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Cervical Spine Angles, Craniocervical Posture, Neck Length, and Oropharyngeal Airway Analyses of Sleep Apnea Patients in Both Supine and Upright Positions: a Retrospective 3-D Imaging Study

Brian Tuan Luong
University of Nebraska Medical Center

CERVICAL SPINE ANGLES, CRANIOCERVICAL POSTURE, NECK LENGTH, AND OROPHARYNGEAL AIRWAY ANALYSES OF SLEEP APNEA PATIENTS IN BOTH SUPINE AND UPRIGHT POSITIONS: A RETROSPECTIVE 3-D IMAGING STUDY

By

Brian Tuan Luong, D.M.D., M.B.A.

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Advisory Committee:

Sundaralingam Premaraj, BDS, MS, PhD, FRCD(C)
Sung K. Kim, DDS
Peter J. Giannini, DDS, MS
Stanton D. Harn, PhD

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The etiology of sleep apnea is complex and multifactorial. It is not surprising that sleep apnea treatment often requires an interdisciplinary team approach. Similarly, an interdisciplinary team of researchers was the foundation for the success of this project. Our team is comprised of orthodontists, dentists, sleep medicine physicians, radiologists, chiropractors, a bioinformatician, and a statistician, all of whom played a critical role in the advancement of our understanding of sleep apnea.

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ABSTRACT

Obstructive sleep apnea (OSA) is one of the most common respiratory disorders. Previous airway studies of OSA subjects have largely relied on 2-D radiographs.

The purpose of this study is to use 3-D imaging to the analyze the relationships among cervical spine angles, craniocervical posture, cervical spine length and the oropharyngeal airway volume in OSA patients in both the supine and upright positions.

Twenty-eight OSA subjects with 3-D imaging were included. Airway, craniocervical posture, spine angles, and spine length were assessed using Dolphin 11.8. Correlation analyses were utilized to detect associations among the recorded and measured variables. Mean differences were determined between the supine and upright subjects. A $p \leq 0.05$ was considered statistically significant.

Significant associations were found: positive associations between apnea-hyponea index (AHI) and age, craniocervical posture and airway volumes, craniocervical posture and cervical vertebrae C1-C2 spinal angle, and spine length and airway volumes. Negative associations were found between craniocervical posture and body mass index (BMI), C2-C3 and C1-C4 angle and age. A 1.767 odds ratio for retrolingual to retro-uvula was found with each increase in spine length. McGregor and McRae angles are nearly perfectly correlated. Subjects in the supine position had significantly greater BMI and oropharyngeal airway dimensions than subjects in the upright position.

Craniocervical extension is positively correlated with increased BMI and negatively correlated with airway volumes; however, spinal angles are not. Subjects in the supine position demonstrated smaller airway volumes than upright subjects. Subject positioning and posture are important consideration in the evaluation of OSA.

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LIST OF ABBREVIATIONS

2-D	Two-dimensional
3-D	Three-dimensional
AHI	Apnea Hypopnea Index
ANS	Anterior Nasal Spine
A-O	Atlas-Occiput
AP	Anteroposterior
BMI	Body Mass Index
C1	Cervical Vertebrae 1
C2	Cervical Vertebrae 2
C3	Cervical Vertebrae 3
C4	Cervical Vertebrae 4
CSA	Central Sleep Apnea
CBCT	Cone Beam Computed Tomography
CFP	Craniofacial Pain Center of Nebraska
CPAP	Continuous Positive Airway Pressure
EEG	Electroenchalogram
EKG	Electrocardiogram
EMG	Electromyogram
EOG	Electrooculogram
ESS	Epworth Sleepiness Scale
FOV	Field of View
HST	Home Sleep Study
lOP	Lower Oropharyngeal Volume
MA	Minimum Cross Sectional Area

MAD	Mandibular Advancement Device
McG	McGregor Line
MDCT	Multi-Detector Computed Tomography
McR	McRae Line
MRI	Magnetic Resonance Imaging
NHP	Natural Head Position or Posture
O	Occiput
OSA	Obstructive Sleep Apnea
PAS	Posterior Airway Space
PGD	Pioneer Greens Dentistry
PNS	Posterior Nasal Spine
PP	Palatal Plane
PSG	Polysomnography
RA	Rheumatoid Arthritis
RDI	Respiratory Disturbance Index
RL	Retro-lingual
RU	Retro-uvula
SBD	Sleep Disordered Breathing
TV	Total Volume
UNMC	University of Nebraska Medical Center Sleep Medicine Clinic
uOP	Upper Oropharyngeal Volume

CHAPTER 1: INTRODUCTION

Sleep Disordered Breathing (SDB) is a common disorder characterized by shallow breaths or pauses in breathing during sleep. Three subcategories of SDB exist: central sleep apnea (CSA), obstructive sleep apnea (OSA), or mixed. CSA is less common and occurs when there is failure of signal transduction from the brain to the breathing apparatus. OSA is more common and occurs when there is momentary but repeated collapse of the airway during respiration. OSA is estimated to affect between 9-28% of adults, typically more common in males than females (Young, Palta et al. 1993). The risk for developing OSA increases with age and body mass index (BMI) (Kapur et al. 2010). For these patients, OSA can dramatically impact their quality of life by impairing neurocognitive performance and inducing excessive daytime sleepiness. Beyond these daytime functional impairments, there may be severe comorbidities such as cardiovascular and neurovascular sequelae (Hirsch Allen, Bansback et al. 2015).

The etiology of OSA is multifactorial and complex. Besides obesity, craniofacial abnormalities and cervical spine pathologies have been associated with OSA. A review paper cited a number of conditions that could contribute to airway obstruction, including: palatine and lingual tonsillar and adenoid hypertrophy, soft palate enlargement, enlarged tongue size and position, mandibular retrognathism, rheumatoid arthritis, osteophytes, osteochondromas, and cervical spine fusion (Khan, Than et al. 2014). These pathologies change the delicate balance in the soft or hard tissues surrounding the upper pharyngeal airway, leading to its collapsibility and subsequent obstruction.

The gold standard for OSA diagnosis involves overnight, attended polysomnography (PSG). Due to its high cost, various home sleep studies (HST) have become an acceptable and valid diagnostic alternative and proven to have high sensitivity and specificity (Ayappa, Norman et al. 2008; Driver, Pereira et al. 2011; Cairns, Wickwire et al. 2014). Moreover, 2- and 3-D imaging studies, using lateral cephalogram or cone beam computed tomography (CBCT) and multi-detector computed tomography (MDCT), have provided researchers and clinicians an excellent window into the anatomy and physiology of how OSA occurs. Studies have shown that there is a high probability of severe OSA with an airway less than $52mm^2$ and low probability if the airway is greater than $110mm^2$ (Lowe, Gionhaku et al. 1986). In addition, these imaging studies provide insight into which treatment modality, surgical versus nonsurgical, should be used.

Imaging studies have enabled researchers to identify additional factors that affect the airway mechanics in OSA. These factors include positional changes, craniocervical (head) posture, cervical spine angles, and neck length. Historically, these studies have largely relied on 2-D lateral cephalograms, which did not fully capture the airway dimensions. Advance 3-D imaging studies, which capture all 3-spatial planes, are superior but are limited in numbers. OSA occurs during sleep when subjects are in the supine position. To date, only 1 study has used CBCT to assess changes in the pharyngeal airway volume of five OSA patients in the supine and upright positions (Camacho, Capasso et al. 2014). In the supine position, total volume and cross sectional areas along the length of the pharyngeal airway were significantly smaller. The authors suggested that the effect of gravity and tissue laxity are contributors to these findings.

Few published studies have directly or indirectly examined the association between cervical spine angles and OSA. A study using lateral cephalograms directly examined the relationship among four cervical spine angles and sleep apnea severity (Dobson, Blanks et al. 1999). The authors found a general kyphotic arrangement of the occiput and upper cervical spine, with the greatest flexion observed in the most severe OSA subjects. The authors hypothesized that injury in this area can result in a loss of pharyngeal airway muscle tonicity, leading to increase airway collapse. Indirect studies have examined the association between cervical spine fusion, disruption of the natural neck alignment, and OSA. One study found that AHI scores, an indicator for sleep apnea severity, increased 5-10 times post spinal fusion surgery (Guilleminault, Li et al. 2003). Reduction in head and neck flexion-extension after spinal fusion was attributed to the development of OSA. For example, a 10-degree increase in head flexion resulted in a 37% reduction in posterior airway space (PAS) (Ota, Neo et al. 2011).

Head posture, or craniocervical posture, has also been associated with OSA. Deviation from a natural head posture in OSA subjects was found as an adaptive mechanism to increase the patency of the airway (Solow, Ovesen et al. 1993; Solow, Skov et al. 1996). In a series of cephalometric studies, Solow found that a forward head position with craniocervical extension increased the lower oropharyngeal airway dimensions. A systematic review identified only one 3-D MRI study, which found a positive correlation between head extension and increased hypopharyngeal airway volume (Gurani, Di Carlo et al. 2016).

An increase in neck circumference has been associated with OSA (Davies, Ali et al. 1992); however, few studies have examined the relationship between neck length and sleep apnea. The few existing studies have reported conflicting conclusions. One study found that a smaller clinical neck length, measured from the hyoid bone to the jugular notch), is associated with increased snoring (Han, Oh et al. 2015). Conversely, a CBCT study showed that an increased neck length was highly predictive of OSA (Kim, Choi et al. 2011). The author hypothesized that a longer but smaller mean cross-sectional area of the airway is more susceptible to collapse.

The purpose of this study is to build on the limited existing knowledge regarding the effects of craniocervical morphology (cervical spine angles and head posture) and body positioning (supine versus upright) on the oropharyngeal airway in OSA subjects using 3-D imaging techniques.

CHAPTER 2: LITERATURE REVIEW

2.1 Sleep Disordered Breathing

Sleep Disordered Breathing (SDB) is a common disorder in which patients experience shallow breaths or one or more pauses in breathing during sleep. Three types of SDB exist: central sleep apnea (CSA), obstructive sleep apnea (OSA), or mixed. Central sleep apnea is the less common type and occurs when the area of the brain that controls breathing fails to properly transmit signals to the breathing muscles. CSA usually involves other medical conditions and can occur concurrently with OSA. OSA is the more common condition where the airway momentarily but repeatedly collapses or becomes blocked during sleep, resulting in shallow breathing or breathing pauses (Garvey, Pengo et al. 2015). In either case, poor sleep can have many consequences including daytime fatigue and sleepiness, neurocognitive impairment, cardiovascular disease and reduced quality of life (Hirsch Allen, Bansback et al. 2015).

2.2 General Overview of Obstructive Sleep Apnea

2.2.1 Prevalence of OSA

OSA is among the most common respiratory disorders. Recent data from a Swiss study estimates the prevalence of OSA to be 23.4% in females and 49.0% in males (Heinzer, Vat et al. 2015). Data from the Wisconsin sleep study suggests a prevalence of 24% in men and 9% in women aged 30-60 years of age, and the prevalence increased with adults (Young, Palta et al. 1993; Young, Peppard et al. 2002). Furthermore, prevalence data suggests that OSA is as common in developing world as western countries (Kapur 2010).

2.2.2 Economic Impact of OSA

OSA has a large economic impact on society and the health care system. Patients with sleep apnea are less productive and are more likely to miss work. Job related injuries are also more common in these patients (AlGhanim, Comondore et al. 2008). Furthermore, untreated OSA patients are at higher risk of motor vehicle accidents, costing society $15.9 billion annually

(Ellen, Marshall et al. 2006). The burden on the health care system includes direct costs of OSA diagnosis and treatment in addition to indirect costs of associated conditions such as obesity, diabetes, depression, and cardiovascular diseases.

2.2.3 Risk Factors

Obesity and OSA

Obesity is one of the strongest risk factors for OSA. Rising rates of obesity will likely result in increased prevalence of OSA. The Wisconsin Sleep Study showed that a 10% increase in body weight conferred a 32% increase in the apnea-hypopnea index (AHI) and a 6-fold increase in the risk of developing moderate to severe OSA (Young, Palta et al. 2009). Furthermore, the Sleep Heart Health Study showed that a weight gain of 10 kilograms over a 5-year period conferred a 5.2 and 2.5 fold increase in the probability of increasing the AHI by 15 events per hour in men and women, respectively (Quan, Howard et al. 1997). Importantly, OSA is present in 41% of patients with a body mass index (BMI) greater than 28 and this number increases to 78% in patients evaluated for gastric bypass surgery (Vgontzas, Tan et al. 1994; Lopez, Stefan et al. 2008)

Age and OSA

In adults, the prevalence of OSA increases with age (Kapur 2010) and is attributed to a number of factors: increase in fat deposition around the pharynx, lengthening of the soft palate, and changes in other parapharyngeal structures (Malhotra, Huang et al. 2006). Interestingly, the Sleep Heart Health Study showed that the prevalence of OSA plateaued after 60 years of age (Quan, Howard et al. 1997) and that the increased risk of all-cause and cardiovascular mortality associated with OSA is limited to middle-aged adults (Young, Palta et al. 1993). This plateau effect can be explained by the cardioprotective adaptation to chronic intermittent hypoxia (Lavie and Lavie 2009).

Gender and OSA

The estimated prevalence of OSA is higher in males (24%) than in females (9%) (Young, Palta et al. 1993). Other studies have demonstrated approximately a 2- to 3-fold higher prevalence of OSA in men (Punjabi 2008). This might be due to physicians having a higher suspicion of this disease in males and a tendency to under-diagnose OSA in females since females may not present with classical symptoms such as loud snoring, witnessed apneas, and excessive daytime sleepiness (Young, Evans et al. 1997).

2.2.4 Comorbidity in OSA

The sequelae of OSA range widely and are linked to many systemic health concerns. Of particular concern is the link between cardiovascular and metabolic disease and OSA.

Cardiovascular Disease

A large body of evidence supports the role of OSA in promoting adverse cardiovascular outcomes, particularly hypertension (McNicholas and Bonsigore 2007). For example, the Sleep Heart Health Study of over 6,000 North American subjects showed that subjects with severe sleep disorder had an odds ratio of 1.37 for prevalence of hypertension compared to those without OSA, even after adjusting for confounding factors (Quan, Howard et al. 1997). Large studies in Europe found similar results (Tkacova, McNicholas et al. 2014). These studies also linked OSA with increased risk of developing coronary artery disease, heart failure, cardiac arrhythmia, and cerebrovascular disease.

Metabolic Disease

A complex relationship exists between OSA, obesity and metabolic diseases (e.g. Type II diabetes). The European sleep study showed that subjects with severe OSA had a twofold increase in the likelihood of having Type II diabetes, even after adjusting for the effects of age and obesity (Tkacova, McNicholas et al. 2014). A large Canadian sleep study of 8,678 reported similar results (Kendzerska, Gershon et al. 2014).

2.2.5 Cervical Spine Abnormalities/Pathologies and OSA

Obstruction in the pharyngeal airway can arise directly from surrounding hard and/or soft tissues. Numerous studies have examined conditions that impact the anterior pharyngeal airway structures such as tonsillar and adenoid hypertrophy, soft palate enlargement, unfavorable hyoid bone position, tongue size and position, abnormal pharyngeal musculature, and maxillomandibular size and retrognathism (Dempsey, Veasey et al. 2010; Edwards and White 2011). Limited studies have examined conditions that impact the posterior airway structures, such as in cervical spine abnormalities.

A number of cervical spine abnormalities and pathologies have been associated with obstructive sleep apnea (Khan, Than et al. 2014). Studies investigating cervical spine morphology and OSA found a high prevalence of cervical spine fusion in these patients. Rheumatoid arthritis has also been linked to both OSA and CSA and the prevalence of sleep apnea in RA patients is estimated to be between 53-79% (Shoda, Seichi et al. 2009). The proposed mechanism for CSA is due to the compression of the medulla by the odontoid process. Osteophytes, or bony projections along joint margins, are signs of bone degeneration and when large enough, may cause compression of the airway. Osteochondromas, or benign tumors of the spine, occur in the posterior cervical spine and can encroach on the pharyngeal space to cause OSA.

2.2.6 Diagnosis

Various diagnostic methods are available for screening and detecting OSA including sleep studies, radiographic studies, endoscopic exams, and surveys. Their indications are discussed below.

Sleep Studies

A wide range of sleep studies are currently available on the market, ranging from overnight attended polysomnography (PSG) to home sleep studies (HST). The Centers for

Medicare and Medicaid Services classification (Phurrough 2009) has broadly categorized these into four groups: Type I (PSG), Type II and III (≥4 channel HST), and Type IV (3-channel HST).

OSA severity is defined by the apnea-hypopnea index (AHI) or respiratory disturbance index (RDI), which indicates the number of complete (apnea) or incomplete (hypopnea) events per hour. AHI values are categorized as: 0-4/hr, none or minimal; 5-15/hr, mild; 15-30/hr, moderate; and >30/hr, severe. Apnea is defined as cessation of airflow for at least 10 seconds. Hypopnea is defined as abnormal respiratory event lasting at least 10 seconds and is accompanied by at least 30% reduction in thoracoabdominal movement or airflow and a 4% decrease in oxygen desaturation. Regardless of the sleep study type, an AHI and/or RDI score will be produced in the report.

Polysomnograms (PSG), a type I sleep study, remains the gold standard for diagnosing and measuring sleep apnea severity. Patients are referred by a physician to a sleep study center, either at a hospital or outpatient facility, where a sleep technician will monitor the patients' sleeping patterns and record various biophysical parameters, typically 12 channels or more, for six or more hours of sleep. These recorded parameters include brain wave activity (EEG), cardiac activity (EKG), ocular movements (EOG), skeletal muscle activation (EMG), breathing functions respiratory airflow, respiratory effort, and oxygen saturation. EEG, EOG and EMG help determine the stages of sleep such as REM sleep. Airflow sensor and respiratory effort detectors identifies apneic and hypopneic events. A report will be generated and interpreted by a physician.

Home sleep studies (HST) are portable monitors that can be used unattended at home. Types II-IV vary by the number of channels with II having a minimum of 7 channels, III having 4 channels and IV having 3 channels. At a minimum, all types will monitor breathing/respiratory effort, oxygen saturation and heart rate.

Numerous validation studies for various Type II and III HST models are available. Three studies pertaining to the HST used in our research (ARES, Medibyte, Nox T3) are briefly described hereafter. A validation study using the ARES Unicorder, a self-applied limited-channel portable monitoring device, was conducted on 97 subjects and their results were compared with the PSG 2 weeks later (Ayappa, Norman et al. 2008). The authors concluded that the ARES provided acceptably accurate OSA indices with high sensitivity and specificity. Similar studies were conducted for the Medibyte and Nox T3. The Medibyte device accurately identified patients without OSA and had a high sensitivity for moderate-to-severe OSA (Driver, Pereira et al. 2011). The Nox T3 demonstrated good agreement with the PSG and had good sensitivity for detecting even mild OSA (Cairns, Wickwire et al. 2014).

While not a sleep study, the Epworth Sleepiness Scale is a widely used, self-administered questionnaire to screen for daytime sleepiness. The higher the ESS score, the higher the propensity for daytime sleepiness. However, validity testing between ESS scores and OSA severity by AHI score demonstrated weak correlation (Manni, Politini et al. 1999; Mihaicuta, Muntean et al. 2006). ESS has also been criticized for its dependency on the patients' subjective reporting, which can be biased depending on their state of mind (Kum, Ozcan et al. 2015). Some clinicians recommend using the ESS questionnaire for screening patients for further diagnostic testing.

Radiographic Studies (2D and 3D imaging studies)

Numerous 2-D and 3-D imaging studies have evaluated the pharyngeal airway dimensions in OSA patients. Conventional 2-D lateral cephalograms are limited to measuring various A-P dimensions along the airway (Zucconi, Ferini-Strambi et al. 1992; Solow, Ovesen et al. 1993; Solow, Skov et al. 1996) whereas 3-D CBCT and MDCT allow for measurements in all 3-planes of space. CBCT and MDCT have been shown to be both accurate and reliable for measuring the dimensions of the airway (Barkdull, Kohl et al. 2008; Shigeta, Ogawa et al. 2008; Ghoneima and Kula 2013; Guijarro-Martinez and Swennen 2013). Moreover, a good correlation among cephalometric and CT parameters of the pharyngeal airway space has been shown (Abramson, Susarla et al. 2010).

There are notable differences between CBCT and MDCT imaging. CBCT has a lower effective radiation dosage, lower cost, easy accessibility and shorter acquisition time compared to MDCT (McCrillis, Haskell et al. 2009; Guijarro-Martinez and Swennen 2013). CBCT has higher resolution but lower soft tissue contrast. However, it has been shown to be reliable in defining the border between soft tissues and empty spaces (i.e. air) and is appropriate for airway assessment (Aboudara, Nielsen et al. 2009). On the contrary, MDCT is superior to CBCT for soft tissue contrast and is suitable for differentiating between various soft tissue borders (i.e. muscles, connective tissues, fat, etc.) of the airway (Lenza, Lenza et al. 2010).

A number of 3-D imaging studies have found significant correlations among sleep apnea severity and airway parameters. A high probability of severe OSA with an airway less than $52mm^2$ and low probability if the airway is greater than $110mm^2$ have been demonstrated (Lowe, Gionhaku et al. 1986). Furthermore, the location, dimension and nature of the obstruction between normal and OSA patients have been compared. The authors found lower total volume, smaller A-P dimension of the minimum cross-section area (OSA 4.6mm; non-OSA 7.8mm), smaller minimum cross-section area (OSA 45.8 mm^2; non-OSA 146.9 mm^2), the location of constriction occurred below the occlusal plane in 70% of the OSA cases, and airways appeared more concave-elliptical versus round-squared in non-OSA subjects (Ogawa, Enciso et al. 2007). The minimum cross-sectional area of the airway changes with the respiratory cycle, with a smaller area noted in both the inspiratory and expiratory phase compared to neutral, and that the most common site of obstruction is in the retropalatal region (Bhattacharyya, Blake et al. 2000).

Endoscopic Examinations

Drug-induced sleep endoscopy (DISE) or flexible nasal endoscopy under anesthesia offers the unique advantage of visualizing the aerodigestive tract, in real-time, for potential sites of obstruction. Additionally, clinicians can identify pathologies such as adenoid and lingual tonsillar hypertrophy, nasal polyps, tongue-base collapse and pharyngeal constriction sites (Al-Hussaini and Berry 2015).

Recent Developments

Recently, two mobile health apps have surfaced and offer an alternative to detecting and monitoring sleep apnea. The first is a novel app that uses snoring sounds to measure OSA severity and works by placing a smartphone on the subject's chest to record and analyze the characteristic frequency of snoring sounds (Sands and Owens 2014). The second is an app that monitors the small movements in the chest and abdomen during breathing. This is achieved by transforming the smartphone into an active sonar system (Nandakumar, Gollakota et al. 2015). Additional research is needed to validate these two innovations. These advances allow for widespread screening for OSA.

2.2.7 Treatment

OSA treatment generally fall into two categories: surgical versus non-surgical.

Surgical

Surgical management of OSA involves a number of procedures that targets the site of obstruction. If the obstruction occurs in the nasal passage, a septoplasty or turbinate reduction may be performed to improve the nasal airway patency. If the obstruction occurs in the retropalatal area, an uvulopalatopharyngoplasty (UPPP) procedure is performed to remove the soft palate, lateral pharyngeal walls and palatine tonsils to widen the pharyngeal airway. Complications associated with UPPP may involve velopharyngeal insufficiencies, dysphagia and nasopharyngeal stenosis and the overall success rate is around 40% (Lefebvre and Moreau 2010). If the obstruction occurs in the tongue-base and hypopharyngeal area, a tongue-base suture suspension or reduction procedures prevent the tongue from collapsing and occluding the pharynx when muscle tonicity is reduced during sleep. If the obstruction is due to poor skeletal proportions such as a retrognathic mandible and/or maxilla, bimaxillary advancement procedure has been shown to be the most effective surgical treatment for OSA (Phan, Wallwork et al. 2016).

A CBCT airway study of OSA subjects post-maxillomandibular advancement procedure showed an average of 2.5-fold increase in total volume of the upper airway space and a 3.5-fold increase in the retropalatal space (Schendel, Broujerdi et al. 2014).

Non-surgical

Continuous positive airway pressure (CPAP) is the primary treatment for OSA. Positive pressure is delivered through the nose via facemasks. For patients with moderate to severe sleep apnea, this is the recommended first-line therapy (Spicuzza, Caruso et al. 2015). However, some patients cannot tolerate either the facemask or the high positive pressure, resulting in lower CPAP (<50%) compliance. For these patients, surgery offers the best alternative whereby the root cause of the obstruction can be eliminated by surgical removal.

For mild to moderate sleep apnea, an alternative therapy using mandibular advancement device (MAD) has been shown to be effective at increasing the airway volume (Kyung, Park et al. 2005). During apnea, the cross-sectional area of the retropalatal and retroglossal levels decreased the most. With the appliance in place, a significant increase in the cross sectional areas at these respective levels were noted to a greater degree in the lateral than sagittal plane.

2.3 Positional Changes in the Airway and OSA

OSA is a dynamic process that occurs throughout the sleep cycle. The site of obstruction can vary depending on the position of sleep. Previous studies examining the changes in the size of the upper airway in the supine versus upright positions used either lateral cephalograms for OSA patients or CBCT for non-OSA patients. Few CT studies have examined the position associated airway changes in OSA patients.

2.3.1 Supine Versus Upright

To date, only one study has examined the airway dimensions of OSA patients in the supine versus upright positions (Camacho, Capasso et al. 2014). The authors initially performed a systematic review to identify previous studies on upright and supine CBCT imaging in OSA patients, but no studies were found. Next, the authors searched internally within the Stanford

Hospital and Clinics for adult OSA patients with polysomnogram (PSG) and CBCT in both the upright and supine positions; five patients matching the inclusion criteria were identified for further investigation. The results showed that the following airway dimensions were smaller when patients were in the supine versus upright position: total upper airway volume decreased from 14.1 to 9.5 cm^3, PNS cross-sectional area decreased from 435 to 226 mm^2, uvula tip cross-sectional area decreased from 170 to 94 mm^2, retrolingual cross-sectional area decreased from 262 to 132 mm^2, tongue base cross-sectional area decreased from 353 to 239 mm^2, and the site of minimum cross-sectional area decreased from 120 to 30 mm^2. Overall, a significant total airway volume decrease of 32.6% and cross-sectional area decrease of 75.9% were noted. The authors suggested that the effect of gravity and tissue laxity are contributors to these findings.

Furthermore, the authors noted that the location of the minimum cross-sectional area was mostly in the tongue base region in the upright group whereas that site shifted to the retropalatal region in the supine group. These findings were consistent with other previous studies, which found the retropalatal region as the most common site with the minimum cross-sectional area. Patients with previous history of tonsillectomy and UPPP demonstrated minimal position-related changes in the airway dimensions.

Lastly, the authors compared these findings with two previous position-related CT studies in non-OSA patients. The first study noted a significant decrease in the retropalatal (41.2%), retrolingual (8.9%), and tongue base (13.4%) regions between the upright versus supine groups (Van Holsbeke, Verhulst et al. 2014). These findings were similar to those found in OSA patients: retropalatal (44.7-48%), retrolingual (49.6%), and tongue base (32.3%). The second study found a decrease in the smallest cross-sectional area of 35.3% (Sutthiprapaporn, Tanimoto et al. 2008).

2.3.2 Supine Versus Lateral

In additional to supine versus upright positioning studies, the effects of lateral positioning in OSA patients have also been examined. One study investigated the upper airway morphology (palatine tonsil size, tongue position, width of fauces and retroglossal space) of OSA patients in the lateral and supine sleeping positions (Soga, Nakata et al. 2009). In 6 patients, a lateral posture decreased the AHI by 50% and more (responders to lateral position) whereas the remaining 25 patients experienced a decrease of less than 50% or even an increase in AHI scores (nonresponders to lateral position). The width of the fauces (distance between palatine tonsils) was significantly larger in the responder group. No differences were noted in the other airway parameters. On the contrary, a DISE study found that when sleep posture is changed from supine to lateral, obstructive due to the tongue base (supine – 71.1%; lateral – 7.1%) and larynx (supine – 70.6; lateral – 60.0%) improved dramatically (Lee, Kim et al. 2015). Obstruction in the lateral position is due to collapsibility of the oropharyngeal lateral walls.

2.4 Spine Alignment and OSA

2.4.1 Normal Spine Alignment

The adult spine, viewed sagittally, exhibits a natural S-shaped curve and has four distinct regions: cervical (neck), thoracic (body), lumbar (lower back), and sacral (tail bone). The cervical and lumbar regions have a slight concave curve whereas the thoracic and sacral regions have a slight convex curve (Figure 2.1). The curves act to absorb shock, maintain balance, and allow range of motion throughout the spinal column. Deviation from this natural curve occurs due to trauma, weak muscles, and poor posture. Long-term imbalance of the spine or mal-alignment can lead to clinical symptoms and degenerative disease (Duval-Beaupere, Schmidt et al. 1992; Katsuura, Hukuda et al. 2001). Abnormal lumbar and cervical spine curvature is called lordosis whereas abnormal thoracic spine curvature is kyphosis (Figure 2.2).

The cervical spine is composed of 7 vertebrae (C1-C7) and consists of two important joints: the atlanto-occipital (occiput-C1) joint for head flexion-extension, and the atlantoaxial (C1-C2) joint for primarily head rotation with some flexion-extension (Figure 2.3). Due to the cervical column's close association with the upper airway, a number of studies have found a relationship between the cervical spine and sleep apnea.

2.4.2 Changes in Spine Alignment with Age, Gender, and BMI

Whole-spine standing radiographic studies have compared the natural aging changes in the cervical sagittal alignment of healthy asymptomatic adults in their 20s and of those older than 60 years (Park, Moon et al. 2013). Specifically, the global thoracolumbar and cervical sagittal alignment was examined using the Cobb method (described in the next section). The results indicated no increase in thoracic kyphosis or lumbar lordosis with age; however, the spine pitches forward into positive sagittal balance while the cervical spine alignment becomes more lordotic with age. These findings suggested that the increased in cervical lordosis was a compensatory mechanism to maintain horizontal gaze. Other studies have found that the C2-C7 angle increased from 8.0 degrees to 19.7 degrees between the 3rd and 8th decade.

Other spine studies have found sagittal alignment differences between genders and BMI groups (Gelb, Lenke et al. 1995; Vedantam, Lenke et al. 1998; Mac-Thiong, Roussouly et al. 2010; Lang-Tapia, Espana-Romero et al. 2011). One study found that the thoracic kyphotic angle and the lumbar lordotic angle decreased with age in famales whereas whereas the lumbar lordotic angle increased while maintaining the same thoracic kyphotic angle (Park, Moon et al. 2013). Another study reported that males have less lumbar lordosis and greater thoracic kyphosis than females (Lang-Tapia, Espana-Romero et al. 2011). These disagreements suggested that other factors, such as BMI, can influence gender differences in spinal alignment.

2.4.3 Measuring Spinal Curvature and Angles

The two most commonly used methods for spinal angle measurements are the Cobbs Method and the Harrison Posterior Tangent Method, which use either horizontal or vertical reference planes. The Cobbs method utilizes horizontal planes tangent to the inferior borders of each cervical vertebrae to create intervertebral angles. Conversely, the posterior tangent method utilizes the vertical planes tangent to the posterior borders of each cervical vertebrae to create intervertebral angles (Figure 2.4). Both methods have shown high reliability in the literature (ICC>0.7); however, the posterior tangent method has a smaller standard error of measurement

(Harrison, Harrison et al. 1998; Harrison DE 1998). Moreover, mathematical models have been applied to examine the cervical spine curvature of patients with varying history of neck pain (Figure 2.5). The authors found that ellipses with different major and minor axis lengths most closely approximate the posterior body of C2-C7 cervical vertebra and that patients with greater chronic neck pain exhibited a larger radius of curvature (Harrison, Harrison et al. 2004). Lastly, good agreement for the evaluation of cervical vertebral morphology was found between lateral cephalograms and CBCT (Sonnesen, Jensen et al. 2013).

2.4.4 Positional Changes and Spinal Angles

From the sagittal view, the cervical spine alignment in the upright position exhibited a more lordotic curvature than in the supine position. This is due to the gravitational force placed on the middle cervical vertebrae, which straightens the cervical curvature. Radiographic studies have demonstrated a difference of five degrees in spinal angles between the supine and upright position (Martensen 2015). Another study compared the cervical spine alignment of patients in the upright (standing conventional lateral cephalograms) versus the supine position (CT scan) and found that patients in the upright position exhibited more cervical spine lordosis (Jun, Chang et al. 2014).

2.4.5 Cervical Spine Angles and OSA

Few studies have directly examined the association between cervical spine angles and OSA. One study examined four cervical spine angles (C1-C2, C1 alone, C1-occiput, and occiput alone) in sleep apnea patients and found that a general kyphotic arrangement of the occiput and upper cervical spine existed in OSA patients, with the greatest extent of flexion in severe sleep apneic patients (Dobson, Blanks et al. 1999). The C1-occiput angle was most predictive of the sleep apnea severity. The authors conjectured that a vertebral injury at this level could impact the outflow of C1 and C2 nerve fibers and result in a loss of pharyngeal airway muscle tonicity (which is innervated by the cervical plexus of nerves), leading to airway collapse. Interestingly, the authors found that the C1-C2 angle does not correlate well with C1-occiput or any other upper cervical angle, suggesting an independent relationship between cervical spine angles and head posture. Furthermore, gender differences were found but should be interpreted cautiously due to a small female sample size. Age was negatively correlated with the atlas angle and positively correlated with C1-occiput angle in moderate-to-severe OSA patients. Moreover, a cephalometric (lateral and posterior-anterior) study examining the association between cervical spine mechanics, sleep apnea severity and positional dependency, found that the Cobb angle of lordosis and atlas angles showed significant negative correlation with OSA severity and positional dependency (Saleh, Sultan et al. 2015).

A number of studies, namely on cervical spine fusion, have indirectly examined the association between cervical spine angles and sleep apnea. In a case report, a 58 year-old female with metastatic breast cancer to the cervical spine required subsequent spine surgery and fusion. Postsurgical airway obstruction was immediately noted and the cause was due to over-flexion of the spine (Lee, Hsieh et al. 2008). Other cervical spine fusion studies have demonstrated post-operative symptoms of sleep apnea with the causative factor attributed to over-flexion of the cervical spine, leading to narrowing and collapsibility of the upper airway (Ataka, Tanno et al. 2010). AHI scores have been shown to increase from 2-2.6 to 11-36 post spinal fusion surgery (Guilleminault, Li et al. 2003). A cephalometric study, examining the relationship between the O-C2 angle and the oropharyngeal space in normal patients, found a strong correlation between the the O-C2 angle (which is often studied in spinal fusion cases) and the narrowest oropharyngeal airway space (nPAS). A 10 degree decrease in O-C2 angle conferred a 37% reduction in nPAS. However, no significant correlation was found between C2-C6 angle and the percent change in nPAS (Ota, Neo et al. 2011).

Two important points of clarification must be stated about the relationship between cervical spine angles and craniocervical head posture (covered in the following section). First, the studies referenced above evaluated both together because they are physiologically and anatomically interconnected structures. For example, the “O-C2” and “C1-occiput” angles are synonymous with craniocervical head posture angles. Second, some studies suggest an independent relation between the two; therefore, further investigation into each is warranted.

2.5 Craniocervical Posture and OSA

Head posture, or craniocervical posture, has been associated with OSA whereby flexion or extension of the head influences the oropharyngeal airway dimensions. The natural head posture/position (NHP) is the upright position of the head of a standing or sitting subject with eyes directed forward so that the visual axis is parallel with the floor. It is unclear what mechanisms are responsible for differences in NHP but one hypothesis states that the primary control is due to the need to maintain a patent airway (Solow, Ovesen et al. 1993; Solow, Skov et al. 1996). Almost all prior studies examining head posture and airway dimensions have made measurements using 2-D cephalometry. Few 3-D imaging studies have ever been performed.

2.5.1 Cephalometric (2-D) Study of Craniocervical Posture

Solow Analysis

Solow and colleagues conducted some of the earliest known cephalometric studies examining the craniofacial morphology and natural head posture in OSA patients (Solow, Ovesen et al. 1993; Solow, Skov et al. 1996). While cephalometry only allows for measurements in the sagittal plane, the author argued that it possesses advantages of consistency over other imaging techniques due to the standardization of patient positioning (i.e. natural head position) and image acquisition protocol. Solow described a number of cephalometric analyses to evaluate head flexion or extension relative to the spinal column (Figure 2.6). At a minimum, craniocervical evaluation requires a cranial (e.g. sella and nasion) and a cervical (e.g. cervical vertebrae 2 and 4) landmark. Additional horizontal and vertical reference lines are added for more in-depth analyses of head and neck inclination.

The authors found that the average craniocervical angulation of OSA subjects was more than two standard deviations above the control group (i.e. more forward inclination of the cervical spine). Solow et al. (1996) repeated the study with a sample of 50 male subjects (mean AHI score of 47 and BMI of 31) and found that extension of the craniocervical angle and forward inclination of the cervical column were highly correlated with an increase in the most caudal airway diameters in OSA subjects (Figure 2.7). These lower oropharyngeal airway landmarks include the uvula, tongue base, and the epiglottis (Figure 2.8). The author suggested that these findings represent a compensatory physiological postural mechanism, which helps maintain airway patency in OSA patients. These physiological adaptations exist in both upright and supine sleeping positions.

The proposed mechanism is best represented by the arc length equation, which can simply be summarized as the arc length = arc radius x central angle. This means that the points furthest away from the fulcrum (i.e. atlanto-occipital joint) of the tilting of the head experiences the greatest change in arc length or airway dimension (Figure 2.9). Said another way, the combination of head extension and cervical spine proclination opens up the lower oropharyngeal airway more than the upper pharyngeal airway. These findings agree with other experimental studies by (Hellsing, McWilliam et al. 1987; Davies, Ali et al. 1992). Hellsing et al. (1987) reported that a 20-degree increase in NHP resulted in an increase in pharyngeal cross-sectional airway dimension. Another study reported a 10-degree increase resulted in about 4mm increase in airway space (Muto, Takeda et al. 2002).

Rocabado Analysis

The Solow Analysis requires a large field of view, including the cranial base. For radiographs with a more limited field of view (i.e. CT neck), the Rocabado Analysis offers a valid alternative.

Rocabado introduced the six cephalometric evaluations for the spinal biomechanics of the head and hyoid position, cervical spine inclination, and airway conditions. Two pertained to head posture, specifically the craniocervical angle and A-O (described below) distance (Rocabado 1983; de Oliveira, Cajaiba et al. 2012). The craniocervical angle is defined as the head posture in relation to the upper cervical posture (flexion or extension of the head) and is formed by the intersection of the McGregor line and Odontoid planes (Figure 2.10). Normal head posture ranges between 96-106 degrees, whereas head extension is less than 96 and head flexion is greater than 106 (Weber, Correa et al. 2012). The A-O distance is the length between the base of the occipital bone and the posterior arch of atlas vertebrae. Normal A-O distances range between 4-9mm, whereas head extension is less than 4mm and flexion is greater than 9mm.

A case control study, comparing the airway dimensions and craniocervical posture (among other variables) of OSA and healthy subjects, found a significant difference between the groups, with a higher head hyperextension and head anteriorization in subjects with greater OSA severity (Piccin, Pozzebon et al. 2016). These findings agreed with the Solow studies and suggest that subjects with OSA are compensated via a forward and extended head posture to increase airway patency.

Other Cephalometric Studies

Other cephalometric studies of head posture utilized analyses largely similar to those described by Solow.

Differences in NHP and the severity of OSA was noted in 252 adult male subjects (Ozbek, Miyamoto et al. 1998). The authors found a high positive correlation between craniocervical extension and forward head posture in OSA severity. Additionally, these patients had a longer and larger tongue, lower hyoid bone position, higher BMI, and smaller nasopharyngeal and hypopharyngeal cross-sectional area.

Studies in children with enlarged tonsils and chronic respiratory problems such as asthma and rhinitis demonstrated an increase in craniocervical extension (Wenzel, Hojensgaard et al. 1985). Moreover, some of the triggers responsible for adaptation of the NHP in children persist in adults. Similarly, another study comparing head postures between 29 children with SDB and the age-gender-matched control groups found that the SDB group exhibited increased head extension and hypopharyngeal airway dimensions compared to the control group (Pirila-Parkkinen, Lopponen et al. 2010).

2.5.2 Three-dimensional Study of Craniocervical Posture

A systematic review examining the effect of head and tongue posture on the pharyngeal airway dimensions in MDCT, CBCT, or MRI identified 4 poor quality and low-level evidence publications (3 MRI and 1 CBCT studies) (Gurani, Di Carlo et al. 2016). Only 1 MRI study directly examined the relationship between head flexion-extension and airway volumes in children with SDB, where the hypopharyngeal airway volume is significantly increased with head extension compared to the neutral head posture. The other two MRI studies examined the effects of head rotations and jaw positioning on airway volumes. The CBCT study only examined the changes in airway volumes with respect to the open and closed jaw position in TMD patients.

2.6 Cervical Spine Length and OSA

Many studies have reported that neck circumference is greater in individuals with OSA due to greater fat deposition around the soft tissues of the upper airway (Davies, Ali et al. 1992). However, other morphometric features such as neck length have not been well studied.

A few studies have clinically and radiographically examined the relationship between neck length and sleep disordered breathing; however, the studies varied widely with respect to how neck length is measured. A clinical study explored the association between neck length and sleep disordered breathing and cardiovascular disease (Han, Oh et al. 2015). The author used a measuring tape to physically measure the midline neck length (MNL- from hyoid bone to the jugular notch) and lateral neck length (LNL-angle of the mandible to the mid-portion of the clavicle). No significant differences were found in neck length between male and female subjects. Male and female habitual snorers were found to have shorter MNLs. However, sleeping patterns (total sleep time, sleep latency, and waking up refreshed) had no correlation with neck length. Subjects with shorter LNL height were associated with metabolic syndrome. In general, short MNL showed a greater correlation than LNL in most categories examined. However, the mechanism for why shorter necks may influence snoring or sleep apnea is unknown.

A few radiographic studies have shown differences in neck length in OSA patients. Small cervical spine lengths (O-C2: 24.8 versus 32.9 mm in controls; O-C6: 87.0 versus 104.6 mm in controls) were significantly associated with the presence of sleep apnea in patients with rheumatoid arthritis (Shoda, Seichi et al. 2009). The author attributed the shortening of cervical spine length to the horizontal atlantoaxial subluxation typically seen in RA patients. On the contrary, CBCTs' of OSA subjects found that OSA cases had larger neck circumferences and larger neck length, as measured from PNS to the second cervical vertebrae (Momany, AlJamal et al. 2016). Similar findings were reported in a study that used MDCT's to examine the relationships among the upper airway length (vertical distance from the hard palate to the hyoid bone) and upper airway volume in severe OSA subjects (Kim, Choi et al. 2011). The authors found that the height adjusted upper airway length showed a significant positive correlation with the AHI score and was a significant variable for predicting the AHI of OSA subjects. However, no significant differences in the upper airway volume and minimum cross sectional areas were detected among the groups. The authors hypothesized that the mean cross sectional area must be decreased in the severe OSA group. This suggested that the lengthening of the upper airway without volumetric change might independently influence the severity of OSA in adults. Furthermore, the correlation between longer UAL and increased UA collapsibility could be explained by Bernoulli's principle where increased air velocity produces decreased pressure. Said another way, if UAL increases without any volume change, then the velocity of airflow through the narrowed airway space should increase with subsequent decrease in intraluminal pressure, which reduces the patency of the airway.

Figure 2.1: Normal Spine Alignment. The natural "S-shaped" alignment of the spine consists of areas of concavity and convexity in the cervical, thoracic, and lumbar regions.

