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CEPHALOMETRIC ASSESSMENT IN OBSTRUCTIVE SLEEP APNEA

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ABSTRACT

BY

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It is reported that some specific craniofacial characteristics are associated with obstructive sleep apnea syndrome (OSAS). To test this finding, the present study developed and assessed a craniofacial index score (CIS) to differentiate OSAS patients from habitual snorers. The CIS was established using discriminant analysis to identify cephalometric and anthropometric measurements that were the best differential functions for a discriminant model. The study population consisted of 28 OSAS patients who had physician-diagnosed OSAS and a Respiratory Disturbance Index (RDI) greater than 20, and 30 habitual snorers. The habitual snorers were persons without any history of symptoms of OSAS and had an RDI less than 20 evaluated by overnight polysomnography (n=17) or no evidence of

significant desaturation on overnight oximetry (n=13). Lateral cephalometric radiographs were taken with subjects seated, using natural head position, at the end of expiration. The radiographs were traced and measured and the CIS was constructed using either a stepwise procedure or forced-entry of all variables. The stepwise method used three variables (H-MP, BMI and P-PNS), and correctly classified 67.9% of the OSAS group and 83% of the snoring group. Using the forced-entry method 82.1% the OSAS group and 86.7% of the snoring group were correctly classified. The findings indicated that cephalometric and anthropometric measurements can be used to identify subjects with and without OSAS. It is hoped that the CIS constructed from cephalometric radiographs may be a useful adjunct diagnostic test to identify individuals predisposed to OSAS.

DEDICATION

TO

ALL PATIENTS WHO ARE SUFFERING

FROM INCURABLE DISEASES

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Learning is an endless process. The author's years of work have not culminated in a new discovery but it is hoped that the present study is an endeavor to broaden a stream of scientific knowledge for a better living for human-beings. The author wishes to express her sincere appreciation and gratitude to those who have contributed to the present study and made this project possible.

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TABLE OF CONTENTS

PAGE

ABSTRACT..... ii

DEDICATION..... iv

ACKNOWLEDGEMENTS..... v

TABLE OF CONTENTS..... viii

LIST OF FIGURES..... x

LIST OF TABLES..... xi

INTRODUCTION..... 1

REVIEW OF THE LITERATURE..... 4

STATEMENT OF THESIS..... 39

METHODS AND MATERIALS..... 40

RESULTS..... 57

DISCUSSION..... 71

SUMMARY AND CONCLUSIONS..... 84

APPENDICES

A. CORRELATION MATRIX..... 87

B. HUMAN INVESTIGATION

CONSENT FORM..... 88

TABLE OF CONTENTS

(CONTINUED)

PAGE

APPENDICES (CONTINUED)

C. APPROVAL OF THE UNIVERSITY REVIEW

COMMITTEE OF HUMAN STUDIES..... 89

GLOSSARY..... 90

REFERENCES..... 98

LISTS OF FIGURES

FIGURE PAGE

1. Conventional linear and angular measurements.....53
2. Cephalometric measurements of the tongue area relative to the intermaxillary area.....54
3. The counterpart analysis (1).....55
4. The counterpart analysis (2).....56
5. All-groups stacked histograms: Summary of classification by forced-entry of all predictor variables.....69
6. All-groups stacked histograms: Summary of classification by stepwise method.....70

LIST OF TABLES

TABLE PAGE

1. Demographic and anthropometric data of the study population..... 58
2. Percentage distribution of the head forms and facial forms.....58
3. Comparison of means of cephalometric variables between OSAS and snoring groups using t-tests..... 60
4. Summary of the correlation among cephalometric, anthropometric and demographic variables.....63
5. Discriminant functions evaluated at group means..... 65
6. Classification results of both methods of variable selection (Forced-entry of all predictive variables and Stepwise method)..... 65
7. Reproducibility of landmark identification and digitizing.....68
8. Reliability of the subjects' natural position.....68

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) has received increased recognition in several medical fields because of multisystem complications associated with the syndrome and the high prevalence of the syndrome in the adult population. Although there have been many significant studies on OSAS, its predisposing factors and pathogenesis are still debated. Anatomic aberration of the pharyngeal airway and/or neurogenic failure to preserve the patency of the pharyngeal airway during sleep are the two most common theories regarding the pathogenesis of the syndrome. Craniofacial anatomical abnormalities related to structural narrowing of the upper airway have been reported in OSAS patients. However, the relationships between naso-respiratory function and facial morphology are still being explored in contemporary research studies.

The effects of airway obstruction on facial growth have been debated in the orthodontic field for many years. Some clinicians and researchers contend that airway impairment alters facial and dental growth. In contrast,

other investigators have reported no change in craniofacial growth with nasal obstruction. The scope of this argument has largely been limited to the growing child. As interest in Obstructive Sleep Apnea Syndrome increases, future arguments concerning respiratory behavior and dentofacial development will likely expand to include the adult population. The application of the existing body of literature concerning craniofacial anatomy and nasorespiratory function may be valuable in determining the relative role of structural features in the pathogenesis and treatment of OSAS.

Dental practitioners are often part of a multidisciplinary team of health professionals treating OSAS patients. The role of the dental professional has been to design and fabricate intraoral appliances that improve the anatomic airway environment. These appliances have been used for patients with OSAS or even snoring subjects without the presence of clinical disease. Interestingly, the appliances that are used to improve the anatomic airway in OSAS patients are similar to the orthopedic appliances orthodontists have been using to correct developing mandibular retrognathia. This increased interest in conservative management of OSAS using intraoral appliances has the potential to expand the scope of future dental and orthodontic practice.

Cephalometry has been used extensively in the fields of orthodontic craniofacial biology and anthropology to record craniofacial form. Recently, it has been also suggested that cephalometry could be a useful adjunctive procedure for assessing craniofacial abnormalities associated with OSAS.

Cephalometry plays an important role in orthodontics not only diagnosis and treatment planning for patients but also longtitudinal studies of craniofacial changes and the results of various treatment intervention strategies. In addition, orthodontists should be familiar with Obstructive Sleep Apnea Syndrome since the dental professional often sees patients for an extended period of time. Long-term changes in craniofacial anatomy of OSAS subjects may be assessed using cephalometric radiographs. Awareness and early recognition of the syndrome are beneficial to the patients as well as the physician managing the disease.

Verification of cephalometric variables that identify craniofacial anatomical risks associated with OSAS may also impact patient care decisions. Compared to other diagnostic techniques used for identifying anatomical structures (Magnetic Resonance Imaging, Computerized Tomography) cephalometry is superior because of its lower cost and reduced radiation exposure. Because of these advantages the use of cephalometry as a diagnostic test for OSAS will be studied.

REVIEW OF THE LITERATURE

OVERVIEW OF OBSTRUCTIVE SLEEP APNEA

A Portrait of an "immensely fat, snoring, hypersomnolent boy" was described in Charles Dickens' classic work The Pickwick Papers[1] in 1837. Over the years, there were numbers of reports in the medical literature of "pickwickian syndrome". Pickwickian syndrome was characterized by symptoms associated with obesity such as excessive sleepiness, cyanosis, pulmonary hypertension, and right sided heart failure.[2] It was not until 1965 when Gastaut and coworkers[3] first began to describe the pickwickian syndrome from the aspect of sleep. They also began to classify sleep-induced apnea syndrome base upon the respiratory patterns seen during sleep. Consequently, the term pickwickian syndrome has been abandoned by most specialists in favor of the more specific designations of the term sleep-induced apnea. Guilleminault et al.,[4] first described sleep apnea as a syndrome and established a sleep laboratory at Stanford University. Since then, there has been a rapid expansion of research studies in sleep-

disordered breathing in United States; however, its pathophysiological mechanism is still debated.

Sleep apnea syndromes are a collection of clinical disorders characterized by recurrent cessation of breathing (apnea and/or hypoventilation) during sleep.[5] Clinical features of the syndromes include: 1). Recurrent hypoxemia and hypercapnia during sleep leading to multiple arousals and sleep fragmentation. 2). Symptoms are reversed when the sleep-induced respiratory disturbances are eliminated. Arousals from sleep and hypoxemia/hypercapnia are believed to be the main contributors to the clinical symptoms and signs. The major clinical symptoms are: altered sleep behavior including snoring, enuresis and sleep walking , excessive daytime sleepiness, intellectual deterioration, sexual dysfunction and personality changes. Clinical features include: reduced sleep latency, obesity, cardiac arrhythmia, bradycardia, hypertension, pulmonary hypertension and polycythemia.

Two distinct clinical syndromes of sleep apnea have been identified based on pathophysiological mechanisms: obstructive and central.[6] The syndrome of central sleep apnea entails a cessation of both respiratory effort and airflow. The obstructive type is characterized by episodes of either obstructive apnea, during which respiratory effort continues despite pharyngeal obstruction to air flow, or of mixed apnea, during which respiratory effort is absent at the beginning of the apnea but then starts again before airflow resumes. The term apnea is defined as a cessation of

airflow for more than 10 seconds; hypopnea is defined as a 50% reduction in airflow associated with a 4% fall in oxygen saturation. Polysomnographic monitoring of sleep behavior is the gold standard for diagnosis of sleep disordered breathing. The apnea index (number of apnea episodes per hour of sleep) is often used to record the results of the polysomnographic study. An apnea index of five or greater is widely used to classify persons with sleep apnea syndrome.[7] However, it is suggested that healthy subjects, especially aging heavy snorers, may exhibit apneas particularly at sleep onset, but in general these episodes are less than 10-15 seconds in duration and are not repetitive.[8] Therefore, the number of episodes of hypoventilation and/or apnea is an arbitrary and inconsistent criterion for the diagnosis of the sleep apnea syndrome. Some investigators have also suggested that the criteria for respiratory disturbances during sleep includes a significant fall in oxygen saturation greater than 4%[9] because the episodes of partial upper airway obstruction or periods of decreased respiratory drive may be as important as frank apnea in the genesis of other clinical features.

Another phenomenon to be considered is hypopnea. Hypopnea is defined by a reduction in air flow often with a decrease in arterial oxygen saturation.[9] The effects of episodes of hypopnea are similar to those seen with typical apnea. Hypopnea has been recorded and reported along with apnea in the recent literature as an Apnea-Hypopnea Index (AHI, or Respiratory Disturbance Index, RDI). The AHI gives a good indication of the severity of the syndrome; however, the predetermined AHI cut off to define

sleep apnea is also somewhat arbitrary.[10] Consequently, the designation of Obstructive Sleep Apnea Syndrome (OSAS) should be clinically applied to those individuals who experience frequent apnea and hypopnea during sleep with pathophysiologic consequences. According to the International Classification of Sleep Disorders[11], diagnostic criteria for OSAS include: excessive sleepiness, frequent episodes of obstructed breathing during sleep, and associated features such as loud snoring. In addition, polysomnographic testing should demonstrate more than five obstructive apneas (greater than 10 seconds in duration) per hour of sleep and one or more of these following signs: frequent arousals from sleep associated with the apneas, bradycardia, arterial desaturation associated with apneic episodes, with or without mean sleep latency of less than 10 minutes.

The incidence and prevalence of sleep apnea syndromes in the United States have not been determined yet. An epidemiological study of Israeli workers by Lavie[12] demonstrated that 0.89% of the samples had symptomatic sleep apnea. Stradling and Crosby[13] suggested that the prevalence of obstructive sleep apnea in a particular population be expected to vary according to the level of obesity as this factor correlates well with the degree of sleep apnea. In their recent study, which recruited one thousand and one English men, aged 35-65 years, they found that 0.3% of this randomly selected population had clinically symptomatic obstructive sleep apnea. They postulated that the prevalence of obstructive sleep apnea in the United States would be higher because 5% of men weigh over 101.6 kg., whereas in the United Kingdom the 95th percentile is

94.4 kg., and only about 2% of men are over 102 kg. This postulation would perhaps be reliable. Phillips et al.,[14] conducted an epidemiological survey of unselected American adult population included 685 people (356 female and 329 male, with a mean age of 50 years) and reported the prevalence of sleep apnea in the general population to approximate 1%. The prevalence in their study is similar to the previously mentioned studies; however, female adults were included in their study. Polysomnographic testing for these sample populations has not been completed. Therefore, the final prevalence may, in fact, be higher.

Obstructive Sleep Apnea Syndrome is predominantly identified in middle aged men. However, post-menopausal women or children with tonsillar and adenoid hypertrophy are other groups particularly prone to sleep apnea.[15-16] Obstructive sleep apnea may also be found in patients with craniofacial anomalies such as Pierre Robin syndrome, Crouzon's syndrome, Apert's syndrome, Pfeiffer's syndrome, Stickler's syndrome and Treacher Collins syndrome.[17] In addition, there have been reported cases of obstructive sleep apnea in Down's syndrome, Acromegaly, Temporomandibular Dysfunction, Hypothyroidism and Myxedema.

Pathophysiologic mechanisms of Obstructive Sleep Apnea Syndrome

There have been numbers of investigations conducted to clarify etiology of the syndrome, but to date no single pathophysiologic mechanism has been identified. It is postulated that the cause of the OSAS is possibly

multifactorial in any one individual or differs in different patients.[18] Factors that determine upper airway patency and may be underlying contributors to the obstruction of the upper airway during sleep include: 1). compliance or collapsibility of upper airway structures; 2). inspiratory muscle function; 3). defective respiratory mechanism; and 4). upper airway geometry.

