameter	p=0.01/p=0.03	p=0.01/p=0.04	p=0.01/p=0.05
Posterior auricular artery distance from the carotid bifurcation	p=0.28/p=0.37	p=0.27/p=0.61	p=0.27/p=0.61
Superficial temporal artery diameter	p=0.02/p=0.01	p=0.03/p=0.04	p=0.01/p=0.02
Superficial temporal artery distance from the carotid bifurcation	p=0.65/p=0.58	p=0.55/p=0.50	p=0.55/p=0.54
Maxillary artery diameter	p=0.21/p=0.12	p=0.12/p=0.15	p=0.12/p=0.05
Maxillary artery distance from the carotid bifurcation	p=0.60/p=0.64	p=0.49/p=0.44	p=0.59/p=0.54

*p-value<0.05 was considered statistically significant

E. INTERNAL AND EXTERNAL DIAMETERS WITHIN THE SAMPLE

E1. Descriptive statistics of the internal and external diameters (mm) at the origin and termination points of the left and right common carotid, internal carotid and external carotid arteries within all individuals.

Measurements	Internal diameter		External diameter		p-value*	
	<i>Median $\pm$ inter-quartile range (mm)</i>		<i>Median $\pm$ inter-quartile range (mm)</i>		Wilcoxon sign rank test	
	Left	Right	Left	Right	Left	Right
Internal diameter origin common carotid artery	9.9 $\pm$ 2.3	9.7 $\pm$ 2.0	9.5 $\pm$ 2.1	9.3 $\pm$ 2.2	p=0.10	p=0.12
Internal diameter origin internal carotid artery	8.7 $\pm$ 1.4	8.2 $\pm$ 1.3	8.1 $\pm$ 1.5	8.0 $\pm$ 1.8	p=0.10	p=0.14
Internal diameter origin external carotid artery	6.6 $\pm$ 2.1	6.1 $\pm$ 2.0	6.4 $\pm$ 2.0	6.2 $\pm$ 2.0	p=0.21	p=0.24
Internal diameter termination common carotid artery	13.2 $\pm$ 2.0	13.4 $\pm$ 2.1	12.9 $\pm$ 2.2	13.0 $\pm$ 2.2	p=0.12	p=0.10
Internal diameter termination internal carotid artery	6.0 $\pm$ 1.0	5.9 $\pm$ 0.9	5.8 $\pm$ 0.9	5.7 $\pm$ 0.9	p=0.16	p=0.15
Internal diameter termination external carotid artery	5.5 $\pm$ 1.1	5.3 $\pm$ 1.0	5.3 $\pm$ 1.0	5.5 $\pm$ 1.0	p=0.24	p=0.21

*p-value<0.05 was considered statistically significant.