(http://www.mayfieldclinic.com/PE-AnatSpine.htm)

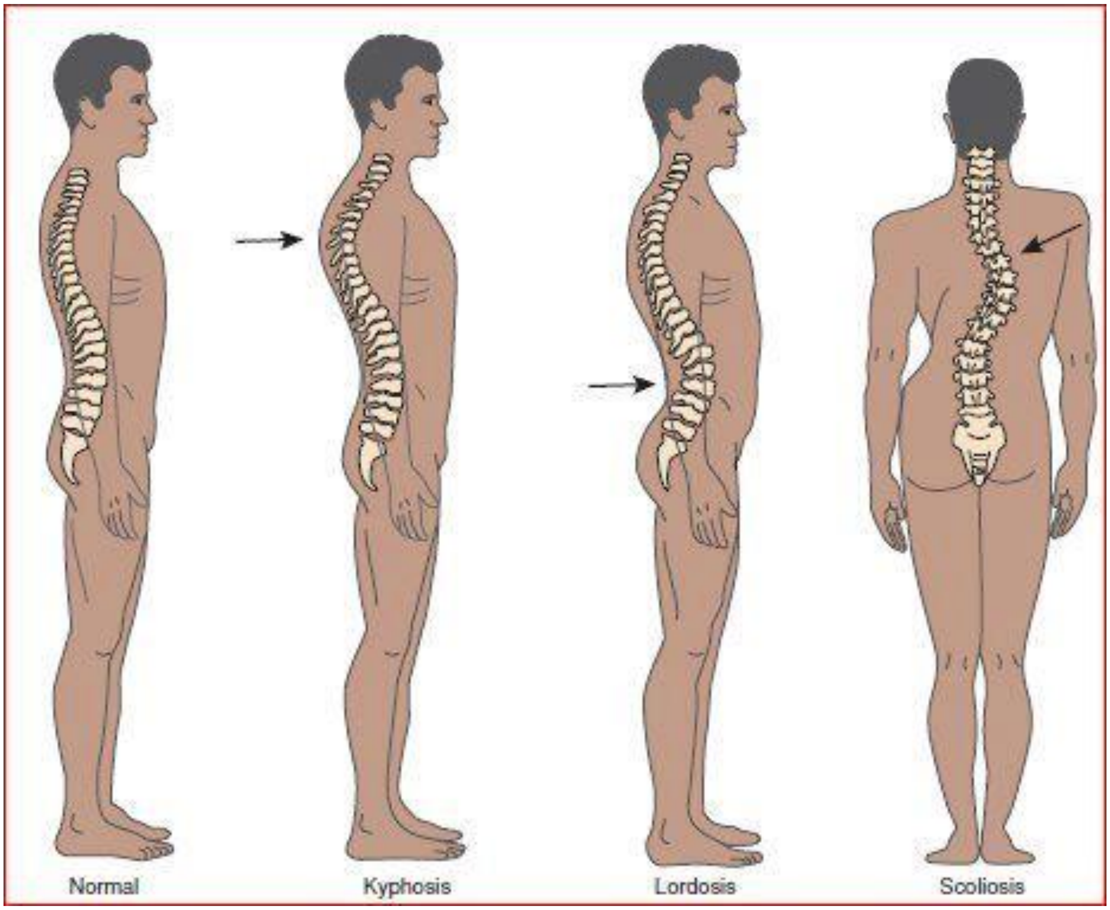
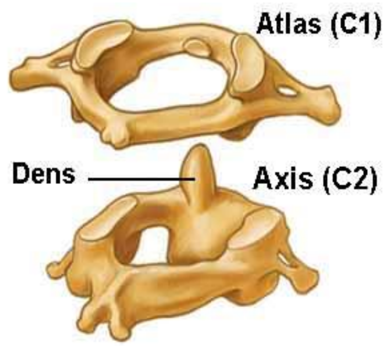
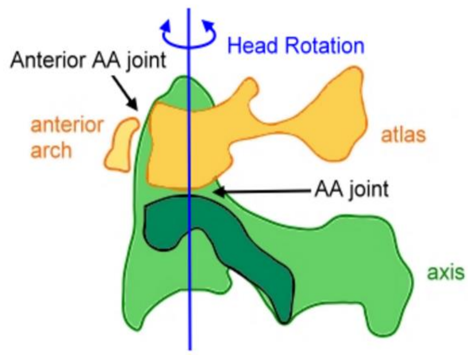


Figure 2.2: Abnormal Spine Curvature. An abnormal curve of the lumbar spine is lordosis where as an abnormal curvature of the thoracic spine is called kyphosis. These terms can be also be used to describe the abnormal curvature of the cervical spine. Abnormal side-to-side curvature is called scoliosis.

(http://www.mayfieldclinic.com/PE-AnatSpine.htm)

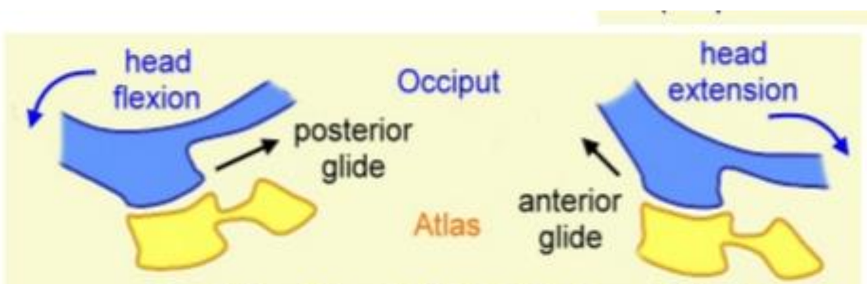


(a)



(b)

Atlantoaxial Joint (Lateral View)



Atlanto-occipital Joint (Lateral View)

(c)

Figure 2.3 (a-c): Anatomy of Cervical Spine and Joint. a) The cervical spine consists of 7 vertebrae. C1 is called atlas and C2 is called axis. **b)** The atlantoaxial joint primarily allows head rotation and some head flexion-extension. **c)** The atlanto-occipital joint allows for head flexion-extension.

http://www.pt.ntu.edu.tw/hmchai/Kines04/KINspine/Spine.htm

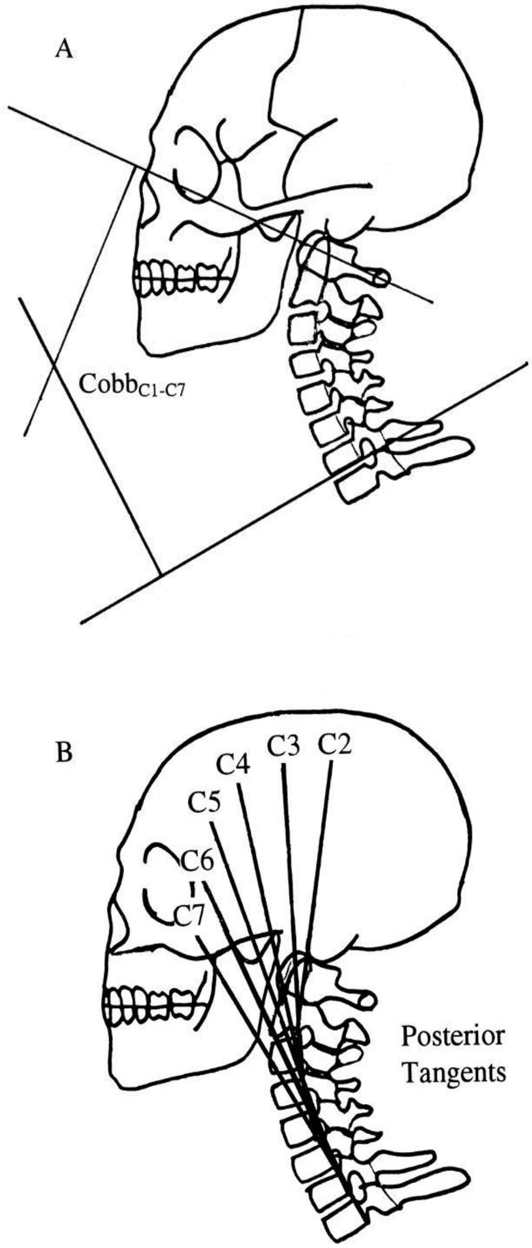
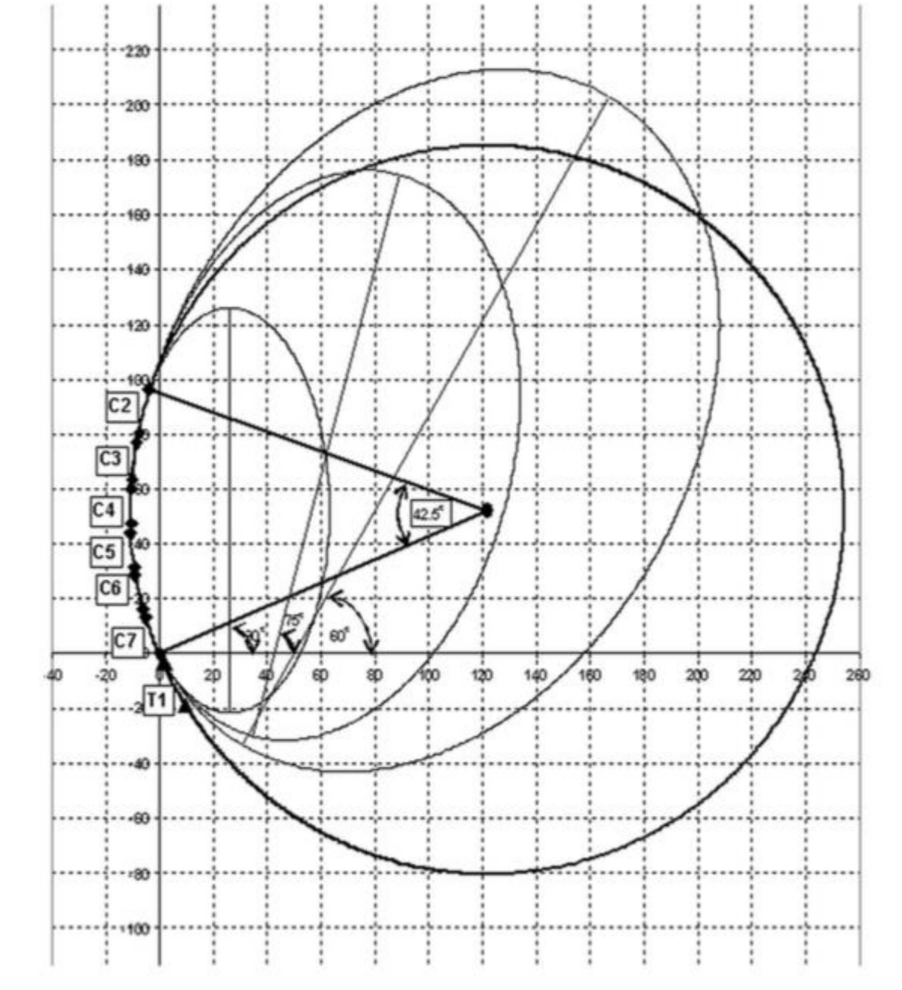


Figure 2.4: Cobb Method versus Harrison Posterior Tangent Method. a) The Cobb method utilizes horizontal planes drawn from the inferior end plates of the cervical vertebrae of interest. **b)** Harrison Posterior Tangent Method utilizes vertical planes drawn from the posterior border of the cervical vertebrae of interest.

(Harrison et al. 2000)



$$\frac{(x-t)^2}{a^2} + \frac{(y-s)^2}{b^2} = 1.$$

Figure 2.5: Elliptical and circular modeling of the normal cervical spine

(Harrison et al. 2004)

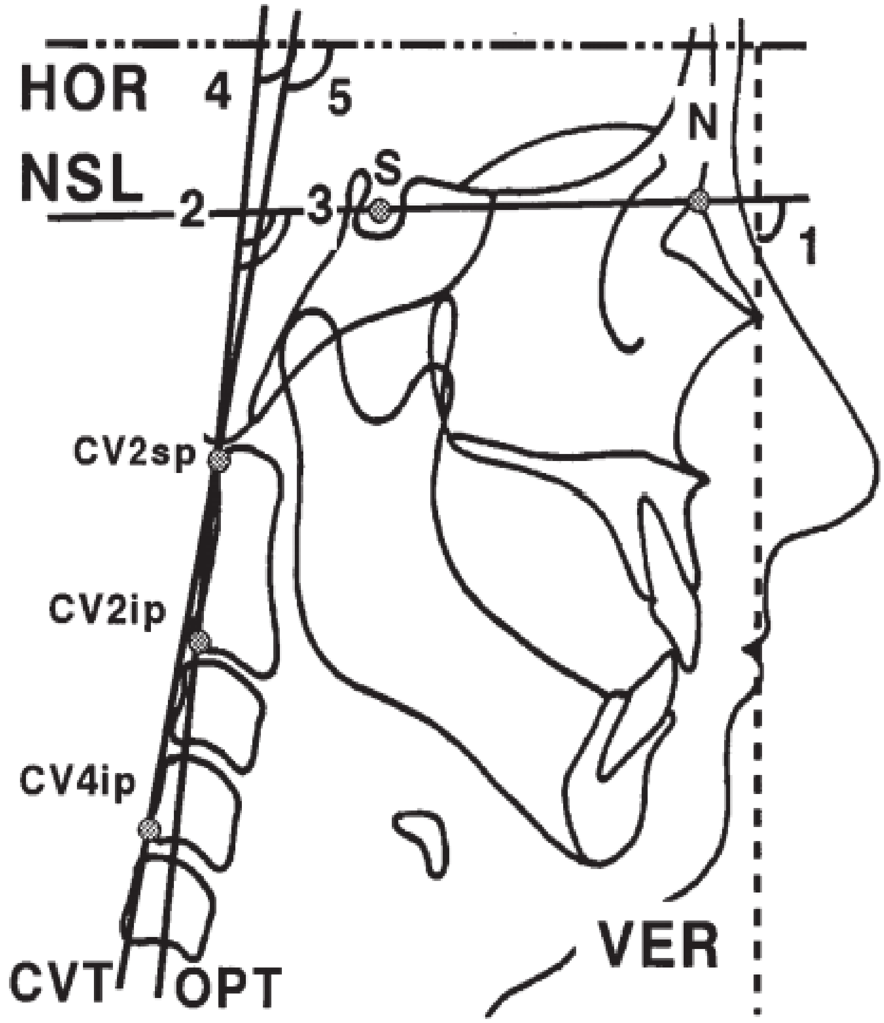


Figure 2.6: Cephalometric landmarks in the Solow Analysis

(Solow et al. 1996)

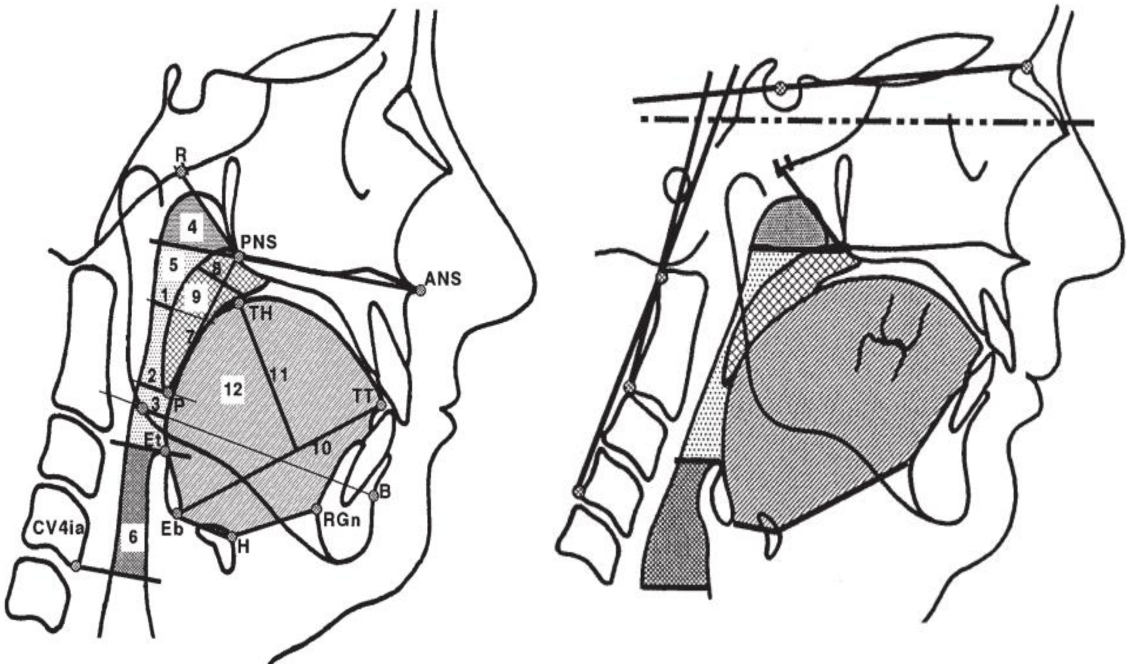


Figure 2.7: Forward head position and craniocervical extension in compensated OSA patients

(Ozbek et al. 1998)

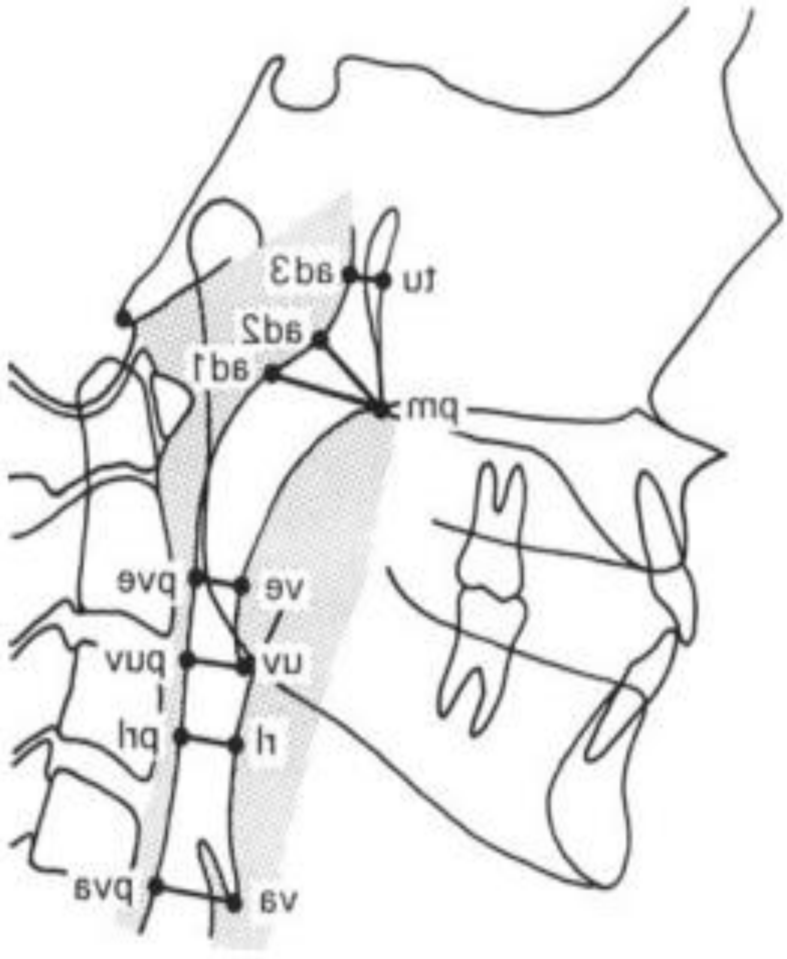


Figure 2.8: Cephalometric landmarks for measuring upper pharyngeal airway dimensions

(Solow et al. 1996)

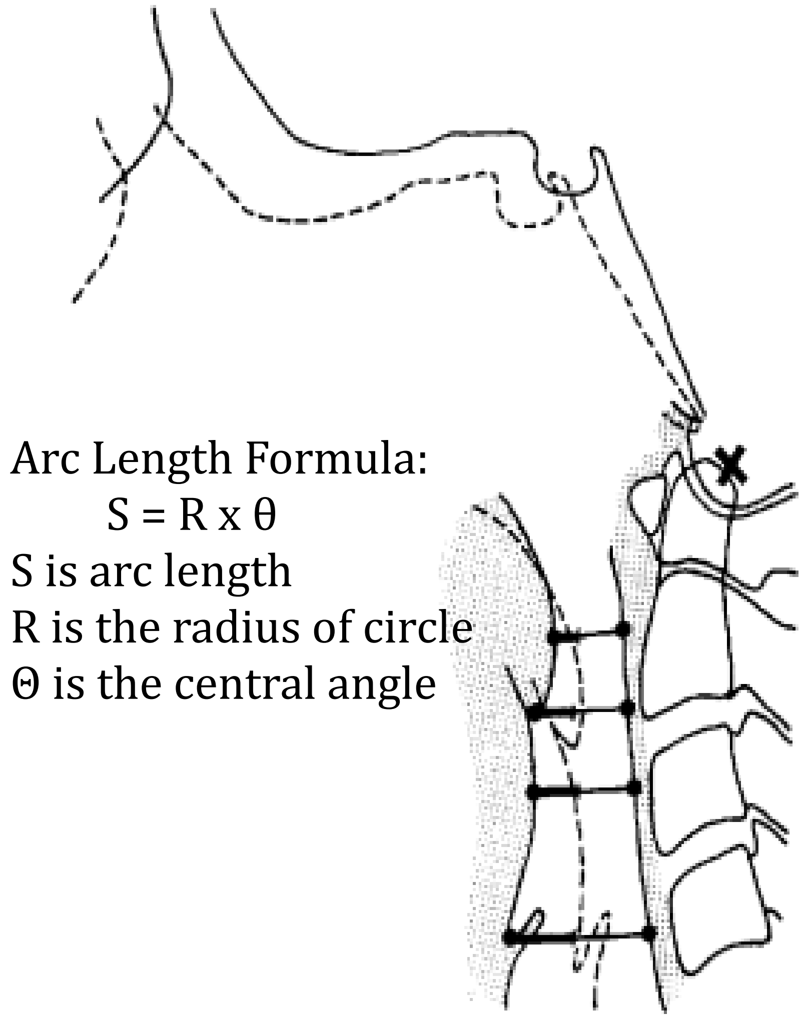


Figure 2.9: Geometry of increased lower oropharyngeal airway dimensions after craniocervical extension

(Solow et al. 1996)

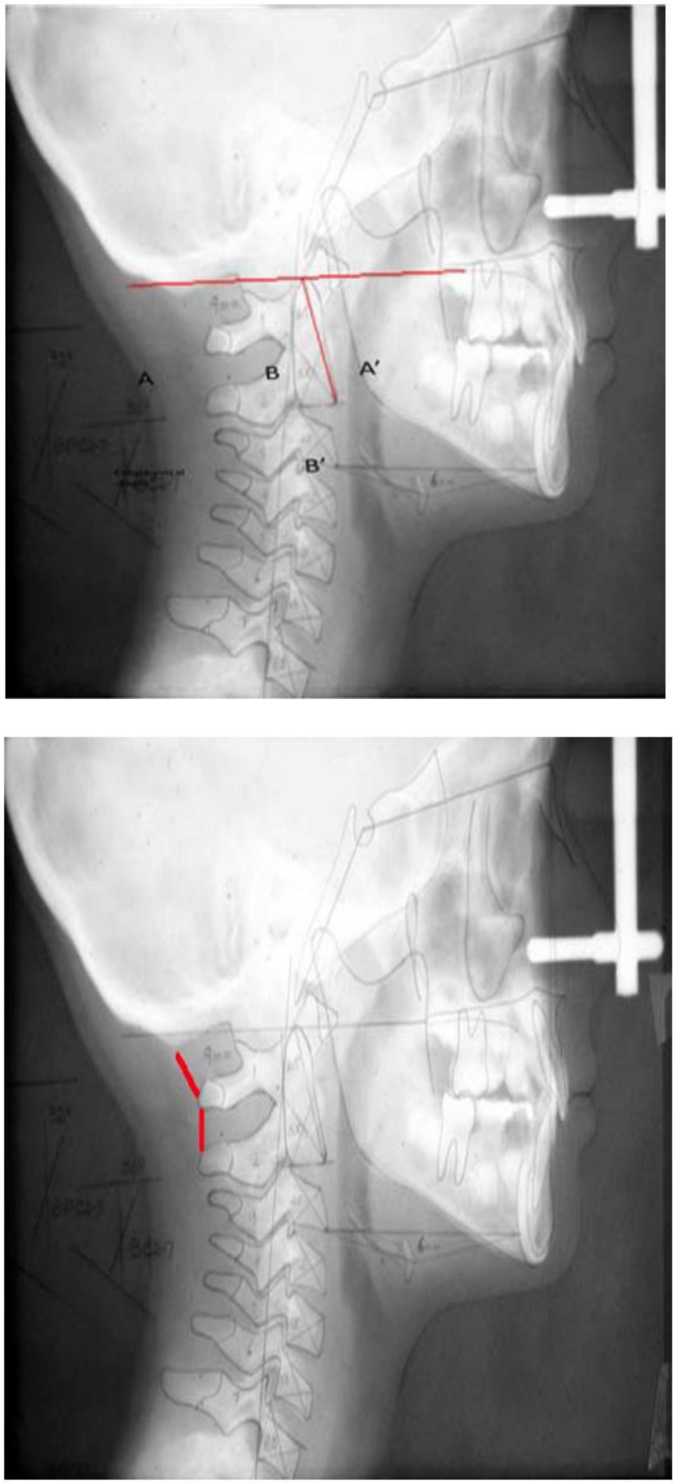


Figure 2.10: Cephalometric landmarks in the Rocabado Analysis

(Oliveira et al. 2012)

CHAPTER 3: STUDY AIMS

3.1 Statement of the Problem

There are three major weaknesses with prior studies examining the associations among cervical spine angles, head posture, neck length, upper airway space, and sleep apnea severity:

1. these studies heavily relied on two-dimensional radiographs, such as whole body x-rays or lateral cephalograms, to make linear and angular measurements. However, two-dimensional radiographic studies do not fully capture the airway in all three spatial planes. The relationship between cervical spine angles, head posture, and sleep apnea severity could be better studied using 3-dimensional imaging and these investigations are yet to be carried out.

2. these studies utilized radiographs of patients in the upright position, which fails to show the true anatomic and physiologic relationship between the airway space and the soft and hard tissue during episodes of obstruction, when subjects are in the supine position for sleep. To our knowledge, there has been one published study comparing positional changes in airway dimension in sleep apnea patients.

3. the body of scientific knowledge on head posture, cervical spine angles, and neck length in sleep apnea patients is generally lacking and this knowledge could be important to improve sleep apnea diagnosis and produce predictable sleep apnea treatment outcomes.

3.2 Null Hypothesis

There are no associations among the variables of oropharyngeal airway dimensions, cervical spine angles (C1-C4), craniocervical posture, cervical spine length, and sleep apnea severity (AHI score). Furthermore, there are no differences in airway dimensions between the upright versus supine subject groups (UNMC and CFP-PGD, respectively).

3.3 Specific aims of current study

The objectives of this study is to determine the following:

- the association between demographic variables (age, gender, body mass index) and the following:

  - Sleep apnea severity
  - Oropharyngeal airway
  - Craniocervical posture
  - Cervical spine angles
  - Cervical spine length

- the effect of patient positioning (supine versus upright) on sleep apnea severity, oropharyngeal airway, craniocervical posture, cervical angles, and cervical spine length variables.
- the association between craniocervical posture and sleep apnea severity and oropharyngeal airway.
- the association between cervical spine angles and sleep apnea severity (AHI) and oropharyngeal airway.
- the association between cervical spine length and sleep apnea severity (AHI) and oropharyngeal airway.
- the association between cervical spine angles and craniocervical posture.
- validity of using the McRae line versus the McGregory line for measuring craniocervical posture.

Table 3.1 contains the description for each variable used in this study.

Table 3.1: Description of Variables

Clinic Variables		
	CFP and PGD	Subjects in both clinics are in the upright position during CBCT scans
	UNMC	Subjects are in the supine position during the MDCT scans
Demographic Variables		
	Age	Numerical age of patient
	Gender	Male or female
	BMI	Body Mass Index is a measure of fat based on height and weight
Sleep Apnea Variable		
	AHI	Apnea-Hypopnea Index is a numerical score which indicates of sleep apnea severity.
Airway Variables		
	TV	Total Volume of the oropharyngeal airway in mm^3
	MA	Minimum Area where the greatest airway constriction occurs, measured in mm^2
	MA (RU/RL)	Location of MA: RU is retro-Uvula, RL is retro-lingual
	uOP	Upper oropharyngeal airway volume in mm^3
	lOP	Lower Oropharyngeal airway volume in mm^3 (TV - uOP = lOP)
Craniocervical Posture Variables		
	MCG_OP	McGregor line to Odontoid Plane angular measurement
	MCR_OP	McRae line to Odontoid Plane angular measurement
	A_O_L	Skull base to posterior mid point of cervical vertebrae 1, in mm
Cervical Spine Angles		
	C1_C2	Cervical vertebrae 1 to cervical vertebrae 2 angle
	C2_C3	Cervical vertebrae 2 to cervical vertebrae 3 angle
	C3_C4	Cervical vertebrae 3 to cervical vertebrae 4 angle
	C1_C4	Cervical vertebrae 1 to cervical vertebrae 4 angle
Cervical Spine Length		
	C2_C3_L	Neck length from cervical vertebrae 2 to cervical vertebrae 3 in mm

CHAPTER 4: MATERIALS AND METHODS

4.1 IRB Approval

The University of Nebraska Medical Center Institutional Review Board (IRB) approved this study protocol (460-15-EX) prior to initiating this study.

4.2 Patient Selection

Subjects with both a completed sleep study, by either polysomnogram (PSG) or home sleep study (HST), and a three-dimensional radiographic scan, with either a multi-detector computed tomography (MDCT) or cone-beam computed tomography (CBCT), were included in this retrospective study. Both PSG and HST diagnostic methods produced an AHI score for evaluation of sleep apnea severity.

Four clinic sites (The University of Nebraska Medical Center Sleep Medicine Clinic – UNMC, The Craniofacial Pain Center of Nebraska – CFP, Pioneer Greens Dentistry – PGD, and The University of California-Los Angeles Radiology Department – UCLA) met the inclusion criteria and were invited to participate in this study. Three clinics (UNMC, CFP, and PGD) accepted our invitation. A fifth site, Dr. Mary Burns' New Hope Orthodontics, was included as backup in case insufficient subjects were identified from the other four sites. Subjects from this clinic partially met the inclusion criteria because they have CBCT scans but no sleep studies. Instead, OSA was evaluated using the Epworth Sleepiness Scale (ESS) survey.

A total of 221 subjects from three primary sites (UNMC – 186, CFP – 22, PGD – 13) were initially screened. Subjects with a history of surgical treatment for OSA (e.g. maxilla-mandibular advancement, uvulopalatopharyngoplasty, and/or other hard-soft tissue therapies), cervical spine surgeries (e.g. spinal fusion, disc replacement, and/or other spine related surgeries), cervical spine diseases or injuries (e.g. severe degenerative diseases, scoliosis, herniated discs, etc.), and other hard-soft tissue pathologies (e.g. cancer) were excluded from this study. Radiographs with low image quality or inadequate field of view of the airway were further excluded from the study. After applying the exclusion criteria, the final sample size totaled 28 subjects (UNMC – 11, CFP – 14, PGD – 3).

Notable differences existed among the clinics and are summarized in Table 4.1, which compares the 5 clinics in this study based on the radiograph quality, type of sleep study, and potential sample size. Greater preference was given to radiographs in the supine position, OSA diagnosis by PSG, and larger potential sample size.

UNMC and UCLA clinics scored higher because of better imaging protocols, better OSA diagnosis, and larger potential sample size. First, the radiographs from these sites scored higher because they were taken in the supine position, which more accurately reflects the airway dimension in sleep apnea, while the CFP, PGD, and New Hope Orthodontics clinic subjects scored lower because they are in the upright position during imaging. Both MDCT and CBCT radiographs generate 3-dimensional volumetric images but MDCT is superior for soft tissue contrast, which might be critical for some clinical conditions but is not critical for airway (empty space) evaluation. Second, the UNMC subjects were examined by sleep medicine physicians and diagnosed by overnight PSG (gold standard) while patients from other clinics were primarily diagnosed by home sleep studies. Again, the New Hope Orthodontic subjects scored the lowest due to the absence of sleep studies. Third, a significant sample size of 186 was identified from the UNMC clinic (described further below).

The patient selection process at each clinic site varied in complexity and is briefly described below. With the assistance of Dr. Purnima Guda, the UNMC selection process began with a computerized search through the medical center's electronic health records (Epic Systems, Madison, WI, USA) for subjects with PSG and head and/or neck CT CPT codes from January 2013 through December 2015. Next, exclusion criteria were applied based on various diagnostic codes and final MDCT scans were de-identified by an X-ray technician and exported for analysis (Figure 4.1). At the other sites, the subjects were manually searched and selected by the attending clinicians. Images were subsequently exported for analyses.

4.3 Image Acquisition

Radiographic scans varied by clinic. All University of Nebraska Medical Center Sleep Medicine Clinic (UNMC) radiographs were taken with either the GE Lightspeed Pro or GE V CT (GE Healthcare, Chicago, IL, USA), which varied by the number of detectors on board, 16 versus 64 respectively. For head CT's, the scan field of view (FOV) is 32 cm and reconstruction is 25 cm with a 0.48mm voxel size. CT head typically captures the image from the vertex of the cranium to about cervical vertebrae 2. For CT neck, the scan field of view is 50cm and the reconstruction is 36cm with a 0.48mm voxel size. CT neck typically captures the image from above sella to the carina. All image acquisitions were performed by one of 18 trained radiology technicians in the radiology department. Subjects were instructed to lie down in the supine position with head rested gently on a towel without any head positioner. Subjects were instructed to adjust themselves into the most comfortable position before scanning. During scanning, which took about 10-15 seconds, subjects were instructed to hold very still to prevent motion artifact.

All radiographic scans from the Craniofacial Pain Center of Nebraska (CFP) were taken with the i-CAT 17-19 CBCT (Imaging Sciences International LLC, Hatfield, PA, USA) with a field of view of 23 cm x 17 cm and a voxel size of 0.3 mm. Subjects were instructed to stand upright and to look straight ahead as if looking into a mirror. They were adjusted to have Frank-Horizontal plane parallel to the floor if possible.

All radiographic scans from the Pioneer Greens Dentistry Clinic were taken with the Galileos GAX5 CBCT (Sirona Dental, Long Island City, NY, USA) with a field of view of 15cm x 15 cm and a voxel size of 0.15mm. Subjects were instructed to stand upright with relaxed back and shoulders and to look straight as if looking into the distant. Subjects would then bite into a bite block to fix the head position.

All radiographic scans from Hope Orthodontics (Dr. Mary Burns) were taken with the Kodak CBCT machine (Carestream Health, Toronto, Canada) with a field of view of 18.4 cm x 20.6 cm and a voxel size of 0.3mm.

All scans from participating clinics were exported in the DICOM file format for analysis in Anatomage Invivo 5 and Dolphin 11.8 Premium.

4.4 Image Analysis

4.4.1 Blinding of Examiner

Both examiners (BL and KS) were blinded to the subjects' age, gender, BMI and AHI values during measurements of the airway parameters, craniocervical posture, cervical spine angles, and cervical spine length. This ensured an unbiased assessment of outcomes. The subjects' demographic information and AHI scores were entered into the database after all measurements were completed.

4.4.2 Testing for Accuracy in the CT Scans of UNMC Subjects

Three significant challenges were encountered while evaluating the images. First, a number of 3-D reconstructions of UNMC maxillofacial and head CT scans showed distortions in both Anatomage and Dolphin, specifically in the A-P dimension. However, the scout and axial images from the innate viewer did not show distortions (Figure 4.2). After consulting Dr. Michael Boska, Professor and Vice Chairman of UNMC Radiology Department, comparative measurements of an easily identifiable landmark were made to test the integrity of the measurements across the different viewing software. Antero-posterior dimensional measurement of the end plate (most inferior aspect) of cervical vertebrae 2 was made in the axial slice using the innate Soma Reviewer Embedded Edition Version 1.9.48.0 (Eagan, MN, USA), Anatomage Invivo Version 5.4.5 (San Jose, CA, USA), and Dolphin 11.8 Premium (Dolphin Imaging & Management Solutions, Chatsworth, CA, USA). The measurement results were 13.37 mm from the Soma Embedded Reviewer, 13.36 mm from Invivo5, and 13.37 from Dolphin (Figure 4.3).

All three measurements were nearly identical and proved that the integrity of the measurements was intact.

4.4.3 The Rationale for Switching from Anatomage to Dolphin

The second challenge occurred in cases where “data overflow” error (i.e. the inability of the software to distinguish between the CT gray values of the background and airway) was present. The Dolphin software with its integrated all-in-one capabilities was better suited for this task than the Anatomage software (Figure 4.3). The differences between the two software are discussed below.

Airway measurements were initially performed in Anatomage Invivo 5 using two separate features – the airway analysis tool for minimum cross-sectional area (MA) measurement and the polygonal sculpting tools for volume measurements. However, each tool has its own advantages and disadvantages. The airway analysis tool was good for determining the MA, but it lacked the ability to reliably and specifically set the airway boundaries, which was critical for determining the location of the MA. On the contrary, the polygonal sculpting tool was good for isolating and determining the airway volume but lacked the ability to calculate the MA. The Dolphin 11.8 Premium software overcame the shortcomings of Anatomage by combining both of these features into one tool.

Our positive experience with the Dolphin software was validated in a study which compared the accuracy of 6 popular imaging software (including Dolphin and Anatomage) used for 3-dimensional analysis. While all six showed high reliability and accuracy, Dolphin showed greater accuracy (smaller error) than Anatomage (Weissheimer, Menezes et al. 2012).

In summary, the Dolphin software was superior for usability, accuracy, and reliability in all situations of airway analysis.

4.4.4 Airway Measurements Using Anatomage Invivo 5

The systematic procedures for identifying, isolating, and measuring the airways were similar in both Anatomage and Dolphin. A brief description of both software methodologies is provided below.

To identify the airway, all scans were first oriented in the mid-sagittal plane using the incisive canal and cervical vertebrae 2 (C-2) as guiding landmarks. The radiolucent airway was easily visualized due to its contrast with the surrounding radiopaque soft and hard tissues (Figure 4.5). Ideally, all scans should be re-oriented along the Frankfort Horizontal plane (Grauer, Cevidanes et al. 2009). However, the UNMC CT neck had a limited field of view and Frankfort-Horizontal plane could not be constructed.

To determine the MA, the airway assessment tool was used by selecting points within the area of interest along the path of the airway. The first and last points set the upper and lower boundaries of the airway. The program automatically calculates the total volume (cc) and the most constricted area (mm^2) shown in Figure 4.5.

To ensure reproducibility of the measurements, the oropharyngeal airway boundaries were chosen based on easily identifiable hard and soft tissue landmarks described in another study (Guijarro-Martinez and Swennen 2013). Table 4.2 describes in detail a modified description of the superior, inferior, anterior, and posterior landmarks used in this study. The total volume is furthered partitioned into the upper (uOP) and lower (lOP) oropharyngeal airway volume (TV = uOP + lOP). The upper and lower oropharyngeal airway are separated by a horizontal plane, parallel to the horizontal aspect of the radiograph, extending from the base of the soft palate and uvula back to the adjacent cervical vertebrae (Figure 4.6). The lower oropharyngeal airway volume is the difference between total airway volume and upper oropharyngeal airway volume.

In Anatomage, the total airway volume was determined using the polygonal sculpting tool to isolate the region of interest using the boundaries described above (Figures 4.7). First, color inversion was used to increase contrast of the airway and to better differentiate the airway from the adjacent hard and soft tissues. Second, unrelated soft and hard tissues were cropped away in the axial, sagittal and coronal planes such that the final product is an isolated airway. Lastly, the software calculated the total volume using the Hounsfeld Unit (HU) parameter of -1000 and -603 (Hart, McIntyre et al. 2015).

4.4.5 Airway Measurement Using Dolphin 11.8

The Dolphin airway measurement tool consisted of three simple steps. First, the boundaries for the total, upper, and lower oropharyngeal airway are set according to the same landmarks described above. Second, a number of "seeds" are placed within the selected area of interest. Third, the threshold value was adjusted using the interactive threshold interval technique (El and Palomo 2010). The airway volumes were then automatically calculated (Figure 4.8). To calculate the MA, the same boundaries in the prior steps are maintained. The upper and lower limits are selected and the MA tool is activated.

The third challenge was encountered with CT neck from 4 UNMC subjects. These radiographs had a limited FOV, which failed to capture PNS. We found in a preliminary study that the palatal plane (ANS to PNS) is related to the tip of the odontoid process (Appendix A). Therefore, a modified technique was used whereby the superior boundary was constructed from the tip of the odontoid process, extending parallel to the horizontal border of the film, to the anterior most border of the film. The anterior border followed the outline of the anterior most aspect of the airway down to the tip of the epiglottis (Figure 4.9). All other boundaries remained the same.

4.4.6 Cervical Spine Angle Measurements Using Dolphin 11.8

In the four-panel view, all radiographs were oriented to the mid-sagittal plane of the cervical spine using the odontoid process of C2 in the coronal slice and the incisive canal in the sagittal slice (Figure 4.8, top). Four angular measurements (C1-C2, C2-C3, C3-C4, and C1-C4) were made using the horizontal lines bordering the superior and inferior borders of each cervical spine vertebrae (Figure 4.10). Cervical angles were assigned the standard kinematic nomenclature in a right-handed Cartesian coordinate system, with lordotic (extension) angles denoted the "-" sign while kyphotic (flexion) angles were denoted the "+" sign (Jackson, Harrison et al. 1993).

4.4.7 Craniocervical Posture Measurements Using Dolphin 11.8

Using the same mid-sagittal view in the cervical spine angle analysis, three craniocervical posture measurements were made. The first two measurements utilized the Rocabado analysis, which consists of an angular and linear measurement. The angular measurement consisted of the McGregor line to the odontoid plane. The linear measurement consisted of a line from the base of the occipital bone to the mid-point of the posterior arch of cervical vertebrae 1. A third measurement, the McRae to odontoid plane angle, was added because PNS was not present in a number of radiographic scans. Figure 4.11 provides detailed descriptions of all craniocervical posture landmarks.

4.4.8 Cervical Spine Length Using Dolphin 11.8

Using the same mid-sagittal view in the previous analyses, the cervical spine length was measured from the tip of the odontoid process of cervical vertebrae 2 to the mid-point, along the inferior border of cervical vertebrae 3 (Figure 4.12).

4.8 Method Error

Intra-examiner and inter-examiner reliability tests were performed to assess the reproducibility of identifying the hard and soft tissue landmarks used in each measurement. For intra-examiner reliability, ten subjects from the three clinics (UNMC – 3, CFP – 6, PGD – 1) were randomly selected two weeks after initial evaluation for repeated measurements of all airway, craniocervical posture, cervical spine angle, and cervical spine length measurements. For inter-examiner reliability, two examiners (B.L. and K.S.) independently repeated all measurements on the same ten subjects. Pearson correlation coefficient was calculated for each variable.

4.9 Statistical Analysis

Fisher exact test was use for the comparison of categorical data due to small sample size. For continuous variables, if data are normal, t-test was used for comparison. If data were not normally distributed, we used nonparametric method. Spearman correlation was used for describing the monotone relationship among numerical variables. Data were analyzed on SAS®9.4 by our study statistician Dr. Jiangtao Luo.

	New Hope Orthodontics	Craniofacial Pain Center	Pioneer Greens Dentistry	UCLA Oral & Maxillofacial Radiology	UNMC Sleep Medicine Clinic
Radiographs Supine (S) Upright (U)	CBCT (U)	CBCT (U)	CBCT (U)	CBCT (S)	MDCT (S)
Diagnosis of OSA	ESS	HST	HST	PSG/HST	PSG
Sample size	36 (20M, 16F)	14	3	~15	11
Overall Score	+	++	++	+++	++++

Table 4.1: Comparison of the five clinic sites

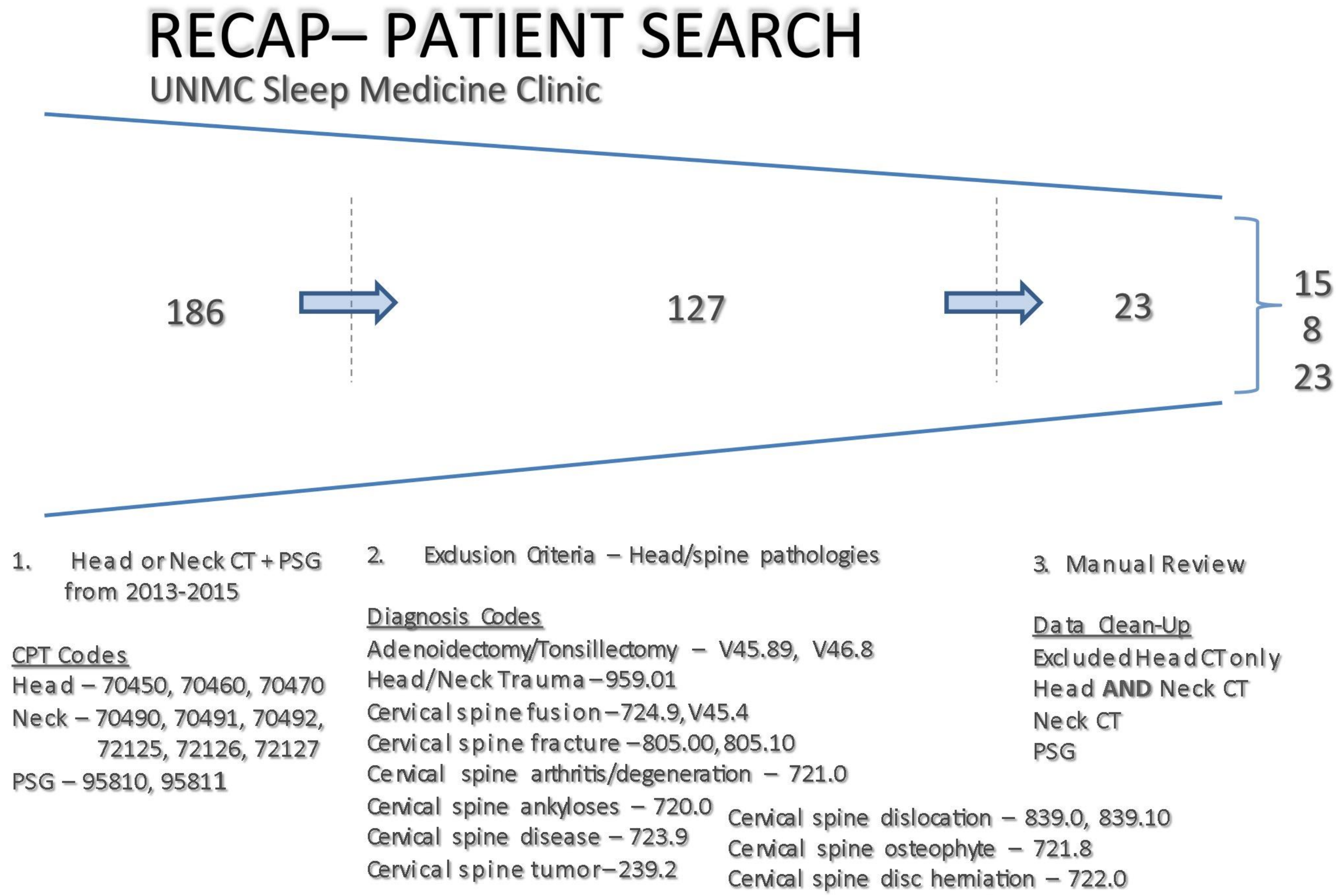


Figure 4.1: UNMC patient filtering process

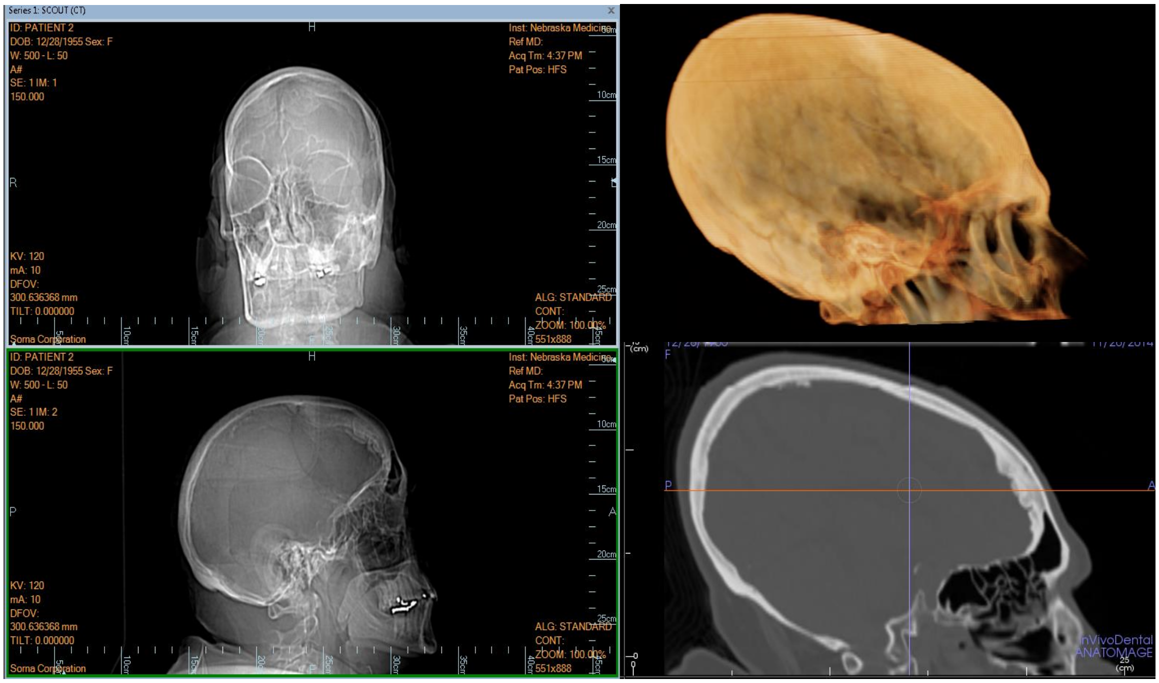


Figure 4.2: Normal views from the scout (left) and distorted 3-D reconstruction (right) from the same UNMC Maxillofacial CT's

Figure 4.3: Comparison of measurement accuracy between innate viewing software (top) and Anatomage (bottom).