1. Upper airway compliance and collapsibility.

The intrinsic passive compliance of the pharyngeal tissues is not easily determined because it is difficult to discriminate it from the effect of muscle activity. It was found in a study which evaluated recently deceased infants that higher suction pressures were required to close the nasopharynx than the oropharynx.[19] In addition, substantially more pressure was needed to close the hypopharynx. Thus, the oropharynx may be the site which is inherently more collapsible.

The resting size of the oropharynx is determined in animal studies by assessing the elastic properties of the airway wall and the degree of muscle activation during resting stage. However, the resting size of the oropharynx has not been assessed in human subjects.[20] Studies using electromyographic activity as an index of pharyngeal function have shown that, during inspiration, the pharyngeal dilator muscles show phasic activation. This is presumed to result in either a larger or less collapsible airway. On the other hand, studies by Remmers et al, Brouillete and Thach, and Mathew et al., demonstrated that reduction in upper airway muscle

activity (such as the genioglossus, geniohyoid) was associated with the onset of upper airway obstruction during sleep.[21,22,23] The usual interpretation of these studies indicated an assumption of a direct relationship between muscle activity and airway patency. Specifically, the activation of dilator muscles decreases upper airway resistance, and inactivation of these muscles increases resistance to airflow.

However, Strohl and Olson[24] proposed an alternative theory that the structural elements inherent in the processes that maintain pharyngeal patency include muscular, nonmuscular and mucosal factors. While the pharyngeal constrictors are attached directly to the pharyngeal mucosa, the rest of the pharyngeal muscles act on the airway indirectly, through their attachments to the tongue and hyoid. In contrast to Brouilette, they found that in anesthetized rabbits the upper airway collapsing pressure did not change significantly with skeletal muscle paralysis but did decrease with death.[25] Based on this assumption, the intrinsic elastic properties of the airway resides partly in the contractile state of the muscle and partly in its associated structures such as connective tissue and blood vessels. In other words, the action of the upper airway muscles causes change in airway size, not compliance of the airway wall. The likelihood of airway collapse is increased if muscle activity is reduced, because the reduction in muscle activity results in a smaller airway not because airway compliance is increased.

Additional evidence supporting this hypothesis was an investigation by Parisi et al.,[26]. They identified a 7 percent increase in pharyngeal volume of normal awake humans after local application of the vasoconstrictor phenylephedrine. These data suggest that vascular mechanisms may affect upper airway size and collapsibility. Another associated factor is mucous stickiness. In a study of anesthetized rabbits injected with methacholine, to increase production of pharyngeal mucus, it was more difficult to close the upper airway, but also more difficult to reopen.[27] Thus, the relative influence of muscular and non-muscular factors should be taken into consideration regarding upper airway compliance.

2. Inspiratory Muscle Function

The role of upper airway muscle function in pathophysiologic mechanism of OSAS has been proposed as follows:

A. Balance of forces

It is hypothesized that obstructive sleep apnea occurs through an imbalance in activity of the upper airway and chest wall muscles.[28-29] Dilating forces are generated by pharyngeal muscle activity and collapsing forces are generated by chest wall muscles. The negative pressure produced when the chest wall muscles contract during inspiration tends to obstruct the upper airway unless it is adequately opposed by the forces produced by the extrathoracic dilating muscles. A modeling experiment in

periodic breathing based on the balance of force concept is postulated by Longobardo et al.,[30]. In addition, this relationship between muscle forces can also be influenced by other factors such as initial airway size, airway collapsibility, reflexes or head position.

B. Critical Pressure Concept

This concept is consistent with the findings that the upper airway tends to collapse in some particular segments on OSAS patients. In this model maximum flow through the upper airway is determined by the pressure within the collapsible upper segment airway.[31] Two factors, upstream resistance and subatmospheric airway driving pressure generated by chest wall muscle contraction, set the transmural pressure within the collapsible segment. In OSAS patients the driving pressure or nasal resistance is either too large or the pharynx is too collapsible leading to upper airway occlusion.

C. Periodic breathing

Hudgel et al.,[32] proposed a concept that periodic breathing produces a mechanical effect on the upper airway during sleep. In their study, periodic breathing was produced in healthy subjects in nonrapid eye movement sleep with mild hypoxia. This resulted in an imbalance in function of the chest wall and upper airway inspiratory muscles. When upper airway inspiratory muscle tonic and phasic inspiratory activity

decreased more than chest wall muscle activity in the hypopneic portion of periodic breathing cycle, upper airway resistance increased significantly. Martin et al.,[33] demonstrated that in OSAS the upper airway resistance gradually increased breath to breath as the apnea approached to the hypopneic portion of the periodic breathing cycle.

3. Defective respiratory control mechanism

Reflexes with afferent receptors in the nasal, pharyngeal and lower respiratory mucosa may alter upper airway caliber through action on respiratory muscle function.[18] The importance of these reflexes is supported by the observation that local anesthesia to the upper airway has been shown to result in obstructive sleep apnea during sleep in healthy individuals[34] and increase in the apnea frequency in OSAS patients.[35] Chadwick et al.,[36] also suggested that the oropharyngeal anesthesia increased the frequency of obstructive apnea hypopnea during sleep but not their duration. Therefore, defective upper airway reflexes may influence the initiation of obstructive respiratory events but not their termination. They postulated that a subtle upper airway neuromuscular reflex may play a role in the maintenance of upper airway patency in normal subjects and that this reflex might not be detectable in patients with OSAS.

4. Upper airway geometry

Any structural alteration that narrows the oropharyngeal or hypopharyngeal airway will increase the tendency for airway collapse by increasing upper airway resistance. Maintenance of normal tidal volume in the face of this increased upper airway resistance requires an increase in negative inspiratory pressure. It also leads to an increase in the velocity of air passing through the site of narrowing. This further reduces intraluminal pressure. For these reasons, there is an increased tendency for pharyngeal collapse at a given site of narrowing during inspiration.[37] The relevance of upper airway size performed during wakefulness to the size of the pharynx during sleep or to the site of obstruction in OSAS is uncertain. Likewise, the relationship between upper airway size and the site of obstruction in OSAS is not clear. However, it is possible that the static upper airway size is one of the precipitating factors developing OSAS. The integration of studies in this topic as well as the effects of dynamic factors such as pharyngeal compliance, reflexes, and inspiratory muscle activity would be meaningful. Combined studies of this type would add to our knowledge and understanding of pathophysiologic mechanisms of OSAS. Multiples modalities have been used to investigate the upper airway of OSAS subjects, nonapneic snorers and normal subjects.[38] These modalities include fiberoptic visualization, fluoroscopy, acoustic reflection, computerized tomography, magnetic resonance imaging and cephalometric radiography. In general, investigators have found that patients with OSAS

have structural narrowing of the upper airway which is the predominant site of initial collapse. Specific findings for each modality will be described:

Fiberoptic visualization

Fiberoptic pharyngoscopy permits examination of the entire upper airway with the mouth closed and the upper airway muscles more relaxed. Using this technique, Borowiecki et al., identified the retropalatal segment of the velopharynx as the dominant site of obstruction during sleep.[39] Thus, a relative narrowing of the upper airway anywhere from the nose to the hypopharynx would be expected to exacerbate a combination of neurophysiologic failure leading to OSAS.[40] Wilms and co-workers studied 25 adult men diagnosed with OSAS. Using fiberoptic technique, they found airway anomalies at the oropharynx level in 76% of the cases. Anomalies were found at the level of hypopharynx in 44% of the cases studied and at the level of the larynx in 8% of cases.[41]

Fluoroscopy

Fluoroscopy was used in investigation performed by Suratt et al.,[42] to observe in awake OSAS patients. They reported upper airway collapse was almost always in the proximal velopharyngeal segment. Using the same technique Katsantonis and Walsh[43] studied patients during sleep that had undergone uvulopharyngopalatoplasty. They reported that for patients who had maximal narrowing and/ or collapse confined to the region of the upper

airway above the midpoint of the body of the second cervical vertebra, 67% responded successfully to uvulopharyngopalatoplasty.

Acoustic reflection technique

Acoustic reflection technique is base on sending sound waves along the respiratory tract.[38] As they travel through the airways, they are partially reflected whenever there is a change in airway cross-sectional area. A microphone positioned at the mouth measures the intensity of the reflections and records their time of arrival relative to the incident wave. Knowing the wave speed and the arrival time of the reflections, the distance from the mouth into the airway can be calculated. Knowledge of the reflection coefficients permits computation of upper airway cross-sectional area. Employing acoustic reflection technique, Rivlin et al.,[44] reported that patients with OSAS appeared to have a smaller pharynx than nonapneic patients. This was true even when the measurements were performed in awake seated subjects. Bradley et al.,[45] found that nonapneic and apneic snorers had similar upper airway cross-sectional area at functional residual capacity; however, the nonapneic snorers had smaller lung volume-related changes in pharyngeal area. In other words, the nonapneic snorers' pharynxes were less collapsible at low lung volume.

Computerized tomography

Studies conducted using conventional computerized tomography (CT) documented that patients with OSAS had smaller minimum upper airway cross-sectional areas than nonobese control subjects.[42,46] When weight-matched subjects have been taken into account, minimum upper airway cross-sectional area has been found to be either smaller[47] or not significantly different[48] from the obese controls. Because of its reduction in scan time and radiation dosage, fast CT scanning was recently used to evaluate of the upper airway passage. Using Fast -CT, Shepard et al.,[49] evaluated the variations in upper airway dimensions with tidal ventilation during wakefulness in 25 OSAS patients. They reported that the lower velopharynx was the smallest and most variable segment. They concluded that upper airway size generally increased during inspiration and decreased toward the end of expiration, coinciding with decreased muscle tone and dissipation of upper airway pressure to atmospheric.

An interesting finding was reported by Burger et al.,[50]. They employed Fast-CT in nonsnoring men, to demonstrate that minimal upper airway cross-sectional area at functional residual capacity and atmospheric pressure was larger in the age 60-79 group than in the younger age (20-39) group. They postulated that the anatomic enlargement and increased upper airway dilator muscle tone, in response to negative pressure loading, may have acted in concert to protect the older men in their study from developing disordered breathing during sleep. CT was also used to determine upper

airway in three dimension. Ryan et al.,[51] evaluated upper airway volume of the consecutive patients with OSAS and correlated the volume measurements to response to uvulopalatopharyngoplasty. They reported that obese patients with OSAS had larger tongues and smaller upper airway volume relative to tongue and soft palate size.

Although computerized tomography has advantages over other methodologies employed to evaluate the upper airway, the major disadvantages of CT are related to the high expense and significant radiation exposure. Fast-CT may reduce the latter but cost of the procedure still limits its clinical uses.[38]

Magnetic resonance imaging

Magnetic resonance imaging (MRI) can provide excellent anatomical detail in a non invasive manner without ionizing radiation. In addition, it is capable of taking an image directly in multiple planes. Three-dimensional upper airway evaluations have been made by Ryan and coworkers.[52] Using MRI taken in sagittal and axial planes, they have shown that patients with OSAS had a decrease in upper airway volume compared to normal subjects. Utilizing advanced computer based image analysis techniques, Hoffman et al., [53-54] reported increased lateral pharyngeal wall thickness and decreased retropalatal cross sectional area in patients with OSAS compared with normal subjects. Rodenstein et al.,[55] utilized midsagittal and transverse MRI sections of the upper airway to measure anteroposterior

and transverse diameters, as well as upper airway cross-sectional area, in normal individuals, snorers and OSAS patients. They reported differences in shape, but not cross-sectional areas, among the three groups. In patients with OSAS, the upper airway was elliptical with the long axis in the sagittal (anteroposterior) plane. In snorers the upper airway was circular. In normal subjects the airway was elliptical in shape with the long axis in coronal (transverse) plane.

Another MRI study of coronal sections of the upper airway to study cross-sectional area was recently reported. The investigators hypothesized that subjects with narrow mandibles would be more likely to have OSAS than those with wide mandibles.[56] They observed a significant correlation between apnea index and area between the mandibular rami at the level of the soft palate and the angle formed by the front teeth and the posterior mandibular rami. In addition to upper airway studies, MRI has also been used to describe adipose tissue distribution. An interesting study conducted by Hoener et al.,[57] indicated excessive deposition of fat around the upper airway of patients with OSAS compared to weight-matched control subjects.

Although MRI is valuable in evaluating the upper airway noninvasively and in three dimensions, there are two disadvantages. First, it requires long scanning time which leads to motion artifacts due to the dynamic changes that occur with tidal ventilation and swallowing. Second, like CT, the high cost of the test limits its clinical use.[38]

Cephalometric Radiography

Cephalometric radiography has been routinely utilized in the fields of orthodontics and otolaryngology to evaluate both skeletal and, to a lesser extent, soft tissues in the craniofacial area. Two-dimensional static images can be obtained in lateral or anteroposterior views. Two methods of orienting the subjects head are routinely used. With both methods, the head is upright and the subject either stands or sits with the head in an orienting device. In the most common reference, soft tissue Frankfort Horizontal is parallel to the floor. In the second method, the subject is oriented with natural head posture. Ear rods are usually used not only to control head posture and symmetry of bilateral structures but also as a constructed cephalometric reference point for some cephalometric analyses.