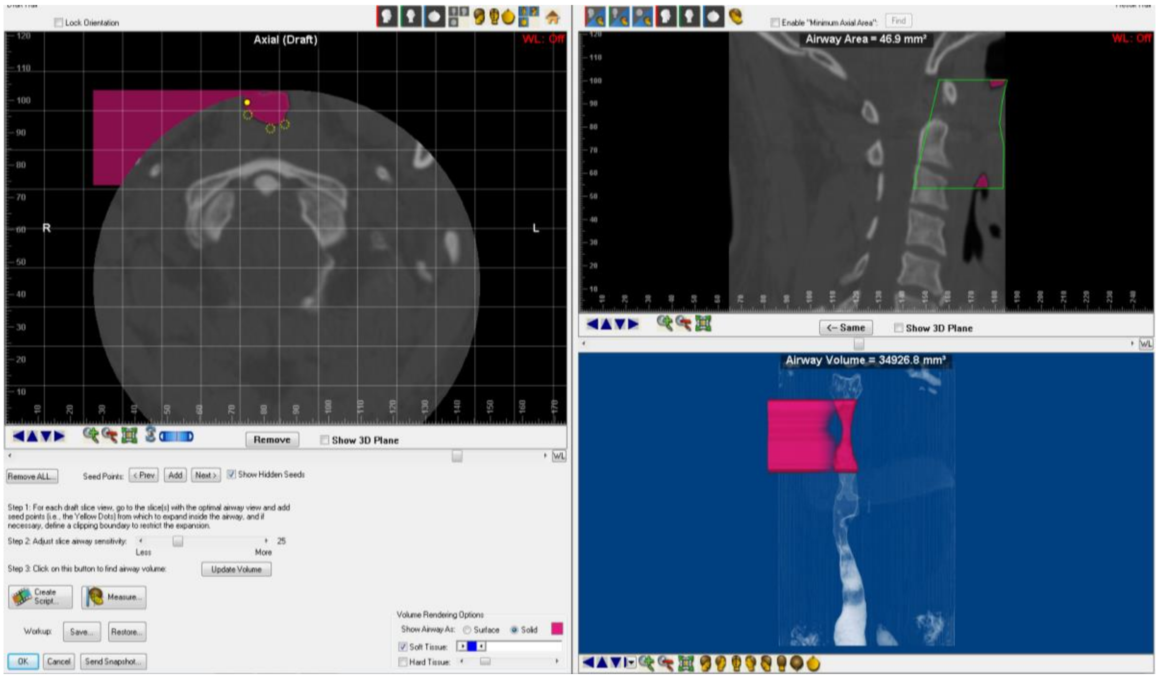


Figure 4.4: Addressing the "data overflow error" in the MDCT scans using Dolphin Premium. Data overflow error occurs when the software fails to distinguish between the pharyngeal airway and the background based on the gray value level.

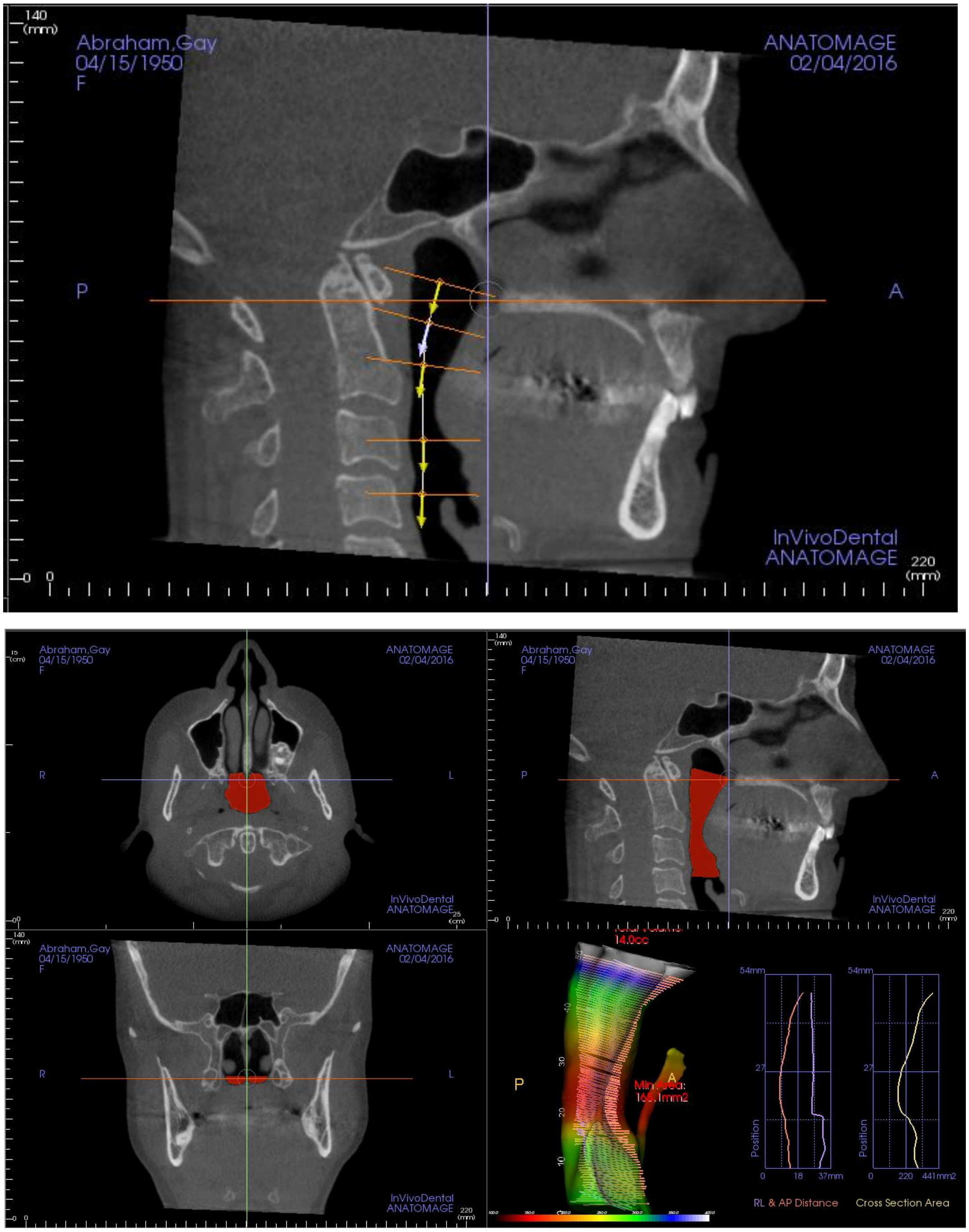


Figure 4.5: Total airway and minimum area measurements using Anatomage Invivo5 airway measurement tool. Points are selected along the area of interest (top) and airway volumes are analyzed (below).

	Boundaries	Plane	Landmarks
Total Volume	Superior	Saggital	Posterior nasal spine (PNS) to the tip of the Odontoid process
	Inferior		Tip of the epiglottis to the posterior border of the adjacent cervical vertebrae along a plane parallel to the horizontal border of the film
	Anterior		PNS to the tip of the epiglottis
	Posterior		Posterior border of the cervical vertebrae at the level of epiglottis to the tip of the odontoid process
Upper Oropharyngeal Volume	Superior	Sagittal	PNS to the tip of the Odontoid process
	Inferior		The base of the uvula to the posterior border of the adjacent cervical vertebrae along a plane parallel to the horizontal border of the film
	Anterior		PNS to the base of the uvula
	Posterior		Posterior border of the cervical vertebrae at the level of uvula to the tip of the odontoid process
Lower Oropharyngeal Volume	Superior	Sagittal	The base of the uvula to the posterior border of the adjacent cervical vertebrae along a plane parallel to the horizontal border of the film
	Inferior		Tip of the epiglottis to the posterior border of the adjacent cervical vertebrae along a plane parallel to the horizontal border of the film
	Anterior		Base of the uvula to the tip of the epiglottis
	Posterior		Posterior border of the cervical vertebrae at the level of epiglottis and uvula

Table 4.2: Cephalometric landmarks for the borders of the oropharyngeal airway

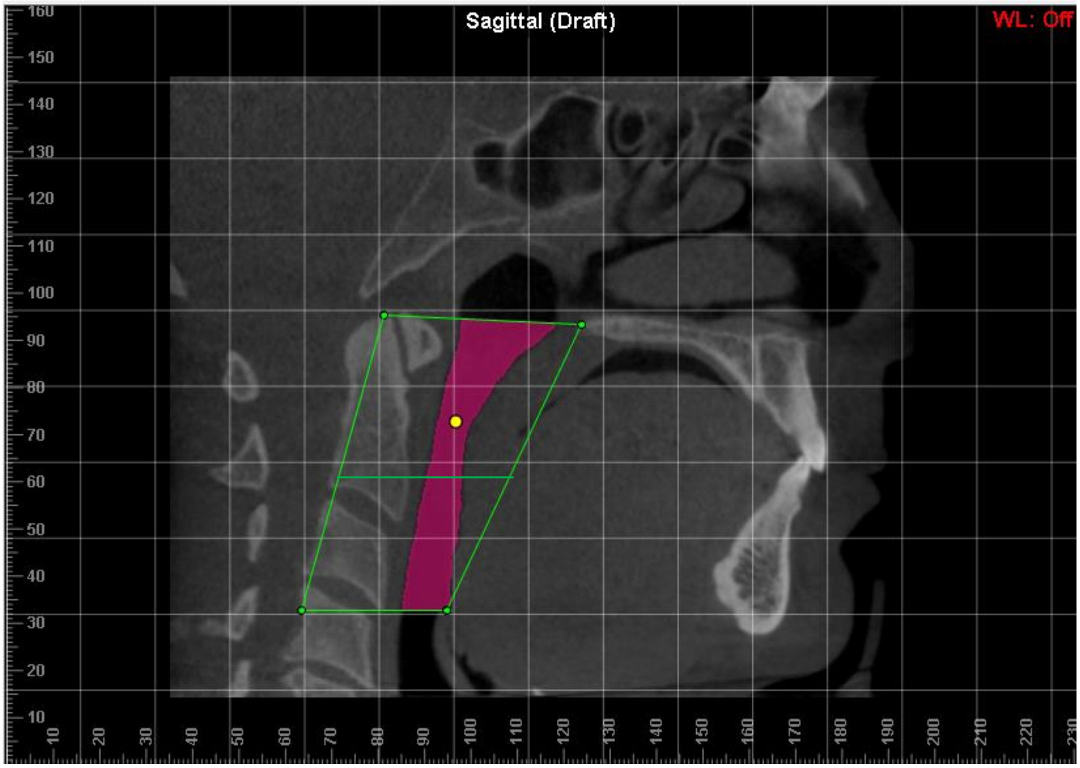


Figure 4.6: Delineating between the upper and lower oropharyngeal airway spaces in Dolphin Software. A horizontal plane, parallel to the horizontal border of the film, at the level of the base of the uvula separates the upper and lower oropharyngeal airway.

Figure 4.7: Airway measurements using Anatomage polygonal sculpting tool. Regions of interest can be initially isolated by cropping away unrelated structures (top). Color inversion allows for contrast between airway and soft tissue structures (middle). The final cropped airway and related volume measurements are at the bottom.

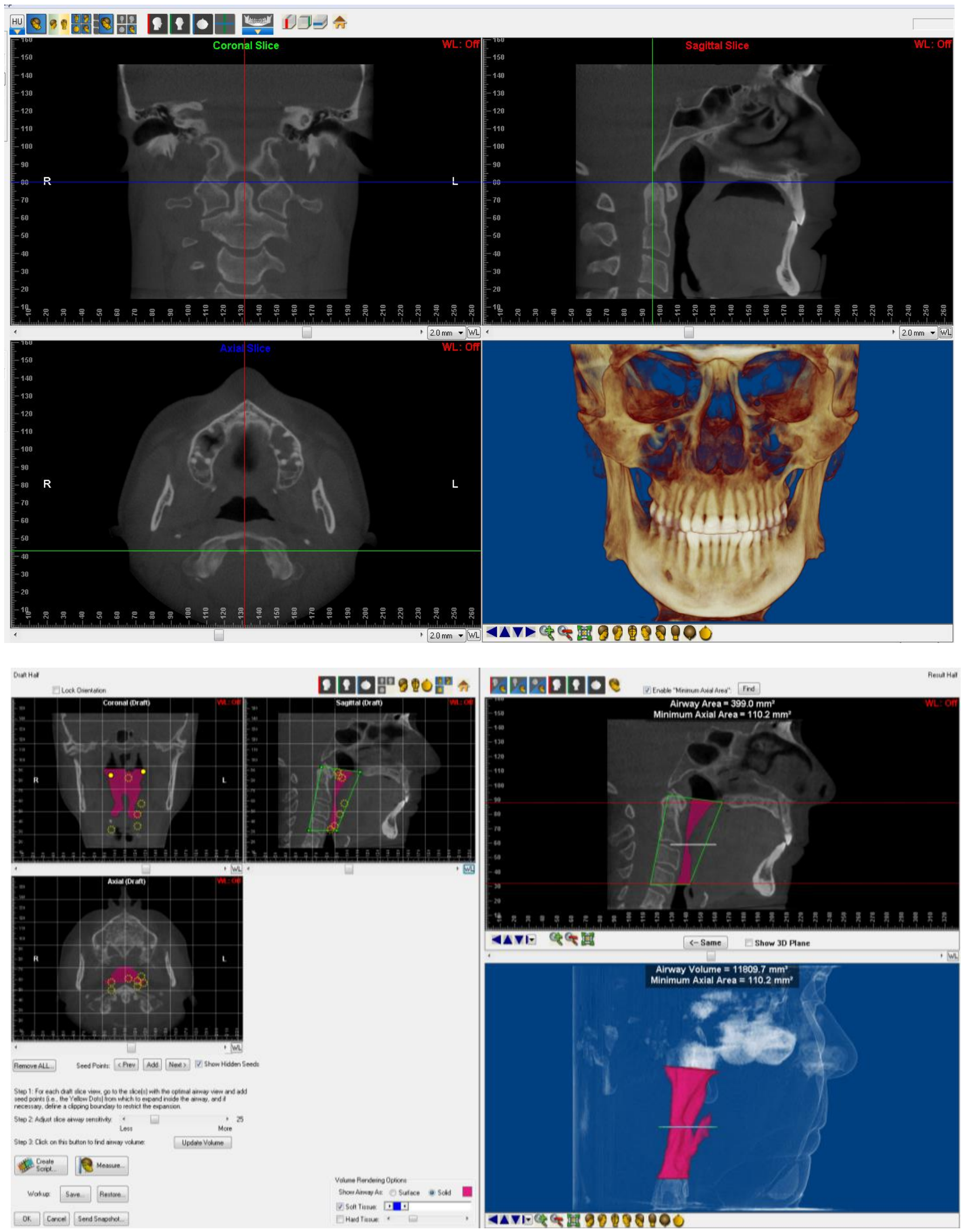


Figure 4.8: Evaluation of the total, upper, and lower oropharyngeal airway spaces in Dolphin Software. The midsagittal plane is set using the 4-panel view to visual the odontoid process and incisive canal (top). The airway volume and minimal cross sectional area tools are located all in one area (bottom).

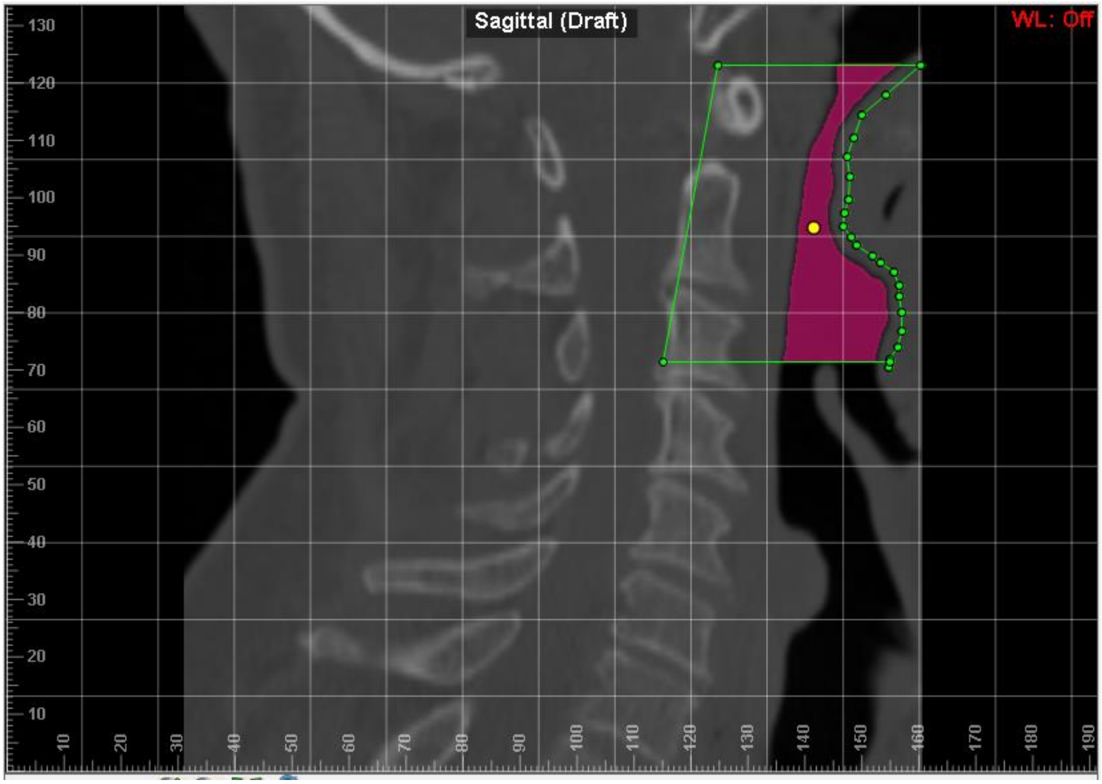


Figure 4.9: Modified method for airway assessment in Dolphin. PNS was not captured in 4 UNMC subjects. The anterior border was modified and was traced along the soft tissue border of the pharyngeal airway.

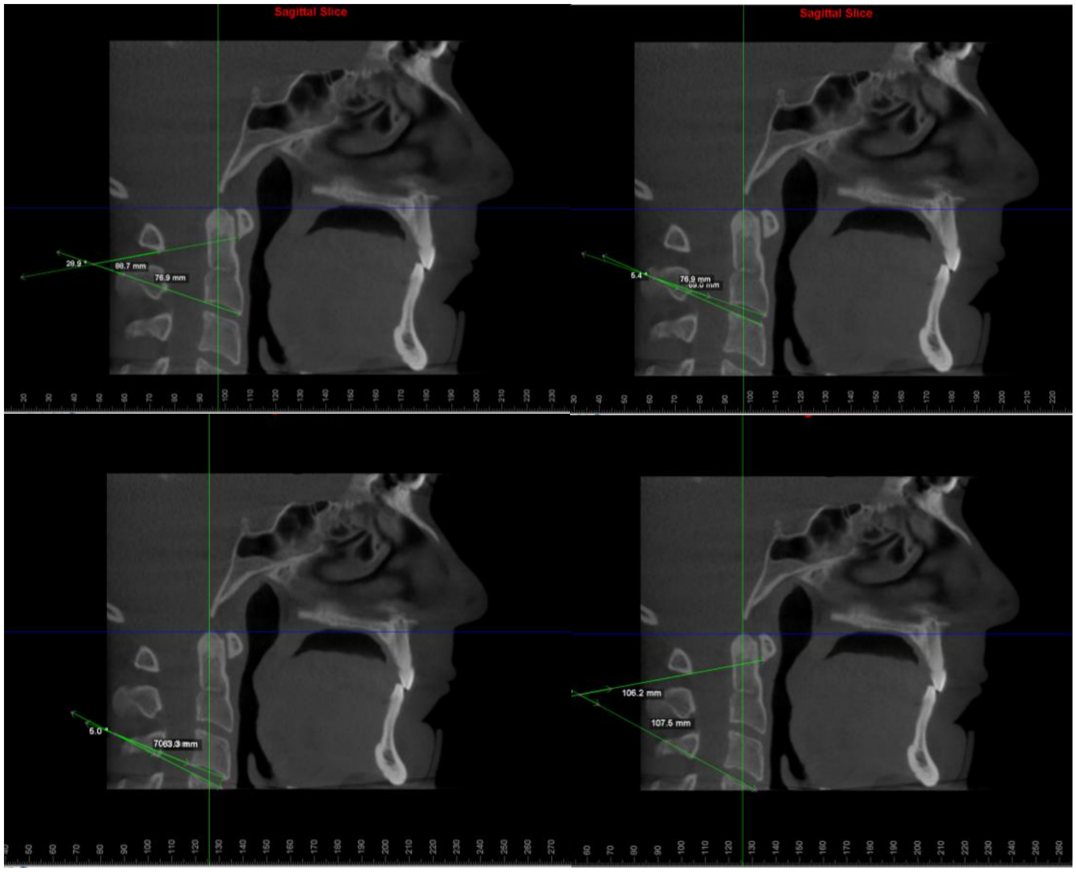


Figure 4.10: Cervical spine angles analysis. C1-C2 (top left), C2-C3 (top right), C3-C4 (bottom left), and C1-C4 (bottom right) spinal angles are determined by drawing horizontal tangent lines to the superior and inferior borders of each respective cervical vertebrae and measuring the angles between each line.

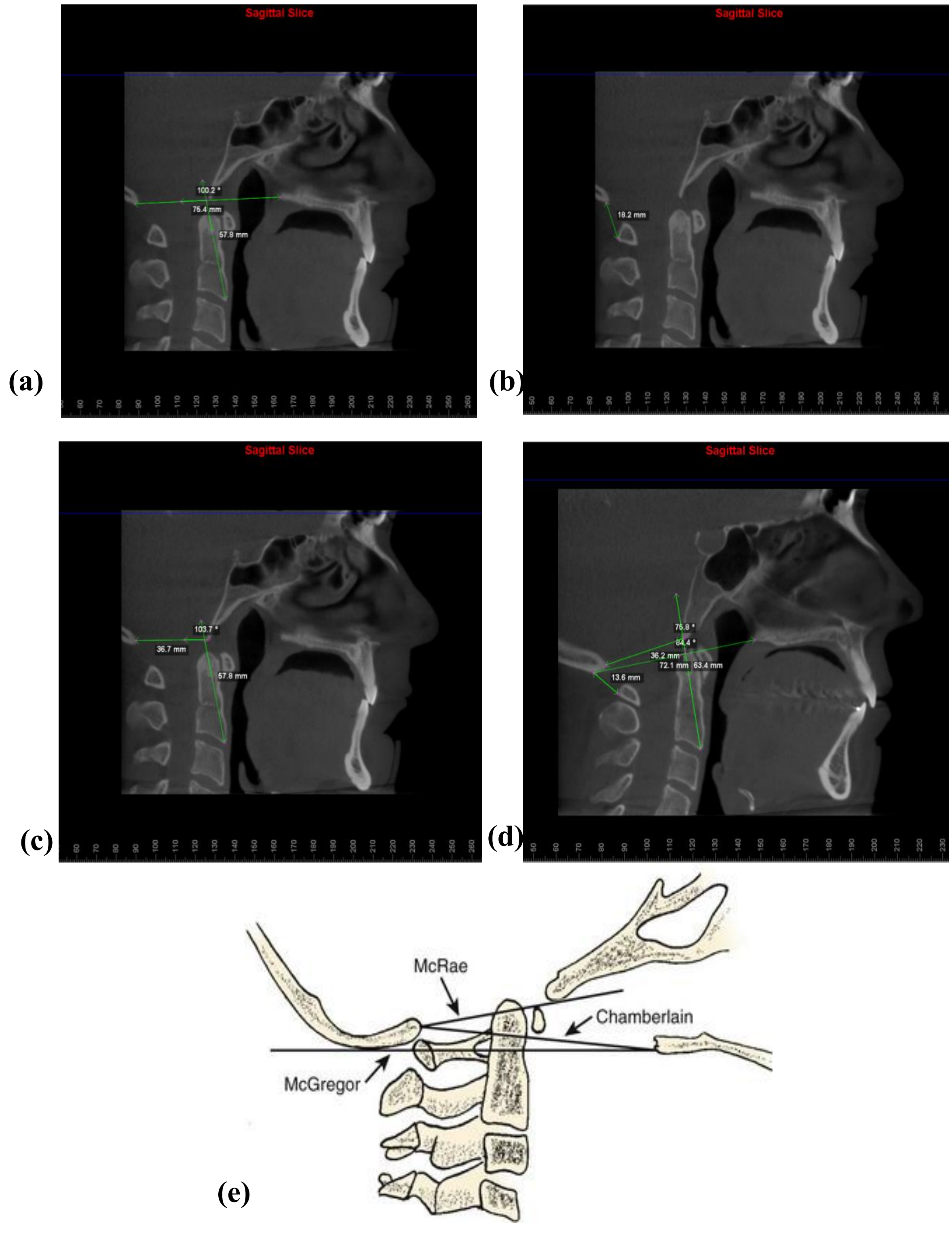


Figure 4.11: Craniocervical posture analysis. Craniocervical angle (a) is measured from the intersection between McGregor line (PNS-occipital base) and odontoid plane (tip of C2 to anterior-inferior point). AO length (b) is measured from the base of the occipital bone to the posterior arch of Atlas (C1). When PNS is not present, the McRae line (e) is used instead. The McRae line is drawn from basion to opisthion (c). Both the McRae and McGregor line angles are measured in all scans when possible (d).

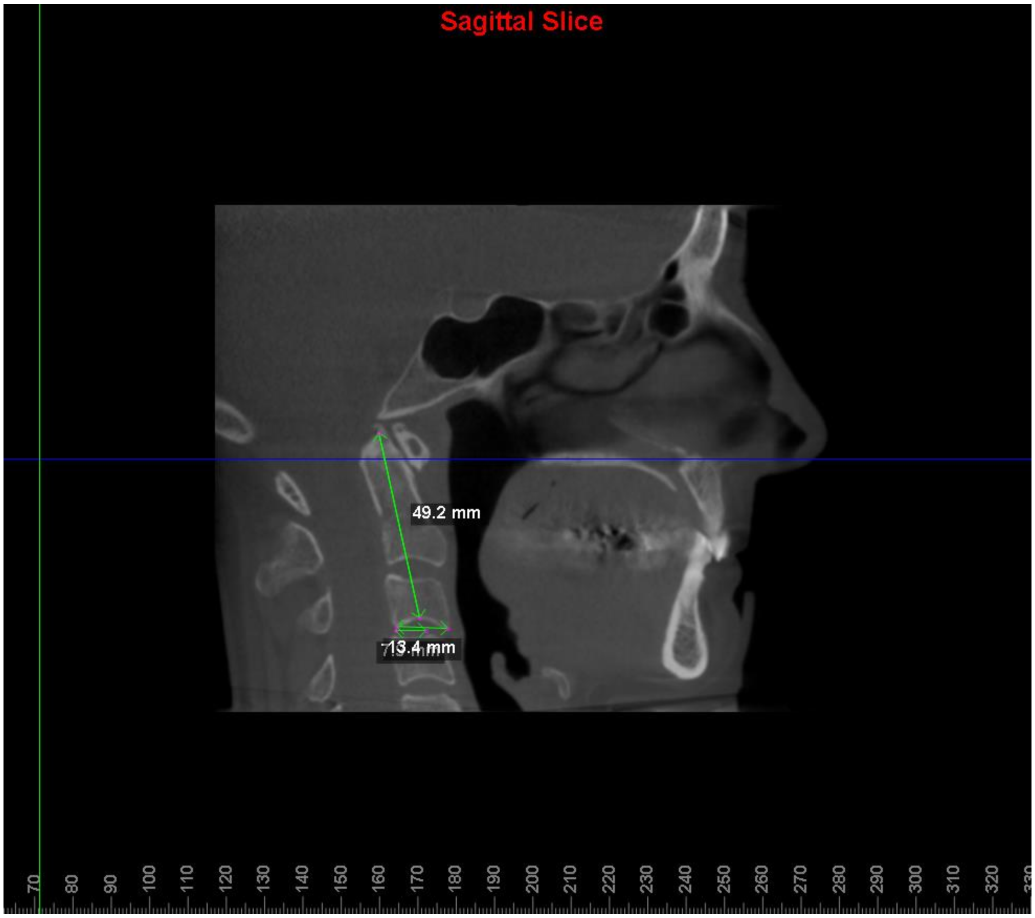


Figure 4.12 : Cervical spine length analysis. The cervical spine length is measured from the tip of the odontoid process of C2 to the mid-point along the inferior end plate of C3.

CHAPTER 5: RESULTS

5.1 General Description of Study Subjects

A total of 28 subjects (17 females, 11 males) were included in this study. The mean age of the "normal" (N=7) sleep apnea group is 39.7 years, the "mild" (N=9) group is 47.6 years, the "moderate" (N=7) is 59.3, and the "severe" (N=5) group is 49.2 years. The mean BMI of the normal group is 31.6, mild group 25.3, moderate 29.1, and severe 30.8.

5.2 Associations between Demographic Variables and Sleep Apnea Severity, Airway Variables, Craniocervical Posture Variables, Cervical Spine Angles, and Cervical Spine Length.

5.2.1 Association between Sleep Apnea Severity (AHI Score) and Demographic Variables (age, gender, and BMI).

Using the nonparametric test, a statistically significant difference (p=0.0384) in AHI score was observed between the male and female groups (11 versus 17, respectively). A summary of the distribution of the Wilcoxon Scores is shown in Figure 5.1. A weak statistical correlation was noted for sleep apnea severity and age (Figure 5.2). No correlation was noted for AHI and BMI.

5.2.2 Association between Airway Variables and Demographic Variables (Age, Gender, and BMI).

No significant associations were noted between total volume and age, gender (p=0.1216), and BMI. No significant associations were noted between minimum cross-sectional area and age (p=0.5185), gender (p=0.6720), and BMI (p=0.1971). No significant associations were noted between location of minimum cross-sectional area and age (p=1), gender (p=0.1741), and BMI (p=0.2607). No significant associations were noted between upper oropharyngeal airway volume and age (p=0.5800), gender (p=0.3880), and BMI (p=0.6119). No significant associations were noted between lower oropharyngeal airway volume and age (p=0.7745) and gender (p=0.0713).

There is a trend that as oropharyngeal airway volume decreases as BMI increases; however, the association is not statistically significant (p=0.0763, Pearson) probably due to a small sample size or an outlier.

5.2.3 Association between Craniocervical Posture Variables and Demographic Variables.

A significant association and Pearson correlation of -0.4405 (p=0.0314) was noted between the McGregor-Odontoid plane angle and BMI (Figure 5.3), but not with age (p=0.6545, Pearson) and gender (p=0.6547, nonparametric test). A significant association and Pearson correlation of -0.4852 (p=0.0089) was noted between between the McRae-Odontoid Plane angle and BMI (Figure 5.4), but not with age (p=0.467, Pearson) and gender (p=0.9406, t-test). A significant negative correlation of -0.5960 (p=0.0008, Spearman) was noted between AO length and BMI (Figure 5.5), but not with age (p=0.5628, Spearman) and gender (p=0.6338).

5.2.4 Association between Cervical Spine Angles and Demographic Variables.

No significant associations were noted between C1-C2 angle and age (p=0.4753, Spearman), gender (p=0.6213, nonparametric), and BMI (p=0.4018 Spearman).

A significant negative correlation of -0.4903 (p=0.0081, Pearson) was noted between C2-C3 angle and age (Figure 5.6), but not gender (p=0.5944) and BMI (p=0.9081).

No significant association was noted between C3-C4 angle and age (p=0.835), gender (p=0.7376), and BMI (p=0.9713).

A significant negative correlation of -0.3935 (p=0.0383) was noted between C1-C4 angle and age (Figure 5.7), but not gender (p=0.2566) and BMI (p=0.9691).

5.2.5 Association between Cervical Spine (C2-C3) Neck Length and Demographic Variables.

No significant association was noted between C2-C3 length and age (p=0.3610) and BMI (p=0.3939). A significant difference (p=0.0001) in C2-C3 length was noted between male (mean 55.5± 4.5mm) and female (50.9± 3.6mm) subjects. All standard error bars represent the upper and lower 95% confidence intervals of each measurement (Figure 5.8). No significant association was noted between C2-C3 length and AHI score (p=0.2951).

5.3 Association between Craniocervical Posture Variables and Sleep Apnea Severity (AHI Score) and Airway Parameters.

5.3.1 Association Between Craniocervical Posture Variables and AHI Score

No significant relationship between craniocervical posture variables and AHI score either as a whole or adjusted by clinic.

5.3.2 Association between Craniocervical Posture Variables and Airway Variables

Total volume (p=0.0487), minimum cross-sectional area (p=0.0025) and upper oropharyngeal airway volume (p=0.0453) are positively correlated with the McGregor-Odontoid plane angle (Figures 5.9-5.11, respectively). Lower oropharyngeal airway volume is correlated with both the McGregor-Odontoid (p=0.0163) and McRae-Odontoid (p=0.0208) plane angles (Figures 5.12-13, respectively). McGregor-Odontoid angle, McRae-Odontoid angle, and AO length are not significantly related to the location of the minimum area by logistic regression model.

5.4 Correlation between McG_OP and McR_OP angles

The McG_OP and McR_OP angles are nearly perfectly correlated base on Pearson correlation analysis (0.7725, p<0.0001). See Figure 5.14.

5.5 Association between Cervical Spine Angles and Sleep Apnea Severity (AHI Score) and Airway Variables.

5.5.1. Association between Cervical Spine Angles and AHI Score

No significant associations were noted between C1-C2 (p=0.2096), C2-C3 (p=0.5288), C3-C4 (p=0.2843), and C1-C4 (p=0.2276) and AHI Score.

5.5.2 Association between Cervical Spine Angles and Airway Variables

For total volume, no significant associations were noted between C1-C2 (p=0.9743), C2-C3 (p=0.6036), C3-C4 (p=0.3504), and C1-C4 (p=0.5258) and TV. For minimum area, no significant associations were noted between spinal angles and MA (p-values of 0.2977, 0.9651, 0.0628, and 0.7633, respectively. For location of minimum area, no significant associations were noted between spinal angles and MA (RU/RL) (p-values of 0.6243, 0.1558, 0.4883, and 0.2126, respectively). For upper oropharyngeal airway volumes, no significant association was noted between spinal angles and uOP (p-values of 0.6307, 0.4812, 0.5997, and 0.8558, respectively). For lower oropharyngeal airway volumes, no significant association was noted between spinal angles and lOP (p-values of 0.0620, 0.9339, 0.5246, and 0.5651, respectively).

5.6 Association between Cervical Spine Length (C2-C3) and Airway Variables

For total volume, a significant but weak positive association (p=0.04003) was noted between spine length and TV (Figure 5.15). For minimum area, no significant association was noted between spine length and MA (p=0.6760).

For MA location, a significant positive association was noted between spine length and MA(RU/RL). For every unit increase of C2-C3 length, the odds of RL to RU is expected to increase 1.767 with 95% confidence interval.

For upper oropharyngeal airway volume, a significant positive association (p=0.0366) was noted between uOP and spine length (Figure 5.16). However, no significant relationship (p=0.3294) was noted between lower oropharyngeal airway volume and cervical spine length.

5.7 Association between Craniocervical Posture and Cervical Spine Angles

A significant positive association of 0.5521 (Pearson, p=0.0052) was noted between McG_OP and C1-C2 angles (Figure 5.17). Similarly, a significant positive association of 0.5768 (Pearson, p=0.0032) was noted between McR_OP and C1-C2 angles (Figure 5.18). The McG_OP is significantly correlated (0.5238) with AO length at the p=0.0086 level. No other associations were noted.

5.8 Clinic Differences (UNMC versus CFP-PGD) in Demographic Variables, Sleep Apnea Severity, Craniocervical Posture, Cervical Spine Angles, and Cervical Spine Length.

5.8.1 Clinic Differences with Demographic Variables (Age, Gender, BMI).

A significant difference (p=0.0382) in BMI was noted between the UNMC (33.5 $\pm$ 10.4) and CFP-PGD (25.8 $\pm$ 4.8) subjects (Figure 5.19). No significant differences (p=0.4268) in the age were noted between UNMC (45.9 $\pm$ 16.7) and CFP-PGD (50.7 $\pm$ 14.4) subjects. No significant differences (p=0.7011, Fisher exact test) in gender was noted between the UNMC and CFP-PGD clinics.

5.8.2 Clinic Differences in Sleep Apnea Severity (AHI score).

No significant differences (p=0.5459) in AHI score were noted between the UNMC (21.4 $\pm$ 32.2) and CFP-PGD (17.2 $\pm$ 18.1) subjects.

5.8.3 Clinic Differences in Airway Variables

Total Volume – A significant mean difference (p=0.0071) of 3,677.0 mm^3 in total airway volume was noted between the UNMC (6,398.6 $\pm$ 2,868.1 mm^3) and CFP-PGD (10,075.6 $\pm$ 3,467.0 mm^3) subjects (Figure 5.20).

Upper Oropharyngeal Volume – A significant mean difference (p=0.0099) of 2,893.1 mm^3 in upper oropharyngeal airway volume was noted between the UNMC (3,835.2 $\pm$ 2,558.9 mm^3) and CFP-PGD (6,728.2 $\pm$ 2,561.6 mm^3) subjects (Figure 5.20).

Lower Oropharyngeal Volume – No significant difference (p=0.2576) in lower oropharyngeal airway volume was noted between the UNMC (2563.5 $\pm$ 1,583.8 mm^3) and CFP-PGD (3,347.3 $\pm$ mm^3) subjects (Figure 5.20).

Minimum Cross-Sectional Area – A significant mean difference (p=0.0099) of 50.7 mm^2 was noted between the UNMC (51.3 $\pm$ 36.8 mm^2) and CFP-PGD (102.0 $\pm$ 52.5 mm^2) subjects (Figure 5.21).

Location of Minimum Area – No significant difference (p=0.2576, Fisher) in the location of the minimum cross-sectional area was noted between the UNMC and CFP-PGD patients. In UNMC subjects, 91% had minimum areas in the retro-uvula versus 9% in the retro-lingual area. Meanwhile in CFP-PGD subjects, 71% had minimum areas in the retro-uvula versus 29% in the retro-lingual area (Figure 5.22).

5.8.4 Clinic Differences in Craniocervical Posture Variables.

A summary of craniocervical posture variables can be found in Figure 5.23.

McGregor-Odontoid Plane Angle – No significant difference (p=0.0753, t-test) in McGregor-Odontoid Plane Angle was noted between UNMC (89.5 ± 4.3 degrees) and CFP-PGD (97.3 ± degrees) subjects.

McRae-Odontoid Plane Angle – No significant difference (p=0.3388, t-test) in McRae-Odontoid Plane Angle was noted between UNMC (89.0 ± 7.5 degrees) and CFP-PGD (92.3 ± 9.5 degrees) subjects.

AO Length – No significant difference (p=0.1150, Wilcoxon) in AO length was noted between the UNMC (12.6 ± 3.5 mm) and CFP-PGD (14.2 ± 3.7 mm).

5.8.5 Clinic Differences in Cervical Spine Angles

A summary of all spinal angles can be found in Figure 5.24.

C1-C2 Cervical Spine Angle – No significant differences (p=0.1581, Wilcoxon) in C1-C2 cervical spinal angle was noted between the UNMC (-29.1 ± 3.3 degrees) and the CFP-PGD (-33.3 ± 8.4 degrees) subjects.

C2-C3 Cervical Spine Angle – No significant differences (p=0.1877, Wilcoxon) in C2-C3 cervical spine angle was noted between UNMC (-4.5 ± 4.0 degrees) and CFP-PGD (-5.8 ± 3.9 degrees) subjects.

C3-C4 Cervical Spine Angles – No significant differences (p=0.2333, t-test) in C3-C4 cervical spine angles was noted between UNMC (-4.1 ± 2.5 degrees) and CFP-PGD (-6.1 ± 6.1 degrees) subjects.

C1-C4 Cervical Spine Angles – No significant differences (p=0.0777, Wilcoxon) in C1-C4 Cervical Spine Angles was noted between UNMC (-33.9 ± 6.0 degrees) and CFP-PGD (-35.1 ± 26.1 degrees) subjects.

5.8.6 Clinic Differences with Respect to Cervical Vertebrae (C2-C3) Neck Length

No significant differences (p=0.7014, t-test) in C2-C3 neck length was noted between UNMC (53.1 ± 2.9 mm) and CFP-PGD (52.5 ± 3.9 mm) subjects (Figure 5.25).

5.9 Method Error

The mean intra-examiner reliability was 0.87 and ranged between 0.54-1.00. The mean intra-examiner reliability was 0.82 and ranged between 0.21-1.00.

Figure 5.1: Gender differences in AHI score

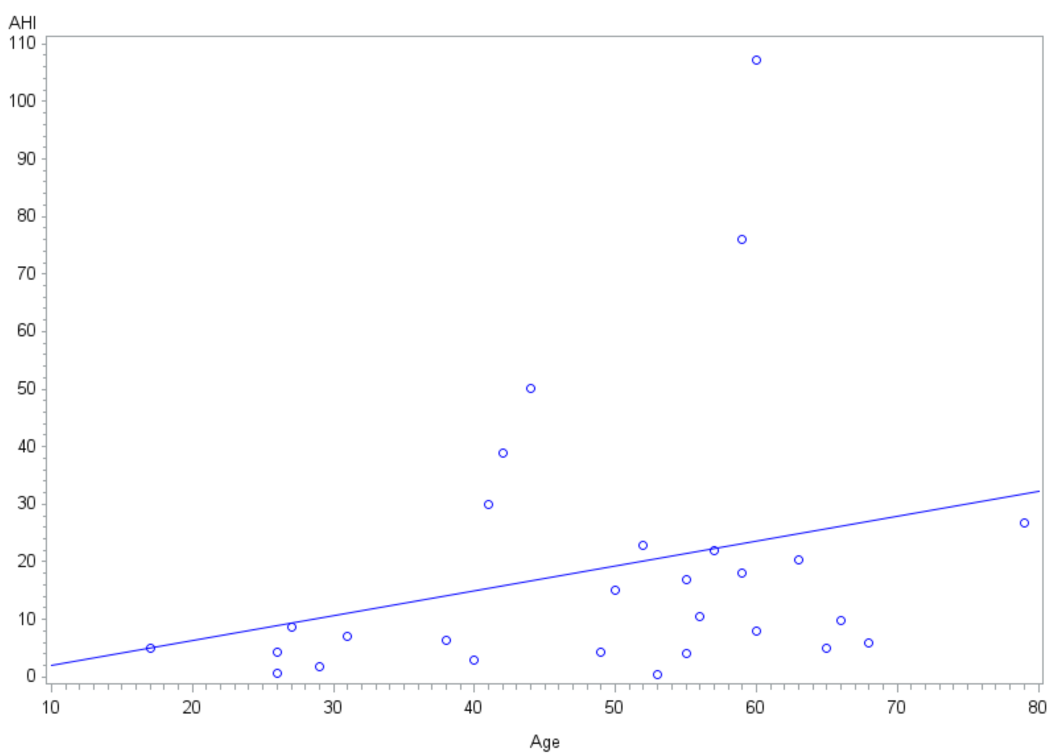


Figure 5.2: Significant positive association between AHI and Age

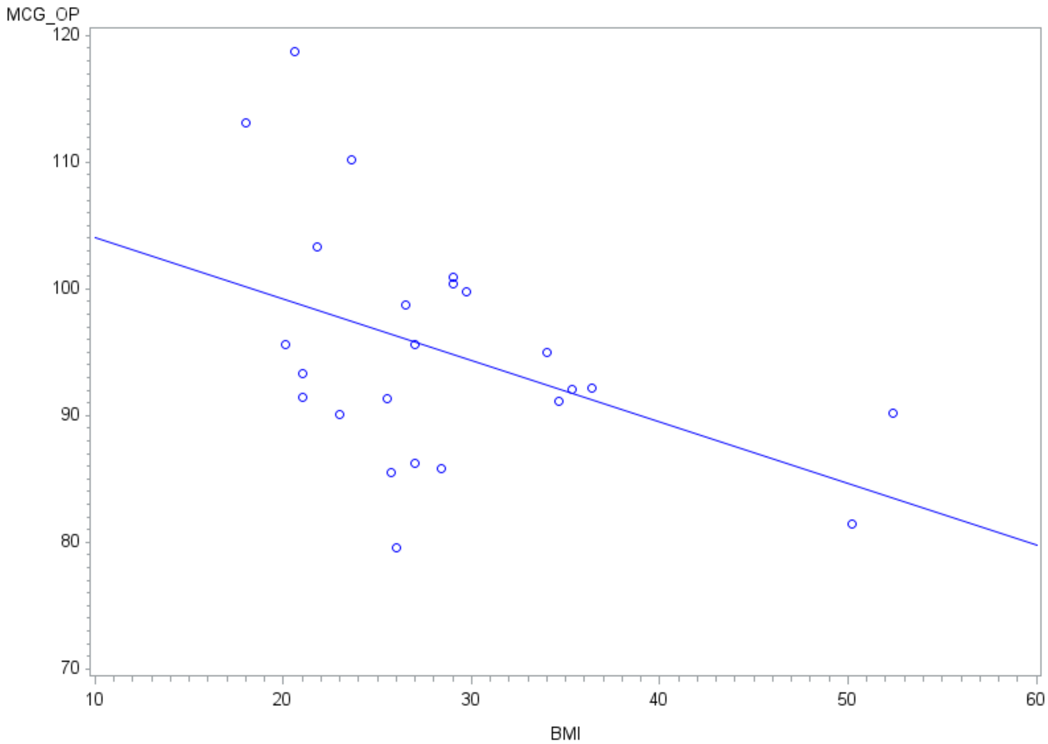


Figure 5.3: Significant negative association between Craniocervical Posture (McG) and BMI

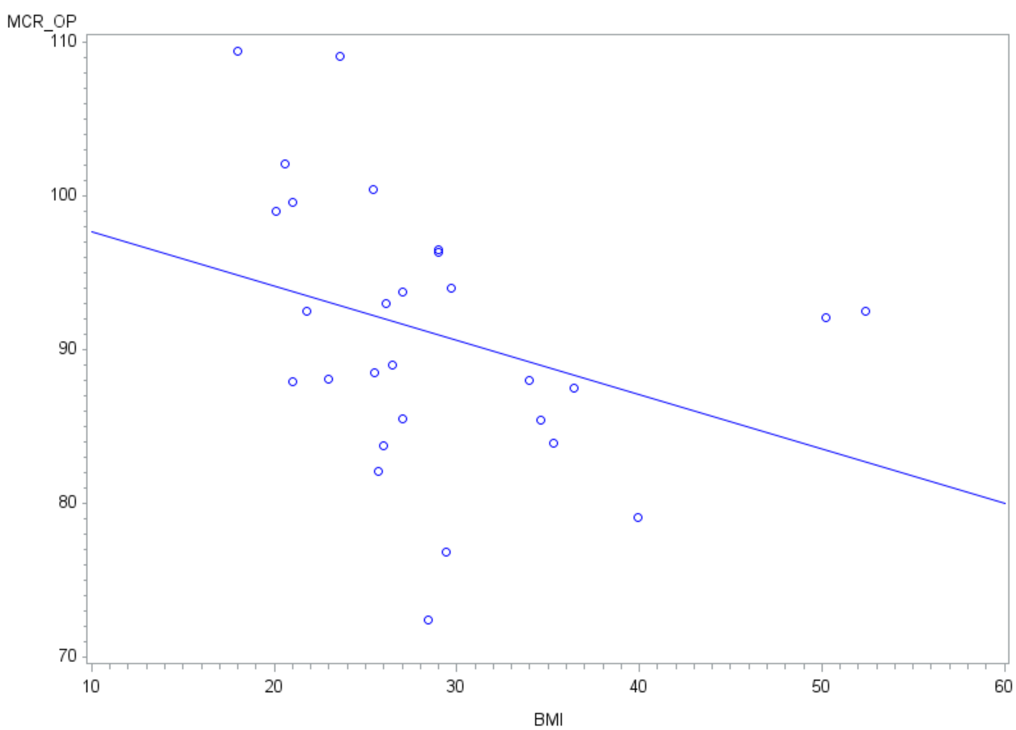


Figure 5.4: Significant negative association between Craniocervical Posture (McR) and BMI

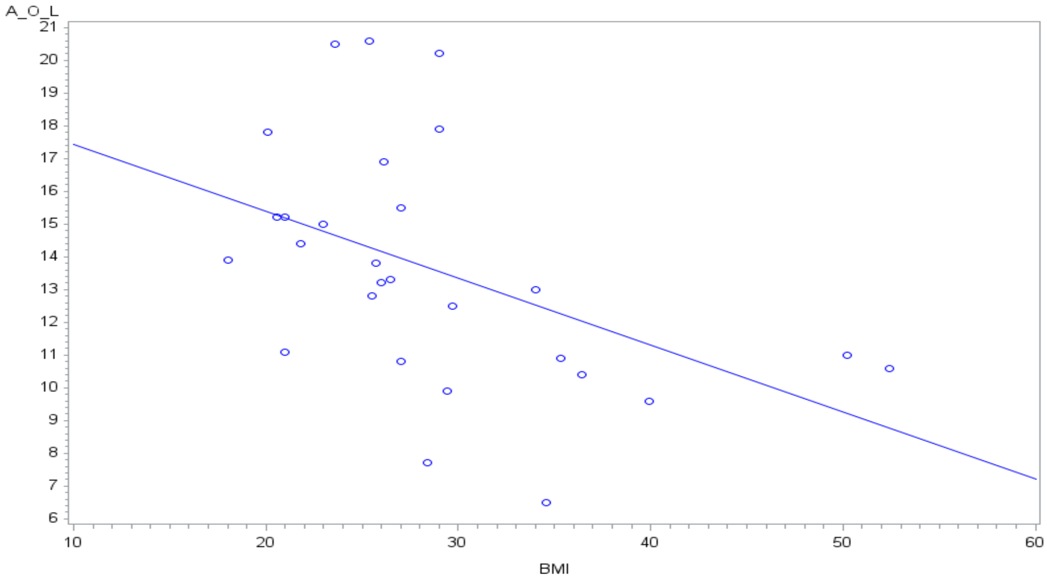


Figure 5.5: Significant negative association between Craniocervical Posture (AOL) and BMI

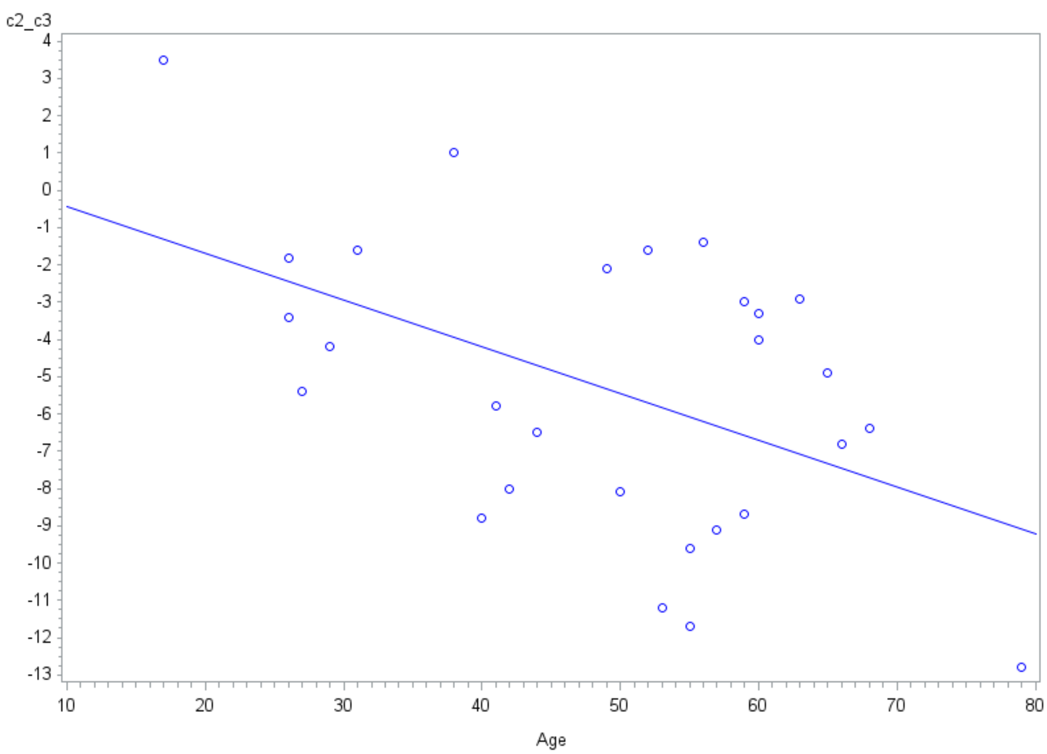


Figure 5.6: Significant negative association between C2-C3 spinal angle and Age

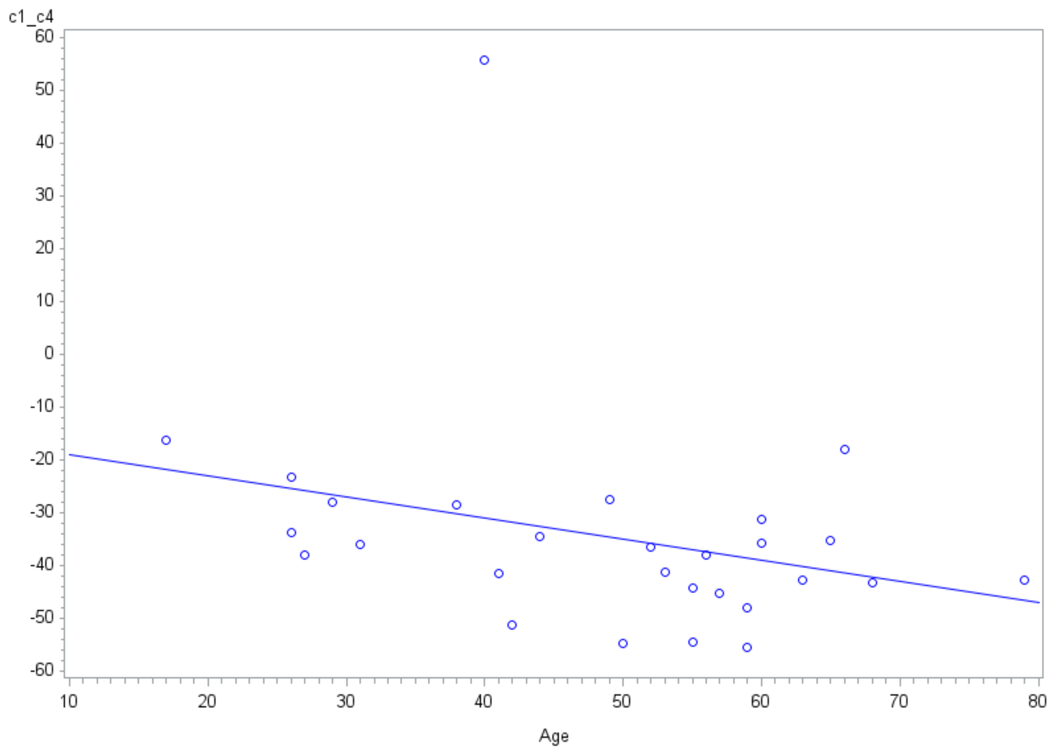
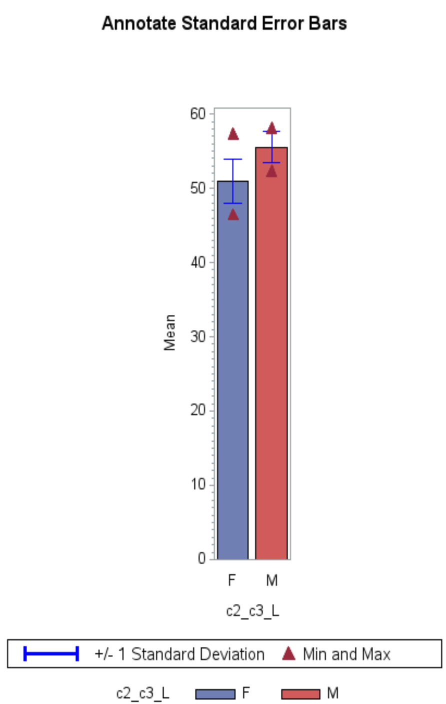


Figure 5.7: Significant negative association between C1-C4 spinal angle and Age



Gender	Mean	95% CI -Lower	95% CI - Upper
F	50.9176	49.386	52.4493
M	55.5364	54.1393	56.9334
Diff (1-2)	-4.6187	-6.7417	-2.4957

Figure 5.8: Gender differences in cervical spine length and gender

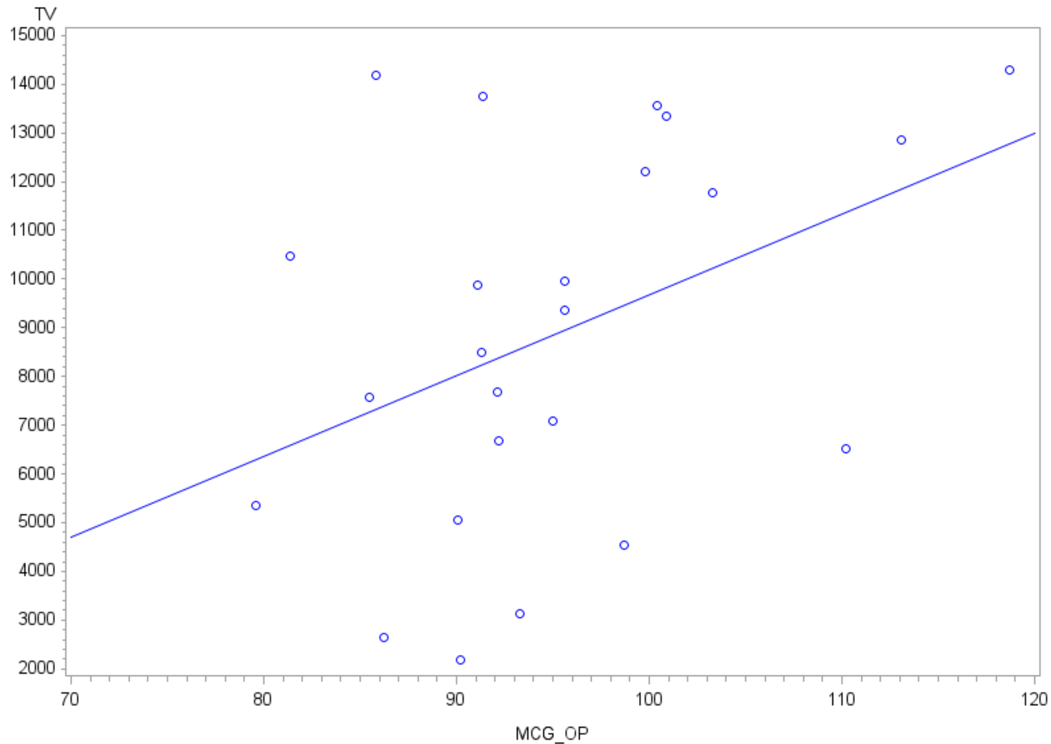


Figure 5.9: Significant positive association between craniocervical posture (McG) and total airway volume (TV)

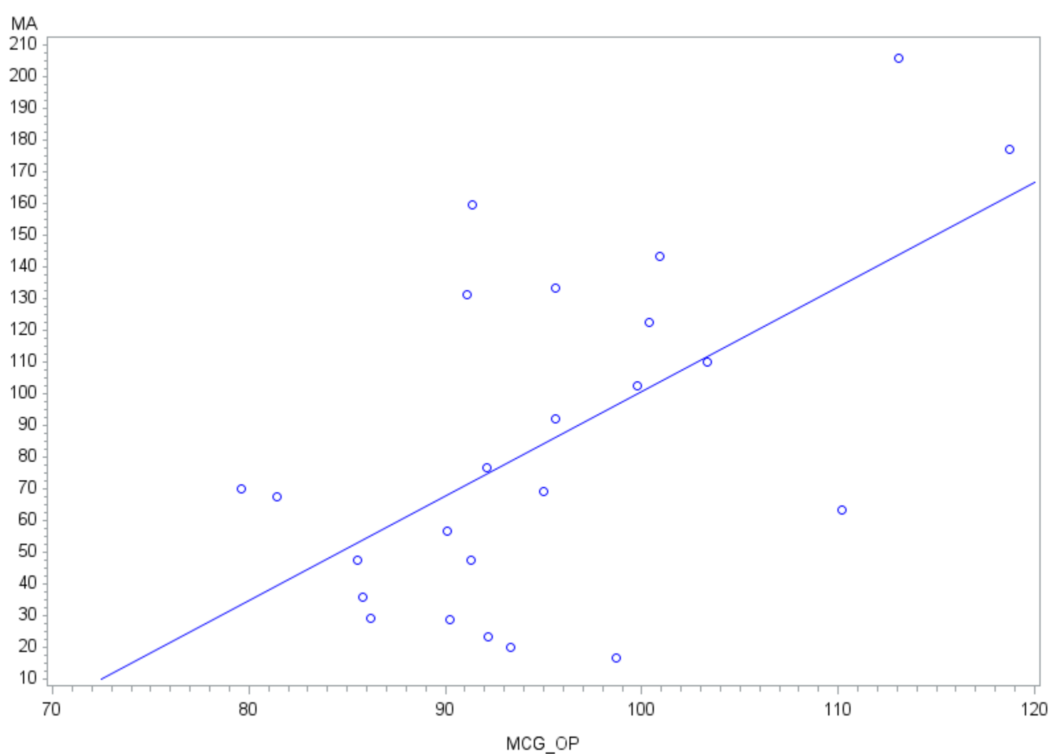


Figure 5.10: Significant positive association between craniocervical posture (McG) and minimum area (MA)

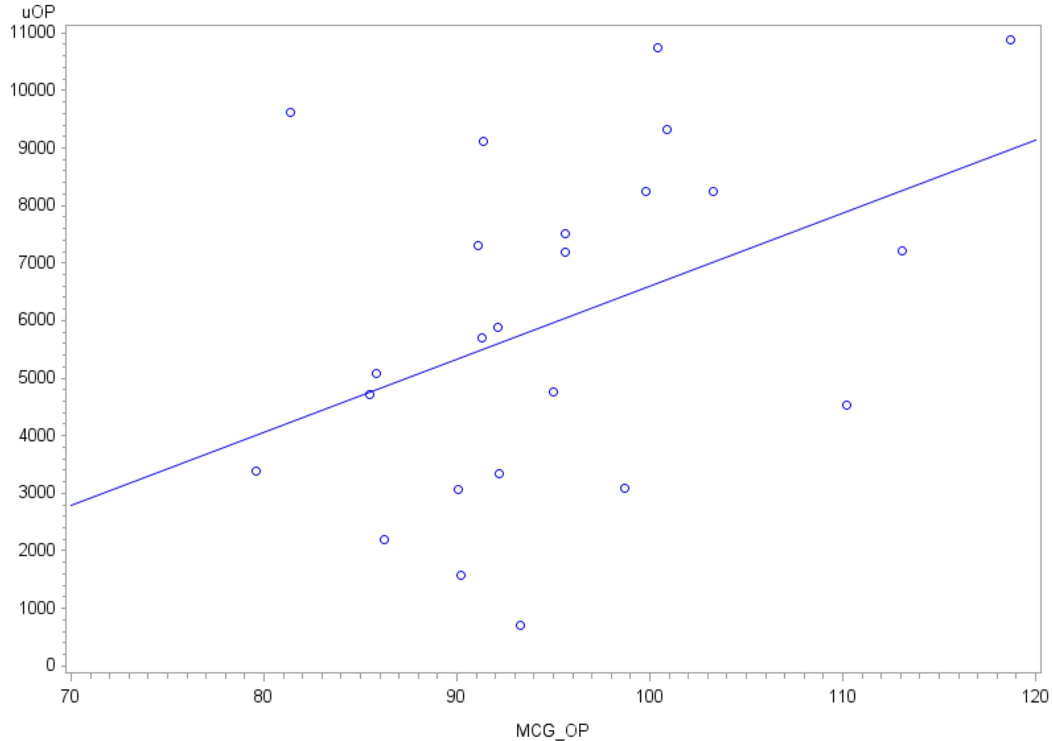


Figure 5.11: Significant positive association between craniocervical posture (McG) and upper oropharyngeal airway (uOP)

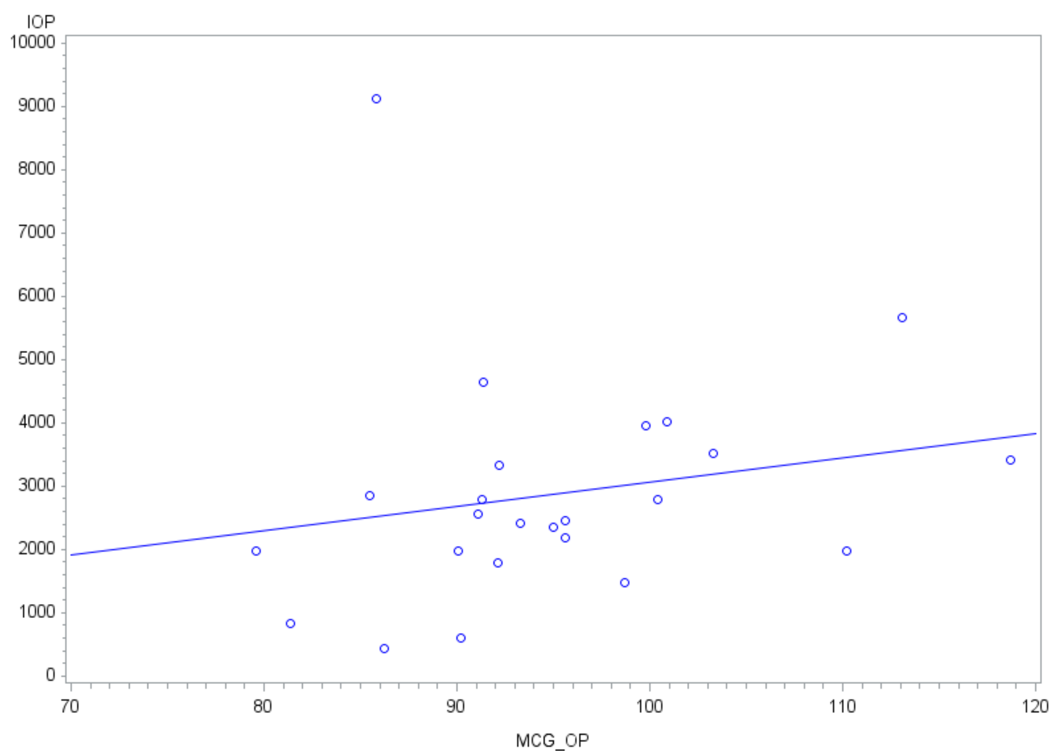


Figure 5.12: Significant positive association between craniocervical posture (McG) and lower oropharyngeal airway (lOP)

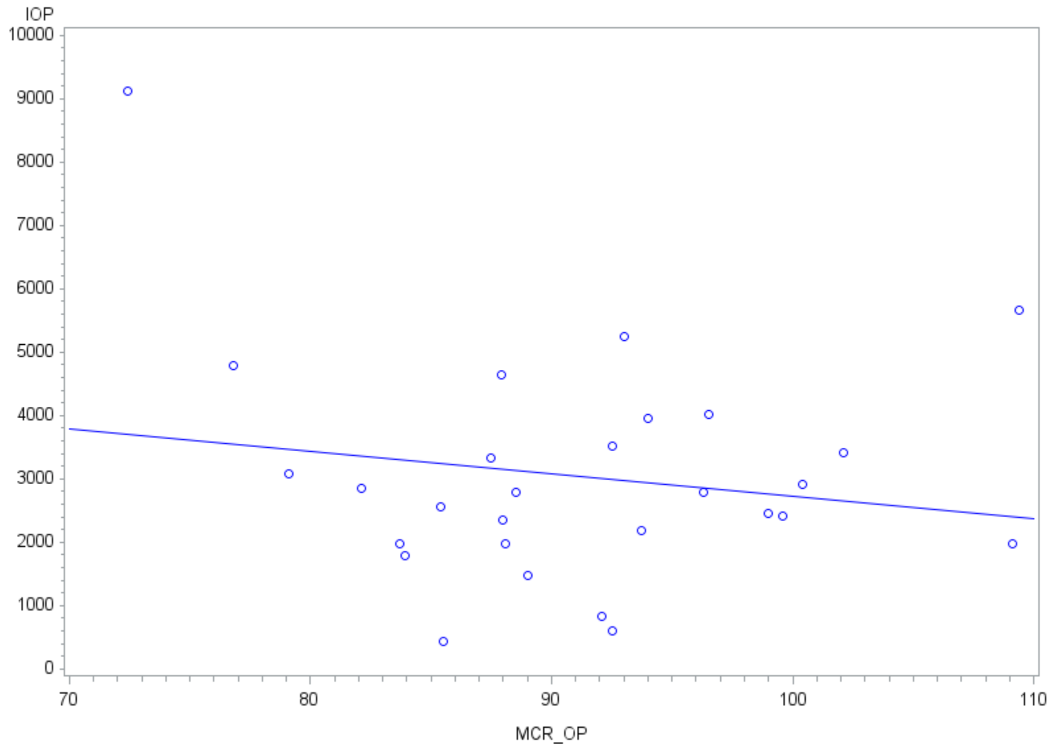


Figure 5.13: Significant negative association between craniocervical posture (McR) and lower oropharyngeal airway (lOP)

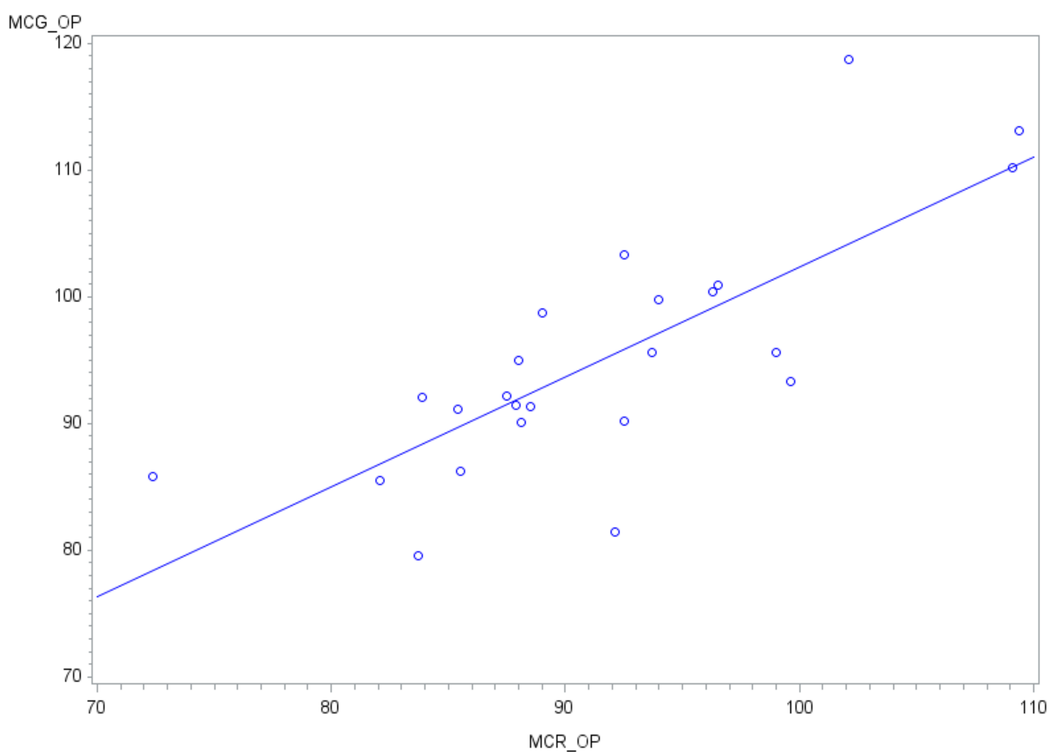


Figure 5.14: Significant positive association between the McGregor angle (McG) and McRae angle (McR)

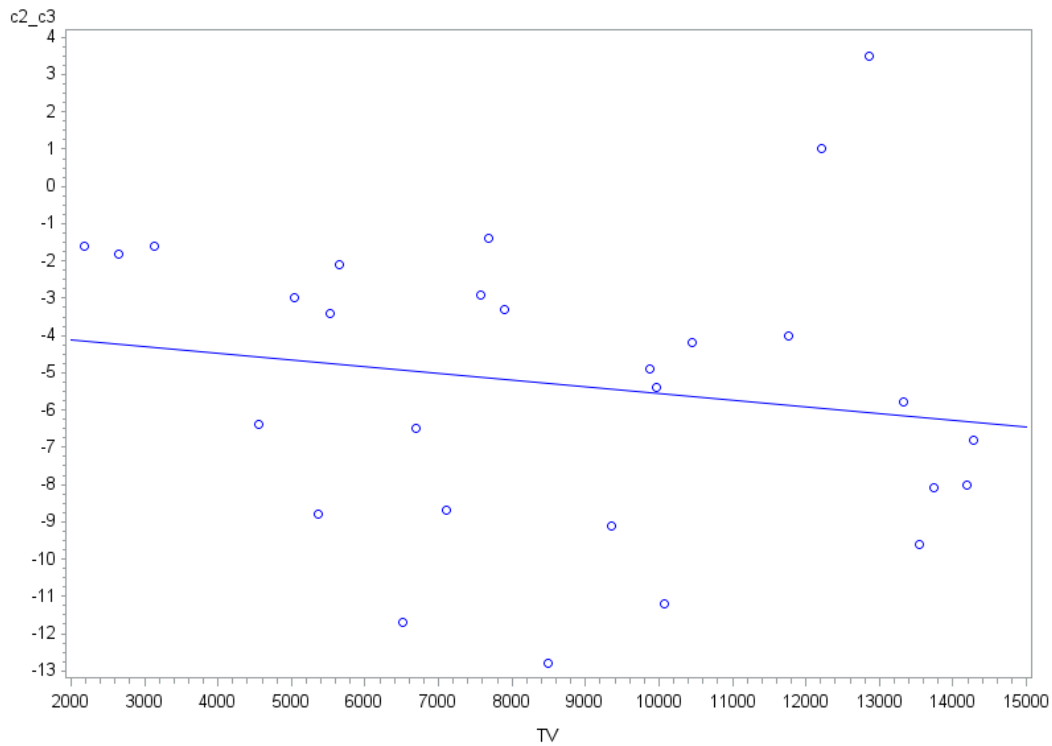


Figure 5.15: Significant negative association between cervical spine length (C2-C3) and total volume (TV)

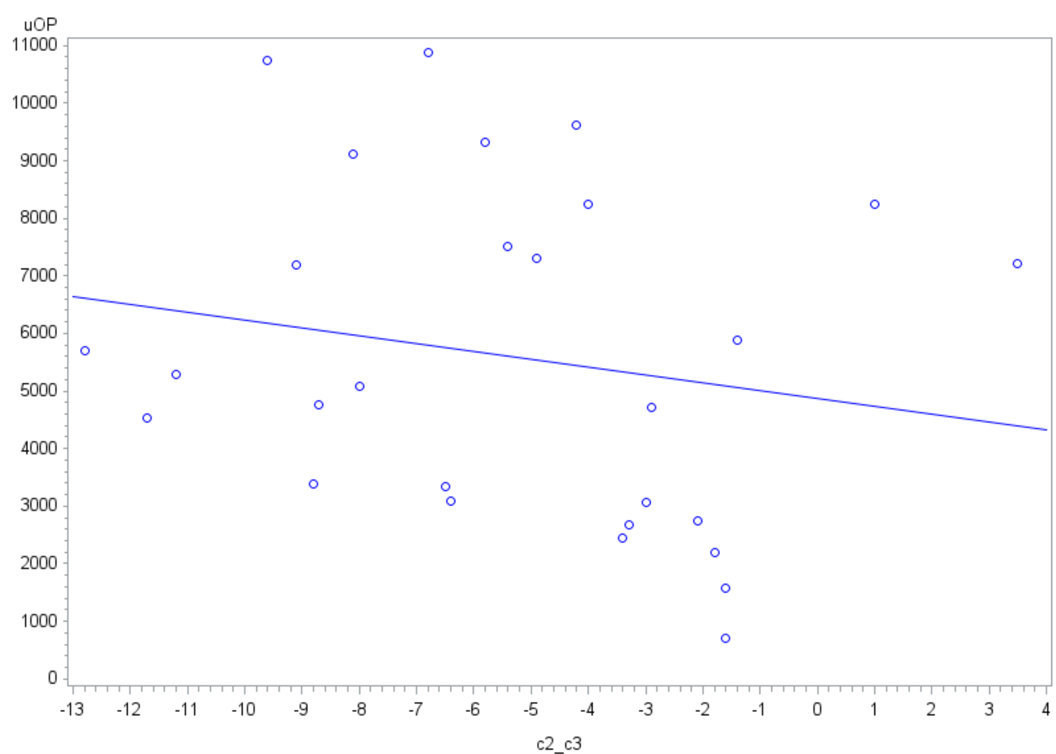


Figure 5.16: Significant negative association between cervical spine length (C2-C3) and upper oropharyngeal volume (uOP)

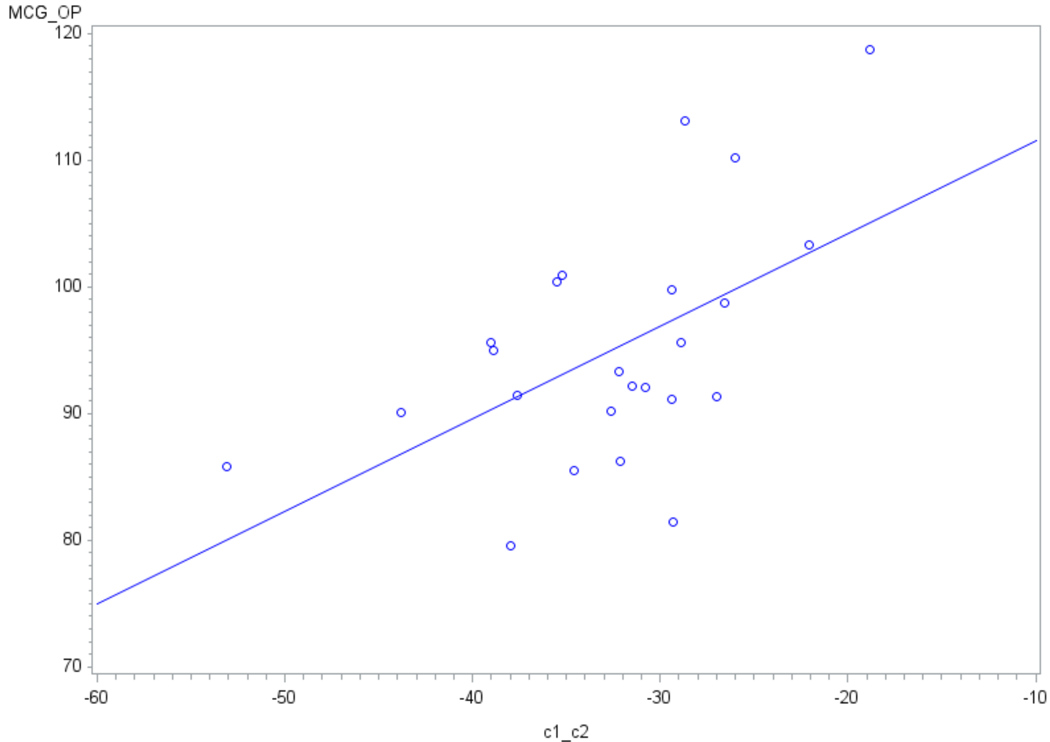


Figure 5.17: Significant positive association between craniocervical posture (McG) and C1-C2 spinal angle

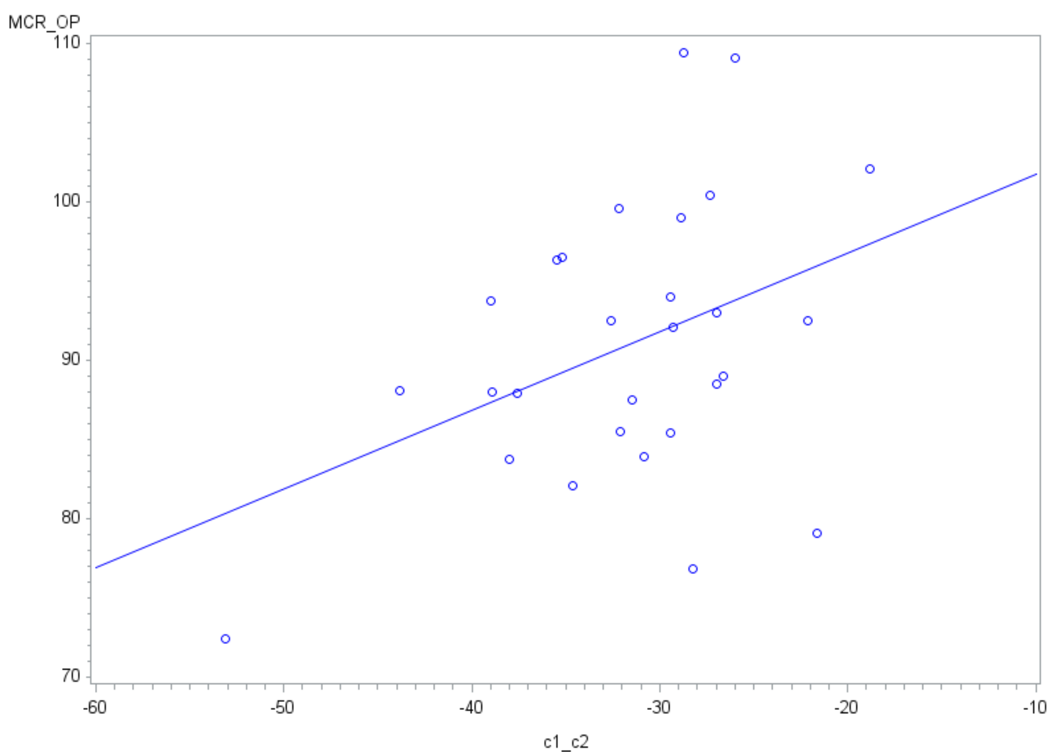


Figure 5.18: Significant positive association between craniocervical posture (McR) and C1-C2 spinal angle

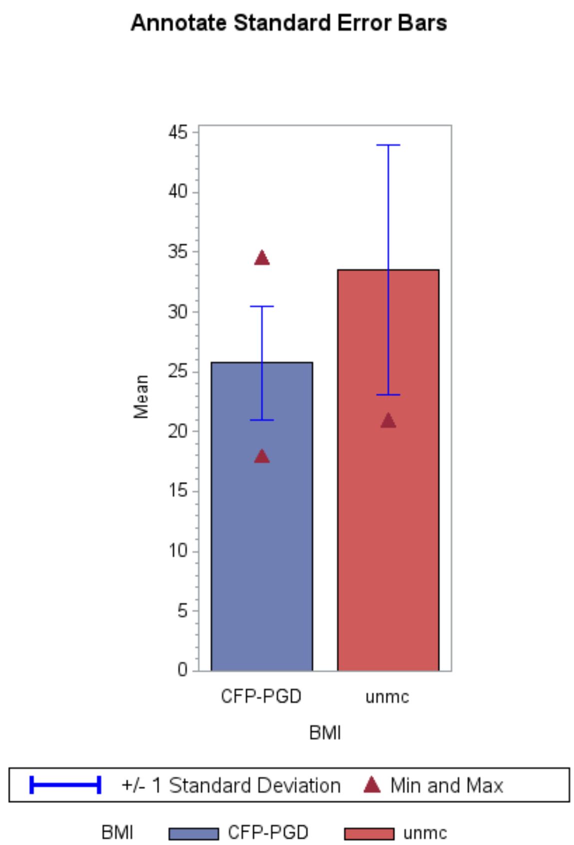


Figure 5.19: Clinic differences in BMI

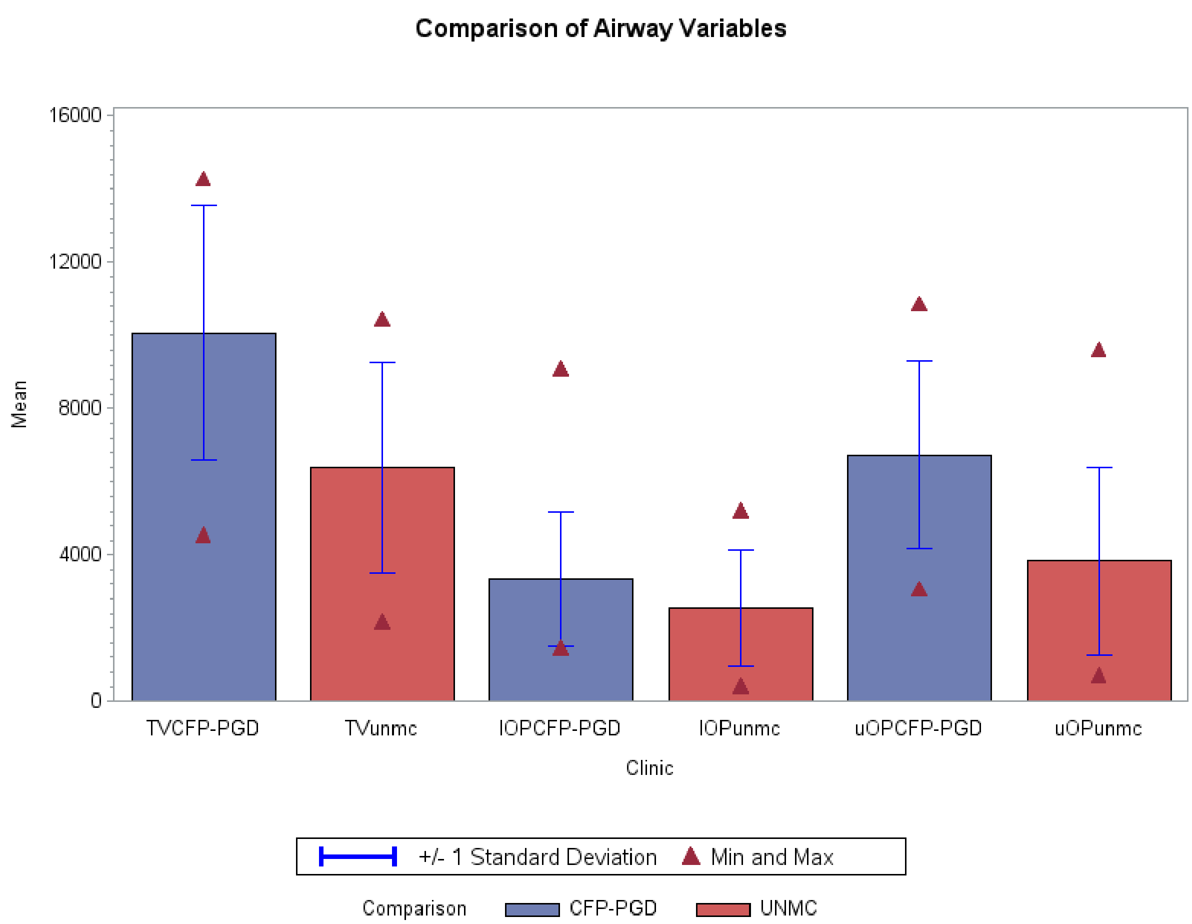


Figure 5.20: Clinic differences in airway parameters (TV, uOP, lOP)