The usage of cephalometric radiography to accurately assess the soft tissue anatomy which defines boundaries of the upper airway is a matter of some debate (especially by specialists other than orthodontists). However, many investigators have concluded that the craniofacial profile derived from cephalometric radiographs has important diagnostic value in both pre and post treatment evaluation. Due to the complexity of the relationships among craniofacial hard and soft tissues, anatomical characteristics may help identify individuals with increased risk of developing Obstructive Sleep Apnea Syndrome. It may also explain the familial link and prevalence of the syndrome by tracing aberrant anatomic features. Over the past decades, attempts to utilize cephalometry as an adjunct diagnostic procedure for

patients with OSAS have increased. Although the degree and accuracy with which upper airway morphology of patients with obstructive sleep apnea can be measured on cephalometric radiographs is sometimes disputed, cephalometrics is still an accepted technique for quantitating hard tissue craniofacial anatomy.

Lowe and Fleetham[58] compared cephalometric and CT data for the same patients, They used correlation coefficients and the results of simple regression analyses between the two and three-dimension of tongue, airway and soft palate variables. They found that metrics for the tongue, soft palate and nasopharynx were significantly correlated but metrics for the oropharynx and hypopharynx were not. It was reported that 40.6% of tongue volume could be predicted by tongue cross-sectional area whereas 20.6% of the variation in soft palate volume could be explained by soft palate cross-sectional area. Lowe's group also suggested that tongue and soft palate shape appear relatively consistent regardless of body position. In addition, they suggested that CT or MRI techniques appear superior to two-dimension cephalometry for these structures. Another interesting finding was that subjects with similar cephalometric variables may reveal different three-dimension CT measurements.

Several studies using cephalometric radiographs have recently suggested that patients with OSAS have craniomandibular and anatomical airway aberration. Measurements derived from cephalometric radiographs of OSAS patients in the upright position and statistically compared to the

same measurements taken on control groups have produced the following results:

Anterior Cranial base- Some investigators have reported that OSAS patients demonstrate a shorter anterior cranial base (Sella-Nasion) than controls.[59,60,61] However, this finding was not supported by Strelzow and his coinvestigators.[62] They found no significant difference of Sella-Nasion length between control and patient groups. Jamieson, et al.,[63] hypothesized that an acute cranial base flexure (<NSBa) leads to abnormal development of the hypopharyngeal soft tissues. However, there are conflicting reports regarding to this angle and patients with OSAS have even been reported to have greater flexion of the cranial base angle[61,62]. In contrast to these reports, Bacon and colleagues[59,60], and Lyberg and his coworkers[65] found similarity of this angle between control and patient groups.

Maxilla- Variations in the shape and position of the maxilla of patients with OSAS have been reported. Several authors reported that the maxilla of patients with OSAS is retropositioned[62,64] and vertically elongate.[62] DeBerry-Borowiecki et al.,[64] also reported elongated hard palate. In contrast, Andersson and coworkers[61] found patients with OSAS had anteroposterior shortening in hard palate but their maxillae are in normal position when compared to nonsnoring controls.

Pharynx- A reduced bony pharynx in OSAS patients has been reported[59,60,65]. Some investigators also demonstrated that there is significant correlation between cranial length and the bony pharyngeal opening.[59,60]

Mandible- A variety of findings have been reported for mandibular size, shape and position. Most studies include mandibular retrognathia as characteristic of patients with OSAS. However, there is still some debate regarding the anatomic site of retrognathia. Some have reported that the finding is due to deficient anteroposterior body length, others implicate a retropositioned mandible, a backward rotated mandible or combination of factors.[59-61, 63-66,67] It has been proposed that patients with OSAS has an increased in lower anterior facial height associated with backward rotation or retruded position of the mandibles.[59,60,62,64,65]

Hyoid Bone- Many studies have found inferior positioning of the hyoid bone in patients with OSAS compared to nonapneic snoring or nonsnoring controls.[62,64,65,67,68,69,70] Partinen et al.,[71] found increased mandibular plane to hyoid bone distance and decreased width of the posterior airway space were significant predictors of elevations in AHI. Because body mass index was highly correlated with AHI, the patient population was subdivided according to BMI and analyzed for the impact of cephalometric variables on the severity of OSAS. Their data suggested the existence of three subgroups of patients. First, those who were morbidly obese but had few cephalometric abnormalities. Second, those who were

not very obese but had major cephalometric abnormalities, and a third group with combined obesity and abnormal cephalometric measurements.

A recent report by Tsuchiya et al.,[72] has confirmed the previous study. Tsuchiya et al., utilized a statistical method, cluster analysis, to divide patients with OSAS into subgroups. The subgroups were then compared to asymptomatic controls with class I malocclusions. The first subgroup consisted of patients with a high apnea index (AI) and low body mass index (BMI). This subgroup was characterized by retruded mandibles with high mandibular plane angles with proclined lower incisors. The second subgroup had a low AI and high BMI ratio. This subgroup was characterized anatomically by inferior positioning of the hyoid bone and large soft palates. Tsuchiya et al., postulated that the patients with a high AI and low BMI ratio have a skeletal mismatch, whereas the patients with a low AI and high BMI have atypical soft tissue structures. These results have given rise to the concept that individuals with favorable craniofacial structures may tolerate massive weight gain without suffering clinical disease. In contrast, patients with abnormal skeletal structures can develop OSAS even in the absence of obesity.[38]

Some recent studies have assessed the predictive value of neck circumference for OSAS. Davies and Stradling[73] have reported that neck size and retroglossal space were significant independent correlates with oxygen saturation dips (>4%) in OSAS patients. They proposed that inferior position of the hyoid bone, elongated soft palate and upward head

extension are secondary phenomena related to variation in neck size. They hypothesized that the upward head position is a response learned by OSAS patients to reduce the increased upper airway resistance caused by a small pharynx. They also suggested that the inferior hyoid bone position is secondary to upward head position. They further proposed that neck obesity results in narrowing of the pharyngeal airway. This narrowing of the pharyngeal airway leads to an increase in hyoid to mandibular plane distance. The latter finding is often seen in OSAS patients and might represent a compensatory response to airway narrowing.

Soft tissue structures- The length, width or area in sagittal dimension of the soft palate is increased in OSAS subjects compared to nonapneic unmatched-weight control subjects.[59-60,62,64-65,67-68,71,74] Lyberg et al.,[74] reported that the area of soft palate, measured in the sagittal plane, occupied 39% of the pharyngeal area in OSAS patients compared to 21% for the unmatched-weight control group. Sites of narrow pharynx have been determined by measuring: 1. the distance from superior posterior surface of the soft palate to pharyngeal wall, 2. tip of the uvula to pharyngeal wall or 3. retroglossal distance to pharyngeal wall. Besides the distance, some investigators determined narrow airway by measuring the area in the mid sagittal plane of nasopharynx, oropharynx and hypopharynx to indicate the area of narrowing. A numbers of studies have reported reduction of posterior airway space in the naso, oro, or hypopharynx in patients with OSAS.[61-65,67-72]

Other investigators have paid more attention to the length, size and/or position of the tongue. This is reasonable because the tongue is one of the major structures of the anterior wall of the pharynx. Many investigators suggested that the tongue may play an important role in obstruction of the airway especially at the hypopharynx level. The tongue may contribute to obstruction in at least two ways. First, there may be reduced muscle activity during particular sleep stage.[21] Second, the shear size of the tongue or its position may contribute to mechanical or physiological changes leading to obstruction of the upper airway. Enlargement of the tongue has been reported in OSAS patients.[59-62,64,65,72] Pae et al.,[70] demonstrated an increase in tongue length measured from tip of the tongue to the base of epiglottis in OSAS patients.

In contrast to this finding, Lyberg et al., did not find a significant difference between tongue length or tongue height. However, they did show increased mass of the tongue as measured by its area in OSAS subjects. In addition, they have reported the lower part of the tongue represented by the vellecular is more caudally situated in OSAS patients. As a consequence, the tongue assumes a more upright position with more of the tongue mass in the hypopharyngeal area. They postulated that the presence of increased tongue mass in the hypopharynx results in depression of the hyoid bone. Hyoid position plays an important role because the hyoid serves as a central anchor for the tongue muscles and thereby partly determines the position of the tongue.

Cephalometric radiography represents a relatively inexpensive method that permits assessment of skeletal and, to a lesser extent, soft tissue elements of the upper airway. The main disadvantages of cephalometry are that it is only a two dimensional static imaging modality and that so far it has been applied primarily to study in awake subjects.[38]

All the previous mentioned modalities have shown that patients with OSAS have craniofacial anatomical abnormalities related to structural narrowing of the upper airway. It is important to note that none of the structural aberrations observed by many diagnostic modalities can be used to establish a cause and effect relationship between craniofacial anatomy and OSAS. Anatomical aberrations thought to be associated with OSAS may be either the result of physiologic compensations to clinical disease or may be underlying factors contributing to the development of clinical illness.

Summary of current theories

Sullivan et al.,[75] summarized current hypotheses which describe pathophysiological mechanism of OSAS as follows:

1. A mechanically narrow airway requiring increased suction pressures to maintain inspiratory airflow; the suction pressure causes closure only during inspiratory efforts during sleep when upper airway muscle tone is reduced. Airway occlusion is not dependent on abnormal loss of muscle tone in sleep.

2. A mechanically narrow airway which is totally dependent on continuing muscle contraction of the dilator muscles for patency. The normal reduction of muscle tone during sleep leads to occlusion. In contrast to theory 1, this model does not require increased suction pressures to produce airway occlusion.

3. Normal airway geometry with excessive loss of muscle tone during sleep, leading to airway narrowing, increasing inspiratory suction pressures and airway collapse.

4. Normal airway geometry, normal upper airway muscles and muscle tone, but abnormal instability of respiratory control causing oscillation and mismatching between diaphragm activity (and thus suction pressure) and upper airway dilator muscles.

5. Abnormal reflex motor responses causing upper airway muscle constriction (e.g., triggering of a gaglike reflex).

Other underlying factors

1. Anthropometric characteristics: Obesity, Neck circumferences, Head form.

Patients with OSAS, the most common type of OSAS, often are overweight and have a short, fat neck, but severe OSAS has also been

documented in persons of normal weight who have normal neck features.[76] The relationship of obesity to the sleep apnea syndrome is not clear. Although the incidence of sleep apnea in men has been shown by Block et al.,[77] to increase with increasing body weight, obese patients accounted for only 40% of one large series of patients with OSAS.[78]

Investigators have demonstrated that significant improvement in obstructive sleep apnea accompanies reduction in body weight.[79,80] Schwartz and coworkers[81] suggested that obesity plays a major role in the pathogenesis of this disorder. Although the mechanism for this decrease in apnea severity is not clear, they hypothesized that decreases in upper airway collapsibility account for decreases in apnea severity with weight loss. They measured the upper airway critical pressure (Pcrit) before and after a reduction in body mass index in thirteen patients with OSAS and compared to thirteen weight-stable controls matched for age, body mass index and gender. The Pcrit was determined by the level of nasal pressure below which maximal inspiratory airflow ceased. They found that in the patients with OSAS, a significant decrease in disordered breathing rate (DBR) and in Pcrit was demonstrated. In contrast, no significant change in DBR and a minimal reduction in Pcrit was observed in the control group. Thus, they concluded that weight loss is associated with decreases in upper airway collapsibility in obstructive sleep apnea.

Obesity indicated by body mass index (W/H^2) is generally used to evaluate effect of weight on prevalence, incidence or severity of OSAS.

Partinen et al.,[71] suggested that body mass index is associated with respiratory disturbance index. How well the body mass index can describe obesity has been investigated by Revicki et al.,[82]. They examined the relationship between various body mass index (BMIs), skin fold measures and laboratory measures of body fat in adult men. It was found that body mass index (Quetelet index, W/H^2) was strongly correlated with weight, hydrostatic and skin fold measurements but not height. They concluded that the Quetelet index is a valid estimate of body fat in respect to their relationship with hydrostatic measurements. However, there is a clinical subjective observation that the patents with OSAS appear to have short and fat necks which are out of proportion to their obesity.[83] This clinical observation suggests that the neck circumference and length of the upper airway may be important in the pathogenesis of the repetitive upper airway obstruction during sleep.

An investigation to observe how increased cervical adipose tissue might affect upper airway function has been conducted in eight rabbits.[84] The rabbits were simulated to have cervical fat accumulation by using lard-filled bags, while additionally using a handhold device to apply measured loads at localized sites along the airway. The investigators reported that upper airway resistance was increased by mass loads, with larger loads having greater effects. The area over the thyrohyoid membrane was more vulnerable to mass loading than adjacent areas. Because mass loading of the upper airway causes changes in its configuration and function, they

speculated that such loading may contribute to the pathogenesis of OSAS associated with obesity.

Katz et al.,[83] reported that AHI correlated with the external neck circumference, the body mass index and the internal circumference of distal pharynx. A recent study has even shown that neck circumference is more predictive of OSAS than general obesity.[85] Hoffstein and Mateika[86] demonstrated that the apnoeic patients had significantly higher body mass index (BMI), neck and abdominal circumferences than non-apneic snorers. When they matched apneic and non-apneic patients exactly one-for-one for BMI and age, there were 156 pairs of subjects. They then found that abdominal circumferences were similar, but the neck circumferences were significantly higher in the apneic group. They concluded that the obese patients with sleep apnoea have fatter necks than equally non-apnoeic snorers, and that the neck circumference could be a significant determinant of apnoea and snoring.

A parallel condition to obstructive sleep apnea/hypopnea syndrome in human beings has been reported in some particular breeds of dogs. The canine version of OSAS is termed brachycephalic airway obstructive syndrome.[87] This syndrome is recognized in brachycephalic breeds that results in varying degrees of upper airway obstruction. The head shape of brachycephalic breeds is caused by an inherited defect in the development of the bones at the base of the skull.[88] This results in a head of normal width but significantly reduced in length, having a facial index (width x

100/length) of more than twice that of mesaticephalic skulls. Breeds such as the English bulldog, Pekingese, Pug and Boston terrier have been selectively bred for these short, wide facial features. The inherent anatomy of the brachycephalic skull contributes to anatomic features such as shortened and distorted nasopharynx, a relatively long and redundant soft palate, stenotic nares, and everted laryngeal saccules.[87] The signs of this syndrome consist of respiratory distress, stridor, reduced exercise tolerance, and in more severe cases, cyanosis and collapse.

Amis et al.,[89] assessed pattern of breathing using tidal breathing flow volume loop (TBFVL) in English bulldogs and Boston Terriers, and found that the dogs did not have a TBFVL shape the same as that considered normal for healthy nonbrachycephalic dogs. Respiration was monitored further in 3 of the studied dogs; results showed that 2 of them presented periodic breathing patterns characterized by multiple episodes of alternating hypopnea and arousal similar to that described in obstructive hypopnea breathing in sleeping people. One of the dogs underwent tracheostomy and the upper airway obstruction was restored and returned to normal rhythm. The investigators speculated that many of anatomic changes described in humans with OSAS are even more pronounced in brachycephalic dogs. These dogs often breathe noisily and snore while sleeping. When brachycephalic dogs are anesthetized, they often develop obstructive sleep apnea and require immediate endotracheal intubation. To date, none of investigations of the relationship between head and facial forms and prevalence of OSAS in humans have been published.

2. Genetic basis.

The importance of inheritance in the expression of OSAS is reported in studies of families with multiple affected members.[90,91] Redline et al.,[92] recently attempted to assess the role of genetics in OSAS by quantitating the degree of familial clustering of symptoms associated with sleep related-breathing disorders. They studied 29 families identified through an index case with OSAS and 21 control families with no relative known to have OSAS. The subjects were studied with standardized questionnaires that ascertained health status and symptoms. It should be noted that the results of polysomnographic study of the subjects have not been reported in their pilot data. Odd ratios of habitual or disruptive snoring, breathing pauses, and excessive daytime sleepiness increased progressively for subjects with increasing numbers of symptomatic relatives. After adjustment for BMI, age and gender, the odd ratios slightly reduced. They summarized that the significantly increased prevalence of symptoms associated with sleep-related breathing disorders in relatives of subjects with OSAS suggested sleep-related breathing disturbances aggregate within families and appear independent of familial similarities in weight.

3. Effects of Position on upper airway

It has been demonstrated that changes in head position affect the upper airway.[93] A change from natural head position to 20 degree extension in healthy adults resulted in changed position of the hyoid bone

and increased cross-sectional dimensions of the pharyngeal airway when measured at retroglossal space at the second and forth vertebra.[94] Solow and associates[95] hypothesized that obstruction of the upper airway triggers a change in cranio-cervical posture which, in growing subjects, could influence the direction of facial development. They assessed the effect of airway obstruction on the posture of the head and the cervical column in 29 patients diagnosed by polysomnography as OSAS. Cephalometric radiographs of the subjects were obtained in natural head posture. They have demonstrated that the patients with OSAS showed markedly larger cranio-cervical angulation and a correspondingly smaller cervical inclination than reference data found in their previous study of normal healthy adults. They postulated that these might be a physiological adaptation to maintain an adequate airway .

Sleep posture may also influence sleep quality and sleep apneic events. In general, patients with the syndrome demonstrate increased respiratory difficulty when they sleep in the supine position. Pae and his colleagues[70] have reported that, when changing from the upright to the supine position, the tongue cross-sectional area of obstructive sleep apnea patients significantly increased, whereas the oropharyngeal area decreased, and the hyoid bone moved anteriorly toward the mandibular symphysis. Fitzpatrick et al.,[96] also assessed effects of supine position on dimensional changes of soft tissues by using cephalometric radiographs. They reported widening of the retroglossal airway, narrowing airway space behind the uvula and inferior anterior positioning of the hyoid bone.

A recent study using roentgenographic evaluation in apneic and nonapneic snorers reported an interesting result.[97] The investigators used three different definition of sleep apnea (AHI of 10, 20, 40) and compared airway dimensions both in upright and supine positions. Only when sleep apnea was defined as AHI >40 /hr. of sleep was there a significant difference in airway dimension at the retropalatal space between apneic and nonapneic snorers. They found that the retropalatal space was a significant predictor of snoring, but not apnea. When exact matching for age and BMI was done, they reported that both groups of patients demonstrated a significant reduction in the retropalatal space on assumption of supine posture. Performing computerized tomography in the supine position, Haponik, et al.,[46] stated that in apneic patients the cross-sectional area of the nasopharynx, oropharynx, and the hypopharynx was significantly reduced. Cartwright[98] demonstrated that the apnea index was twice as high during the time spent sleeping on back as it was when sleeping in the side position. Investigators[99] also suggested that sleep position training may be appropriate as a single or interim treatment for patients with OSAS who have position related obstruction.

Treatment for obstructive sleep apnea

Several treatments of OSAS should be considered, including surgical, mechanical and medical approaches. Treatment should be instituted to each individual based upon the patient's disability and cooperation. Proper diagnosis is extremely important in selecting treatment

modalities. Successful treatment of OSAS requires that therapy be individualized according to the patients' needs. Patients may benefit from simple treatment of risk factors for respiratory disturbances during sleep. Sleep position training and weight reduction programs should be considered in obese patients who have positioned related obstruction. A trial of nasal continuous positive air pressure(Nasal CPAP) is probably the first step in the treatment.[100] CPAP may act as a pneumatic splint and passively open the upper airway to prevent obstructive apnea.[28] Surgical correction of pathologic narrowing of the upper airway caused by enlarged tonsils, nasal polyps, macroglossia, or micrognathia can improve signs and symptoms of sleep apnea. Therefore, surgical operations such as uvulopalatopharyngoplasty, tonsillectomy, mandibular advancement, and tracheostomy, may be indicated in selective cases.[28] Medical therapy can be attempted, but there is insufficient data to suggest a high rate of success.[99]

For some patients, mechanical devices offer an alternative to surgical management of the obstruction. The Tongue Retaining Device (TRD) is an intraoral appliance designed to reduce snoring by holding the tongue in a forward position. The tongue is retained in a specially shaped compartment by suction. The TRD prevents the retrolapse of the flaccid tongue into the oropharynx. Cartwright et al.,[101] suggested that TRD can be used alone or in conjunction with other treatments to improve nocturnal respiration of the patients with wide range of apnea severity. It is also utilized in OSAS

patients with position-related obstruction and body weight not greater than 50% above the ideal weight.

Bonham et al.,[102] studied the use of cephalometrics and overnight polysomnographic monitoring to analyze the effects of a modified functional appliance on airway, sleep, and respiratory disturbances in OSAS patients. The patients were fitted with appliances designed to hold the mandible in an anterior-inferior position. A reduction in the rate of obstructive events is attributed to the effect of the appliance on the anatomical configuration of the oropharyngeal structures.[101] Another design of functional appliance by the same mode of function was introduced and named as nocturnal-airway-patency appliance (NAPA).[103] The appliance was designed to keep the airway open during sleep by 1) posturing the tongue more anteriorly 2) inhibiting wide jaw opening 3) assuring adequate air intake through the mouth whenever nasal obstruction exists. However, there is some controversy about the effects of prolonged traction on the TMJ.

Rider[104] studied the use of removable Herbst Appliance in treatment for OSAS. Its mechanism advanced the mandible and tongue to a predetermined position whether the mouth is opened or closed. However, the effectiveness of the oral removable appliance in repositioning the lower jaw for the obstructive sleep apnea patients has to be verified further. What mechanisms of the appliance relieve obstruction of the airway, and how effective the appliance is in various degree of severity of the obstructive

sleep apnea condition need to be investigated. The oral removable appliance may be another compromised, alternative treatment for OSAS.

In conclusion, obstructive sleep apnea has received increased recognition in several medical fields because of the serious systemic effects of the disease. In addition, the prevalence of the syndrome has been proven to be higher than suspected based on a epidemiological survey. Although, there has been significant research on OSAS, the intricacy of its predisposing factors and pathogenesis are still debated. Anatomic factors and/or neurogenic failure to preserve the patency of the pharyngeal airway during sleep, are two common theories for the pathogenesis of the syndrome. The use of the cephalometric technique for clinical decision making in OSAS has the potential of expanding the scope of future dental practice. However, to our knowledge the existing medical literature contains many cephalometric studies which have been based on inadequate designs and/or imprecise cephalometric technique. Construction of a Craniofacial Index Score (CIS) may provide a useful adjunct diagnostic procedure to evaluate individuals at risk for developing OSAS, which may impact treatment decisions. Such a diagnostic tool may be used in place of more costly MRI or CT scans.

STATEMENT OF THESIS

The purpose of this cross sectional study was to test a hypothesis that some craniofacial features are associated with subjects' risk factor for developing Obstructive Sleep Apnea Syndrome (OSAS). Over a period of two years, cephalometric radiographs and anthropometric measurements were collected on a group of patients with OSAS, and compared to a group of self-reported habitual snorers who do not have clinical symptoms of OSAS. Specific aims of the present study were:

1. To develop and assess a craniofacial index score (CIS) derived from cephalometric and antropometric measurements in order to differentiate OSAS patients from other snorers.

2. To find a subset of craniofacial variables that have equal or more predictive value in discriminating OSAS patients from snorers.

The derived Craniofacial Index Score (CIS) is useful to determine the validity of using cephalometric and anthropometric measurements as a

diagnostic test to identify patients at risk for Obstructive Sleep Apnea Syndrome. This CIS will be tested in the future as the second phase of the present study.

MATERIALS AND METHODS

1. Study Population

The purpose of the present study was to develop and assess an index score of craniofacial characteristics associated with OSAS. Over a period of two years, cephalometric and anthropometric measurements were collected on 58 Caucasian subjects (28 OSAS and 30 snorers). The study population consisted of 24 male and 4 female subjects diagnosed with OSAS, and 25 male and 5 female self-reported habitual snorers without clinical symptoms of OSAS. The subjects' age, sex, height and weight were recorded. Rather than the actual height and weight, Quetelet's index or the Body Mass Index (weight / height2, (kg / m^2)) was used in data analysis.

OSAS Subjects Twenty-nine patients referred by their physician for investigation of suspected abnormal breathing during sleep were recruited from the Division of Pulmonary and Critical Care, Department of Medicine, University Hospitals of Cleveland (U-HC), or the Department of Neurology

(U-HC) or the Sleep Disorders Center of the Veteran's Administration Hospital of Cleveland. The OSAS subjects had a clinical history of excessive daytime sleepiness, episodes of obstructed breathing during sleep and loud snoring. Twenty seven subjects underwent a standard polysomnographic study for either a half night or one night and had a respiratory disturbance index (apnea and hypopnea/ hr) greater than 20. Two subjects were evaluated by oxygen saturation monitoring (Criticare Pulse Oximeter model # 501 plus) over two nights and had repetitive episodes of arterial oxygen desaturation more than 4% from base line with the cumulative percentages of time spent at normal saturation below 90%. All subjects received CPAP treatment. One subject was excluded from analysis because the patient had a uvulopharyngopalatoplasty (UPPP) before cephalometric radiographs could be taken.

Snoring Subjects The control group consisted of habitual snorers recruited from three sources. Twenty of the controls were referred to the Division of Pulmonary and Critical Care, University Hospitals of Cleveland (U-HC), or the Department of Neurology (U-HC) for evaluation of heavy snoring and to rule out OSAS. Ten of the twenty were evaluated by oxygen saturation monitoring (Criticare Pulse Oximeter model # 501 plus) over two nights. None of these patients had a clinical history of active daytime sleepiness. In addition, the pulse oximeter showed no evidence of repetitive episodes of desaturation indicating a lack of substantial apneic acitvity. Standard overnight polysomnographic study was performed in ten of the

twenty snorers. These ten patients had a respiratory disturbance index less than 20 and lacked clinical symptoms of OSAS.

Three snoring subjects were recruited using a local advertisement asking for snoring subjects to participate in a research study. These three patients experienced snoring but lacked signs and symptoms of OSAS. Oxygen saturation was monitored (Criticare Pulse Oximeter model # 501 plus) in this group for two nights. There was no evidence of repetitive episodes of desaturation.

Seven of the controls were referred by Dr. Susan Redline, an Assistant Professor of Medicine and Co-Director of the Sleep Disorders Center at the Veteran Administration Hospital of Cleveland. These seven subjects were participants in an epidemiological study of genetic risk factors for OSAS. Subjects participated in the present study were neither relatives of patients with OSAS in the subject group nor relatives of each other. These seven subjects had a history of habitual snoring with no signs and symptoms of OSAS. They were evaluated for abnormal sleep-breathing conditions using a portable home monitor (Edentec Monitoring System, model 4700 Scanner or Edentracell, Eden Prairie, MN). Their respiratory disturbance index was less than 20.