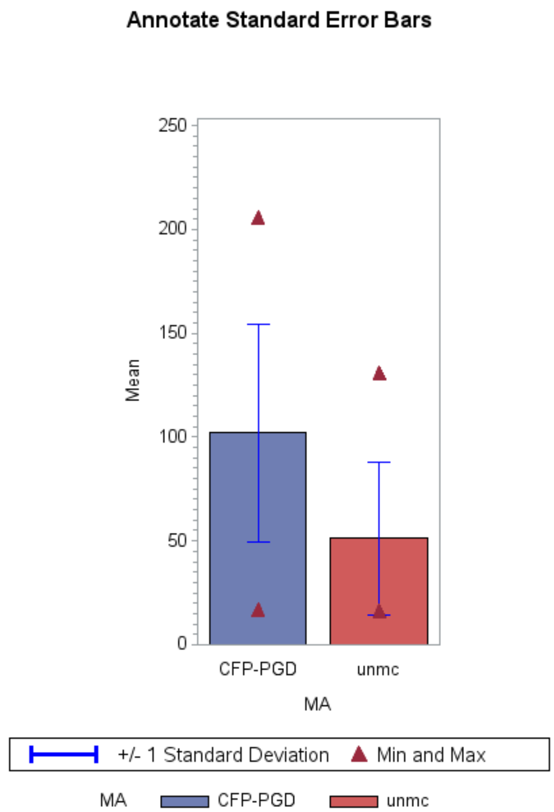


Figure 5.21: Clinic differences in MA

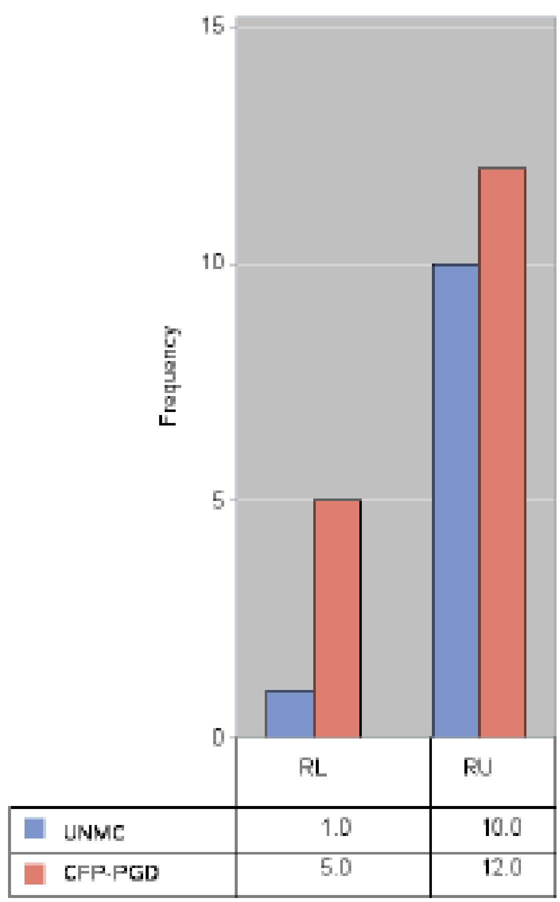


Figure 5.22: The frequency of the minimum area (MA) location between the clinics

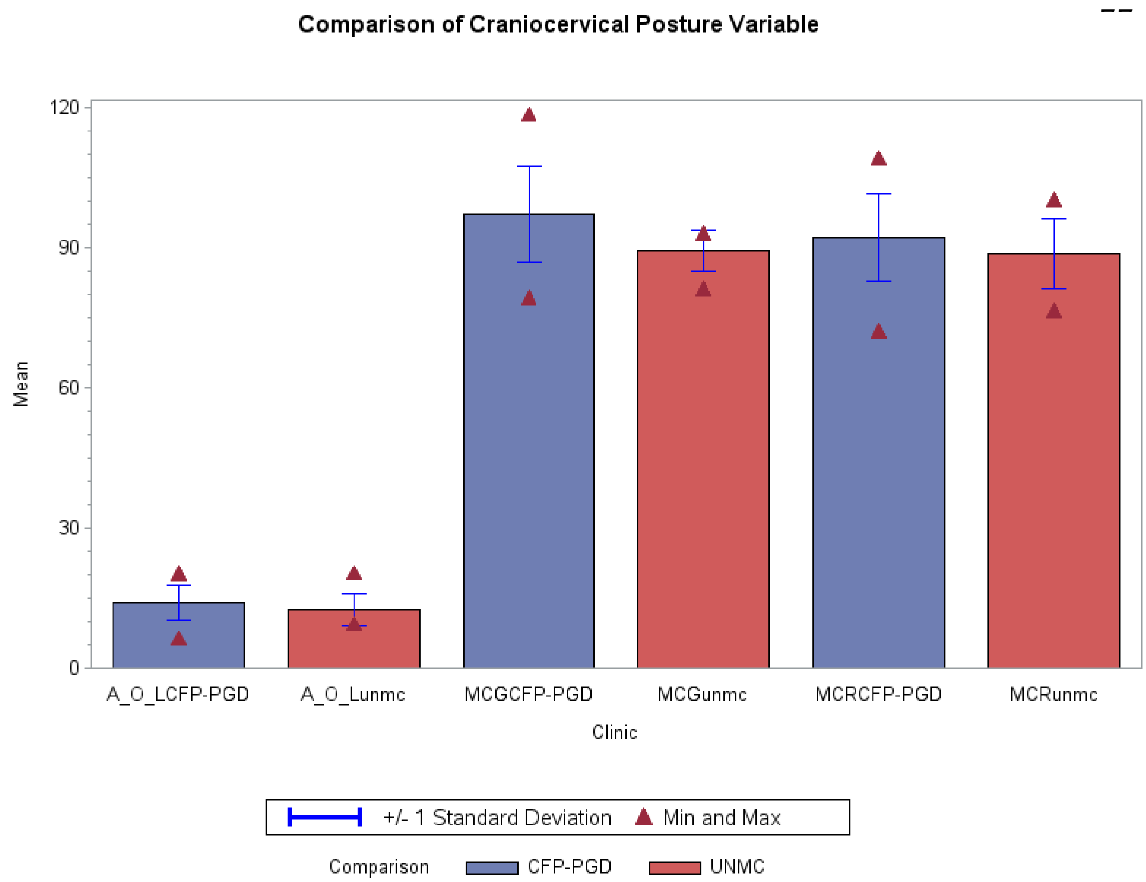


Figure 5.23: Clinic differences in craniocervical posture (McG, McR, AOL)

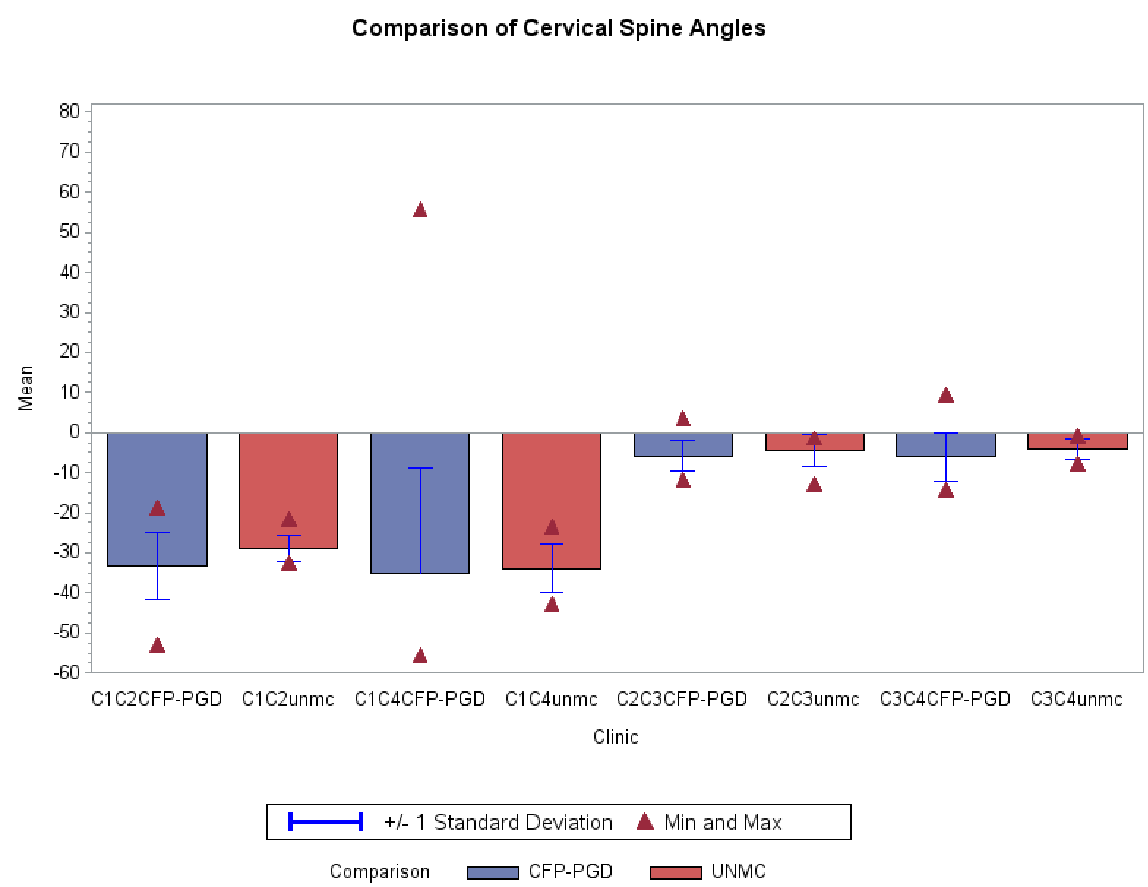


Figure 5.24: Clinic differences in cervical spine angles (C1-C2, C2-C3, C3-C4, C1-C4)

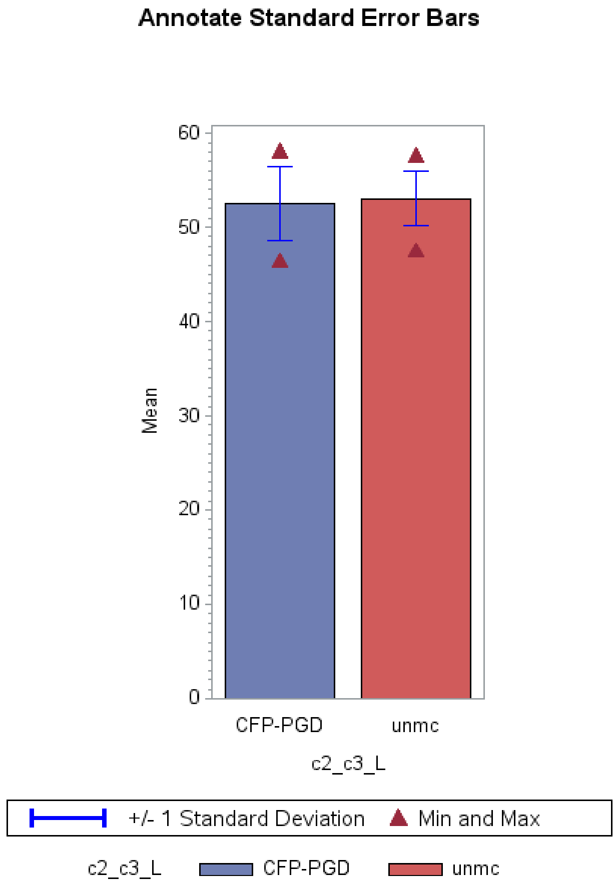


Figure 5.25: Clinic differences in neck length (C2-C3_L)

CHAPTER 6: DISCUSSION

6.1 Method of Error

Substantial to almost perfect agreement was noted in both the intra- and inter-examiner reliability tests. The intra-examiner reliability mean was 0.87 and ranged between 0.54 and 1.00. The inter-examiner reliability mean was 0.82 and ranged between 0.21and 1.00. As reported in other studies, scores above 0.61 represents substantial agreement and above 0.81 represents almost perfect agreement (Landis and Koch 1977). However, the wide range indicated that some measurements were more reliable than others.

Airway measurements were more reliable than any other measurements with an intra-examiner correlation of 0.96 (0.85-1.00) and inter-examiner correlation of 0.95 (0.81-1.00). TV, uOP and MA had nearly perfect intra- and inter-examiner reliability. First, this is due to the reproducibility of the hard tissue landmarks used to define the boundaries of the airway, which allows for consistent accuracy of volumetric measurements. Secondly, the Dolphin software's integrated tools allows for airway volume and MA to be calculated in one area, which is superior to Anatomage.

Cervical spine length was the second most reliable measurement with an intra-examiner mean of 0.96 and inter-examiner mean of 0.96. Both C2 and C3 cervical vertebrae were easily identifiable on radiographs.

Craniocervical posture measurements were the third most reliable with an intra-examiner mean of 0.96 (0.93-0.98) and inter-examiner mean of 0.84 (0.77-0.89). The Rocabado analysis was easily reproducible as well as our modified method using McRae line.

On average, cervical spine angles had good agreement but exhibited a wide range. The intra-examiner mean was 0.68 with a range of 0.54-0.83 while the inter-examiner mean was 0.64 and with a range of 0.21-0.96. The low reproducibility of the cervical spine angles was due to the difficulty of clearly identifying the borders of each cervical vertebrae. In instances where the intervertebrae distance is small, it was hard to delineate the exact border of each vertebrae.

6.2 Rationale for Combining Patients for Analyses

Four UNMC patients presented with neck CT's which failed to show PNS. For these subjects, a modified technique was used to assess airway parameters (see methods section). No statistical differences were noted between airway parameters in subjects with neck CT's and head CT's (Appendix E2.1); therefore, these scans were combined for analyses.

Besides BMI and airway parameters, there were no statistical differences in cervical spine angles, craniocervical posture, and neck length between the UNMC and CFP-PGD subjects. Therefore, these subjects were combined. Intra-clinic analyses will be needed to rule out the effects of BMI on other correlation analyses.

6.3 Demographic Differences in OSA Subjects

There was a significant difference in AHI scores between the males and female subjects. This is in line with previous research on gender differences in the prevalence of OSA. Both the Wisconsin and Swiss sleep studies mentioned previously showed that the prevalence of OSA in males are two-three folds higher than females (Young, Palta et al. 1993; Young, Evans et al. 1997; Young, Peppard et al. 2002; Punjabi 2008; Young, Palta et al. 2009).

There was a weak statistical correlation between AHI and age in our study. This agrees with previous studies which showed that the prevalence of OSA increases with age (Kapur 2010) due to increased fat deposition around the pharynx, lengthening of the soft palate, and changes in parapharyngeal structures (Malhotra, Huang et al. 2006).

Surprisingly, our study failed to show a statistically significant association between BMI and AHI scores, though a positive trend can be observed. BMI and AHI are highly correlated. The Sleep Heart Health Study showed that a weight gain of 10 kg can confer a 2.5 fold increase in the chances of increase the AHI score by 15 (Quan, Howard et al. 1997). Trend that as oropharyngeal airway volume decreases, BMI increases but not statistically significant (p=0.0763). This might be due to a small sample size where a few outliers could potentially skew the overall results.

6.4 Changes in Cervical Spine Angles, Craniocervical Posture, and Airway Dimensions in the Supine (UNMC) versus Upright (CFP-PGD) Positions

No differences in cervical spine angles or craniocervical posture were noted in the supine versus upright position in this study. Regarding positional changes in cervical spine angles, a 5-degree decrease in cervical spine angle has been shown in the supine position and the author attributed it to gravitational forces (Martensen 2015). Another study found an increase cervical lordosis in the upright position (Jun, Chang et al. 2014). No studies have examined changes in head posture in the supine position.

Our study showed a significant difference in total volume, upper oropharyngeal airway, and minimum cross sectional area between the clinics (UNMC<CFP-PGD). Subjects in the supine position (UNMC) exhibited a significantly smaller total airway volume (6,398.6 mm^3) compared to the subjects in the upright position (CFP-PGD), which had a mean volume of 10,075.6 mm^3. The minimum cross sectional area was significantly smaller in the supine group (51.3 mm^2) compared to the upright group (102.0 mm^2). These findings agreed with the study by Camacho et al. (2014), which showed a significant decrease in the total upper airway volume from 14,100 to 9,500 mm^2. The minimum cross-sectional area also decreased from 120 to 30 mm^2.

6.5 Cervical Spine Angles Parameters

A significant negative correlation was noted between C2-C3 angle (-0.4903) and C1-C4 angle (-0.3935) with age. This implies that the cervical spine alignment becomes more lordotic with age. Due to a lack of normative data, controversy exists regarding whether the cervical spine becomes more lordotic or kyphotic with age (Kim, Lenke et al. 2014). Some authors believe that with age and disc degeneration, the spine becomes more kyphotic (straightens) whereas others believe the spine becomes more lordotic in order to maintain gaze (Park, Moon et al. 2013). Our results should be interpreted with caution for two reasons. First, the sample size is quite small (n=28). Second, the UNMC subjects were in the supine position with a few patients having their necks supported by a pillow during CT scans.

6.6 The Relationship between Cervical Spine Angles and Craniocervical Posture

Significant positive association was noted between the McG and McR angles and the C1-C2 angle. This is not surprising since McG and McR are measurements of head extension and flexion. The atlanto-axial joint of C1-C2 allows for mostly head rotation but also some head flexion. This implies that the upper head-neck joints involved in head flexion-extension are related.

6.6 Craniocervical Posture Parameters

To date, no CBCT study examining the relationship between head posture and OSA subjects is reported. The Solow studies showed a significant increase in the AP dimension of the lower oropharyngeal airway with craniocervical extension (Solow, Ovesen et al. 1993; Solow, Skov et al. 1996). Our study found a significant positive correlation between craniocervical angulation and total volume, upper oropharyngeal volume, lower oropharyngeal volume, and minimum cross sectional area. This implies that airway volume increases with head flexion, not extension. These results conflict with findings from previous cephalometric and 3-D imaging studies (Muto, Takeda et al. 2002), which reported a 10-degree increase resulted in about 4mm increase in airway space. Gurani et al. (2016) reported a MRI study which showed head extension resulted in an increase hypopharyngeal airway volume. These disagreements might be due to differences in the way the radiographs were taken. UNMC subjects have MDCT's taken in the supine position where a small pillow is sometimes placed under the neck, which could tilt the head. However, patients are instructed to adjust their head and/or pillow into a more comfortable position before image acquisition. Likewise, the CFP-PGD subjects were instructed to be in the natural head position/posture. However, it is unclear if all subjects were consistently positioned this way.

Interestingly, significant negative associations were noted between McG-Odontoid plane angle (-0.4405), McR-Odontoid plane angle (-0.4852), and AO Length (-0.5960), and BMI. This implies that head extension is highly correlated with BMI. For every unit increase in BMI, a half-degree increase in head extension is noted. These results tend to agree with those proposed by Solow et al. (1996). Craniocervical extension from the natural head position is an adaptive mechanism used in OSA subjects, who typically have high BMI, as a way to increase airway patency.

The normal values for the Rocabado parameters for head extension-flexion is 96-106 degrees or 4-9mm. Our study showed that the UNMC subjects were in an extended head position (89.5 $\pm$ 4.3 degrees) whereas the CFP-PGD exhibited a normal position (97.3 $\pm$ 10.2 degrees). Although these differences were not statistically significant, the differences could be related to patient positioning since UNMC subjects were in the supine position. Moreover, the UNMC subjects had higher AHI and BMI values and lower airway volumes, which could imply that these patients were in the compensated extended head position to maintain airway patency (Hellsing, McWilliam et al. 1987; Solow, Skov et al. 1996; Piccin, Pozzebon et al. 2016).

6.7 Modified Method for Evaluating Craniocervical Posture

Almost all prior cephalometric studies examining head posture have used variations of Solow or Rocabado analyses. These analyses depend largely on a wide field of view and the presence of craniofacial structures such as nasion, sella, and PNS. For subjects with hospital CT's that have limited field of view, a modified method from the Rocabado analysis using the McRae line, instead of the McGregor line, was used in this study. A nearly perfect correlation was found between McGregor and McRae angles (0.77). In fact, whenever a significant correlation was found with the McGregor angle, a similar effect was detected with the McRae angle.

6.8 Cervical Spine Length Parameters

Significant difference in C2-C3 length was noted between male versus female. This is expected since statural differences between genders have been well established in the literature. On average, males are taller than females (Graber and Swain 1985). Furthermore, studies that quantified the differences in neck geometry between males and females found that most anthropometric parameters were significantly smaller in females compared to males. Female C3-C7 vertebrae were smaller in the A-P direction and were weaker than male necks in both flexion and extension (Vasavada, Danaraj et al. 2008). Furthermore, other studies found that males have longer upper airway length than females and proposed that these gender differences could partially explain the predisposition of men to OSA (Malhotra, Huang et al. 2002; Ronen, Malhotra et al. 2007).

Significant but weak positive association was noted between spine length and TV. In addition, a significant positive association was noted between the upper oropharyngeal airway and spine length. Our finding partially agrees with Kim et al. (2011), who found that longer neck length did not result in increased upper pharyngeal airway volume.

Another interesting finding was that for every unit increase in spine length, there is a 1.767 increase in the odds of the minimum constriction area shifting from the retro-lingual to the retro-uvula area. Camacho et al. (2014) noted that the most common site of constriction was located in the retropalatal (uvula) area. To our knowledge, there is no study specifically examining the relationship between neck length and the location of the minimum area.

6.9 Study Limitation

The first major limitation of this study is a small sample size of twenty-eight subjects. In general, the smaller the sample size, the more noise is seen in the results. For example, we expected to see a correlation between AHI and BMI; however, no statistical significance was detected in this dataset, which could be due to the small sample size.

The second major limitation is the heterogeneity of the subject pool, which automatically introduces variability in the data. Subjects were recruited from three different clinic sites, each with different demographics and radiology protocol. First, there are major differences between the UNMC and CFP-PGD subjects. UNMC hospital patients had CT scans for other health conditions that were unrelated to sleep apnea. These patients likely presented with more complex medical histories and potentially significant medical comorbidities compared to the CFP-PGD patients. Secondly, the radiology protocols varied among the three clinics. The UNMC radiology department has 18 radiology technicians who might have slightly different routines for capturing CT's. The CFP and PGD clinics used different CBCT machines that have different head positioners. It is widely known within the dental field that there is no standardized protocol for capturing CBCTs. In fact, a few patients were noted to have a slightly open mouth position or a retruded tongue position.

The third major limitation is inherent in the use of CBCT's and MDCT's to scan the airway. While both imaging techniques have been validated for use in sleep apnea studies, they represent snapshot images of a dynamic process that occurs during sleep. Other imaging techniques such as the four-dimensional MDCT (Wagnetz, Roberts et al. 2010) or the drug-induced sleep endoscopy (DISE) are better equipped at capturing airway volumes and location of minimum cross sectional area in real time.

6.10 Future Studies

Future studies can proceed in multiple directions. This is a pilot study with a small sample size of 28 subjects. Consequently, a number of anticipated correlations, such as BMI vs. AHI score, were absent. These associations have been shown in previous studies (Young, Palta et al. 1993; Quan, Howard et al. 1997). In fact, no correlations between AHI scores and any airway variables, particular minimum cross sectional area, were detected. A larger sample size may be needed to detect these associations.

Cervical spine angles should be further examined since no associations were detected in this study between cervical spine angles and airway volumes or AHI scores. For example, a follow up correlation study of UNMC patients who have a history of cervical spine fusion (i.e. loss of cervical spine lordosis), diagnosis of sleep apnea by overnight polysomnography, and head/neck CT may increase our understanding of the effects of cervical spine angles in sleep apnea.

The concept of craniocervical posture requires further investigation. Solow et al. (1996) demonstrated from cephalometric studies that forward head posture and head extension increased the A-P dimension of the lower pharyngeal airway along multiple sagittal planes. A repeat study using 3-D imaging to measure the cross sectional area along these pharyngeal reference points (e.g. tip of uvula, vellecula epiglottis, velum palati, etc.) will elucidate the actual airway changes during head posturing.

Lastly, evaluation of neck length represented a small component of this study. Our preliminary results, combined with findings from previous studies, suggest further investigation into this topic. Future studies can examine the interaction among neck length, airway volume, and airflow resistance modeling.

CHAPTER 7: CONCLUSION

To date, no CBCT studies have examined the relationship among craniocervical posture, cervical spine angles, and the upper pharyngeal airway space in OSA subjects. Our study showed that craniocervical posture could significantly impact the airway dimension. Cervical spine angles, in the absence of spine pathology, have little to no impact on the airway space. However, the atlanto-axial joint, which allows for mostly head rotation and some flexion-extension, may impact the upper airway space. Furthermore, our study showed that airway dimensions are significantly decreased in the supine position, which is typically the sleeping position. For clinicians who frequently order MDCT's, we proposed using the McRae line for evaluating head posture in limited view neck CT's. Altogether, these findings may help providers better assess the clinical parameters for OSA.

LITERATURE CITED

Aboudara, C., I. Nielsen, et al. (2009). "Comparison of airway space with conventional lateral headfilms and 3-dimensional reconstruction from cone-beam computed tomography." Am J Orthod Dentofacial Orthop **135**(4): 468-479.

Abramson, Z. R., S. Susarla, et al. (2010). "Three-dimensional computed tomographic analysis of airway anatomy." J Oral Maxillofac Surg **68**(2): 363-371.

Al-Hussaini, A. and S. Berry (2015). "An evidence-based approach to the management of snoring in adults." Clin Otolaryngol **40**(2): 79-85.

AlGhanim, N., V. R. Comondore, et al. (2008). "The economic impact of obstructive sleep apnea." Lung **186**(1): 7-12.

Ataka, H., T. Tanno, et al. (2010). "Occipitocervical fusion has potential to improve sleep apnea in patients with rheumatoid arthritis and upper cervical lesions." Spine (Phila Pa 1976) **35**(19): E971-975.

Ayappa, I., R. G. Norman, et al. (2008). "Validation of a self-applied unattended monitor for sleep disordered breathing." J Clin Sleep Med **4**(1): 26-37.

Barkdull, G. C., C. A. Kohl, et al. (2008). "Computed tomography imaging of patients with obstructive sleep apnea." Laryngoscope **118**(8): 1486-1492.

Bhattacharyya, N., S. P. Blake, et al. (2000). "Assessment of the airway in obstructive sleep apnea syndrome with 3-dimensional airway computed tomography." Otolaryngol Head Neck Surg **123**(4): 444-449.

Cairns, A., E. Wickwire, et al. (2014). "A pilot validation study for the NOX T3(TM) portable monitor for the detection of OSA." Sleep Breath **18**(3): 609-614.

Camacho, M., R. Capasso, et al. (2014). "Airway changes in obstructive sleep apnoea patients associated with a supine versus an upright position examined using cone beam computed tomography." J Laryngol Otol **128**(9): 824-830.

Davies, R. J., N. J. Ali, et al. (1992). "Neck circumference and other clinical features in the diagnosis of the obstructive sleep apnoea syndrome." Thorax **47**(2): 101-105.

de Oliveira, L. B., F. Cajaiba, et al. (2012). "Comparative analysis of assessment of the craniocervical equilibrium through two methods: cephalometry of Rocabado and cervical range of motion." Work **41 Suppl 1**: 2563-2568.

Dempsey, J. A., S. C. Veasey, et al. (2010). "Pathophysiology of sleep apnea." Physiol Rev **90**(1): 47-112.

Dobson, G. J., R. H. Blanks, et al. (1999). "Cervical Angles in Sleep Apnea Patients: A Retrospective Study." J. Vertebral Subluxation Res. **3**(1): 1-15.

Driver, H. S., E. J. Pereira, et al. (2011). "Validation of the MediByte(R) type 3 portable monitor compared with polysomnography for screening of obstructive sleep apnea." Can Respir J **18**(3): 137-143.

Duval-Beaupere, G., C. Schmidt, et al. (1992). "A Barycentremetric study of the sagittal shape of spine and pelvis: the conditions required for an economic standing position." Ann Biomed Eng **20**(4): 451-462.

Edwards, B. A. and D. P. White (2011). "Control of the pharyngeal musculature during wakefulness and sleep: implications in normal controls and sleep apnea." Head Neck **33 Suppl 1**: S37-45.

El, H. and J. M. Palomo (2010). "Measuring the airway in 3 dimensions: a reliability and accuracy study." Am J Orthod Dentofacial Orthop **137**(4 Suppl): S50 e51-59; discussion S50-52.

Ellen, R. L., S. C. Marshall, et al. (2006). "Systematic review of motor vehicle crash risk in persons with sleep apnea." J Clin Sleep Med **2**(2): 193-200.

Garvey, J. F., M. F. Pengo, et al. (2015). "Epidemiological aspects of obstructive sleep apnea." J Thorac Dis **7**(5): 920-929.

Gelb, D. E., L. G. Lenke, et al. (1995). "An analysis of sagittal spinal alignment in 100 asymptomatic middle and older aged volunteers." Spine (Phila Pa 1976) **20**(12): 1351-1358.

Ghoneima, A. and K. Kula (2013). "Accuracy and reliability of cone-beam computed tomography for airway volume analysis." Eur J Orthod **35**(2): 256-261.

Graber, T. M. and B. F. Swain (1985). Orthodontics, current principles and techniques. St. Louis, C.V. Mosby Co.

Grauer, D., L. S. Cevidanes, et al. (2009). "Working with DICOM craniofacial images." Am J Orthod Dentofacial Orthop **136**(3): 460-470.

Guijarro-Martinez, R. and G. R. Swennen (2013). "Three-dimensional cone beam computed tomography definition of the anatomical subregions of the upper airway: a validation study." Int J Oral Maxillofac Surg **42**(9): 1140-1149.

Guilleminault, C., K. K. Li, et al. (2003). "Anterior cervical spine fusion and sleep disordered breathing." Neurology **61**(1): 97-99.

Gurani, S. F., G. Di Carlo, et al. (2016). "Effect of Head and Tongue Posture on the Pharyngeal Airway Dimensions and Morphology in Three-Dimensional Imaging: a Systematic Review." J Oral Maxillofac Res **7**(1): e1.

Han, T. S., M. K. Oh, et al. (2015). "Relationship between Neck Length, Sleep, and Cardiovascular Risk Factors." Korean J Fam Med **36**(1): 10-21.

Harrison, D. D., D. E. Harrison, et al. (2004). "Modeling of the sagittal cervical spine as a method to discriminate hypolordosis: results of elliptical and circular modeling in 72 asymptomatic subjects, 52 acute neck pain subjects, and 70 chronic neck pain subjects." Spine (Phila Pa 1976) **29**(22): 2485-2492.

Harrison, D. E., D. D. Harrison, et al. (1998). "Reliability of spinal displacement analysis of plain X-rays: a review of commonly accepted facts and fallacies with implications for chiropractic education and technique." J Manipulative Physiol Ther **21**(4): 252-266.

Harrison DE, H. D., Cailliet R, et al. (1998). "Reliability of spinal displacement analysis on plain x-rays: a review of commonly accepted facts and fallacies with implications for chiropractic education and technique." J of Manipulative Ther **21**(4): 252-266.

Hart, P. S., B. P. McIntyre, et al. (2015). "Postsurgical volumetric airway changes in 2-jaw orthognathic surgery patients." Am J Orthod Dentofacial Orthop **147**(5): 536-546.

Heinzer, R., S. Vat, et al. (2015). "Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study." Lancet Respir Med **3**(4): 310-318.

Hellsing, E., J. McWilliam, et al. (1987). "The relationship between craniofacial morphology, head posture and spinal curvature in 8, 11 and 15-year-old children." Eur J Orthod **9**(4): 254-264.

Hirsch Allen, A. J., N. Bansback, et al. (2015). "The effect of OSA on work disability and work-related injuries." Chest **147**(5): 1422-1428.

Jackson, B. L., D. D. Harrison, et al. (1993). "Chiropractic biophysics lateral cervical film analysis reliability." J Manipulative Physiol Ther **16**(6): 384-391.

Jun, H. S., I. B. Chang, et al. (2014). "Is it possible to evaluate the parameters of cervical sagittal alignment on cervical computed tomographic scans?" Spine (Phila Pa 1976) **39**(10): E630-636.

Kapur, V. K. (2010). "Obstructive sleep apnea: diagnosis, epidemiology, and economics." Respir Care **55**(9): 1155-1167.

Katsuura, A., S. Hukuda, et al. (2001). "Kyphotic malalignment after anterior cervical fusion is one of the factors promoting the degenerative process in adjacent intervertebral levels." Eur Spine J **10**(4): 320-324.

Kendzerska, T., A. S. Gershon, et al. (2014). "Obstructive sleep apnea and incident diabetes. A historical cohort study." Am J Respir Crit Care Med **190**(2): 218-225.

Khan, A., K. D. Than, et al. (2014). "Sleep apnea and cervical spine pathology." Eur Spine J **23**(3): 641-647.

Kim, E. J., J. H. Choi, et al. (2011). "Upper airway changes in severe obstructive sleep apnea: upper airway length and volumetric analyses using 3D MDCT." Acta Otolaryngol **131**(5): 527-532.

Kim, H. J., L. G. Lenke, et al. (2014). "Cervical Lordosis Actually Increases With Aging and Progressive Degeneration in Spinal Deformity Patients." Spine Deformity **2**: 410-414.

Kum, R. O., M. Ozcan, et al. (2015). "A new suggestion for the Epworth Sleepiness Scale in obstructive sleep apnea." Eur Arch Otorhinolaryngol **272**(1): 247-252.

Kyung, S. H., Y. C. Park, et al. (2005). "Obstructive sleep apnea patients with the oral appliance experience pharyngeal size and shape changes in three dimensions." Angle Orthod **75**(1): 15-22.

Landis, J. R. and G. G. Koch (1977). "The measurement of observer agreement for categorical data." Biometrics **33**(1): 159-174.

Lang-Tapia, M., V. Espana-Romero, et al. (2011). "Differences on spinal curvature in standing position by gender, age and weight status using a noninvasive method." J Appl Biomech **27**(2): 143-150.

Lavie, P. and L. Lavie (2009). "Unexpected survival advantage in elderly people with moderate sleep apnoea." J Sleep Res **18**(4): 397-403.

Lee, C. H., D. K. Kim, et al. (2015). "Changes in site of obstruction in obstructive sleep apnea patients according to sleep position: a DISE study." Laryngoscope **125**(1): 248-254.

Lee, Y. H., P. F. Hsieh, et al. (2008). "Upper airway obstruction after cervical spine fusion surgery: role of cervical fixation angle." Acta Anaesthesiol Taiwan **46**(3): 134-137.

Lefebvre, E. and R. Moreau (2010). Snoring : causes, diagnosis and treatment. New York, Nova Science Publishers.

Lenza, M. G., M. M. Lenza, et al. (2010). "An analysis of different approaches to the assessment of upper airway morphology: a CBCT study." Orthod Craniofac Res **13**(2): 96-105.

Lopez, P. P., B. Stefan, et al. (2008). "Prevalence of sleep apnea in morbidly obese patients who presented for weight loss surgery evaluation: more evidence for routine screening for obstructive sleep apnea before weight loss surgery." Am Surg **74**(9): 834-838.

Lowe, A. A., N. Gionhaku, et al. (1986). "Three-dimensional CT reconstructions of tongue and airway in adult subjects with obstructive sleep apnea." Am J Orthod Dentofacial Orthop **90**(5): 364-374.

Mac-Thiong, J. M., P. Roussouly, et al. (2010). "Sagittal parameters of global spinal balance: normative values from a prospective cohort of seven hundred nine Caucasian asymptomatic adults." Spine (Phila Pa 1976) **35**(22): E1193-1198.

Malhotra, A., Y. Huang, et al. (2006). "Aging influences on pharyngeal anatomy and physiology: the predisposition to pharyngeal collapse." Am J Med **119**(1): 72 e79-14.

Malhotra, A., Y. Huang, et al. (2002). "The male predisposition to pharyngeal collapse: importance of airway length." Am J Respir Crit Care Med **166**(10): 1388-1395.

Manni, R., L. Politini, et al. (1999). "Sleepiness in obstructive sleep apnea syndrome and simple snoring evaluated by the Epworth Sleepiness Scale." J Sleep Res **8**(4): 319-320.

Martensen, K. (2015). Radiographic Image Analysis. St. Louis, Saunders.

McCrillis, J. M., J. Haskell, et al. (2009). "Obstructive sleep apnea and the use of cone beam computed tomography in airway imaging: a review." Semin Orthod. **1**: 63-69.

McNicholas, W. T. and M. R. Bonsigore (2007). "Sleep apnoea as an independent risk factor for cardiovascular disease: current evidence, basic mechanisms and research priorities." Eur Respir J **29**(1): 156-178.

Mihaicuta, S., D. Muntean, et al. (2006). "[Excessive diurnal somnolence--causes, mechanisms, therapeutical approach]." Pneumologia **55**(1): 13-18.

Momany, S. M., G. AlJamal, et al. (2016). "Cone Beam Computed Tomography Analysis of Upper Airway Measurements in Patients With Obstructive Sleep Apnea." Am J Med Sci **352**(4): 376-384.

Muto, T., S. Takeda, et al. (2002). "The effect of head posture on the pharyngeal airway space (PAS)." Int J Oral Maxillofac Surg **31**(6): 579-583.

Nandakumar, R., S. Gollakota, et al. (2015) "Contactless Sleep Apnea Detection on Smartphones." MobiSys, 45-57.

Ogawa, T., R. Enciso, et al. (2007). "Evaluation of cross-section airway configuration of obstructive sleep apnea." Oral Surg Oral Med Oral Pathol Oral Radiol Endod **103**(1): 102-108.

Ota, M., M. Neo, et al. (2011). "Impact of the O-C2 angle on the oropharyngeal space in normal patients." Spine (Phila Pa 1976) **36**(11): E720-726.

Ozbek, M. M., K. Miyamoto, et al. (1998). "Natural head posture, upper airway morphology and obstructive sleep apnoea severity in adults." Eur J Orthod **20**(2): 133-143.

Park, M. S., S. H. Moon, et al. (2013). "The effect of age on cervical sagittal alignment: normative data on 100 asymptomatic subjects." Spine (Phila Pa 1976) **38**(8): E458-463.

Phan, N. T., B. Wallwork, et al. (2016). "Surgery for adult patients with obstructive sleep apnoea: A review for general practitioners." Aust Fam Physician **45**(8): 574-578.

Phurrough, S. (2009). "Decision memo for sleep testing for obstructive sleep apnea (OSA) (CAG-00405N)." from http://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=227.

Piccin, C. F., D. Pozzebon, et al. (2016). "Craniocervical Posture in Patients with Obstructive Sleep Apnea." Int Arch Otorhinolaryngol **20**(3): 189-195.

Pirila-Parkkinen, K., H. Lopponen, et al. (2010). "Cephalometric evaluation of children with nocturnal sleep-disordered breathing." Eur J Orthod **32**(6): 662-671.

Punjabi, N. M. (2008). "The epidemiology of adult obstructive sleep apnea." Proc Am Thorac Soc **5**(2): 136-143.

Quan, S. F., B. V. Howard, et al. (1997). "The Sleep Heart Health Study: design, rationale, and methods." Sleep **20**(12): 1077-1085.

Rocabado, M. (1983). "Biomechanical relationship of the cranial, cervical, and hyoid regions." J Craniomandibular Pract **1**(3): 61-66.

Ronen, O., A. Malhotra, et al. (2007). "Influence of gender and age on upper-airway length during development." Pediatrics **120**(4): e1028-1034.

Saleh, A., I. Sultan, et al. (2015). "Alteration in cervical spine mechanics in obstructive sleep apnea syndrome patients." Egyptian Journal of Chest Diseases and Tuberculosis **64**(4): 897-902.

Sands, S. A. and R. L. Owens (2014). "Does my bed partner have OSA? There's an app for that!" J Clin Sleep Med **10**(1): 79-80.

Schendel, S. A., J. A. Broujerdi, et al. (2014). "Three-dimensional upper-airway changes with maxillomandibular advancement for obstructive sleep apnea treatment." Am J Orthod Dentofacial Orthop **146**(3): 385-393.

Shigeta, Y., T. Ogawa, et al. (2008). "Gender- and age-based differences in computerized tomographic measurements of the orophaynx." Oral Surg Oral Med Oral Pathol Oral Radiol Endod **106**(4): 563-570.

Shoda, N., A. Seichi, et al. (2009). "Sleep apnea in rheumatoid arthritis patients with occipitocervical lesions: the prevalence and associated radiographic features." Eur Spine J **18**(6): 905-910.

Soga, T., S. Nakata, et al. (2009). "Upper airway morphology in patients with obstructive sleep apnea syndrome: effects of lateral positioning." Auris Nasus Larynx **36**(3): 305-309.

Solow, B., J. Ovesen, et al. (1993). "Head posture in obstructive sleep apnoea." Eur J Orthod **15**(2): 107-114.

Solow, B., S. Skov, et al. (1996). "Airway dimensions and head posture in obstructive sleep apnoea." Eur J Orthod **18**(6): 571-579.

Sonnesen, L., K. E. Jensen, et al. (2013). "Cervical vertebral column morphology in patients with obstructive sleep apnoea assessed using lateral cephalograms and cone beam CT. A comparative study." Dentomaxillofac Radiol **42**(6): 20130060.

Spicuzza, L., D. Caruso, et al. (2015). "Obstructive sleep apnoea syndrome and its management." Ther Adv Chronic Dis **6**(5): 273-285.

Sutthiprapaporn, P., K. Tanimoto, et al. (2008). "Positional changes of oropharyngeal structures due to gravity in the upright and supine positions." Dentomaxillofac Radiol **37**(3): 130-135.

Tkacova, R., W. T. McNicholas, et al. (2014). "Nocturnal intermittent hypoxia predicts prevalent hypertension in the European Sleep Apnoea Database cohort study." Eur Respir J **44**(4): 931-941.

Van Holsbeke, C. S., S. L. Verhulst, et al. (2014). "Change in upper airway geometry between upright and supine position during tidal nasal breathing." J Aerosol Med Pulm Drug Deliv **27**(1): 51-57.

Vasavada, A. N., J. Danaraj, et al. (2008). "Head and neck anthropometry, vertebral geometry and neck strength in height-matched men and women." J Biomech **41**(1): 114-121.

Vedantam, R., L. G. Lenke, et al. (1998). "Comparison of standing sagittal spinal alignment in asymptomatic adolescents and adults." Spine (Phila Pa 1976) **23**(2): 211-215.

Vgontzas, A. N., T. L. Tan, et al. (1994). "Sleep apnea and sleep disruption in obese patients." Arch Intern Med **154**(15): 1705-1711.

Wagnetz, U., H. C. Roberts, et al. (2010). "Dynamic airway evaluation with volume CT: initial experience." Can Assoc Radiol J **61**(2): 90-97.

Weber, P., E. C. Correa, et al. (2012). "Craniocervical posture: cephalometric and biophotogrammetric analysis." Braz J Oral Sci. **11**(3): 416-421.

Weissheimer, A., L. M. Menezes, et al. (2012). "Imaging software accuracy for 3-dimensional analysis of the upper airway." Am J Orthod Dentofacial Orthop **142**(6): 801-813.

Wenzel, A., E. Hojensgaard, et al. (1985). "Cranio-facial morphology and head posture in children with asthma and perennial rhinitis." European Journal of Orthodontics **7**: 83-92.

Young, T., L. Evans, et al. (1997). "Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women." Sleep **20**(9): 705-706.

Young, T., M. Palta, et al. (2009). "Burden of sleep apnea: rationale, design, and major findings of the Wisconsin Sleep Cohort study." WMJ **108**(5): 246-249.

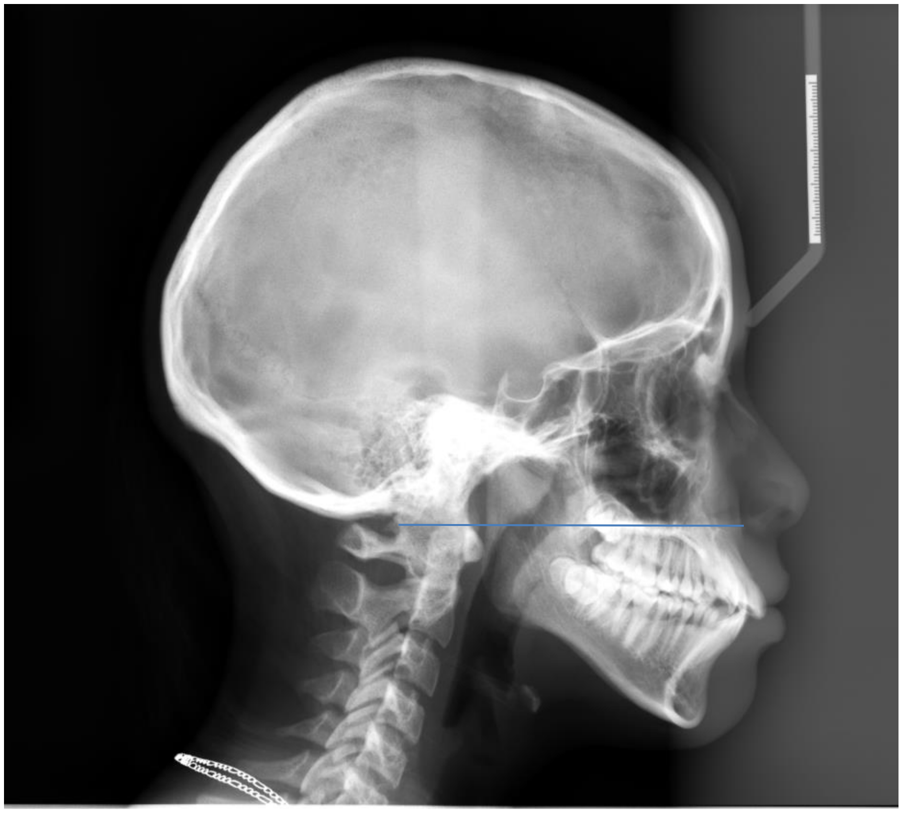
Young, T., M. Palta, et al. (1993). "The occurrence of sleep-disordered breathing among middle-aged adults." N Engl J Med **328**(17): 1230-1235.

Young, T., P. E. Peppard, et al. (2002). "Epidemiology of obstructive sleep apnea: a population health perspective." Am J Respir Crit Care Med **165**(9): 1217-1239.

Zucconi, M., L. Ferini-Strambi, et al. (1992). "Habitual snoring with and without obstructive sleep apnoea: the importance of cephalometric variables." Thorax **47**(3): 157-161.