Standard overnight polysomnographic study included: oronasal airflow measured with thermister, respiratory effort assessed by surface chest wall and abdominal electromyography, arterial saturation assessed by finger pulse oximeter (Nellcor N-200 Pulse Oximeter, Nellcor Inc., CA), and

sleep stages evaluated by electroencephalography (EEG), electro-oculography (EOG), electrocardiography (ECG) and submental and tibial electromyography (EMG). Recordings were obtained with a polygraph (Grass Model 78 Research Polysomnograph, Grass Instrument Co., MA). A respiratory event (apnea or hypopnea) was defined as a cessation or discernible reduction in airflow, lasting at least 10 seconds, and associated with either a 4 percent or greater decrease in oxygen saturation, or a 2 percent or greater decrease in oxygen saturation accompanied by an arousal. The respiratory disturbance index (RDI) was calculated by the total sum of apneas and hypopneas divided by total sleep time.

2. Collection of data

Anthropometric and cephalometric technique

The subject's head was measured using spreading calipers according to standard anthropometric methods.[105] Classification of head form (Brachycephaly, Mesocephaly, or Dolichocephaly) was done by using the cephalic index (ratio between cranial width and cranial length). Classification of facial type (Euryprosopic, Mesoprosopic, or Leptoprosopic) was obtained by calculating the ratio of bizygomatic width measured from the frontal radiograph to facial height measured from the lateral radiograph according to Montagu.[105] The measurements were corrected for magnification before calculation.

To clarify the outline of the oropharyngeal soft tissues, each subject swallowed a tablespoon of Barium Sulfate Esophageal Cream (Esophotrast, Roer Pharmaceutical Corp.) prior to radiography. Lateral cephalograms were recorded using natural head posture in the upright seated position at the end of the expiration phase, with the posterior teeth in light contact, and without swallowing. To ensure that the subject was awake and did not swallow when the radiographs were taken, the subject had to respond to the investigator's directions by raising his finger, and the exposure was made as the finger was being raised. Natural head posture was obtained by having the subject look into his own pupils reflected in a mirror located at eye level.[106] Head position was recorded as an angle relative to an extracranial horizontal line obtained by a fluid level device with a metallic line.[107] The most reproducible head position was used as the natural head posture.

Lateral head radiographs were traced on 0.003 inch matte acetate paper with 0.3 mm. H lead pencil. All landmarks were located and digitized by the same investigator. Linear, angular, and area variables were computed using a digitizing tablet (Summagraphics® Inc.) and customized software developed for two-dimensional morphologic analysis of anatomy (GeoCalc, courtesy Drs. John Blank, Robert Mensforth, Cleveland State University). Additionally, other soft tissue and bony structures in the upper respiratory compartment were measured (Glossary and figures 1-2). The relationship between skeletal and soft tissue components was determined by the ratio of the tongue area to the intermaxillary space in the sagittal

plane as previously reported by Vig and Cohen[108] The Counterpart Analysis of Enlow[109] was used to analyze cranial base alignment and ramus width relative to the cranial base.(figure 3-4) The counterpart analysis is based on an individual's own anatomical features and does not require a separate control group for comparison.

The mean enlargement factor of the cephalometric radiographs was 6.6 % for both subject and control groups.

Errors made in landmark identification and for digitizing method, were estimated by examining duplicate tracings of 25% of the lateral head films (N=15 pairs). Selection of radiographs was randomly done at least three weeks apart. Tracings were done on 0.003 inch matte acetate paper with a 0.3 mm H lead pencil. Nine randomly selected cephalometric variables of the second tracing were digitized and computed by the same investigator and then compared to the same variables of the first tracing. Comparison of equality of means using paired t-tests and Pearson's Simple Correlation Coefficients were used to examine the reproducibility of landmark identification. The reliability of a subject's natural head position was tested by randomly selecting fourteen subjects and recording the natural head position before and after taking the radiograph. Comparison between the means of the first and second natural head position records was then performed using paired t-tests. Pearson's Simple correlation was also calculated. P-values of less than 0.05 and 0.001 were used to determine

statistically significant difference and correlation of the means at time 1 and time 2 , respectively.

3. DATA ANALYSIS

(a) Cephalometric Analysis

In addition to traditional cephalometric landmarks, some soft tissues and structures in the upper respiratory compartment were included in the present study . Definitions of landmarks and measurements are presented in Glossary.

The counterpart analysis of Enlow was used to analyze cranial base rotation and relative width of the ramus compared to the cranial base.

(b) Statistical Analysis

The objective of the study was to compute a Craniofacial Index Score (CIS) that differentiates the snorers who have apneas (OSAS) and those who do not have apneas (snorers). The independent variables measured on a continuous scale included the following: 22 anatomic variables derived from the cephalometric radiographs, head posture, ratio of the cranial index to facial index, age and Body Mass Index (kg / m^2). Sex was determined as a dichotomous variable. The analysis for the present study proceeded as follows:

1. Descriptive Statistics

Means and standard deviations were calculated for all continuous independent variables. In addition, histograms were plotted to examine normality of the variables.

2. Comparison of Equality of the Means

As a first step, t-tests (equal variance) were used for comparison of equality of the means between the two groups. A p-value of less than 0.002 using Bonferroni's correction [P-value of 0.05 divided by total number of variables (0.05 / 27 = 0.002)] was used to determine statistical significance. The t-tests were helpful to in identifying trends in the data.

3. Constructing the Craniofacial Index

In order to differentiate subjects with OSAS from snorers, multivariate statistical procedures were used to adjust for various independent variables in the model. By considering the variables together, interrelationships among variables were incorporated and provided more important information. The present study utilized discriminant analysis to classify the subjects.

Discriminant analysis is a statistical procedure concerning with the problem of distinguishing between two or more populations on the basis of

observation on several variables. This statistical method attempts to establish a rule, or discriminant function that can be used to classify each individual. The discriminant function assigns some new individuals to the correct population when it is not known from which of the populations the individuals come.[110] The better the discriminant function, the better of the groups are divided.

It was suspected that the 22 cephalometric variables might correlate with each other. However, the degree to which they were correlated was not known. Therefore, linear correlation was computed in order to determine interdependencies among these variables. It was decided that a subset of the 22 cephalometric variables would be chosen if several variables were very highly correlated with each other ($P \leq 0.001$). This was, perhaps, the more efficient way to deal with a study involving numbers of variables, particularly cephalometric variables, but a small sample size. Besides, the final variables chosen were in accordance to results of the previously reviewed studies.

For the discriminant model, two main methods of variable selection were compared. First, all of the final cephalometric and anthropometric variables selected were forced to enter the linear discriminant model and then into the appropriate discriminant functions. The observations were finally reclassified according to the functions.

For the second method, a step-wise procedure was used to find a subset of the given variables which best performed this assignment. This

procedure was useful to determine if some variables were more important in discriminating between the two groups. Variable selection criteria for the step-wise discriminant procedure in the present study were to minimize the Wilks' Lambda and the Mahalanobis' Distance. These two methods were chosen to compare whether the variables selected were the same.

Wilks' Lambda is the ratio of the within-groups sum of squares to the total sum of squares. The small value of the lambda indicates that within-group variability is small compared to the total variability which means most of the total variability is attributable to differences between the means of the two groups.[111] At each stepwise session, variables that result in the smallest Wilks' Lambda for the discriminant function were selected for entry.

Mahalanobis distance (D^2) is a generalized measure of the distance between the two groups, and is used to correct for the effect of correlation between the independent variables.[112] The Mahalanobis' distances between all pairs of groups were calculated first. The variable that has the largest D^2 for the two groups that are closest (have the smallest D^2 initially) is selected for inclusion.

Finally, the discriminant function that best classified the subjects was used to calculate the Craniofacial Index Score (CIS). The equation used for the discriminant function calculation was as follows:

$$D = B_o + B_1 X_1 + B_2 X_2 + ... + B_K X_K$$

where the X's are the values for the independent variables, and the B's are coefficients estimated from the data. Unstandardized coefficients were used for calculation of the function score.

The equation given above was calculated for the two groups (OSAS and snorers) using the group mean for the X's and the coefficients. Consequently, the mean function scores for the two groups were computed. The best dividing point for the classification of the two groups was midway between the mean scores for the groups.[112] The average mean score was the separating boundary that classified OSAS from other regular snorers. Thus, the CIS that was used for classification is described below:

$$CIS = 1/2 \text{ (mean score for OSAS + mean score for snorers)}$$

The effectiveness of the discriminant function was also computed. Relative variability of the actual discriminant scores within and between groups was interpreted as the eigenvalue. The eigenvalue is a ratio of the between-groups to within-groups sums of square.[112] A large eigenvalue (between-groups variability is high compared to within-group variability) is characteristic of a good discriminant function. Canonical correlation, another indicator of effectiveness, was also calculated. The canonical correlation measures the degree of association between the discriminant scores and the groups.[112] The correlation is equivalent to the square root of the ratio of the between-groups sum of squares to the total sum of squares and represents the proportion of the total variance attributable to differences

between the groups. A large correlation value is associated with a good discriminant function.

All computations were performed using Statistical Package for the Social Sciences (SPSS-PC+ for windows).

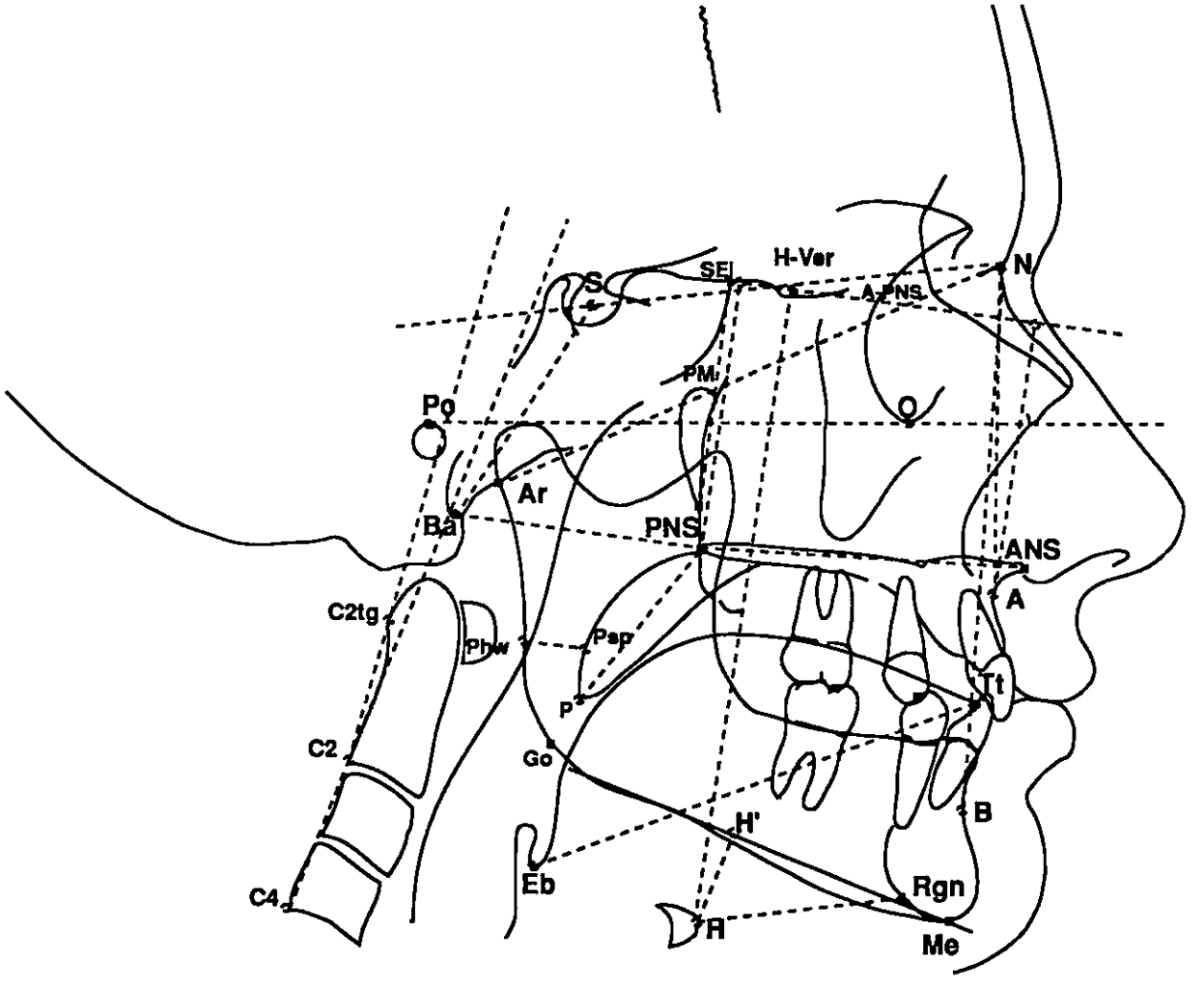


Figure.1 Conventional linear and angular measurements (see definition in GLOSSARY)

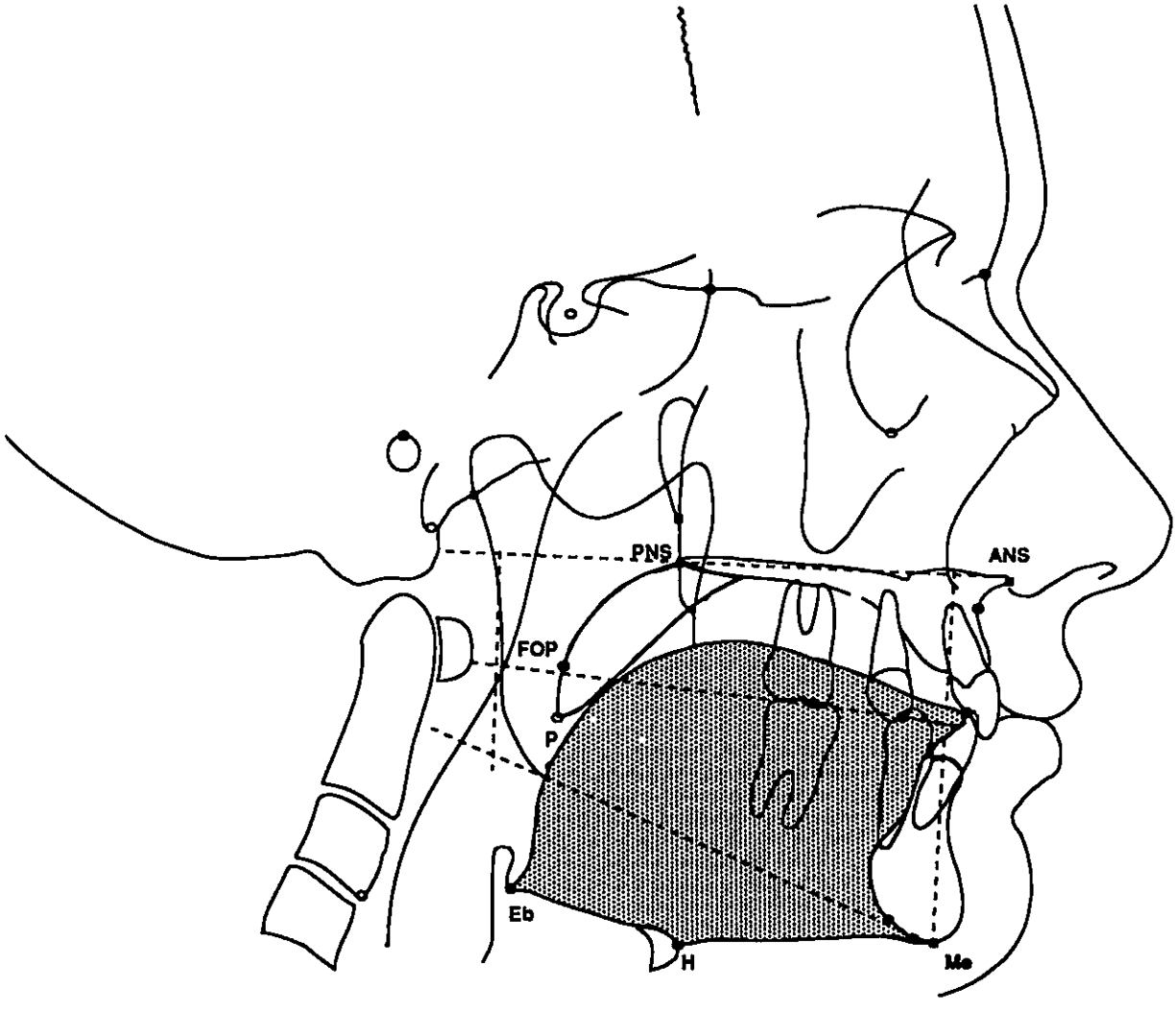


Figure. 2 Soft tissue area and soft tissue relationship to skeletal structures (see definition in GLOSSARY)

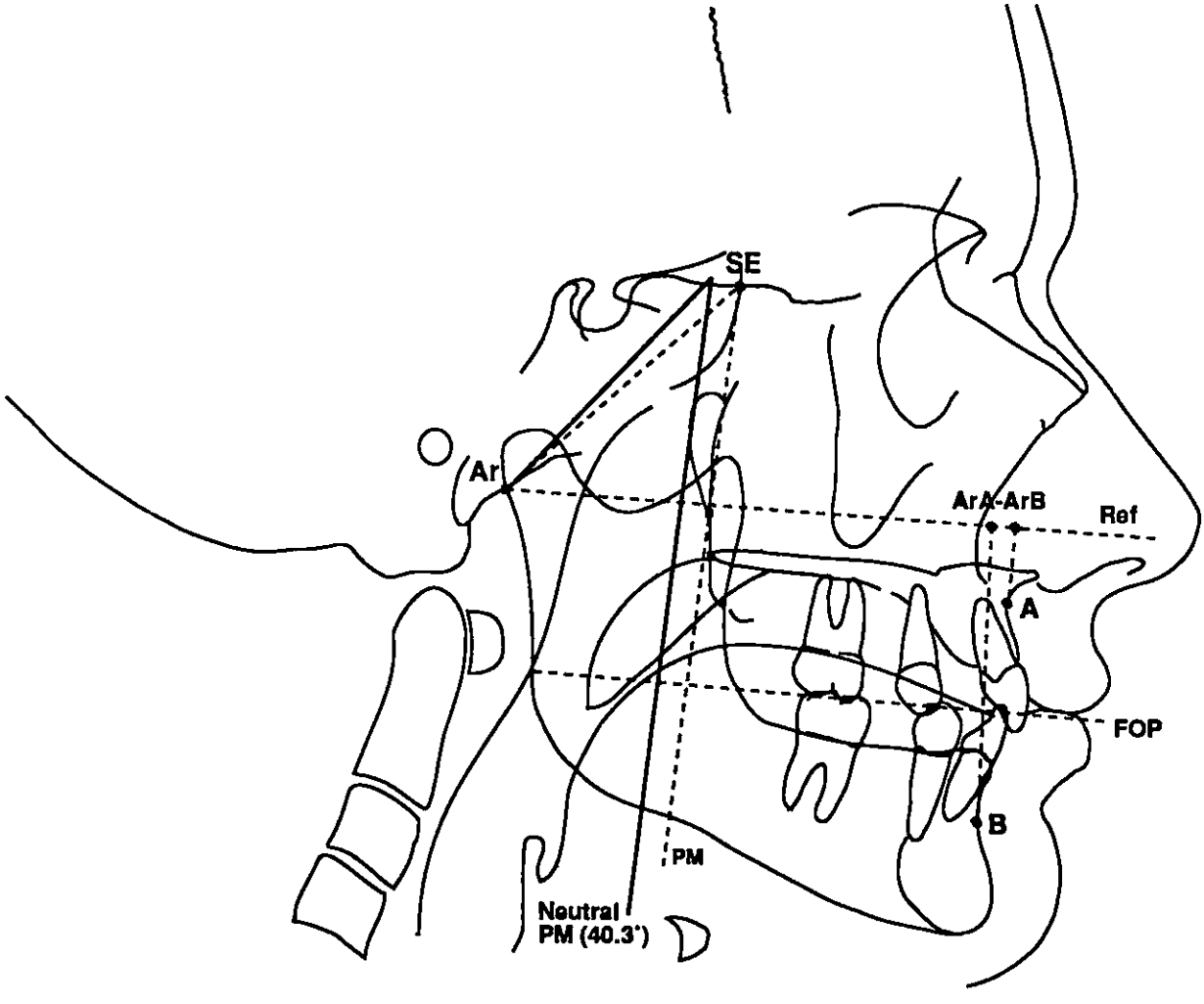


Figure. 3 The Counterpart Analysis. This diagram demonstrates the effects of rotational alignment of the individual's own MCF compared with the neutral MCF on corresponding maxillary and mandibular placement. A clockwise (+) alignment is shown. (see GLOSSARY for definition); the relative comparison of cumulative maxillary length from Ar to A point with cumulative mandibular point from Ar to B point is demonstrated. (See GLOSSARY for definition)

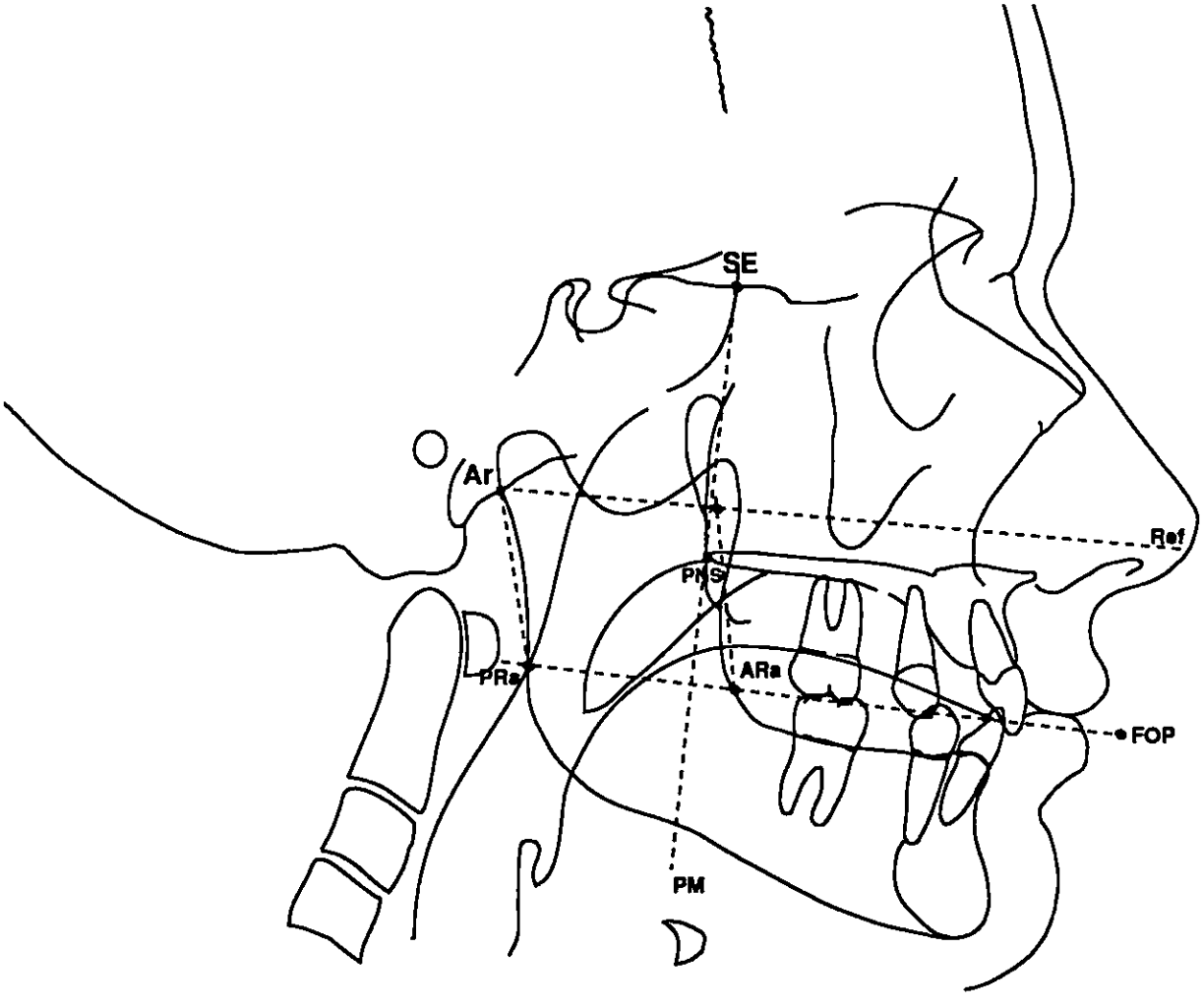


Figure. 4 The Counterpart Analysis. This diagram demonstrates comparison of the horizontal dimensions of the MCF with the width the ramus. The diagram shows a protrusive (-) mandibular effect (see GLOSSARY for definition).

RESULTS

The demographic and anthropometric data for the subjects involved in the study are presented in TABLE 1. Age, the ratio of cranial index to facial index of the OSAS group were not statistically different from the snoring group. Percentage distribution of subjects'head forms and facial forms is demonstrated in Table 2. The mean cranial index for both groups represented a Mesocephalic head form whereas their mean facial index represented a Leptoprosopic facial form. Conversely, the Body Mass Index (weight / height^2 (kg/m^2)) of the subjects with OSAS was significant greater than the control group ($P \leq 0.001$). Polysomnographic monitoring of the OSAS group demonstrated moderate to severe apnea (mean AHI =52.92 ± 27.59). The controls who underwent polysomnographic monitoring had a mean AHI 5.1± 3.92 which represented mild apneic severity.

TABLE 1. Demographic and anthropometric data of the study population.

Variables	SNORE MEAN	SNORE SD	OSAS MEAN	OSAS SD	P-VALUE	
Male:Female	25:5		24:4			
AGE	49.60	14.29	47.36	12.86	0.533	
BMI(kg/m2)	31.81	4.91	42.34	13.49	0.000	***
CI/FI	0.84	0.08	0.84	0.07	0.797	
Head Position	3.85	5.15	4.98	4.56	0.380	
AHI	5.10*	3.92	52.92**	27.59	-	

* For 17 subjects; ** For 26 subjects; ***P≤0.002

Table 2. Percentage distribution of the head forms and facial forms

	Head Forms			Facial Forms		
GROUPS	Brachy-cephalic (≥81.0)	Meso-cephalic (76-80.9)	Dolicho-cephalic (≤75.9	Eurypro-sopic (≤84.9)	Mesopro-sopic (85-89.9)	Leptopro-sopic (≥90.0)
SNORER (%)	20	63.3	16.7	-	13.3	86.7
OSAS (%)	46.2	42.9	10.7	3.6	7.1	89.3

Cephalometric Assessment

Equality of means of cephalometric variables between groups was tested using t-tests. Because of the high number of comparison tests of the means of the two groups, Bonferroni Criteria for significance level was calculated. A P-value of 0.002 was used to assign statistical significance. Comparison of the cephalometric anatomic variables are presented in Table 3 and will be summarized for each anatomic region as follows:

-Basicranium: There were no significant differences of the cranial base angle (<BaSN) and the middle cranial fossa rotation (MCF) between the two groups.