APPENDIX

Appendix A: Raw Data from Orthodontic patients – palatal plane to tip of Odontoid Process



Patient	Age	PP-C2 (above, at, below C2)
1	18	Below
2	16	At
3	26	Below
4	16	Below
5	16	Above
6	15	At
7	26	Below
8	16	At
9	15	Above
10	50	Below

Appendix B: Raw Data from Measurements made with Anatomage

Patient ID	CT Date	CT Type	Exclude?	CT assessment note	DOB	Age	Gender	BMI	AHI Score	Total Volume (cc) Method 1*	Total Volume (cc) Method 2**	Minimum Area (mm2)	Location of min area	C1/C2 Angle (degrees)	C2/3 Angle (degrees)	C3/4 Angle (degrees)	C4/C5 Angle (degrees)	C1/C4 Angle
1	4/28/2015	Cervical spine CT w/o contrast			2/23/1956	60	M			16.4	14.5	11.4	C2		2.3	10.2	3.8	
2	11/28/2014	Maxillofacial CT w/o contrast	Yes	Does not cover area of interest	12/28/1955	61	F											
3	7/26/2015	Head CT w/o Contrast	Yes	Does not cover area of interest	2/7/1959	57	M											
4	2015	Head CT	Yes	Does not cover area of interest	9/21/1950	66	M											
5	4/2/2015	Soft tissue neck CT w/ contrast			5/22/1964	52	F			7.1		27.8			6.1	9.6	18.1	
7	2012, 2015	Soft tissue neck CT w/ contrast and cervical spine w/o contrast	Yes	Error (poor resolution)	7/20/1987	29	M											
8	4/15/2015	Soft tissue neck CT w/ contrast	Yes	Error (poor resolution)	6/25/1990	26	F											
9	2007, 2012, 2013	Soft neck w/ contrast and Cervical spine CT w/o contrast		2007	3/1/1985	31	F			7.8		37.6			4.3	3.5	3.7	
				2012						7.3		36.7			2.1	3.1	1.9	
				2013						11.8		31.1						
	12/22/2013	Soft tissue neck CT w/ contrast	Yes?	Error (overflow)	1/22/1982	34	F											
11	2013 and 2014	Soft tissue neck CT w/ contrast			5/3/1958	58	M			2.4					7.8	6.4	2.5	
12	2015	Soft tissue neck CT w/ contrast			6/1/1972	44	M			12.2		24.9			3.6	3.7	3.2	
13	4/9/2014	Soft tissue neck CT w/ contrast			9/24/1960	56	F			10.7		72.4			1.4	2.7	3.2	
14	3/4/2015	Cervical spine CT w/o contrast	Yes	Presence of soft tissue pathology	8/23/1939	77	F											
15	2011, 2014	Cervical spine CT w/o contrast	Yes	Presence of spinal path	3/29/1949	67	M			16.4		80						
16	5/30/2015	Cervical spine CT w/o contrast	Yes	Does not cover area of interest	8/13/1980	36	M											
17	2010, 2013, 2014	Cervical spine CT w/o contrast		2010 ok; 2013 & 2014 error	12/31/1967	49	M			6.3		2.9			2.8	1.4	2.3	
18	8/21/2015	Cervical spine CT w/o contrast	Yes	Presence of spinal fusion	8/7/1944	72	M											
19	2012, 2015	Cervical spine CT w/o contrast	Yes	Presence of spinal fusion	8/14/1974	42	F											
20	11/24/2014	Cervical spine CT w/o contrast		Only Method 2 works	5/26/1990	26	F				13.4				1.9	3.2	6.1	
21	10/10/2014	Cervical spine CT w/o contrast		Error (either volume overflow OR image not axial)	3/23/1983	33	M											
22	2013, 2014	Cervical spine CT w/o contrast		2013	8/30/1937	79	M			16.6		51.3						
				2014						12.3	11.9	44.5			13.2	5.8	2.8	
23	9/13/2014	Cervical spine CT w/o contrast		Only Method 2 works	8/21/1963	53	F				23.8				12	3.4	6.8	

Appendix C: Raw Data from Measurements made with Dolphin

Clinic	Age	Gender	BMI	AHI	TV	MA	MA (RU/RL)	uOP	lOP	MCG_OP	MCR_OP	A_O_L	c1_c2	c2_c3	c3_c4	c1_c4	c2_c3_L
cfp	66	F	20.6	9.7	14288.20	176.9	RU	10869.70	3418.50	118.7	102.1	15.2	-18.8	-6.8	4.1	-18.0	49.2
cfp	55	F	23.6	4.0	6521.40	63.2	RU	4542.10	1979.30	110.2	109.1	20.5	-26.0	-11.7	-12.4	-44.4	46.5
cfp	50	M	21.0	15.0	13748.00	159.3	RL	9112.20	4635.80	91.4	87.9	11.1	-37.6	-8.1	-9.7	-54.8	58.2
cfp	17	F	18.0	5.0	12863.60	205.6	RU	7202.70	5660.90	113.1	109.4	13.9	-28.7	3.5	9.5	-16.3	49.4
cfp	59	M	34.0	76.0	7098.60	69	RU	4757.10	2341.50	95.0	88.0	13.0	-38.9	-8.7	-9.6	-55.5	53.2
cfp	40	F	26.0	3.0	5363.00	69.8	RU	3384.70	1978.30	79.6	83.7	13.2	-38.0	-8.8	-14.3	55.8	52.4
cfp	60	F	21.8	8.0	11769.00	110.1	RU	8254.80	3514.20	103.3	92.5	14.4	-22.1	-4.0	-7.5	-35.7	47.9
cfp	41	M	29.0	30.0	13331.70	143.1	RU	9310.50	4021.20	100.9	96.5	20.2	-35.2	-5.8	-4.2	-41.6	55.1
cfp	57	F	27.0	22.0	9359.20	92	RL	7179.30	2179.90	95.6	93.7	15.5	-39.0	-9.1	-7.8	-45.4	52.9
cfp	65	F	34.6	5.0	9872.90	131	RU	7314.70	2558.20	91.1	85.4	6.5	-29.4	-4.9	-1.9	-35.3	49.4
cfp	59	F	23.0	18.0	5041.90	56.7	RU	3071	1970.90	90.1	88.1	15.0	-43.8	-3	-7.9	-48.1	48
cfp	55	F	29.0	17.0	13546.8	122.4	RL	10751.1	2795.70	100.4	96.3	17.9	-35.5	-9.6	-9.9	-54.5	57.4
cfp	27	M	20.1	8.7	9969.20	133.1	RL	7505.90	2463.30	95.6	99.0	17.8	-28.90	-5.40	-5	-38.00	57.50
cfp	38	M	29.7	6.4	12204.20	102.3	RL	8249.40	3954.80	99.8	94.0	12.5	-29.4	1	-3.4	-28.60	58.1
pgd	63	F	25.7	20.3	7573.5	47.4	RU	4717.9	2855.6	85.5	82.1	13.8	-34.6	-2.9	-3	-42.7	52.5
pgd	42	M	28.4	39.0	14183.2	35.7	RU	5073.7	9109.5	85.8	72.4	7.7	-53.1	-8	-7.8	-51.2	55.2
pgd	68	F	26.5	6.0	4550.3	16.7	RU	3083.3	1467	98.7	89.0	13.3	-26.6	-6.4	-12.7	-43.2	50
unmc	79	M	25.5	26.7	8484.20	47.3	RL	5705.00	2779.20	91.3	88.5	12.8	-27.0	-12.8	-4.4	-42.8	53.4
unmc	52	F	52.4	22.8	2173.50	28.5	RU	1582.80	590.70	90.2	92.5	10.6	-32.6	-1.6	-1.1	-36.5	51.8
unmc	29	M	50.2	1.8	10457.60	67.3	RU	9619.10	838.50	81.4	92.1	11.0	-29.3	-4.2	-2.6	-28.1	57.7
unmc	26	F	27.0	0.7	2639.50	29.0	RU	2198.00	441.50	86.2	85.5	10.8	-32.1	-1.8	-2.0	-33.9	50.3
unmc	31	F	21.0	7.0	3128.40	20	RU	708.20	2420.20	93.3	99.6	15.2	-32.2	-1.6	-1.7	-36.0	51.1
unmc	44	M	36.4	50.1	6685.80	23.4	RU	3349.70	3336.10	92.2	87.5	10.4	-31.5	-6.5	-6.7	-34.6	52.4
unmc	56	F	35.3	10.4	7675.50	76.4	RU	5883.60	1791.90	92.1	83.9	10.9	-30.8	-1.4	-5.7	-38.0	52.8
unmc	49	M	25.4	4.2	5654.10	30.7	RU	2752.70	2901.40		100.4	20.6	-27.3	-2.1	-0.9	-27.5	54.6
unmc	26	F	39.9	4.3	5515.80	94.9	RU	2438.20	3077.60		79.1	9.6	-21.6	-3.4	-4.9	-23.3	47.6
unmc	60	M	26.1	107.2	7905.50	16.1	RU	2670.20	5235.30		93.0	16.9	-27.0	-3.3	-7.8	-31.4	55.5
unmc	53	F	29.4	0.5	10064.80	130.9	RU	5279.20	4785.60		76.8	9.9	-28.2	-11.2	-6.9	-41.2	56.4

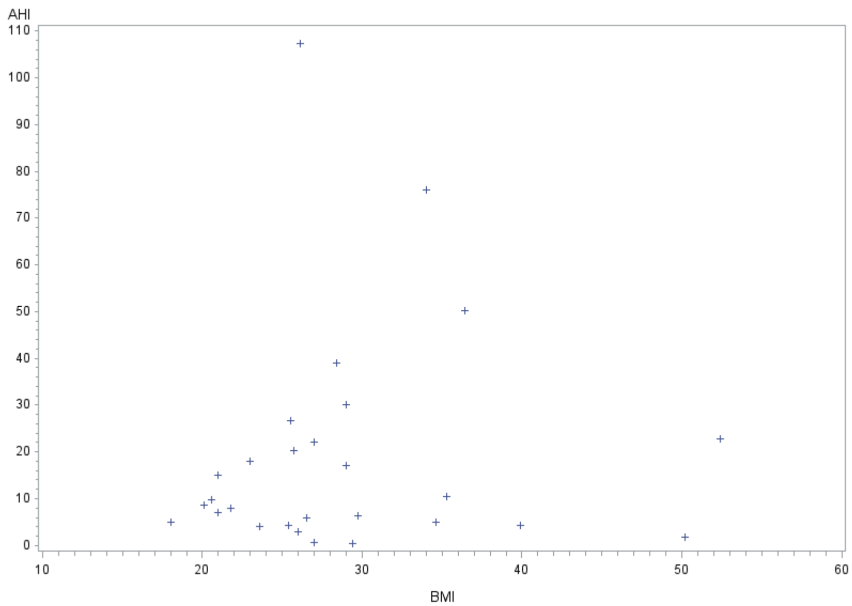
Appendix D: Raw Data from Inter- and Intra-examiner Reliability

	Clinic	Age	Gender	BMI	AHIScore	TV	MA	MA (RU/RL)	uOP	lOP	MCG_OP	MCR_OP	A_O_L (mm)	c1_c2	c2_c3	c3_c4	c1_c4	c2_c3_L
Original Data	cfp					5041.90	56.70	RU	3071.00	1970.90	90.1	88.1	15.0	-43.8	-3.0	-7.9	-48.1	48.0
	cfp					13546.80	122.40	RL	10751.10	2795.70	100.4	96.3	17.9	-35.5	-9.6	-9.9	-54.5	57.4
	cfp					9969.20	133.10	RL	7505.90	2463.30	95.6	99.0	17.8	-28.9	-5.4	-5.0	-38.0	57.5
	cfp					6521.40	63.20	RU	4542.10	1979.30	110.2	109.1	20.5	-26.0	-11.7	-12.4	-44.4	46.5
	cfp					5363.00	69.80	RU	3384.70	1978.30	79.6	83.7	13.2	-38.0	-8.8	-14.3	55.8	52.4
	cfp					11769.00	110.10	RU	8254.80	3514.20	103.3	92.5	14.4	-22.1	-4.0	-7.5	-35.7	47.9
	pgd					7573.50	47.40	RU	4717.90	2855.6	85.5	82.1	13.8	-34.6	-2.9	-3.0	-42.7	52.5
	unmc					5654.10	30.70	RU	2752.70	2901.40	93.3	99.6	15.2	-32.2	-1.6	-1.7	-36.0	51.1
	unmc					7675.50	76.40	RU	5883.60	1791.90	92.1	83.9	10.9	-30.8	-1.4	-5.7	-38.0	52.8
	unmc					10064.80	130.90	RU	5279.20	4785.60		76.8	9.9	-28.2	-11.2	-6.9	-41.2	56.4
Intraexaminer	cfp					5119.70	56.70	RU	3165.70	1954.00	89.7	85.7	16.2	-43.4	-4.9	-10.6	-46.2	47.4
	cfp					13658.50	122.40	RL	10776.00	2882.50	101.4	93.6	17.1	-32.7	-12.3	-17.2	-55.7	57.7
	cfp					9949.50	133.20	RL	7425.00	2524.50	97.1	98.2	17.4	-28.0	-4.8	-7.0	-39.0	57.0
	cfp					6639.40	63.30	RU	5097.50	1541.90	109.2	108.4	20.7	-32.4	-3.9	-15.9	-41.3	46.9
	cfp					5288.90	69.80	RU	3276.00	2012.90	84.4	75.8	13.0	-37.5	-7.4	-13.2	-50.9	51.6
	cfp					11809.70	110.20	RU	8289.40	3520.30	100.5	93.8	15.3	-22.7	-4.9	-6.5	-34.2	47.5
	pgd					7719.30	49.40	RU	5133.40	2585.90	86.2	82.6	14.5	-34.5	-3.0	-3.4	-42.9	51.3
	unmc					5532.30	30.70	RU	2871.70	2660.60	91.3	100.3	15.7	-31.1	-3.8	-2.2	-37.0	50.9
	unmc					7940.80	81.70	RU	5849.00	2091.80	91.4	82.3	12.6	-34.8	-3.0	-2.2	-37.2	52.2
	unmc					10304.20	132.60	RU	5259.90	5044.30		78.2	10.4	-34.5	-5.0	-6.9	-41.3	56.1
Interexaminer	cfp					5103.60	56.70	RU	3216.70	1886.90	89.7	89.5	16.1	-38.9	-4.5	-8.4	-49.4	47.1
	cfp					14211.70	122.40	RL	11174.60	3037.10	97.9	92.2	17.4	-34.1	-13.4	-11.5	-55.7	57.8
	cfp					10213.70	133.10	RL	7349.40	2864.30	88.8	91.6	18.8	-30.0	-4.5	-7.0	-41.0	57.1
	cfp					6543.10	60.10	RU	3572.10	2971.00	105.3	100.2	20.5	-25.8	-2.0	-12.1	-45.3	46.9
	cfp					5324.00	69.80	RU	3225.40	2098.60	80.3	75.3	12.8	-40.7	-8.7	-14.1	-54.2	51.9
	cfp					11860.30	110.20	RU	7371.10	4489.20	96.0	86.6	15.9	-21.1	-4.9	-6.5	-34.9	46.5
	pgd					6789.60	36.90	RU	4598.90	2190.70	80.0	76.8	15.5	-35.7	-3.5	-6.2	-48.0	51.8
	unmc					5944.40	33.40	RU	2823.30	3121.10	86.8	89.6	15.8	-32.8	-1.5	-1.0	-34.1	50.0
	unmc					8203.20	88.60	RU	5857.70	2345.50	83.2	82.0	16.6	-30.3	-8.2	-4.5	-35.8	52.7
	unmc					10594.40	140.10	RU	5315.00	5279.40		79.2	11.3	-30.1	-6.8	-2.2	-36.3	54.9

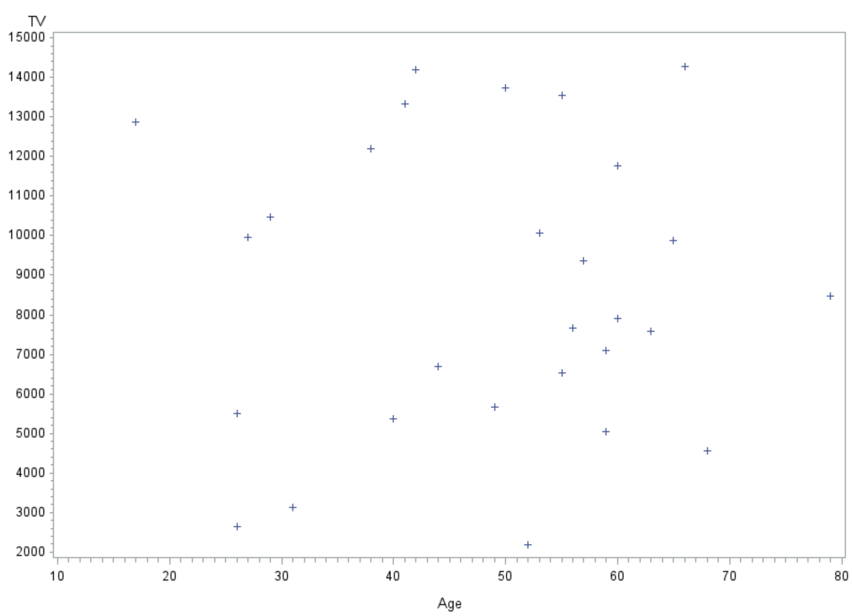
Appendix E: Statistical Analyses

E1. Correlation Analyses

1. AHI and BMI: No obvious correlation



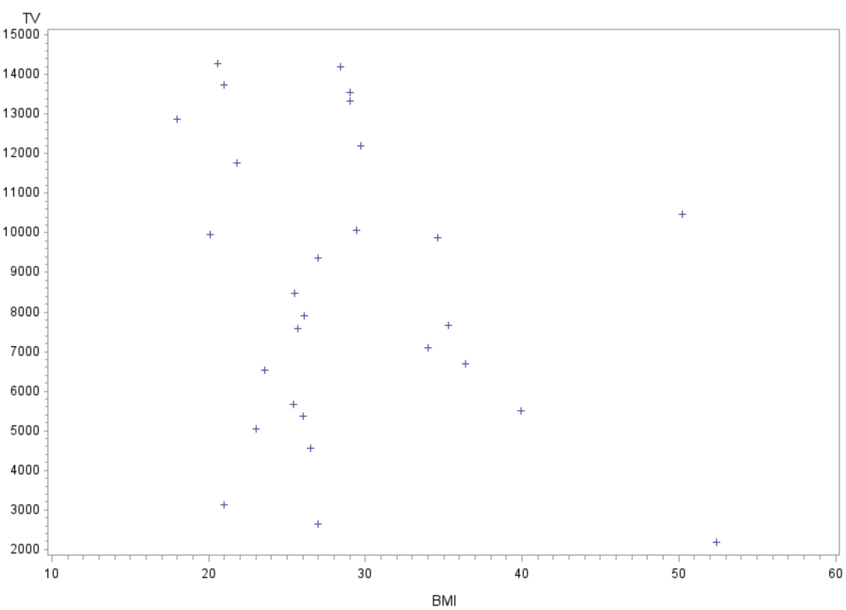
2. TV and AGE: No significant association



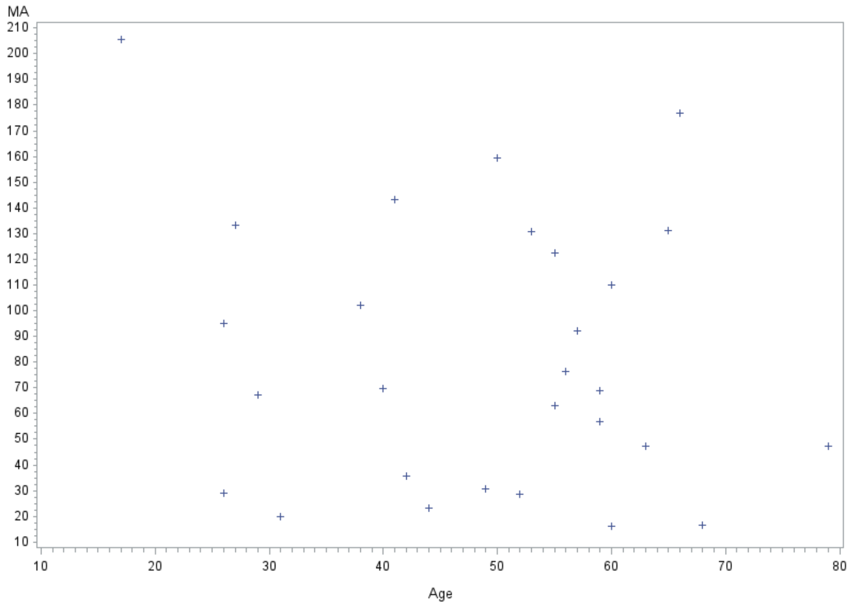
3. TV and Gender: No significant association (p=0.1216)

Gender	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
F		7761.6	5772.4	9750.8	3868.8	2881.4	5888.1
M		9974.7	7929.5	12020.0	3044.4	2127.2	5342.7
Diff (1-2)	Pooled	-2213.1	-5056.1	629.9	3574.3	2814.8	4898.3

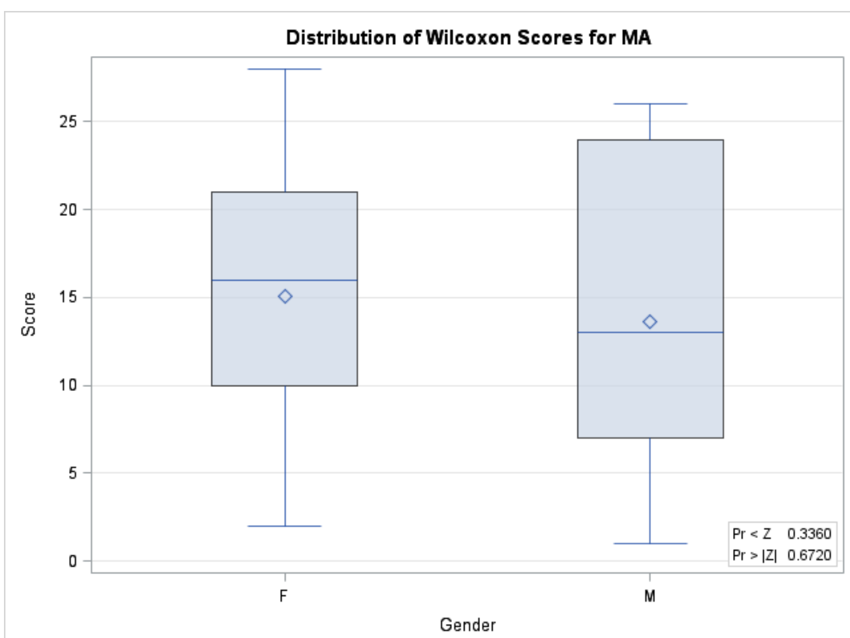
4. TV and BMI: No significant association



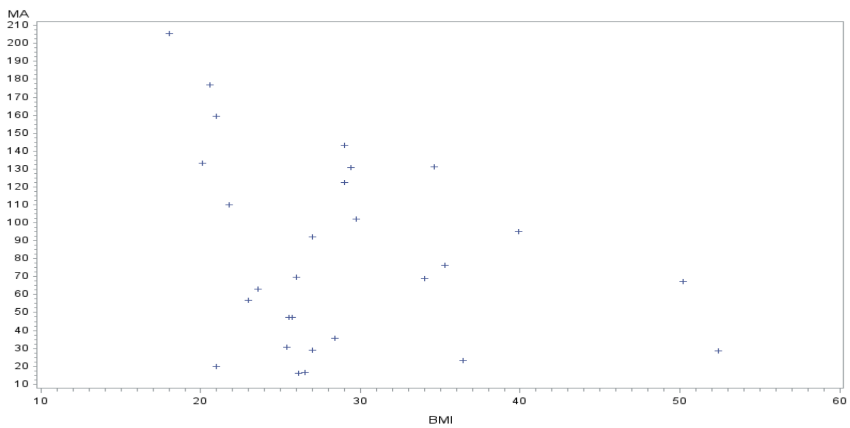
5. MA and Age: No significant association. Pearson correlation = -0.12733 (p=0.5185)



6. MA and Gender: No significant association. Wilcoxon rank test (p=0.6720)



7. MA and BMI: No significant association. Spearman correlation = -0.1971 (p=0.1350)



8. MA(RU/RL) and AGE: No significant association. Wilcoxon p=1

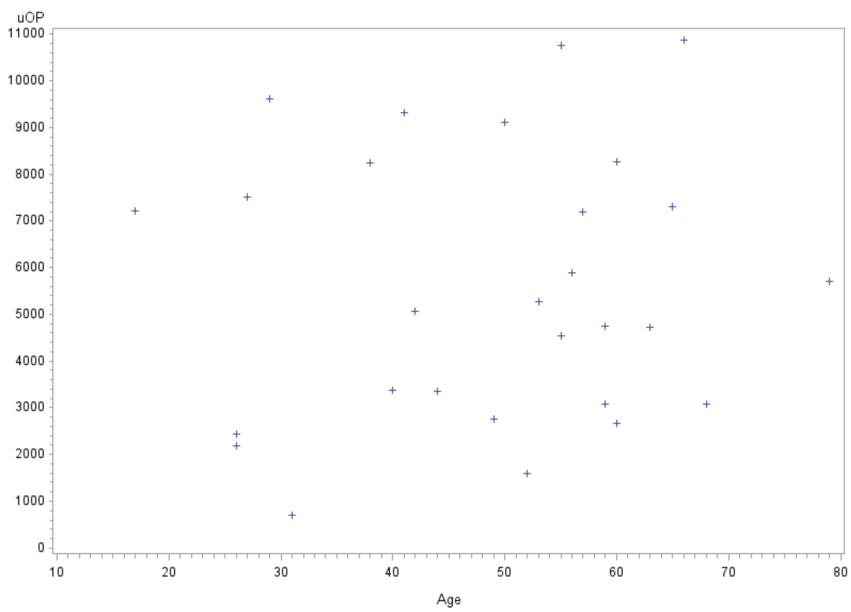
MARUL	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
RL		51.0000	32.3330	69.6670	17.7876	11.1032	43.6262
RU		48.2273	41.6184	54.8362	14.9058	11.4678	21.3014
Diff (1-2)	Pooled	2.7727	-11.9028	17.4483	15.5017	12.2078	21.2440

9. MA(RU/RL) and Gender: No significant association. Fisher exact test p = 0.1741

10. MA(RU/RL) and BMI: No significant association (p=0.2607)

MARUL	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
RL		25.3833	21.1472	29.6194	4.0365	2.5196	9.9001
RU		29.7409	25.7763	33.7056	8.9420	6.8795	12.7786
Diff (1-2)	Pooled	-4.3576	-12.1480	3.4328	8.2289	6.4804	11.2772

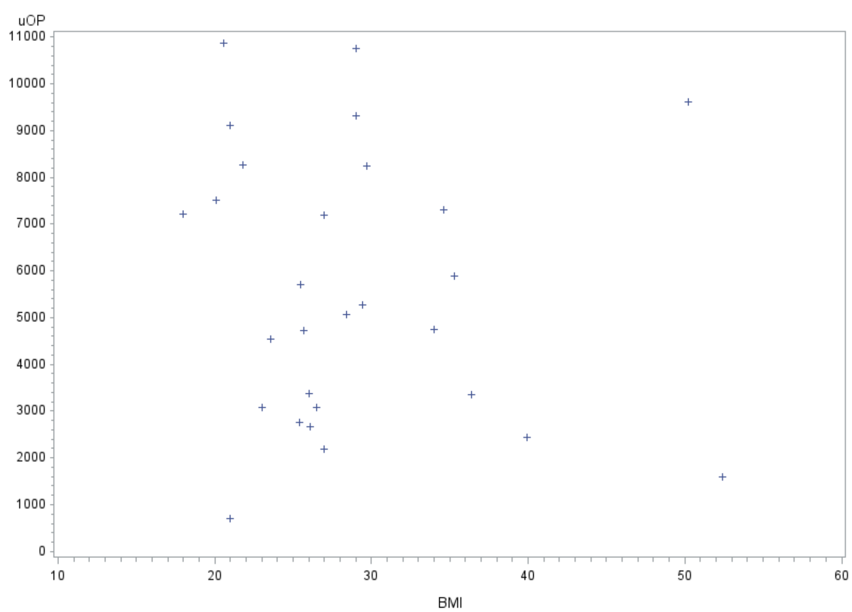
11. uOP and Age: No significant association (p=0.5800)



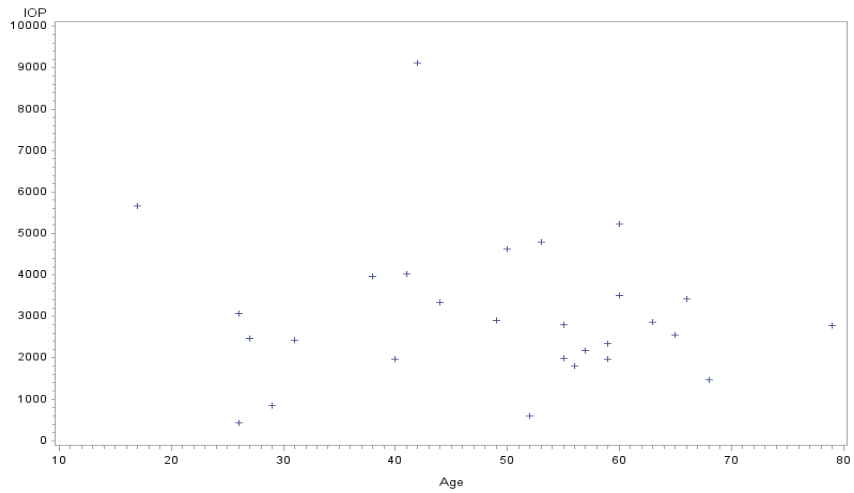
12. uOP and Gender: No significant association (p=0.3880)

Gender	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
F		5203.6	3639.7	6767.5	3041.8	2265.4	4629.4
M		6191.4	4391.1	7991.7	2679.8	1872.4	4702.9
Diff (1-2)	**Pooled**	-987.8	-3300.7	1325.1	2907.9	2290.0	3985.1

13. uOP and BMI: No significant association. Wilcoxon p=1



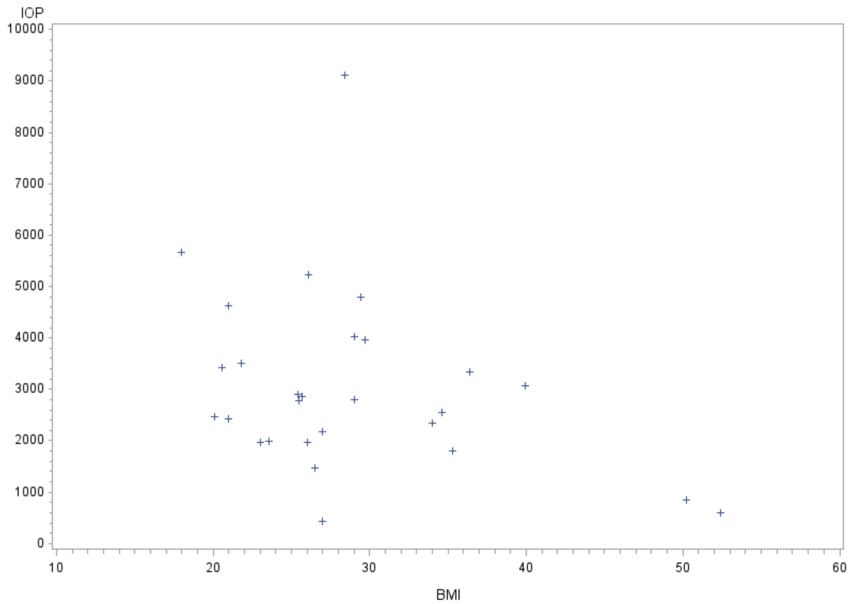
14. lOP and AGE: No significant association (p=0.7745, Spearman)



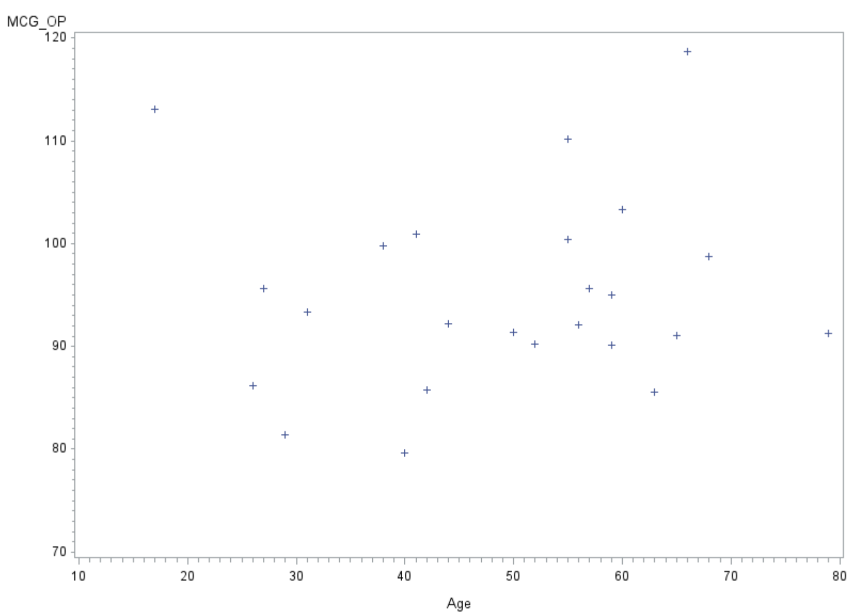
15. lOP and Gender: No significant association (p=0.0713)

Gender	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
F		2558.0	1878.3	3237.7	1322.0	984.6	2012.1
M		3783.3	2346.1	5220.6	2139.4	1494.8	3754.4
Diff (1-2)	Pooled	-1225.3	-2564.8	114.1	1684.0	1326.2	2307.8

16. lOP and BMI: There is a trend that as lOP decreases, BMI increases. The association is not statistically significant (p=0.0763, Pearson).



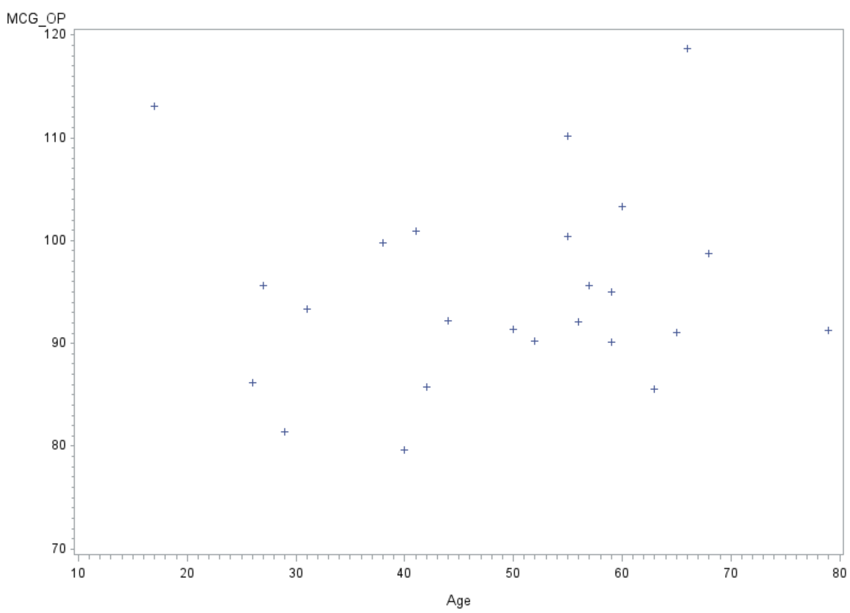
17. McG_OP and Age: No significant association (p=0.6545, Pearson)



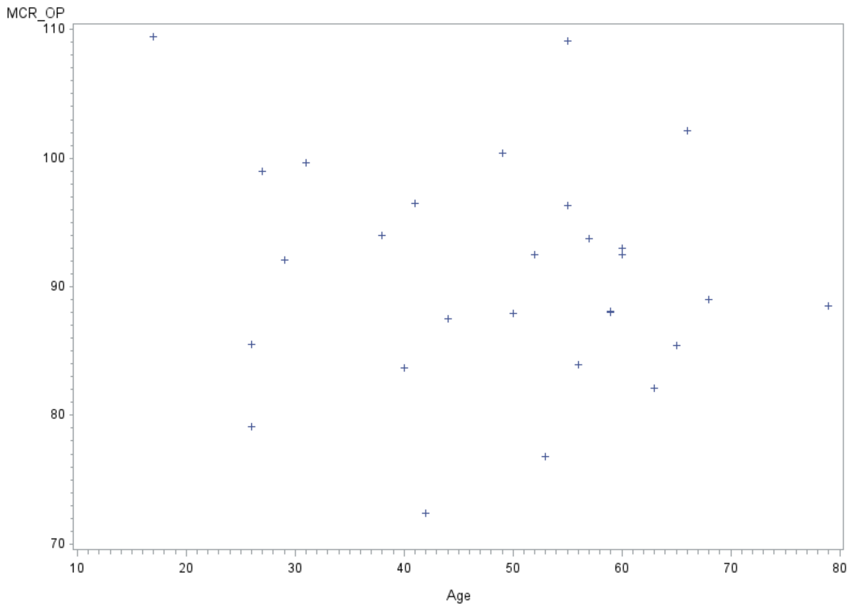
18. McG_OP and Gender: No significant association (p=0.6547, Nonparametric test)

Gender	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
F		96.5400	90.4822	102.6	10.9390	8.0088	17.2519
M		92.6000	87.8115	97.3885	6.2296	4.2078	11.9344
Diff (1-2)	Pooled	3.9400	-4.3675	12.2475	9.5006	7.3477	13.4466

19. McG_OP and Age: No significant association (p=0.6545, Pearson)



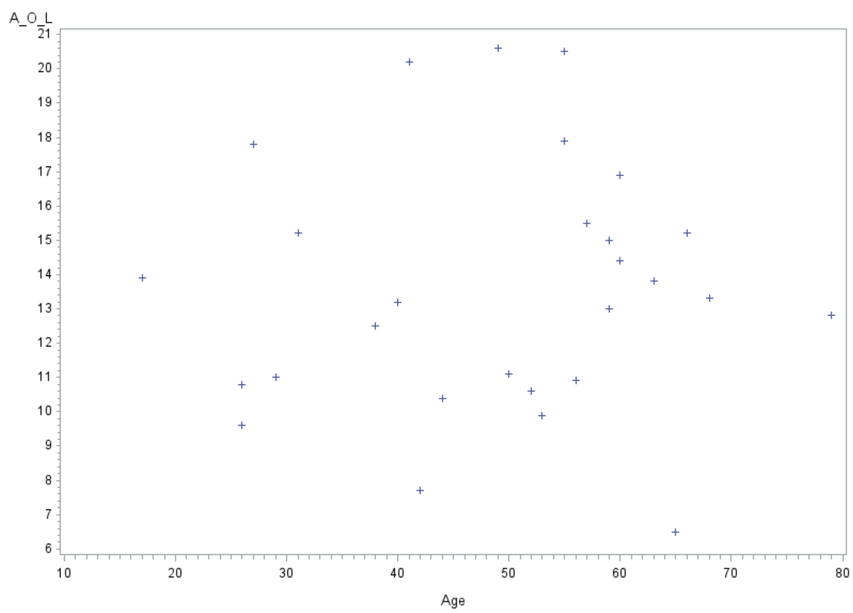
20. McR_OP and Age: No significant association (p=0.467, Pearson)



21. McR_OP and Gender: No significant association (p=0.9406, T-test)

Gender	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
F		91.1059	86.1223	96.0895	9.6928	7.2189	14.7518
M		90.8455	85.7308	95.9602	7.6133	5.3196	13.3609
Diff (1-2)	Pooled	0.2604	-6.8586	7.3795	8.9504	7.0486	12.2659

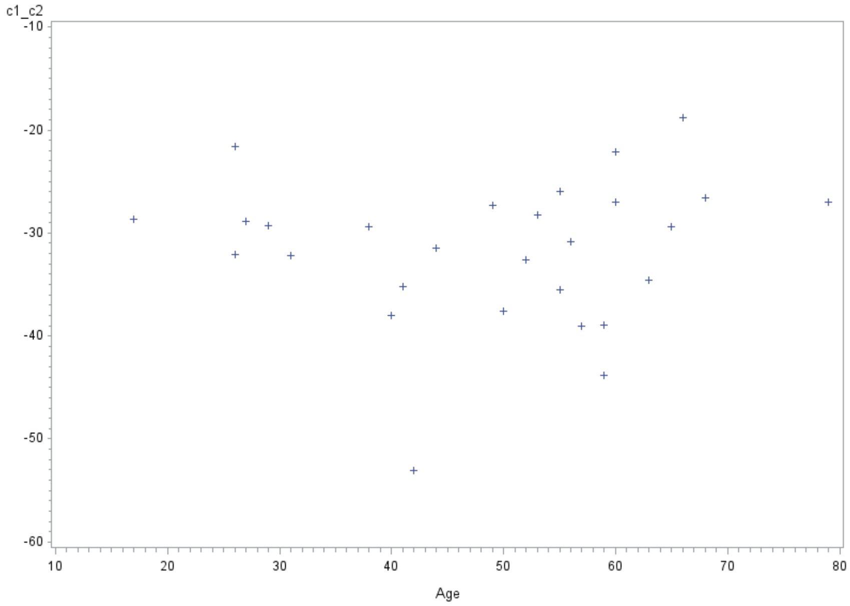
22. AO_L and Age: No significant association (p=0.5628, Spearman)



23. AO_L and Gender: No significant association (p=0.6338)

Gender	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
F		13.3059	11.5786	15.0331	3.3594	2.5020	5.1128
M		14.0000	11.1529	16.8471	4.2379	2.9611	7.4373
Diff (1-2)	Pooled	-0.6941	-3.6545	2.2663	3.7219	2.9311	5.1006

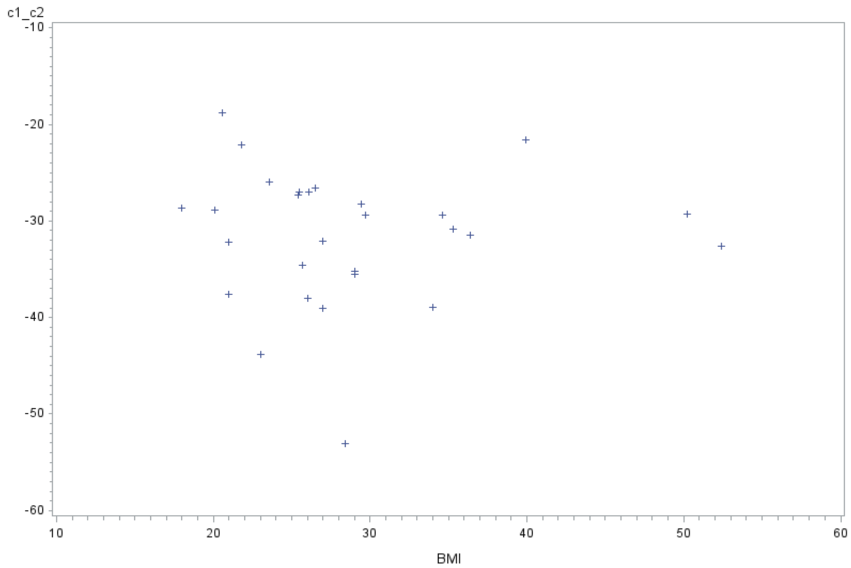
24. C1_C2 and Age: Middle ages tend to have smaller C1_C2 angle. Spearman correlation not significant (p=0.4753)



25. C1_C2 and Gender: No significant association (p=0.6213, nonparametric test)

Gender	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
F		-30.5882	-33.9619	-27.2146	6.5616	4.8869	9.9863
M		-33.2000	-38.4667	-27.9333	7.8395	5.4776	13.7578
Diff (1-2)	Pooled	2.6118	-3.0200	8.2435	7.0805	5.5760	9.7033

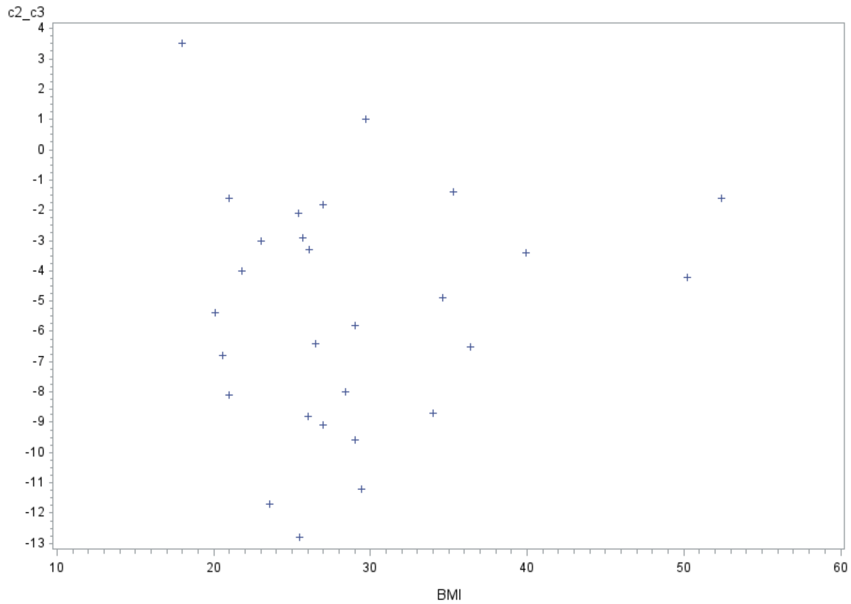
26. C1_C2 and BMI: No significant association (p=0.4018, Spearman)



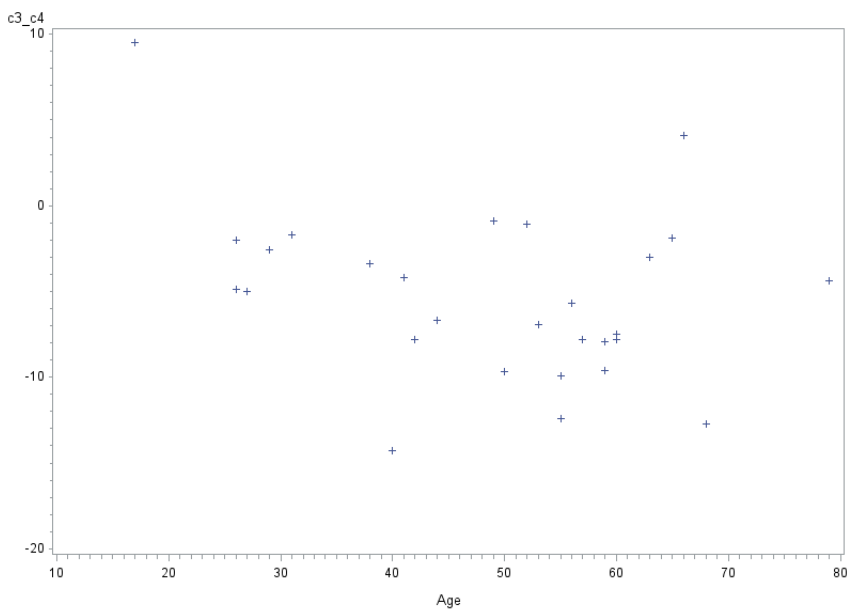
27. C2_C3 and Gender: No significant association (p=0.5944)

Gender	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
F		-4.9824	-7.1002	-2.8645	4.1192	3.0679	6.2691
M		-5.8091	-8.2950	-3.3231	3.7004	2.5855	6.4939
Diff (1-2)	Pooled	0.8267	-2.3257	3.9792	3.9634	3.1212	5.4315

28. C2_C3 and BMI: No significant association (p=0.9081)



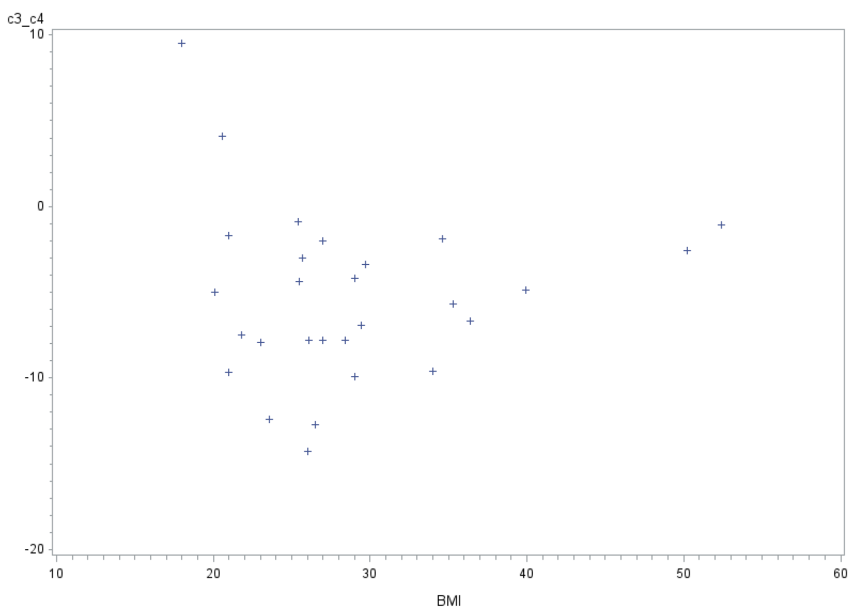
29. C3_C4 and Age: No significant association (p=0.0835, Pearson)



30. C3_C4 and Gender: No significant association (p=0.7376, Wilcoxon)

Gender	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
F		-5.0647	-8.1944	-1.9350	6.0872	4.5335	9.2642
M		-5.6455	-7.5852	-3.7057	2.8873	2.0174	5.0671
Diff (1-2)	Satterthwaite	0.5807	-2.9539	4.1154	5.0999	4.0162	6.9890

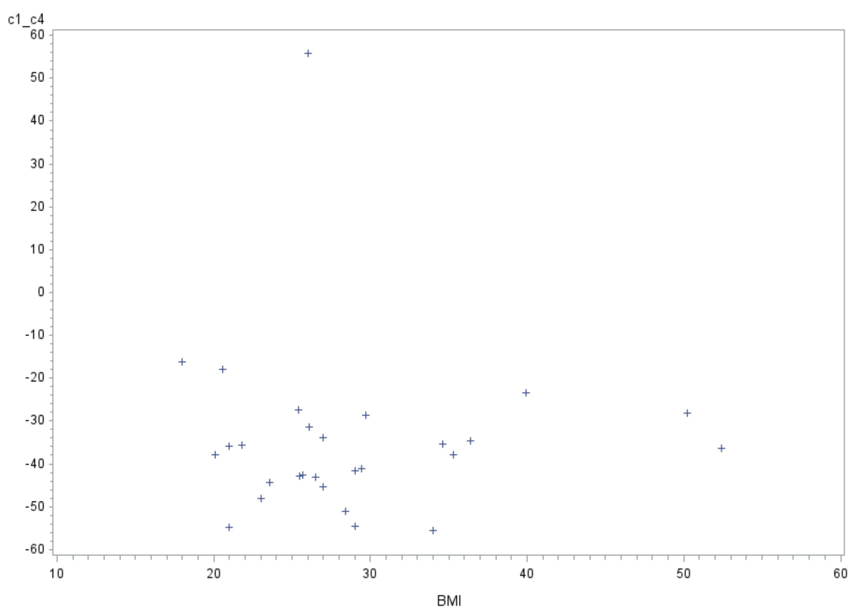
31. C3_C4 and BMI: No significant association (p=0.9713, Spearman)



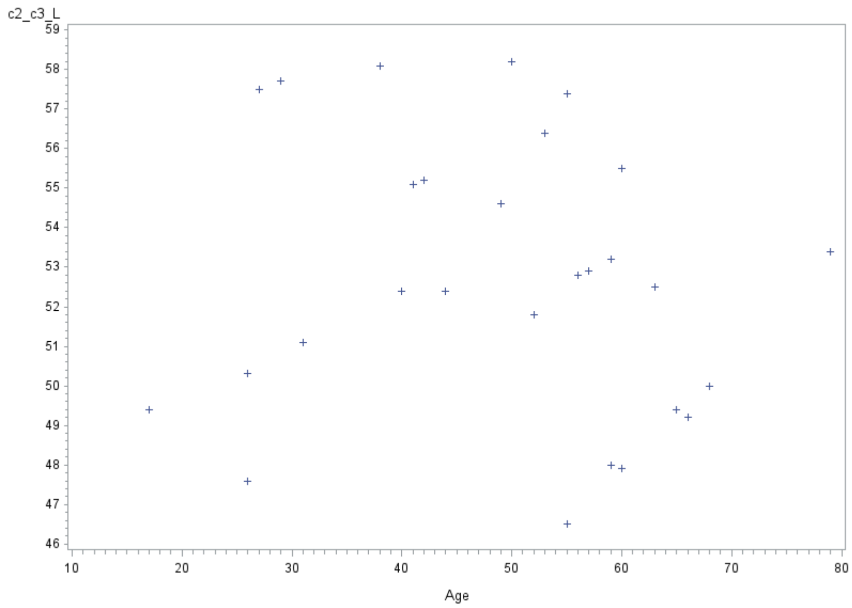
32. C1_C4 and Gender: No significant association (p=0.2566)

Gender	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
F		-31.5706	-44.2612	-18.8800	24.6826	18.3828	37.5651
M		-39.4636	-46.5953	-32.3320	10.6156	7.4173	18.6296
Diff (1-2)	Satterthwaite	7.8930	-6.1366	21.9227	20.4512	16.1057	28.0270

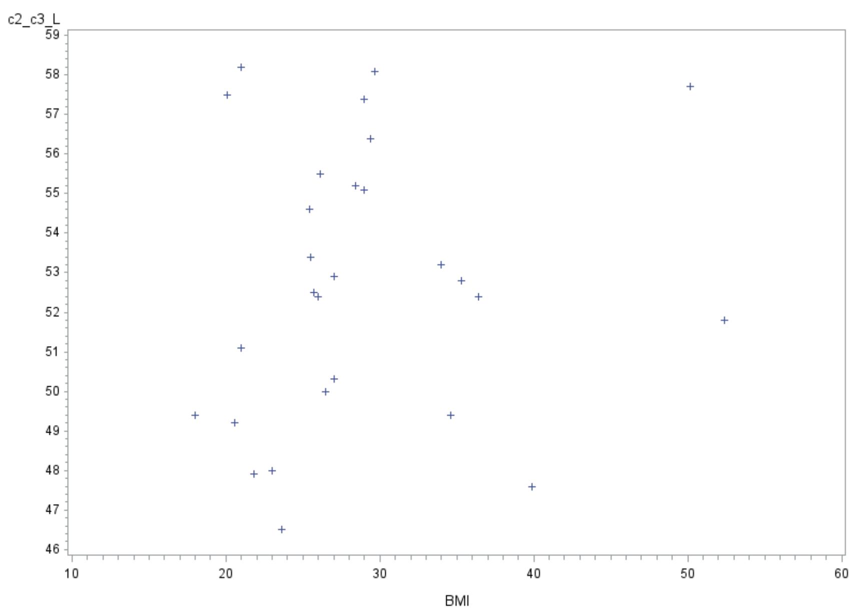
33. C1_C4 and BMI: No significant association (p=0.9691)



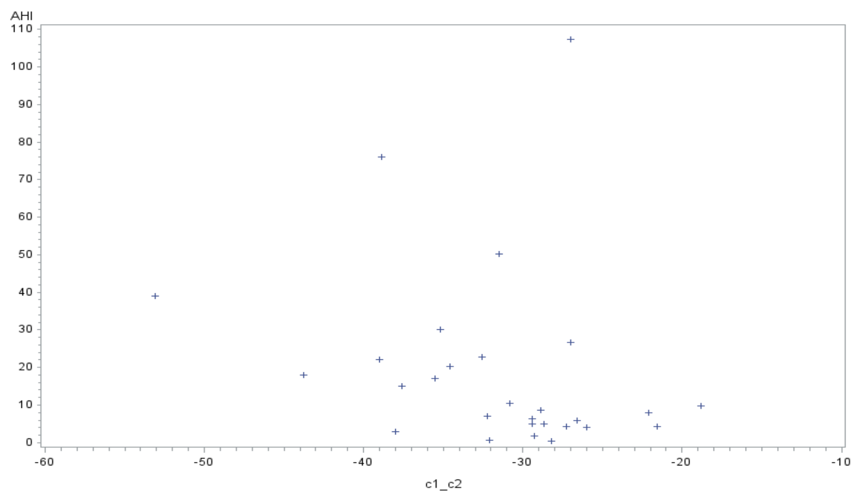
34. C2_C3_L and Age: No significant association (p=0.3610)

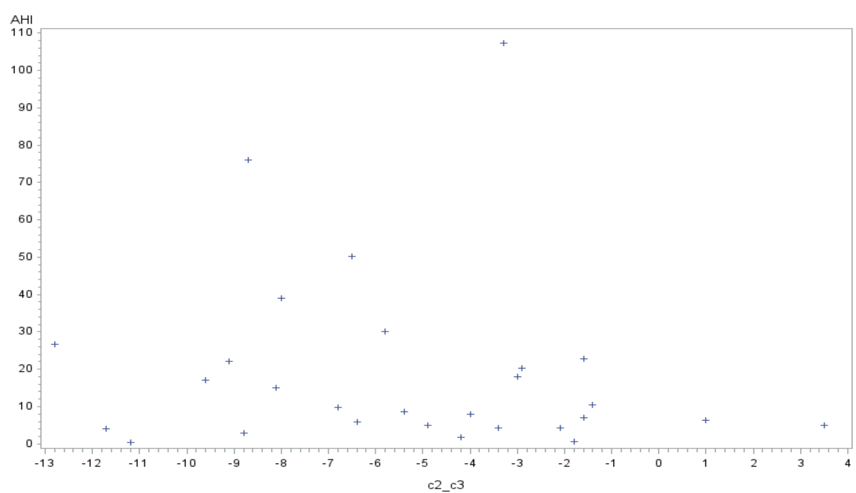


35. C2_C3_L and BMI: No significant association (p=0.3939)

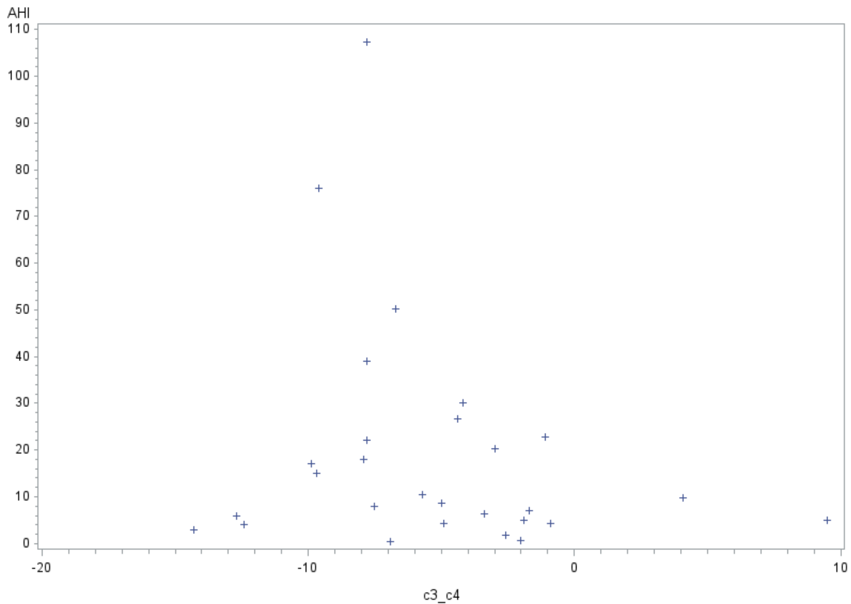


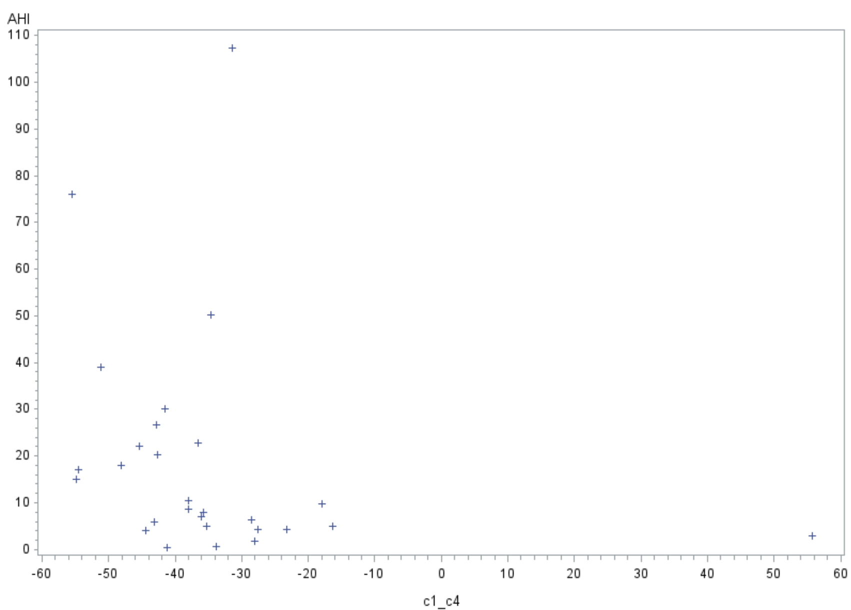
36. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and AHI. No significant associations





36 Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and AHI



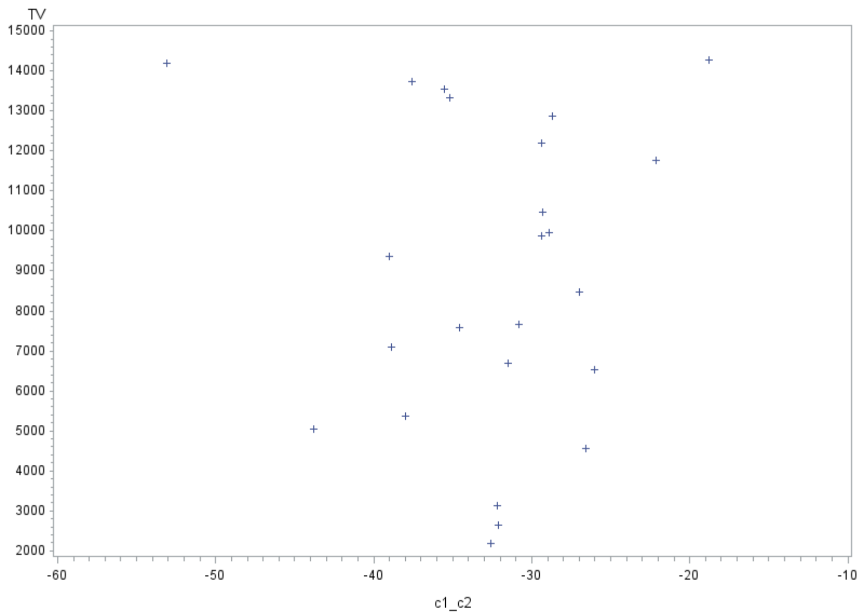


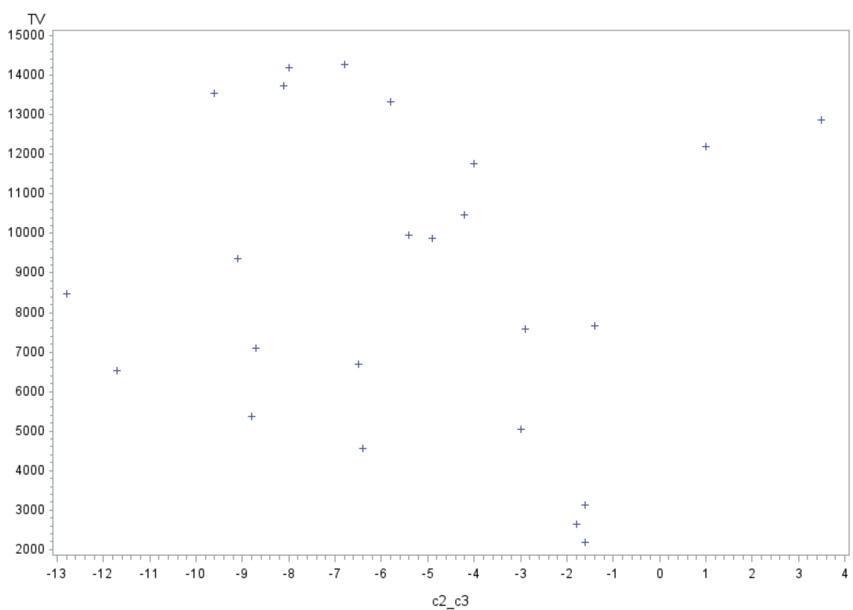
36. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and AHI. No significant associations

Pearson Correlation Coefficients, N = 28
Prob > |r| under H0: Rho=0

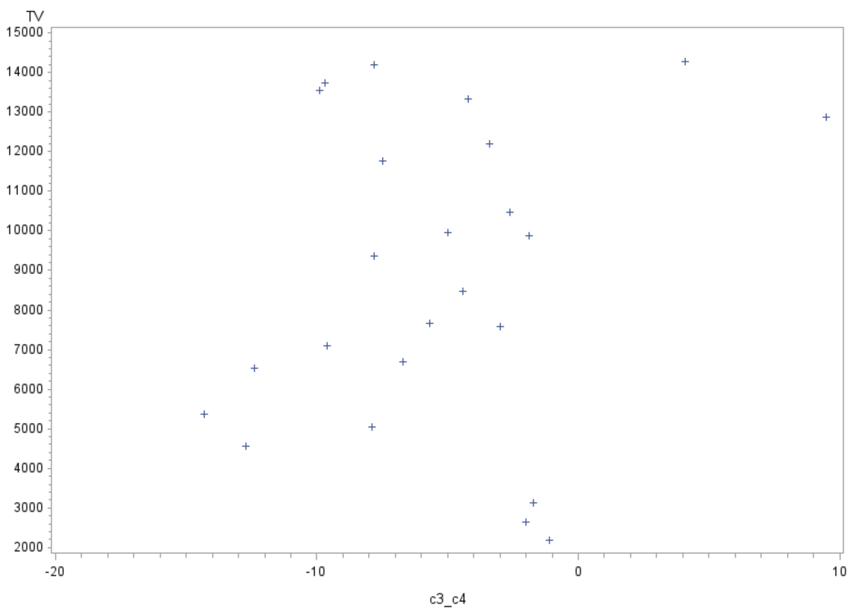
	AHI	c1_c2	c2_c3	c3_c4	c1_c4
AHI	1.00000	-0.24464	-0.12423	-0.20964	-0.23553
		0.2096	0.5288	0.2843	0.2276
c1_c2	-0.24464	1.00000	0.14812	0.32649	0.17839
	0.2096		0.4519	0.0899	0.3637
c2_c3	-0.12423	0.14812	1.00000	0.62276	0.14613
	0.5288	0.4519		0.0004	0.4581
c3_c4	-0.20964	0.32649	0.62276	1.00000	0.05190
	0.2843	0.0899	0.0004		0.7931
c1_c4	-0.23553	0.17839	0.14613	0.05190	1.00000
	0.2276	0.3637	0.4581	0.7931	

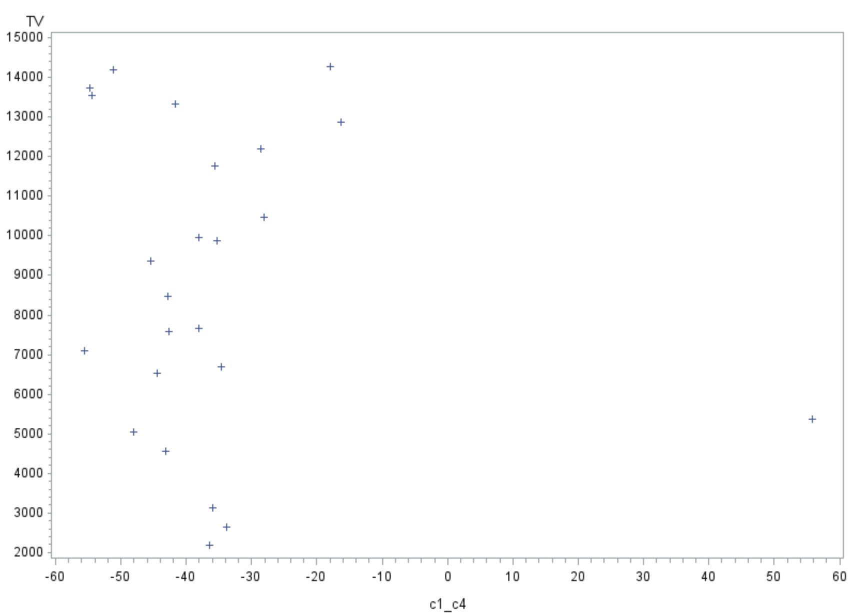
37. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and TV. No significant associations.





37. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and TV



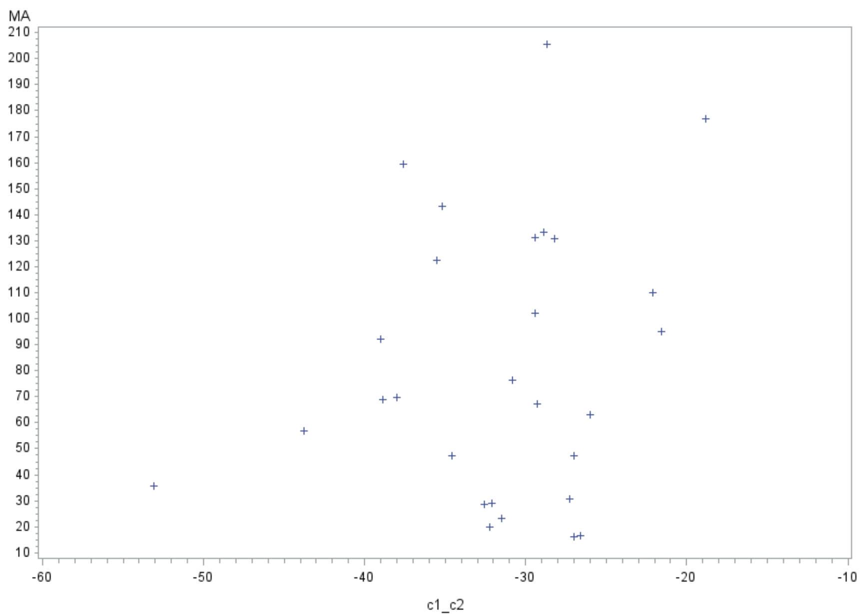


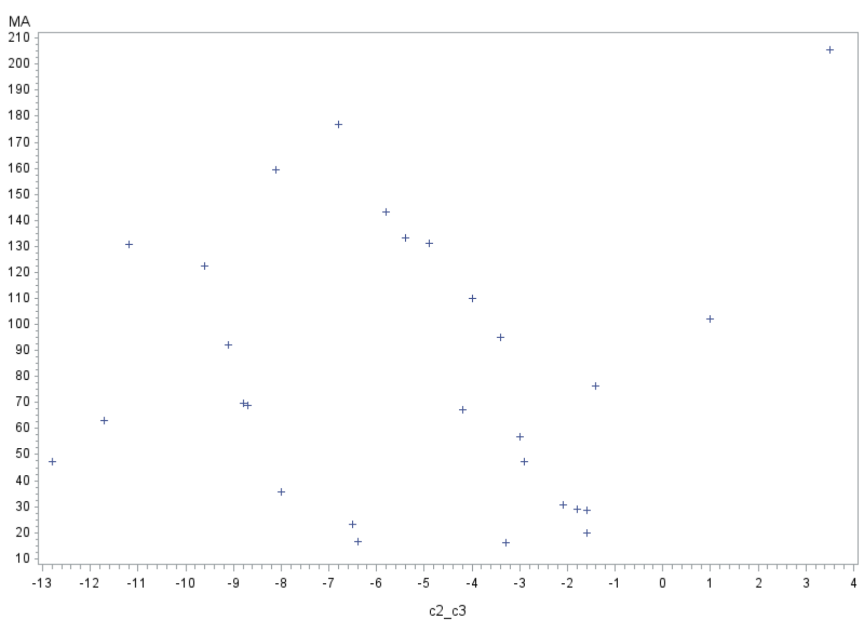
37. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and TV. No significant associations

Pearson Correlation Coefficients, N = 24
Prob > |r| under H0: Rho=0

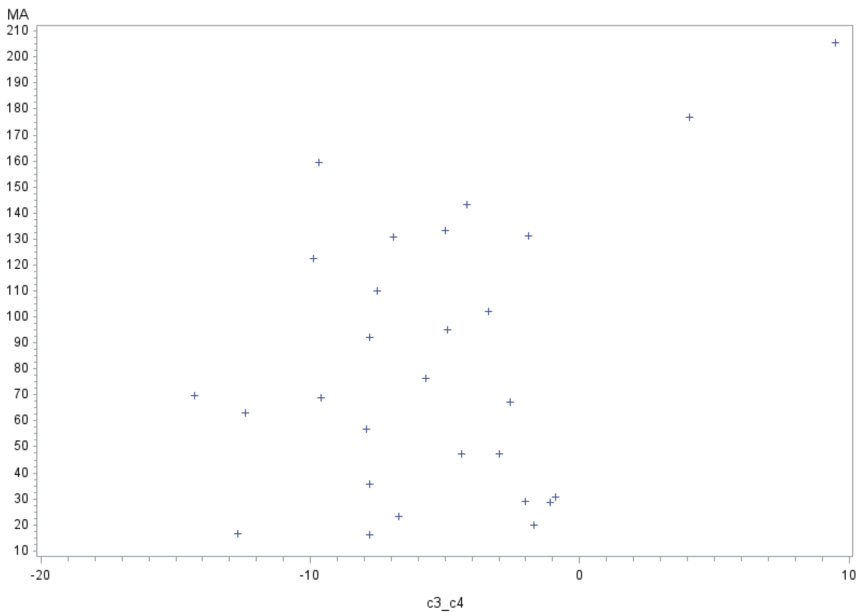
	TV	c1_c2	c2_c3	c3_c4	c1_c4
TV	1.00000	0.00694	-0.11161	0.19933	-0.13617
		0.9743	0.6036	0.3504	0.5258
c1_c2	0.00694	1.00000	0.13416	0.34979	0.15101
	0.9743		0.5320	0.0938	0.4812
c2_c3	-0.11161	0.13416	1.00000	0.64127	0.11281
	0.6036	0.5320		0.0007	0.5997
c3_c4	0.19933	0.34979	0.64127	1.00000	0.03916
	0.3504	0.0938	0.0007		0.8558
c1_c4	-0.13617	0.15101	0.11281	0.03916	1.00000
	0.5258	0.4812	0.5997	0.8558	

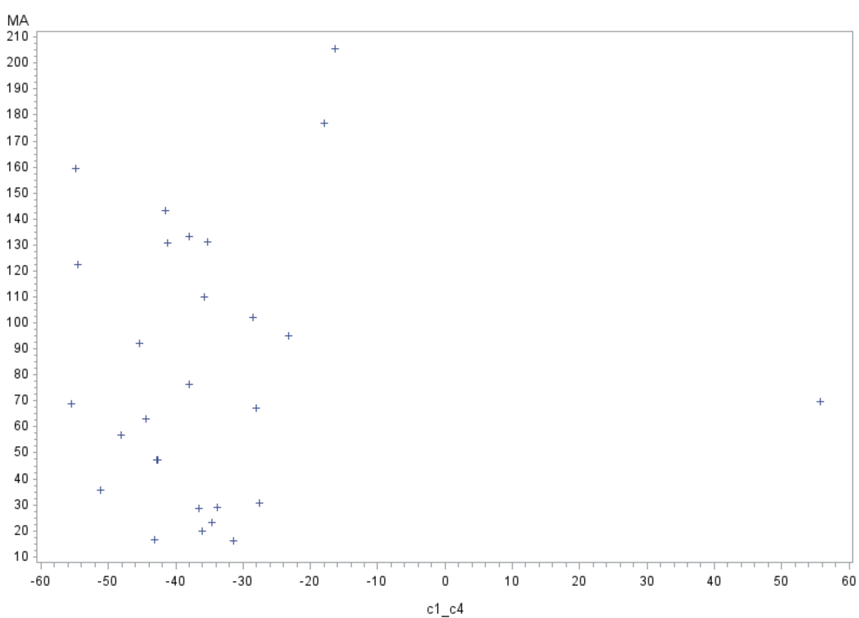
38. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and MA. No significant associations





38. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and MA. No significant associations





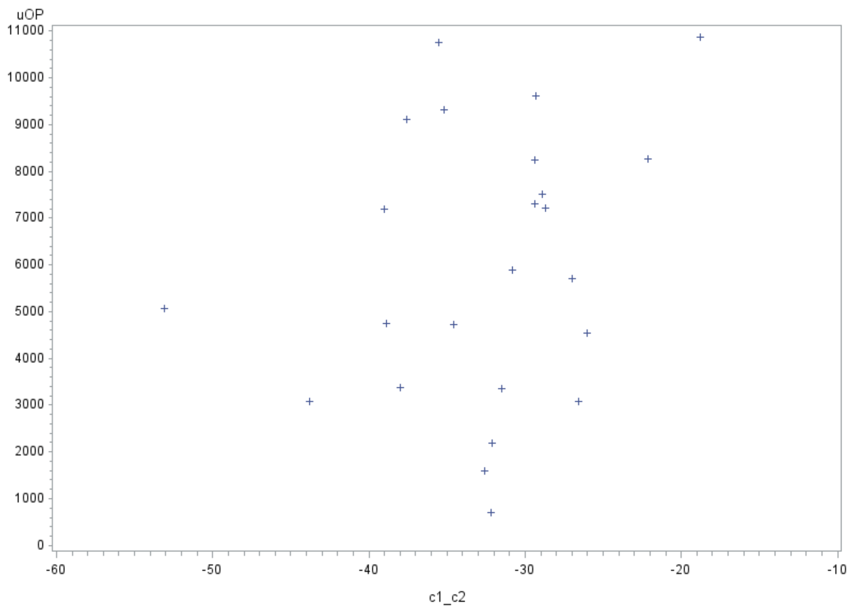
38. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and MA. No significant associations

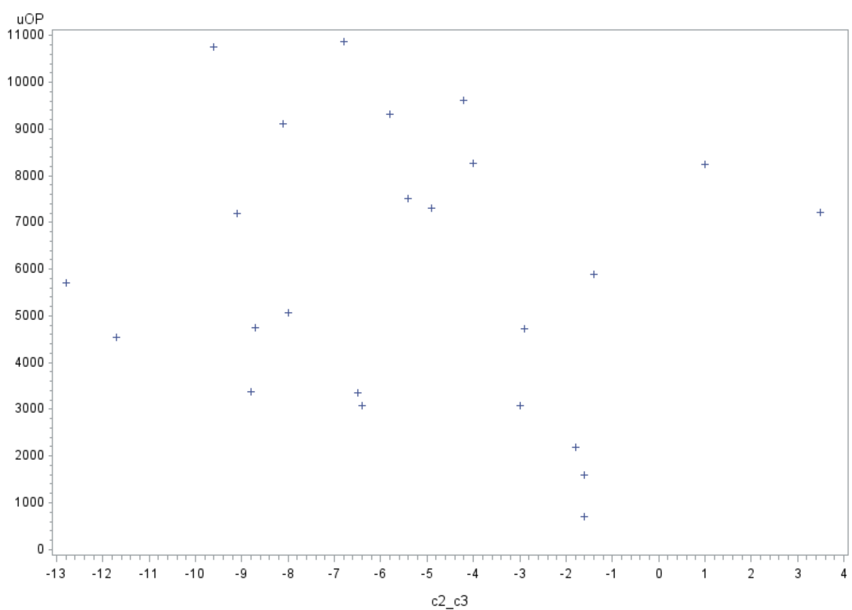
Pearson Correlation Coefficients, N = 28
Prob > |r| under H0: Rho=0

	MA	c1_c2	c2_c3	c3_c4	c1_c4
MA	1.00000	0.20403	0.00866	0.35617	0.05959
		0.2977	0.9651	0.0628	0.7633
c1_c2	0.20403	1.00000	0.14812	0.32649	0.17839
	0.2977		0.4519	0.0899	0.3637
c2_c3	0.00866	0.14812	1.00000	0.62276	0.14613
	0.9651	0.4519		0.0004	0.4581
c3_c4	0.35617	0.32649	0.62276	1.00000	0.05190
	0.0628	0.0899	0.0004		0.7931
c1_c4	0.05959	0.17839	0.14613	0.05190	1.00000
	0.7633	0.3637	0.4581	0.7931	

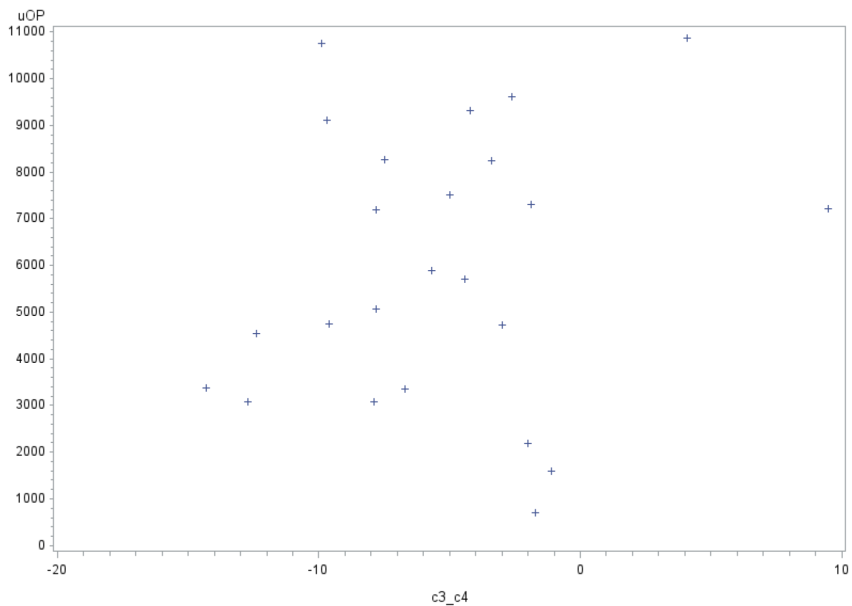
T-test does not show any significant differences of (C1_C2, C2_C3, C3_C4, C1_C4) between two subgroup of MA(RU/RL) with corresponding p-values 0.6243, 0,1558, 0.4483, and 0.2126.

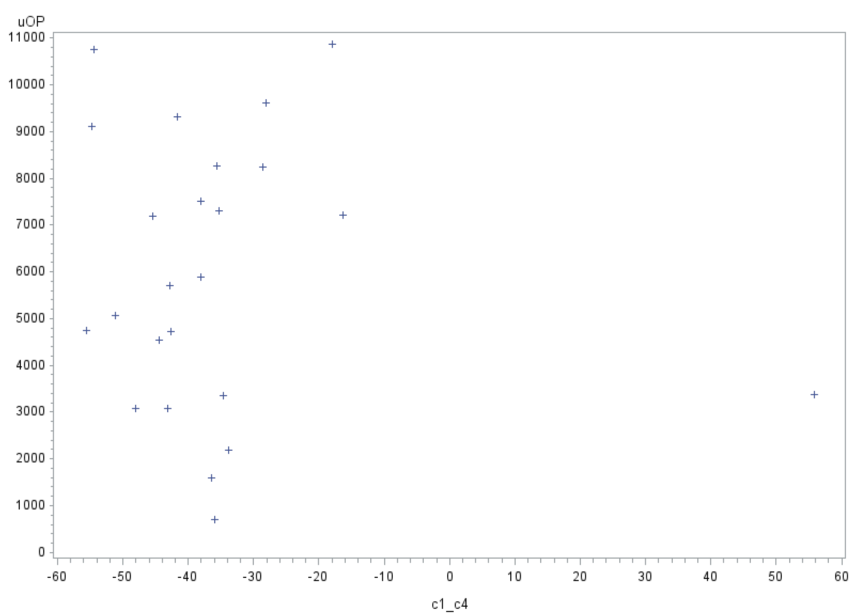
39. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and uOP. No significant associations





39. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and uOP. No significant associations



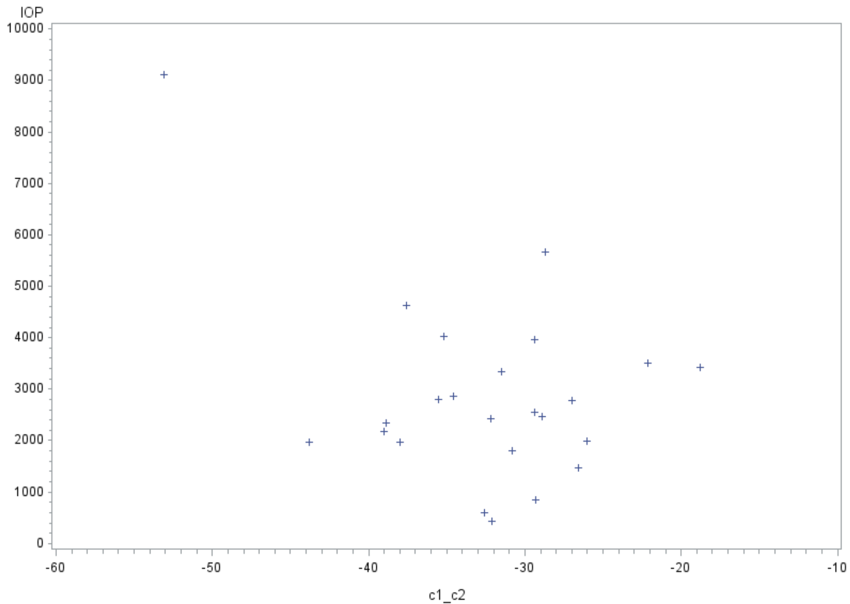


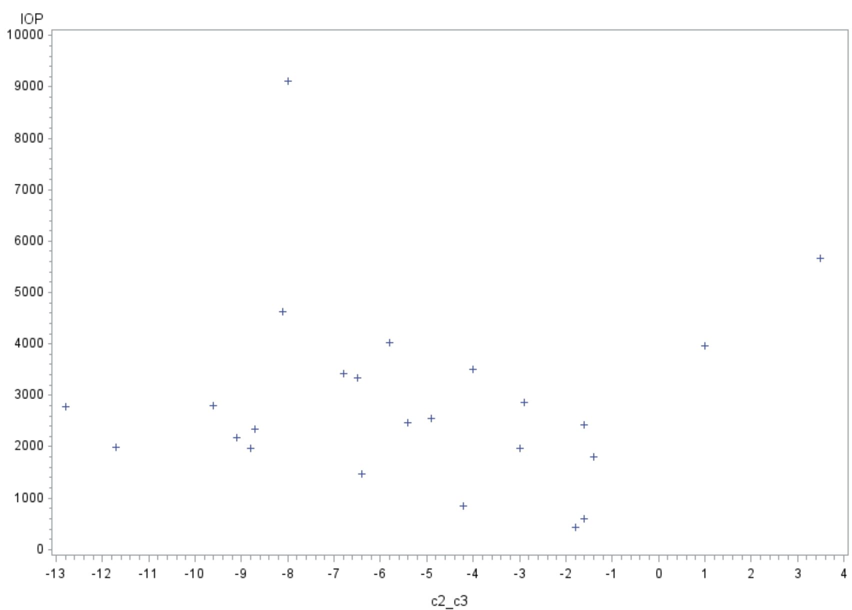
39. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and uOP. No significant associations

Pearson Correlation Coefficients, N = 24
Prob > |r| under H0: Rho=0

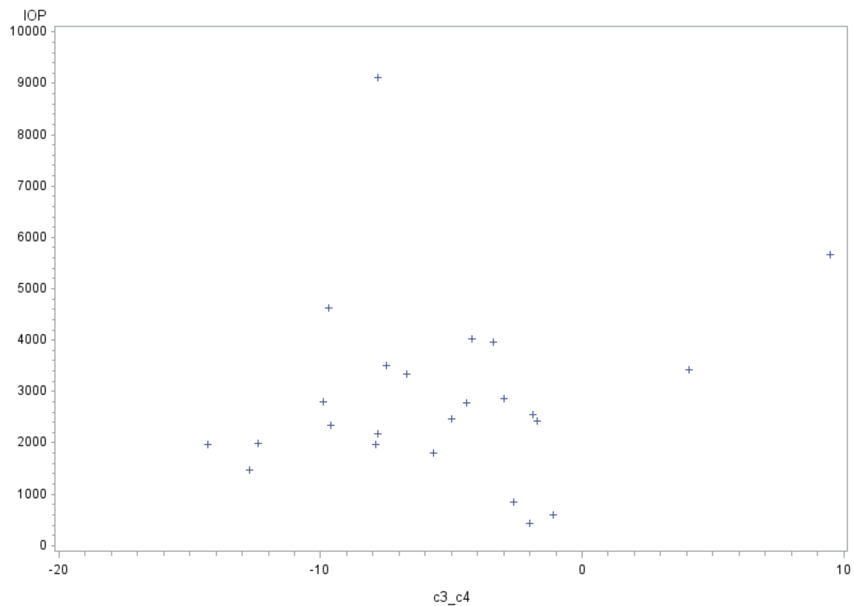
	uOP	c1_c2	c2_c3	c3_c4	c1_c4
uOP	1.00000	0.24858	-0.13640	0.17880	-0.10339
		0.2415	0.5251	0.4032	0.6307
c1_c2	0.24858	1.00000	0.13416	0.34979	0.15101
	0.2415		0.5320	0.0938	0.4812
c2_c3	-0.13640	0.13416	1.00000	0.64127	0.11281
	0.5251	0.5320		0.0007	0.5997
c3_c4	0.17880	0.34979	0.64127	1.00000	0.03916
	0.4032	0.0938	0.0007		0.8558
c1_c4	-0.10339	0.15101	0.11281	0.03916	1.00000
	0.6307	0.4812	0.5997	0.8558	

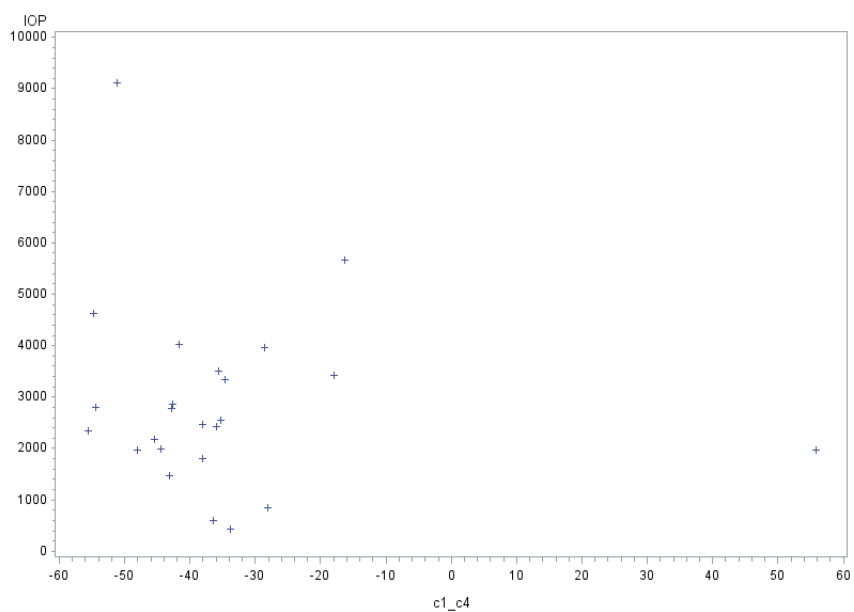
40. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and IOP. No significant associations





40. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and IOP. No significant associations