-Maxilla: The maxillary position in both groups as determined by the position of A point and the pterygomaxillary fissure relative to the cranial base (<SNA and <ArN-PM) did not appear to be different. In addition, there was no significant difference in effective dimension of the maxilla (A-PNS, maxillary length projected to the reference line in mid-sagittal plane). In both subjects with OSAS and snorers, anteroposterior dimension of the bony pharynx (PNS-Ba) was not significantly different.

-Mandible: The anteroposterior position of the mandible as given by the position of B point relative to the cranial base (<SNB) between the OSAS and snoring groups was not significantly different. The ramus width

Table 3. Comparison of means of cephalometric variables between OSAS and snoring groups using t-tests. (***P≤0.002)

		SNORE (25M,5F) MEAN	SNORE SD	OSAS (24M,4F) MEAN	OSAS SD	P-VALUE	
Cranial base	MCF	0.04	2.14	-0.35	3.94	0.639	
	<BaSN	128.86	4.63	128.79	6.18	0.963	
Maxilla	<SNA	81.75	3.51	81.20	4.65	0.610	
	<ArN-PM	56.81	3.47	56.46	5.01	0.760	
	A-PNS	51.42	4.06	51.62	4.84	0.865	
	PNS-Ba	47.33	3.73	46.66	3.92	0.504	
Mandible	Ram/MCF	1.79	3.34	2.80	4.31	0.323	
	<SNB	79.12	3.94	78.10	4.54	0.363	
	ArA-ArB	-0.19	4.66	0.45	3.93	0.576	
Hyoid	H-MP	18.01	6.05	24.94	6.43	0.000	***
	H ver	125.54	9.64	132.23	9.46	0.010	
Neck	<C2C4-SN	107.39	7.93	114.39	8.36	0.002	***
	<C2-SN	100.10	7.63	105.81	9.78	0.016	
Head post.	FH-Hor	4.17	4.24	5.36	4.64	0.310	
Soft tissue	Phw-Psp	7.71	3.52	6.28	2.50	0.083	
	P-PNS	41.05	4.70	44.93	6.77	0.013	
	TI	84.91	7.47	90.54	6.75	0.004	
	T area	4269.95	456.06	4629.02	494.23	0.006	
Ratio	AntrMxHt	73.52	6.30	73.38	5.02	0.931	
	PostrMxHt	42.49	6.79	46.36	7.59	0.045	
	InMxLth	84.41	5.69	81.14	7.08	0.057	
	T/InMx area	0.89	0.10	0.96	0.09	0.008	

relative to the middle cranial fossa width (RAM / MCF) was smaller in the OSAS group and this resulted in a mandibular retrusive effect. However, the difference was not statistically significant. Both groups had no difference in maxillo-mandibular dentoalveolar relation (ArA-ArB) which was represented by an orthognathic dentoalveolar skeleton.

-Hyoid bone: There was a significantly different hyoid bone position relative to the mandibular plane (H-MP) between the OSAS and snoring groups ($P \leq 0.001$). The hyoid bone position (H Ver) of the subjects with OSAS also had a tendency to be more inferior than the snoring group when related to the subjects' cranial reference plane ($P \leq 0.01$).

-Neck: The subjects with OSAS had more obtuse cranio-cervical angles represented by $<C_2C_4$-SN than the snorers ($P \leq 0.002$). In contrast, the difference in head posture relative to the true horizontal plane (FH-Hor, Head Position) between the two groups was not statistically significant.

-Oropharyngeal soft tissue: The Soft Palate of the OSAS group had a tendency for greater length than the control group ($P=0.013$). However, there was no difference in the posterior-superior airway space between groups. For the tongue length and area in sagittal dimension, the OSAS group demonstrated a tendency to an increase in tongue length and larger tongue area than the control group. However, the differences failed to reach the prospectively defined statistical significance ($P=0.004$, $P=0.006$, respectively).

-Ratio between hard and soft tissues: The ratio of tongue area to intermaxillary area was higher in the OSAS group compared to the snoring group ($P \leq 0.008$). However, this trend was not statistically significant. For the intermaxillary space itself, the posterior maxillary height of the subjects with OSAS seemed to be longer while the intermaxillary length tended to be shorter when compared to the snorers ($P=0.045$, $P=0.057$, respectively).

Cephalometric variables appeared to reveal differences between the OSAS and snoring groups. This was most evident in the soft tissue measurements.

Constructing the Craniofacial Index

Histograms of each variable were plotted in order to examine the normality of the variables, . The diagrams presented only a marginal departure from the normal distribution. Linear correlation was computed for all of the original 22 cephalometric and 4 anthropometric variables. The total correlation matrix is presented in appendix A. Sex (a dichotomous variable) did not provide additional information for the discriminant function. Thus, it was not included as a independent variable when all variables were forced into the discriminant function.

The original cephalometric and anthropometric variables were reduced to 13 cephalometric and 4 anthropometric predictor variables by selecting the variables according to their degree of correlation ($P \leq 0.001$)

and according to previous studies. The correlation among the variables is concluded in Table 4. These final 17 predictor variables were entered in a linear discriminant model and subjected to two methods of variable selection.

Table 4. Summary of the correlation among cephalometric, anthropometric and demographic variables. (*** Degree of correlation P≤0.001)

Cranial	Maxilla	Mandible	Hyoid	Tongue	T/InMX	Neck
MCF	<SNA	Ram/MCF	H-MP	T area	H-MP	<C2C4-SN
<ArN-PM	MCF	<SNB	H Ver	TI	InMxLth	<C2-SN
<SNA	<ArN-PM	MCF	TI	H-MP	T area	<SNA
<SNB	<SNB	<ArN-PM	T area	<C2C4-SN		<SNB
Ram-MCF	<C2C4-SN	<SNA	T/InMx	<C2-SN		H-MP
PNS-Ba	<C2-SN	InMxLth.	<C2C4-SN	T/InMx		TI
InMxLth.		<C2C4-SN	<C2-SN	P-PNS		Wt
CI				Wt		
				FI		

***The total correlation matrix is presented in appendix A.

-Entering all of the final predictor variables: All 17 predictor variables were forced into the discriminant function. Unstandardized discriminant coefficients were then computed. These coefficients resulted in a value of

the discriminant function that separated the cases into two groups. A Craniofacial Index Score (calculated by averaging discriminant functions evaluated at group means) for this method was 0.03505. The mean canonical discriminant functions for each group are presented in Table 5. Classification results and Histograms are summarized in Table 6 and figure 6. When all variables were forced into the discriminant function, the percentage of cases correctly classified in the OSAS and snoring groups were 82.10 % and 86.70 %, respectively. The overall percentage of grouped cases correctly classified was 84.48 %. Effectiveness of the discriminant function was additionally evaluated by the eigenvalue and canonical discriminant correlation as indicated in the Table 6.

-The stepwise procedure: Two different criteria for variable selection were used. Each, the Wilks' Lambda and the Malahanobis' distance, resulted in similar findings. For the stepwise procedure, the first variable that entered the discriminant function model was H-MP. At the following steps, BMI and the soft palate length (P-PNS) were included in the model, respectively. Unstandardized discriminant function coefficients for the entered variables were estimated. The best discriminant formula was as follows:

$$D= -7.4276-0.0905\ (H\text{-}MP)+0.0632\ (BMI)+0.0737\ (P\text{-}PNS).$$

Table 5. Discriminant functions evaluated at group means.

	Method 1 (Forced-entry)	Method 2 (Stepwise)
Group1	-0.9814	-0.7622
Group2	1.0515	0.8166
CIS	0.03505	0.0272

Table 6. Classification results of both methods of variable selection (Forced-entry of all predictive variables and Stepwise method)

Actual Group	No. of Cases	%correctly classified Forced-entry (*,††)	%correctly classified Stepwise(*,††)
Snoring	30	26(86.7%)	25(83.3%)
OSAS	28	23(82.1%)	19(67.9%)
	*eigenvalue	1.0687	0.6446
	††canonical correlation	0.7188	0.6261

The selected variables in the step-wise procedure resulted in a value of the discriminant function score that best separated cases into two groups. A Craniofacial Index Score for this procedure was 0.0272. The mean canonical discriminant function for each group is presented in Table 5. Summary of the classification results by the step-wise procedure is also indicated in Table 6. Histograms of the classification are illustrated in Fig 7. By using the step-wise method, the percentage of cases correctly classified in the OSAS and snoring groups were 67.9 % and 83.3 %, respectively. Compared to the first method, the step-wise procedure , which selected only important discriminant variables into the model, can classify subjects less efficiently. Additionally, in the step-wise procedure, a smaller eigenvalue and canonical correlation coefficient were found. When compared to the first method, this indicated that between-group variability is less relative to within-group and total variability.

In conclusion, the effectiveness of the discriminant function was greater when all predictor variables were forced into the discriminant function. The discriminant function equation for the best model derived from the "forced all" variable method is given as follows:

D= -7.465-0.0163(<BaSN)+0.0486(<C2C4-SN)+0.1055(A-PNS)
-0.0127(Age)+0.0618(BMI)+0.1105(H-MP)+2.5907(CI/FI)
-0.0547(InMxLth)+0.0799(MCF)+0.1074(P-PNS)-0.0282(Phw-Psp)-0.0572(PNS-Ba)+0.0127(RAM/MCF)-3.5778(T/InMx)
-0.0002(T area)-0.0236(TI)-0.0971(Head Post).

Means of the nine randomly selected cephalometric variables traced at time1 (T1) and time2 (T2) are demonstrated in Table 7. Reproducibility Coefficients for landmark identification and digitizing were calculated. None of the means of the nine cephalometric variables traced at time 1 and time 2 showed significant differences ($P \geq 0.05$). There were also highly significant correlation between the cephalometric variables traced at time1 and time2 ($P \leq 0.001$).(Table 7) The reliability of the fourteen subjects' natural head position was tested on the records of head position before and after taking the radiographs. The means of the first and second natural head position records demonstrated no significant differences ($P \geq 0.05$). The reliability coefficient of the subjects' natural head position records before and after taking the radiographs was also highly correlated ($P \leq 0.001$).(Table 8)

Table 7. Reproducibility of landmark identification and digitizing.

	Variables								
(N=15 pairs)	<BaSN	MCF	<SNA	RAM/ MCF	P-PNS	Phw-Psp	H-MP	<C2C4-SN	T/InMx
MEAN T1	127.87	-1.30	81.07	3.82	43.10	6.26	24.02	111.61	0.962
SD	5.53	4.63	3.73	5.24	6.86	3.00	6.58	8.50	0.058
MEAN T2	127.74	-1.29	80.95	3.69	42.53	6.49	24.24	110.94	0.975
SD	5.40	4.34	3.88	5.72	6.77	2.84	6.67	8.43	0.068
P-Value (Paired t-tests)	0.579	0.962	0.409	0.729	0.210	0.210	0.320	0.294	0.055
Cor. Coefficient.	0.988	0.988	0.989	0.967	0.992	0.976	0.992	0.960	0.943
P-value (2-tail)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

TABLE 8. Reliability of the subjects' natural head position.

(N=14 pairs)	MEAN DIFF. (T1-T2)	SD	P-value (Paired t-test)	Corr.Coeff.	P-value (2-tail)
Head Posture	-0.214	5.42	0.487	0.985	0.000

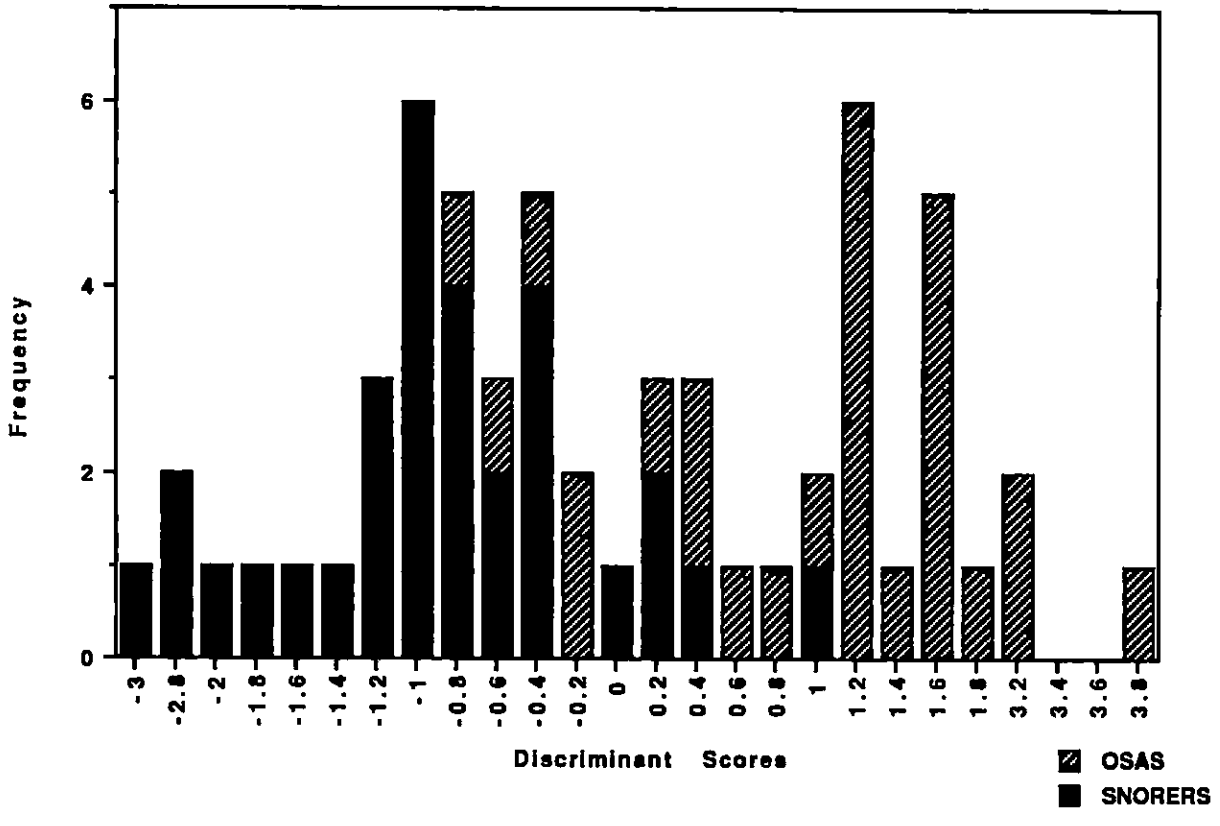


FIGURE 5. ALL-GROUPS STACKED HISTOGRAM : Summary of classification by the forced-entry method.