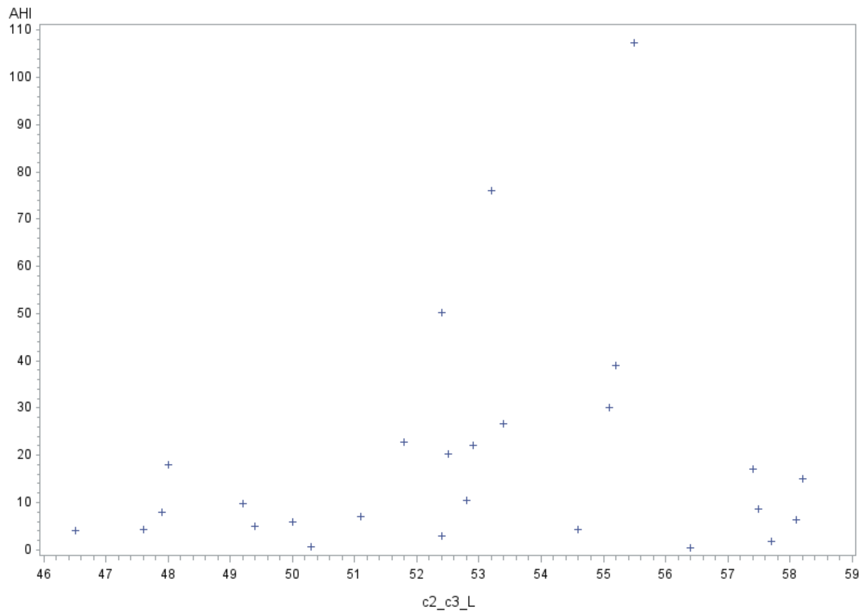


40. Cervical spine angles (C1-C2, C2_C3, C3_C4, C1_C4) and lOP. No significant associations

Pearson Correlation Coefficients, N = 24
Prob > |r| under H0: Rho=0

	lOP	c1_c2	c2_c3	c3_c4	c1_c4
lOP	1.00000	-0.38656	-0.01787	0.13656	-0.12359
		0.0620	0.9339	0.5246	0.5651
c1_c2	-0.38656	1.00000	0.13416	0.34979	0.15101
	0.0620		0.5320	0.0938	0.4812
c2_c3	-0.01787	0.13416	1.00000	0.64127	0.11281
	0.9339	0.5320		0.0007	0.5997
c3_c4	0.13656	0.34979	0.64127	1.00000	0.03916
	0.5246	0.0938	0.0007		0.8558
c1_c4	-0.12359	0.15101	0.11281	0.03916	1.00000
	0.5651	0.4812	0.5997	0.8558	

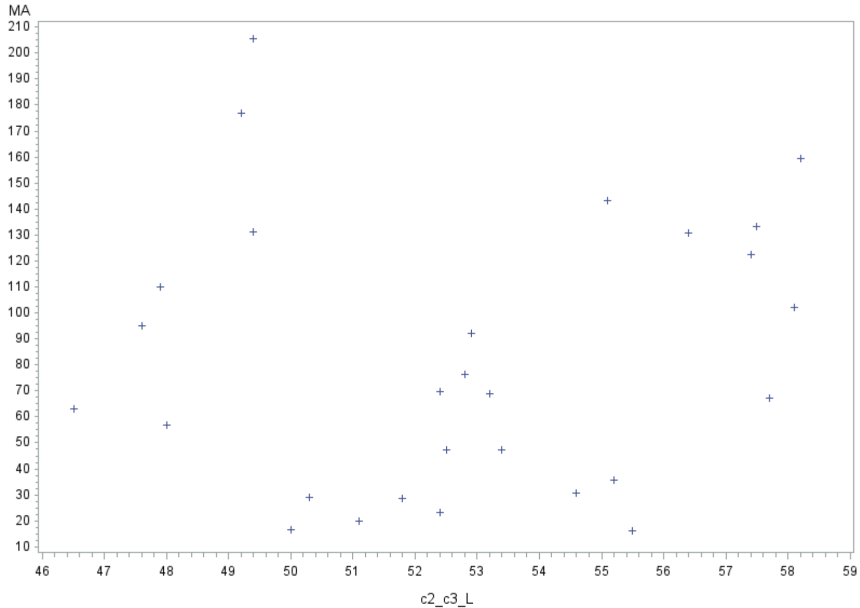
41. Cervical spine length (C2_C3_L) and AHI. No significant associations



Pearson Correlation Coefficients, N = 28
Prob > |r| under H0: Rho=0

	AHI	c2_c3_L
AHI	1.00000	0.20507 0.2952
c2_c3_L	0.20507 0.2952	1.00000

42. Cervical spine length (C2_C3_L) and MA. No significant associations



Pearson Correlation Coefficients, N = 28
Prob > |r| under H0: Rho=0

	MA	**c2_c3_L**
MA	1.00000	0.08260 0.6760
c2_c3_L	0.08260 0.6760	1.00000

43. Relationship among craniocervical posture, spinal angles, airway variables and AHI score

Pearson Correlation Coefficients, N = 24
Prob > |r| under H0: Rho=0

	MCG_OP	MCR_OP	A_O_L	c1_c2	c2_c3	c3_c4	c1_c4	AHI
MCG_OP	1.00000	0.77253 <.0001	0.52375 0.0086	0.55210 0.0052	0.04417 0.8376	0.33711 0.1072	-0.13717 0.5227	-0.10896 0.6123
MCR_OP	0.77253 <.0001	1.00000	0.68244 0.0002	0.57678 0.0032	0.12458 0.5619	0.36557 0.0790	0.02578 0.9048	-0.31754 0.1305
A_O_L	0.52375 0.0086	0.68244 0.0002	1.00000	0.21898 0.3039	-0.22432 0.2920	-0.14437 0.5009	-0.05737 0.7900	-0.10574 0.6229
c1_c2	0.55210 0.0052	0.57678 0.0032	0.21898 0.3039	1.00000	0.13416 0.5320	0.34979 0.0938	0.15101 0.4812	-0.44941 0.0276
c2_c3	0.04417 0.8376	0.12458 0.5619	-0.22432 0.2920	0.13416 0.5320	1.00000	0.64127 0.0007	0.11281 0.5997	-0.33060 0.1146
c3_c4	0.33711 0.1072	0.36557 0.0790	-0.14437 0.5009	0.34979 0.0938	0.64127 0.0007	1.00000	0.03916 0.8558	-0.19725 0.3556
c1_c4	-0.13717 0.5227	0.02578 0.9048	-0.05737 0.7900	0.15101 0.4812	0.11281 0.5997	0.03916 0.8558	1.00000	-0.37255 0.0730
AHI	-0.10896 0.6123	-0.31754 0.1305	-0.10574 0.6229	-0.44941 0.0276	-0.33060 0.1146	-0.19725 0.3556	-0.37255 0.0730	1.00000
TV	0.40647 0.0487	0.13540 0.5282	0.09671 0.6530	0.00694 0.9743	-0.11161 0.6036	0.19933 0.3504	-0.13617 0.5258	0.02557 0.9056
MA	0.58835 0.0025	0.48611 0.0160	0.25549 0.2282	0.26655 0.2080	0.12625 0.5566	0.41073 0.0462	0.09413 0.6617	-0.21406 0.3152
uOP	0.41218 0.0453	0.26681 0.2076	0.21547 0.3119	0.24858 0.2415	-0.13640 0.5251	0.17880 0.4032	-0.10339 0.6307	-0.12546 0.5591
lOP	0.20166 0.3447	-0.14193 0.5083	-0.14159 0.5093	-0.38656 0.0620	-0.01787 0.9339	0.13656 0.5246	-0.12359 0.5651	0.25713 0.2252

43. Relationship among craniocervical posture, spinal angles, airway variables and AHI score

Pearson Correlation Coefficients, N = 24 Prob > |r| under H0: Rho=0				
	TV	MA	uOP	lOP
MCG_OP	0.40647 0.0487	0.58835 0.0025	0.41218 0.0453	0.20166 0.3447
MCR_OP	0.13540 0.5282	0.48611 0.0160	0.26681 0.2076	-0.14193 0.5083
A_O_L	0.09671 0.6530	0.25549 0.2282	0.21547 0.3119	-0.14159 0.5093
c1_c2	0.00694 0.9743	0.26655 0.2080	0.24858 0.2415	-0.38656 0.0620
c2_c3	-0.11161 0.6036	0.12625 0.5566	-0.13640 0.5251	-0.01787 0.9339
c3_c4	0.19933 0.3504	0.41073 0.0462	0.17880 0.4032	0.13656 0.5246
c1_c4	-0.13617 0.5258	0.09413 0.6617	-0.10339 0.6307	-0.12359 0.5651
AHI	0.02557 0.9056	-0.21406 0.3152	-0.12546 0.5591	0.25713 0.2252
TV	1.00000	0.75458 <.0001	0.89392 <.0001	0.69010 0.0002
MA	0.75458 <.0001	1.00000	0.78770 <.0001	0.33801 0.1062
uOP	0.89392 <.0001	0.78770 <.0001	1.00000	0.29251 0.1654
lOP	0.69010 0.0002	0.33801 0.1062	0.29251 0.1654	1.00000

43. Relationship among craniocervical posture, spinal angles, airway variables and AHI score

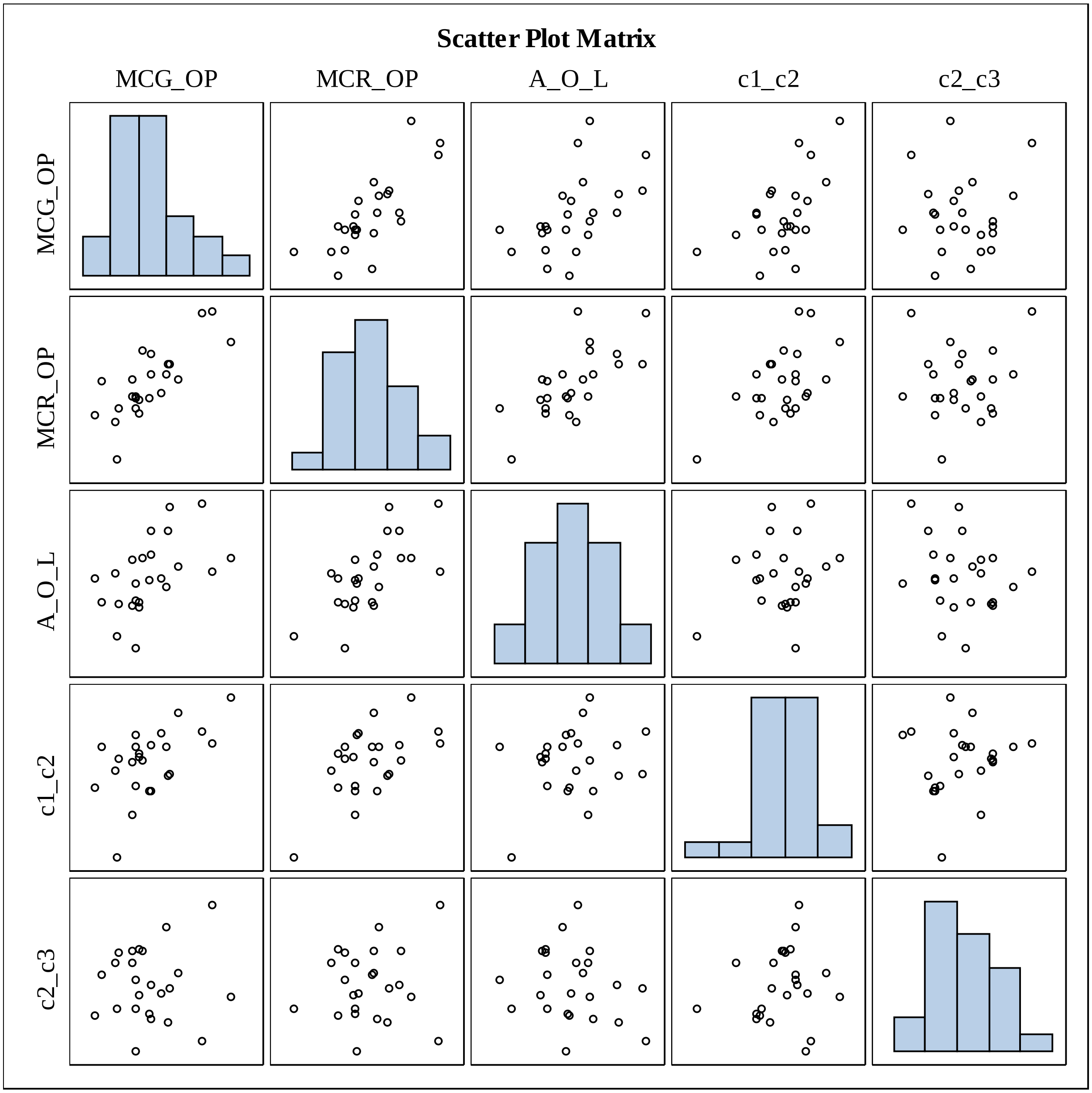
Spearman Correlation Coefficients, N = 24
Prob > |r| under H0: Rho=0

	MCG_OP	MCR_OP	A_O_L	c1_c2	c2_c3	c3_c4	c1_c4	AHI
MCG_OP	1.00000	0.78904 <.0001	0.61331 0.0014	0.49543 0.0138	-0.06568 0.7604	0.02719 0.8997	-0.00761 0.9718	-0.00348 0.9871
MCR_OP	0.78904 <.0001	1.00000	0.70422 0.0001	0.45803 0.0244	0.03980 0.8535	0.25359 0.2318	0.13919 0.5166	-0.18269 0.3929
A_O_L	0.61331 0.0014	0.70422 0.0001	1.00000	0.12049 0.5749	-0.25076 0.2372	-0.20183 0.3443	-0.19922 0.3507	-0.03697 0.8638
c1_c2	0.49543 0.0138	0.45803 0.0244	0.12049 0.5749	1.00000	0.14615 0.4956	0.32362 0.1229	0.47803 0.0181	-0.46999 0.0205
c2_c3	-0.06568 0.7604	0.03980 0.8535	-0.25076 0.2372	0.14615 0.4956	1.00000	0.63810 0.0008	0.48282 0.0169	-0.28012 0.1849
c3_c4	0.02719 0.8997	0.25359 0.2318	-0.20183 0.3443	0.32362 0.1229	0.63810 0.0008	1.00000	0.58330 0.0028	-0.13136 0.5406
c1_c4	-0.00761 0.9718	0.13919 0.5166	-0.19922 0.3507	0.47803 0.0181	0.48282 0.0169	0.58330 0.0028	1.00000	-0.57416 0.0033
AHI	-0.00348 0.9871	-0.18269 0.3929	-0.03697 0.8638	-0.46999 0.0205	-0.28012 0.1849	-0.13136 0.5406	-0.57416 0.0033	1.00000
TV	0.37225 0.0732	0.19917 0.3508	0.13351 0.5340	0.07480 0.7283	-0.18004 0.3999	0.07306 0.7344	-0.04262 0.8433	0.14655 0.4944
MA	0.47793 0.0182	0.35877 0.0851	0.33181 0.1132	0.13612 0.5260	-0.03479 0.8718	0.11698 0.5862	0.12785 0.5516	-0.11524 0.5918
uOP	0.41009 0.0466	0.29615 0.1600	0.23092 0.2776	0.23396 0.2712	-0.17700 0.4080	0.07871 0.7147	0.05566 0.7961	-0.02131 0.9213
lOP	0.39008 0.0595	0.14307 0.5048	0.10133 0.6376	0.00478 0.9823	-0.07436 0.7298	0.09698 0.6521	-0.04740 0.8259	0.32964 0.1157

43. Relationship among craniocervical posture, spinal angles, airway variables and AHI score

Spearman Correlation Coefficients, N = 24 Prob > |r| under H0: Rho=0				
	TV	MA	uOP	lOP
MCG_OP	0.37225 0.0732	0.47793 0.0182	0.41009 0.0466	0.39008 0.0595
MCR_OP	0.19917 0.3508	0.35877 0.0851	0.29615 0.1600	0.14307 0.5048
A_O_L	0.13351 0.5340	0.33181 0.1132	0.23092 0.2776	0.10133 0.6376
c1_c2	0.07480 0.7283	0.13612 0.5260	0.23396 0.2712	0.00478 0.9823
c2_c3	-0.18004 0.3999	-0.03479 0.8718	-0.17700 0.4080	-0.07436 0.7298
c3_c4	0.07306 0.7344	0.11698 0.5862	0.07871 0.7147	0.09698 0.6521
c1_c4	-0.04262 0.8433	0.12785 0.5516	0.05566 0.7961	-0.04740 0.8259
AHI	0.14655 0.4944	-0.11524 0.5918	-0.02131 0.9213	0.32964 0.1157
TV	1.00000	0.74696 <.0001	0.89652 <.0001	0.77391 <.0001
MA	0.74696 <.0001	1.00000	0.82000 <.0001	0.50783 0.0113
uOP	0.89652 <.0001	0.82000 <.0001	1.00000	0.51826 0.0095
lOP	0.77391 <.0001	0.50783 0.0113	0.51826 0.0095	1.00000

43. Relationship among craniocervical posture, spinal angles, airway variables and AHI score

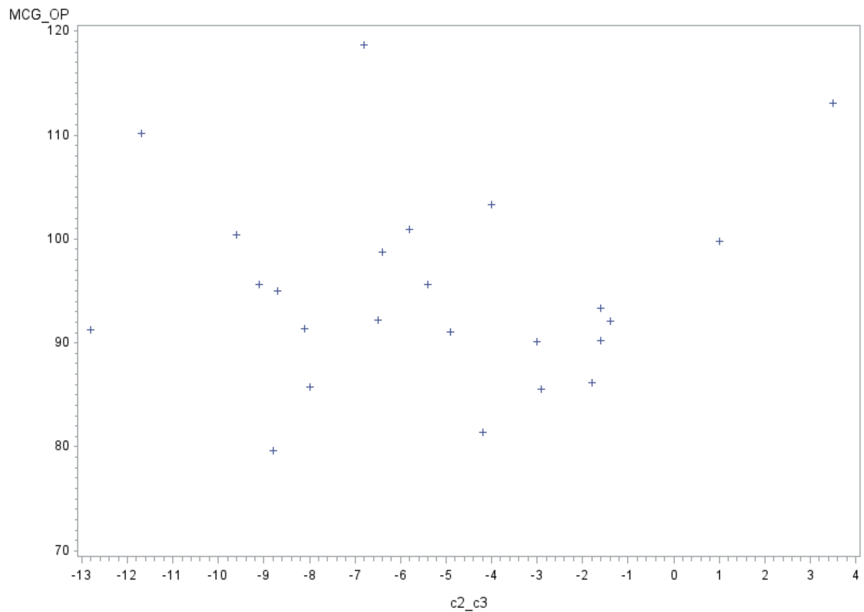


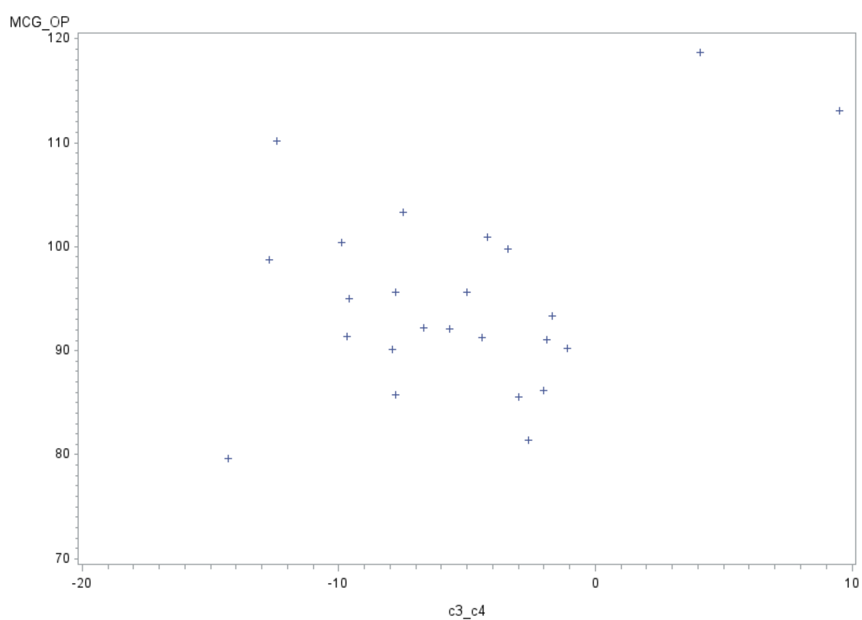
44. Craniocervical posture (McG) and spinal angles. Significant association found with C1_C2

Pearson Correlation Coefficients, N = 24
Prob > |r| under H0: Rho=0

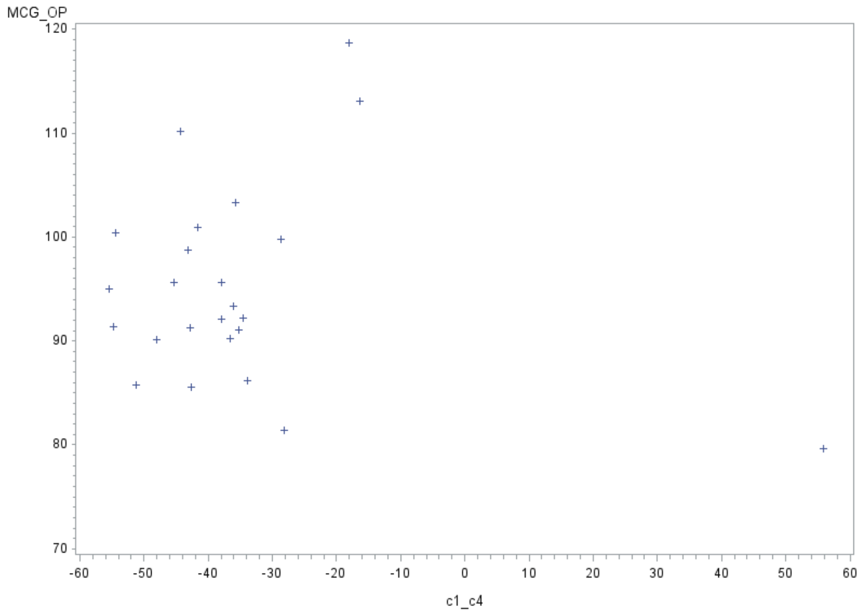
	MCG_OP	MCR_OP	c1_c2	c2_c3	c3_c4	c1_c4
MCG_OP	1.00000	0.77253	0.55210	0.04417	0.33711	-0.13717
		<.0001	0.0052	0.8376	0.1072	0.5227
MCR_OP	0.77253	1.00000	0.57678	0.12458	0.36557	0.02578
	<.0001		0.0032	0.5619	0.0790	0.9048
c1_c2	0.55210	0.57678	1.00000	0.13416	0.34979	0.15101
	0.0052	0.0032		0.5320	0.0938	0.4812
c2_c3	0.04417	0.12458	0.13416	1.00000	0.64127	0.11281
	0.8376	0.5619	0.5320		0.0007	0.5997
c3_c4	0.33711	0.36557	0.34979	0.64127	1.00000	0.03916
	0.1072	0.0790	0.0938	0.0007		0.8558
c1_c4	-0.13717	0.02578	0.15101	0.11281	0.03916	1.00000
	0.5227	0.9048	0.4812	0.5997	0.8558	

44. Craniocervical posture (McG) and spinal angles. Significant association found with C1_C2





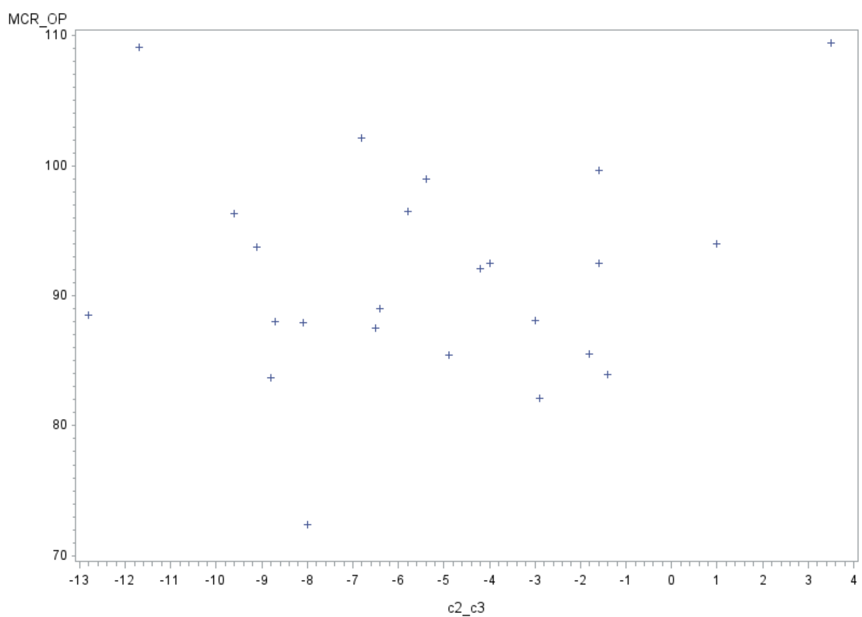
44. Craniocervical posture (McG) and spinal angles. Significant association found with C1_C2



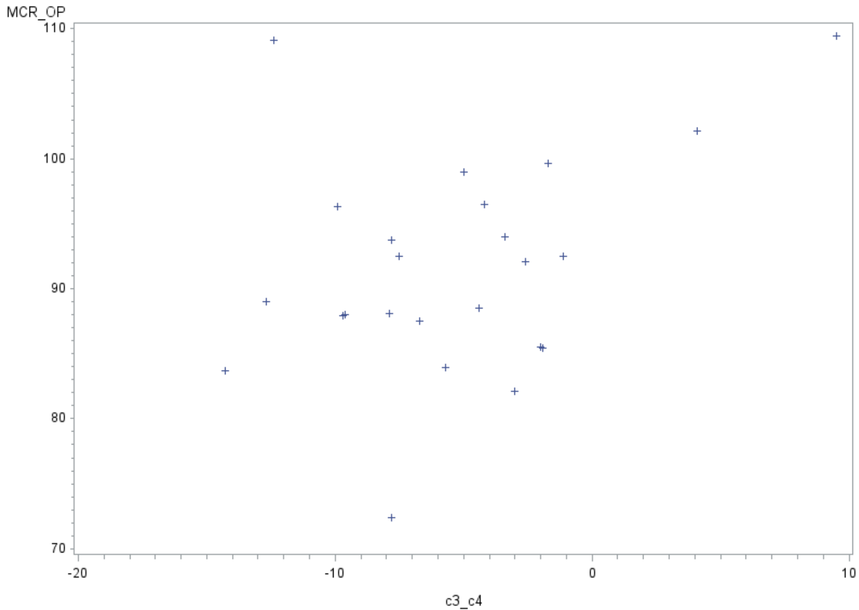
45. Craniocervical posture (McR) and spinal angles. Significant association found with C1_C2

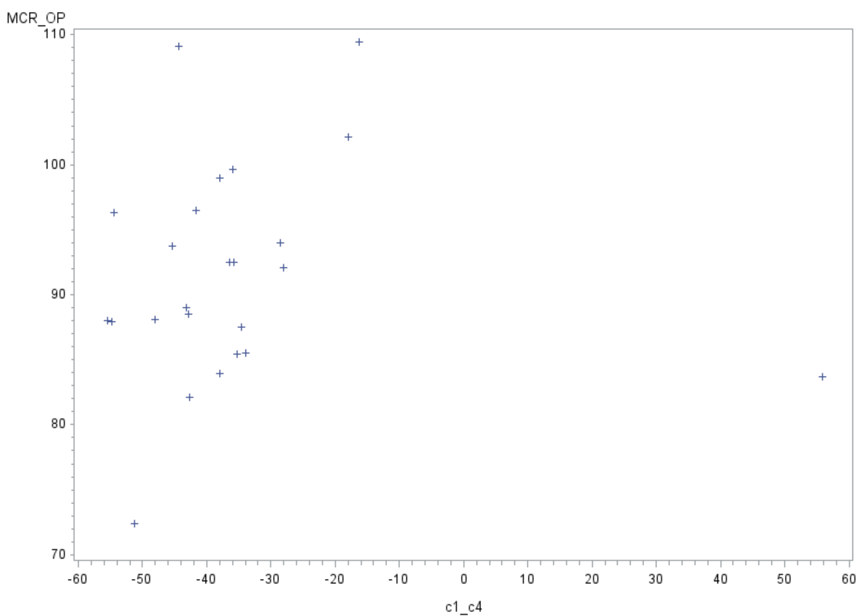
Linear model also shows that MCR_OP is significantly related to c1_c2.

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	111.4797740	7.64641843	14.58	<.0000001
c1_c2	0.6005515	0.23388785	2.57	0.0188379
c2_c3	-0.2160013	0.51380929	-0.42	0.6789155
c3_c4	0.4039905	0.40279995	1.00	0.3284853



45. Craniocervical posture (McR) and spinal angles. Significant association found with C1_C2





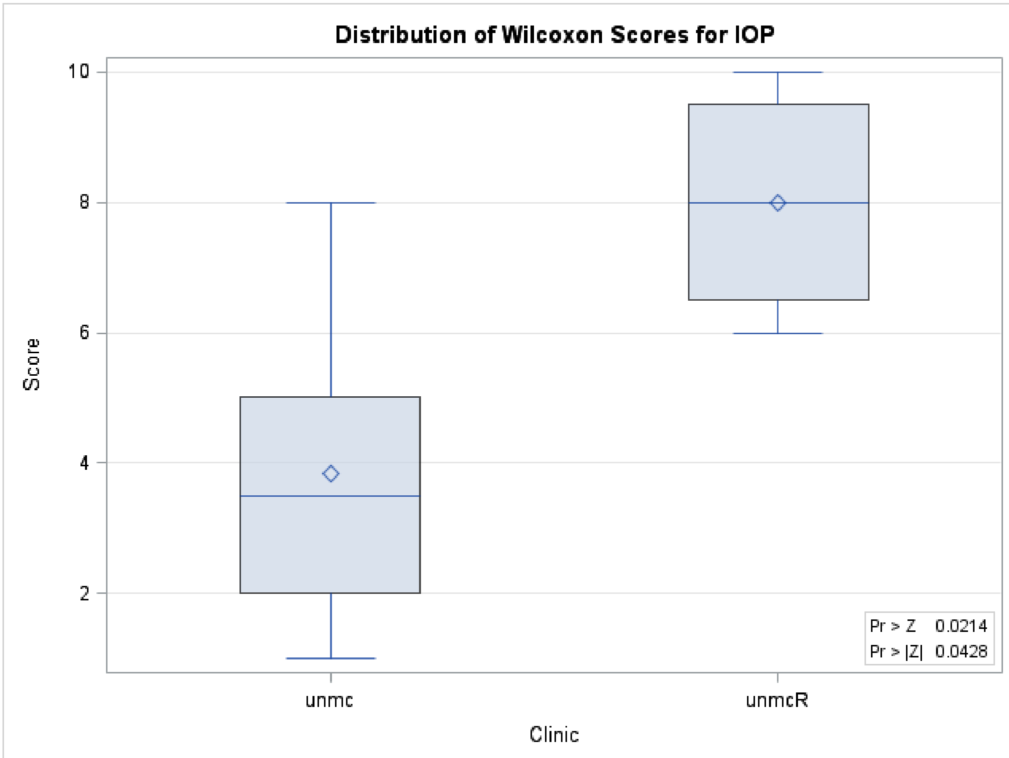
46. Categorizing spinal angles and head posture results by sleep apnea severity

The MEANS Procedure

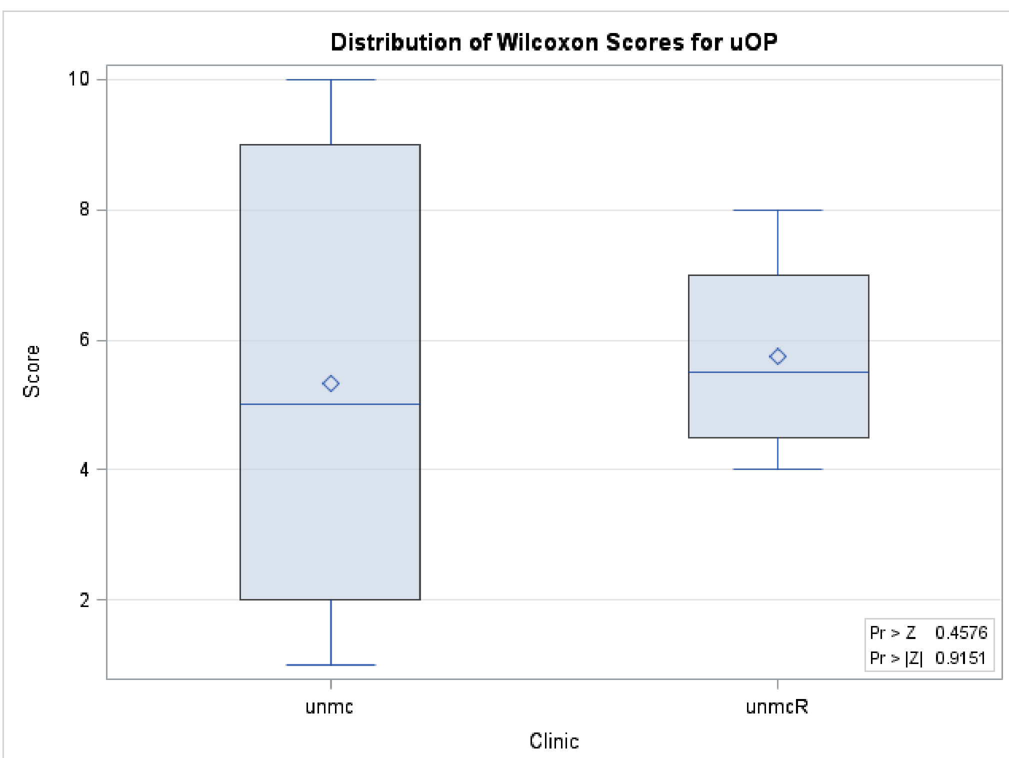
Cat	N Obs	Variable	Mean	Std Error	Std Dev	Lower 95% CL for Mean	Upper 95% CL for Mean
mild	**9**	**TV**	9591.26	1266.07	3798.22	6671.69	12510.82
		uOP	6563.59	1006.68	3020.05	4242.17	8885.01
		lOP	3027.67	425.7947393	1277.38	2045.78	4009.55
		MCG_OP	100.6333333	3.1976120	9.5928359	93.2596269	108.0070397
modera	**7**	**TV**	8561.01	1592.88	4214.37	4663.37	12458.66
		uOP	6017.04	1229.29	3252.41	3009.07	9025.02
		lOP	2543.97	459.4973194	1215.72	1419.62	3668.32
		MCG_OP	92.0714286	1.7824160	4.7158295	87.7100137	96.4328434
normal	**4**	**TV**	6245.38	1622.75	3245.51	1081.05	11409.70
		uOP	4935.98	1632.73	3265.46	-260.1063607	10132.06
		lOP	1309.40	394.8829405	789.7658809	52.7062451	2566.09
		MCG_OP	89.3500000	7.0881944	14.1763888	66.7922019	111.9077981
severe	**4**	**TV**	10324.83	1991.22	3982.44	3987.88	16661.77
		uOP	5622.75	1285.08	2570.15	1533.06	9712.44
		lOP	4702.08	1509.06	3018.12	-100.4311932	9504.58
		MCG_OP	93.4750000	3.1356485	6.2712970	83.4959669	103.4540331

E2. Mean Differences

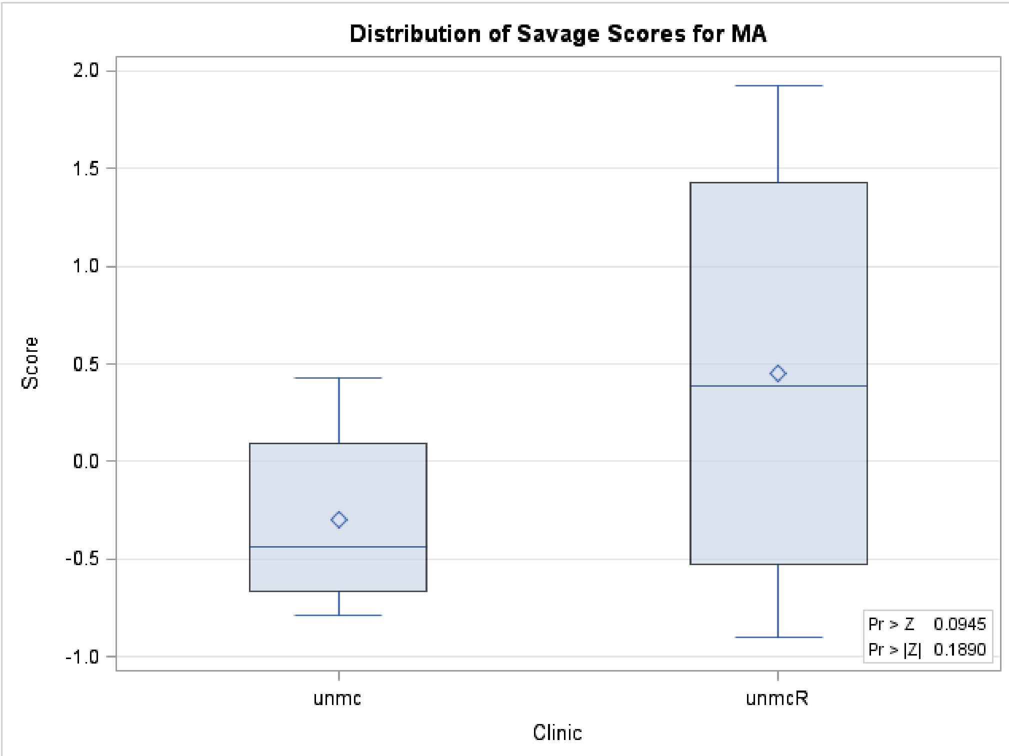
1. Differences in craniocervical posture within UNMC subjects: head CT (UNMC) versus neck CT (UNMCR)



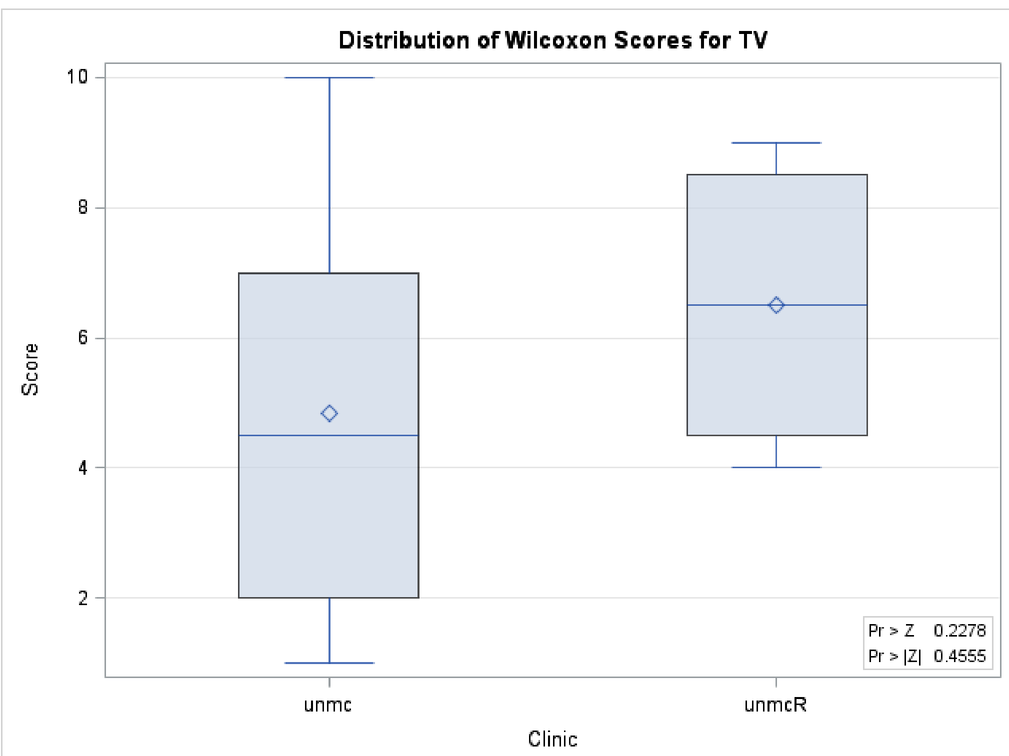
uOP: No significant difference (p=0.9151).



MA: no significant difference (p=0.1890).



TV: no significant difference observed (p=0.455).



2. Clinic differences in age. No significant difference (p=0.4268)

Private	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
No(UNMC)		45.9091	34.6738	57.1444	16.7240	11.6853	29.3494
Yes(cfp+pgd)		50.7059	43.2845	58.1273	14.4342	10.7501	21.9678
Diff (1-2)	Pooled	-4.7968	-17.0103	7.4167	15.3553	12.0926	21.0434

3. Clinic differences in gender. No significant difference (p=0.7011, Fisher exact test)

4. Clinic differences in AHI. No significant difference (p=0.5459)

5. Clinic differences in lOP. No significant difference (p=0.2576)

Private	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
No		2563.5	1499.4	3627.5	1583.8	1106.6	2779.5
Yes		3347.3	2397.8	4296.9	1846.8	1375.5	2810.7
Diff (1-2)	Pooled	-783.9	-2176.1	608.3	1750.3	1378.4	2398.7

5. Clinic differences in McG_OP. No significant difference (p=0.0753)

Private	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
No		89.5286	85.5918	93.4653	4.2566	2.7430	9.3734
Yes		97.3412	92.1015	102.6	10.1910	7.5899	15.5100
Diff (1-2)	Pooled	-7.8126	-16.1675	0.5423	8.9707	6.9379	12.6967

6. Clinic differences in McR_OP. No significant difference (p=0.3388, t-test)

Private	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
No		88.9909	83.9287	94.0531	7.5352	5.2650	13.2237
Yes		92.3059	87.4246	97.1871	9.4938	7.0707	14.4489
Diff (1-2)	Pooled	-3.3150	-10.3083	3.6783	8.7923	6.9240	12.0492

7. Clinic differences in AO_L. No significant difference (p=0.1150, Wilcoxon)

Private	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
No		12.6091	10.2519	14.9663	3.5087	2.4516	6.1575
Yes		14.2059	12.2853	16.1264	3.7354	2.7820	5.6850
Diff (1-2)	Pooled	-1.5968	-4.4999	1.3063	3.6499	2.8743	5.0019

8. Clinic differences in C1_C2 angle. No significant difference (p=0.1581, Wilcoxon)

Private	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
No		-29.0545	-31.2689	-26.8401	3.2962	2.3031	5.7846
Yes		-33.2706	-37.5755	-28.9657	8.3728	6.2358	12.7428
Diff (1-2)	Satterthwaite	4.2160	-0.4665	8.8985	6.8789	5.4173	9.4271

9. Clinic differences in C2_C3 angle. No significant difference (p=0.1877, Wilcoxon)

Private	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
No		-4.5364	-7.2235	-1.8492	3.9998	2.7947	7.0194
Yes		-5.8059	-7.8064	-3.8054	3.8909	2.8978	5.9217
Diff (1-2)	Pooled	1.2695	-1.8589	4.3979	3.9332	3.0974	5.3901

10. Clinic differences in C3_C4 angle. No significant difference (p=0.2333, t-test)

Private	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
No		-4.0636	-5.7529	-2.3744	2.5145	1.7569	4.4127
Yes		-6.0882	-9.2048	-2.9717	6.0615	4.5145	9.2252
Diff (1-2)	Pooled	2.0246	-1.9557	6.0049	5.0042	3.9409	6.8580

11. Clinic differences in C1_C4. No significant difference (p=0.0777, Wilcoxon)

Private	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
No		-33.9364	-37.9344	-29.9383	5.9512	4.1582	10.4439
Yes		-35.1471	-48.5833	-21.7109	26.1327	19.4629	39.7721
Diff (1-2)	Satterthwaite	1.2107	-12.6029	15.0243	20.8298	16.4038	28.5458

12. Clinic differences in C2_C3_L. No significant difference (p=0.7014, t-test)

Private	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
No		53.0545	51.1018	55.0073	2.9067	2.0309	5.1010
Yes		52.5235	50.5267	54.5203	3.8837	2.8925	5.9107
Diff (1-2)	Pooled	0.5310	-2.2847	3.3467	3.5400	2.7878	4.8513

E3. Inter- and Intra-examiner Reliability Tests

1. Reliability Test: p-value table from paired t-test or nonparametric

Comparisons	Origin vs IntraEx	Origin vs InterEx	*IntraEx* vs InterEx
TV	0.0805	0.2463	0.5395
MA	0.1198	0.6036	0.9426
uOP	0.1797	0.2668	0.1778
lOP	0.7741	0.0655	0.0637
MCG_OP	0.8740	0.0026	0.0005
MCR_OP	0.1959	0.0061	0.0392
A_O_L (mm)	0.1061	0.0579	0.0815
c1_c2	0.2897	0.9310	0.3060
c2_c3	0.5758	0.9119	0.4728
c3_c4	0.2816	0.9095	0.2379
c1_c4	0.3623	0.3363	0.4035
c2_c3_L	0.1094	0.1094	0.3662

2. Pearson correlation and corresponding p-value for testing H0: correlation=0

Comparisons	Origin vs IntraEx (p-value H0: correlation=0)	Origin vs InterEx (p-value H0: correlation=0)	*IntraEx* vs InterEx (p-value H0: correlation=0)
TV	1.00000 <.0001	1.00000 <.0001	1.00000 <.0001
MA	1.00000 <.0001	0.98788 <.0001	0.98788 <.0001
uOP	1.00000 <.0001	1.00000 <.0001	1.00000 <.0001
lOP	0.85455 0.0016	0.80606 0.0049	0.76970 0.0092
MCG_OP	0.96667 <.0001	0.86667 0.0025	0.86667 0.0025
MCR_OP	0.92727 0.0001	0.89091 0.0005	0.85455 0.0016
A_O_L (mm)	0.97576 <.0001	0.76970 0.0092	0.80606 0.0049
c1_c2	0.71125 0.0211	0.96364 <.0001	0.77204 0.0089
c2_c3	0.64635 0.0435	0.21277 0.5551	0.64526 0.0439
c3_c4	0.82675 0.0032	0.85455 0.0016	0.86930 0.0011
c1_c4	0.53659 0.1098	0.51672 0.1262	0.96657 <.0001
c2_c3_L	0.96364 <.0001	0.96364 <.0001	0.96364 <.0001