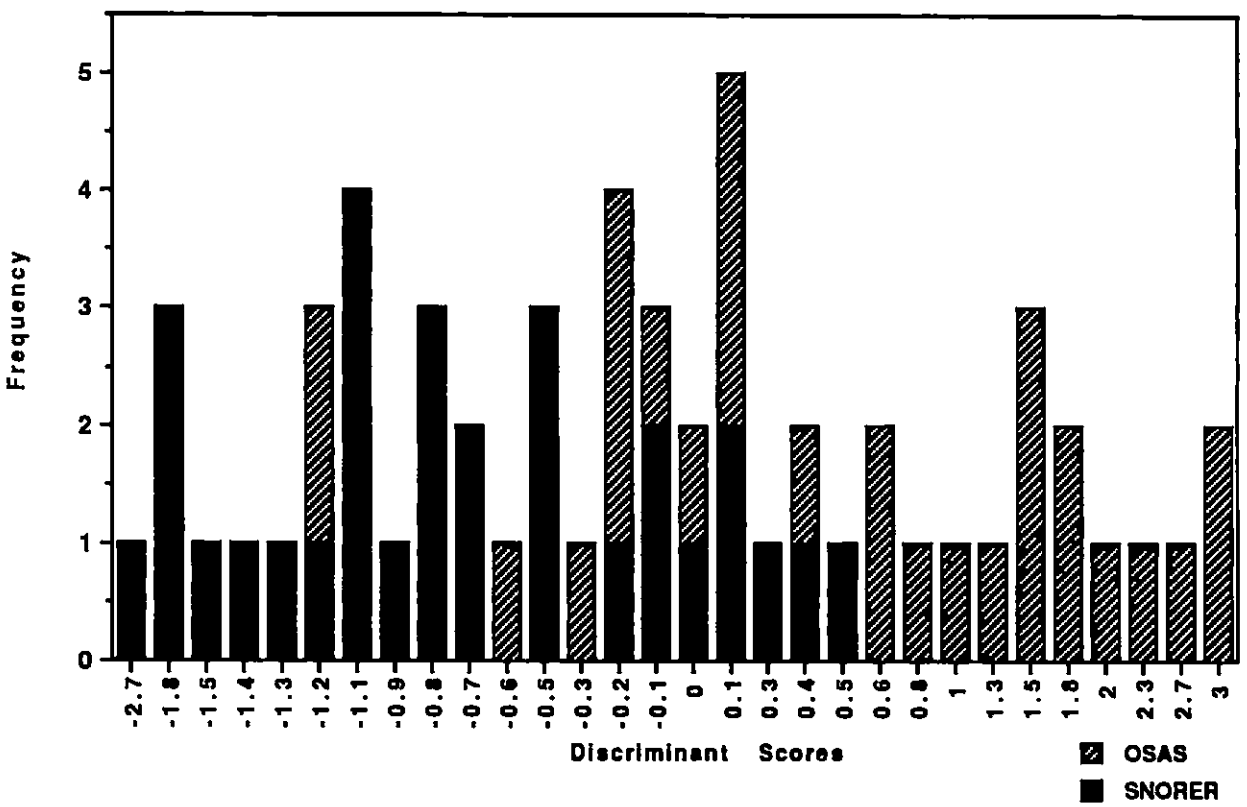


FIGURE 6. ALL-GROUPS STACKED HISTOGRAM : Summary of classification by stepwise method.

DISCUSSION

Recently, some studies have stated that cephalometric radiographs can be used to identify subjects' anatomical risks for developing Obstructive Sleep Apnea. Some authors have even recommended cephalometrics as a routine diagnostic test as well as an adjunct to treatment planning.[59-72] Many investigators have demonstrated that the craniofacial hard and soft tissue structure of patients with OSAS is different from non diseased controls. However, there is a lack of controlled clinical studies demonstrating the utility of using cephalometric radiographs as a diagnostic test to identify patients at risk for OSAS. In an attempt to test the validity of using cephalometric radiographs to identify patients at risk for OSAS, an index was first constructed from anthropometric and cephalometric variables.

Discriminant analysis is a statistical technique used to classify subjects based on risk factor variables and to develop procedures for predicting group membership for new cases. There are a variety of valid methods for selecting variables to be included in the discriminant model.

Stepwise variable selection is one method for determining which variables discriminate between the two groups. This procedure includes the most predicting variable in the discriminant model and terminates when there are no more variables that meet the selection criteria. This procedure has one limitation. Variables with low individual discriminant power may be ignored even though they may have high discriminant power when considered as part of a group. The stepwise procedure will not allow these variables to enter the discriminant model. Because of this limitation, the present study used another method to select variables for the index. The second method forces all the variables into the model.

When using the stepwise method, only three variables met the selection criteria. These variables reflected, or were related to, the soft tissues (H-MP, BMI and P-PNS). Using this model, 19 of the 28 cases (67.9%) in the OSAS group were correctly classified. In the snoring group, 25 of the 30 cases (83.3%) were correctly classified. However, the classification rate increased when we forced all the variables into the equation. Using this method, there were 23 of the 28 cases (82.1%) correctly classified in the OSAS group and 26 of the 30 cases (86.7%) in the snoring group.

In addition, findings from the present study indicated that approximately 39% (Canonical correlation in the stepwise procedure $r=0.63$, $r^2=0.39$) of total variance of the discriminant score was attributable to between-group variability. However, approximately 52% (Canonical

correlation in forced all variable method $r=0.72$, $r^2=0.52$) of total variance of discriminant score was attributable to differences between the groups when all anthropometric and cephalometric variables were included in the model. Therefore, inclusion of anthropometric, soft and hard craniofacial cephalometric variables improved the discriminant function to a considerable extent.

Bacon and his colleagues[60] attempted to classify 43 subjects with OSAS and 40 un-matched controls derived from students in a Dental School by using the stepwise procedure in the discriminant analysis. They demonstrated that four cephalometric variables entered the discriminant model were: the soft palate length, the sagittal dimension of upper face, the anterior cranial base length and the lower face height. But it is important to note that , in their model, they did not adjust the subject's weight which was found to play an important role in developing OSAS. Thus, they were able to conclude that 93% of the study population could be correctly classified using these four cephalometric variables. To our knowledge, Bacon's and the present studies are only two studies that attempted to use the discriminant analysis to determine cephalometric predictor variables which are important to distinguish subjects with and without OSAS.

Several studies have stated that upper airway collapse is a result of interrelated anatomical and functional factors. The structural relationship between soft and hard tissues surrounding the airway passage is an important area to discuss. Obesity is considered to be a predisposing factor

in the development of airway occlusion. Using cephalography, Partinen et al.,[71] studied the relationship between abnormal upper airway anatomy and body mass in 157 OSAS patients. They found when the BMI is low, the severity of airway collapse, as assessed by the respiratory disturbance index (RDI), appears associated with abnormal craniofacial cephalometric findings. They have further stated that when BMI increases, particularly in obese patients with a BMI>30, the RDI appears to be less dependent on the cephalometric results.

Further support for the hypothesis that OSAS patients may belong to two groups based on the pathogenesis of the disease can be found in the recent literature. Tsuchiya and coworkers[72] proposed that there are subtypes of OSAS who are likely to have a different pathogenesis. They classified patients with OSAS on the basis of the amount of obesity and the severity of their OSAS and then evaluated craniofacial and demographic data by means of multiple regression analysis. The OSAS patients were subdivided using cluster analysis into two groups: a group with high Apnea Index (AI) and low BMI , and a group with low AI and high BMI. In the first group, a high AI was related to a large skeletal anteroposterior discrepancy, a steep mandibular plane, and an inferoanterior position of the hyoid bone. In contrast, a high AI was associated with a large tongue and a small upper airway in the latter group. They concluded that in high AI / low BMI ratio patients with moderately obese, skeletal abnormalities may be more important etiologic factors, whereas atypical soft tissue structures (a large

tongue and/or soft palate possibly related to obesity) may result in a small upper airway of the patients with a low AI and high BMI.

The findings of the present study seem compatible to their postulation and also support the hypothesis that craniofacial or anatomic risk factors may have varying contributions to the development of clinical disease. The most important discriminant factors extracted by the stepwise method included position of the hyoid bone, soft palate length, and BMI. The first two cephalometric variables as well as BMI are all related to obesity. When using the forced-entry method, the additional anthropometric and cephalometric variables were helpful in distinguishing between subjects with and without OSAS. In particular, the relative relationship between hard and soft tissues may have more impact on determining the static size of the airway passage. Because the Craniofacial Index Score (CIS) derived from the present study included the BMI in the model, confounding factors such as effects of weight and height on craniofacial hard and soft tissue structures were already controlled.

Cephalometric craniofacial abnormalities have been demonstrated in the patients with OSAS when compared to either habitual snorers or nonsnorers.[59-74] However, the list of the significant differences in variables reported by different investigators varies considerably. When comparing cephalometric craniofacial variables in each anatomic region between subjects with and without OSAS, the present study showed very few significant differences. This was particularly true for skeletal measurements.

This finding was contrary to the results of some studies, and consistent with others. One possible reason for these controversial findings is the difference in the control group to whom subjects with OSAS were compared. The control group in the present study consisted of habitual snorers who had an RDI less than 20, whereas in some other studies control groups comprised of normal, nonsnoring, adolescents. Another reason may be due to the statistical methods employed. Some studies used multiple comparisons of a large number of variables. Repeated t-tests are likely to provide random significance (1/22). To be conservative in estimation of significance when multiple comparisons are made, Boferronis'correction method was used in the present study. This resulted in a conservative level of significance at p-value of 0.002. Thus, many cephalometric variables measured in the present study had a trend towards significance in stead of having statistical significance. Bacon[59-69] and Partinen[71] also used Bonferroni Criteria in their statistical analysis. However, the rest of the studies did not use such correction.

All previous investigations as well as the present study seem in agreement on one anatomic difference. The position of the hyoid bone is lower in OSAS patients.[62,64,65,67-70] Additionally, it appeared that the soft palate of the patients with OSAS is longer, wider and has a greater area in sagittal dimension.[59,60,62,64,65,67,68,71,74] A number of studies have reported reduction of posterior airway space in the naso, oro, or hypopharynx in patients with OSAS[61-65,67-72]; this finding was not demonstrated in the present study.

Position of the hyoid bone was found to be related to apnea severity.[62,64,71,72] The present study also found that position of the hyoid bone relative to the mandibular plane (H-MP) was the most important predictor variable in the discriminant function using the stepwise procedure. Unfortunately, this measurement is subject to a high degree of physiologic variation. Davies and Stradling[73] have proposed that the inferior position of the hyoid bone, elongated soft palate and upward head extension are secondary phenomena related to variation in neck size. They speculated that OSAS patients adapted to the increased upper airway resistance, due to mass loading of the neck area, by extending their head in an upward position. This secondarily resulted in an inferior hyoid bone position. Thus, in their opinion, an increase in hyoid to mandibular plane distance might represent a compensatory response to airway narrowing and not a predisposing factor.

It has been stated that changes in head position affect the hyoid bone position and the upper airway.[93] Tallgren and Solow[93] examined hyoid bone position and craniocervical posture in an adult dentate sample. They demonstrated that the hyoid bone position correlated both with facial morphology and head and cervical posture. They further indicated that the distance from the hyoid bone to the mandible (H-MP) and from the hyoid bone to the cervical column were greater in older age groups (30-49, 50-81 years) compared to a younger group (20-29 years). A change from natural head position to 20 degree extension in healthy adults resulted in changed position of the hyoid bone and increased cross-sectional dimensions of the

pharyngeal airway when measured at retroglossal space at the second and forth vertebra.[94]

Solow and associates[95] assessed the effect of airway obstruction on the posture of the head and the cervical column in OSAS patients. Cephalometric radiographs of the subjects were obtained in natural head posture. They found that the patients with OSAS showed markedly larger cranio-cervical angulation (<C2-SN) than reference data found in their previous study of normal healthy adults. Interestingly, they did not find a significant difference in the cranio-vertical posture (SN-True Vertical). Thus, they postulated that these changes might be physiological adaptations to maintain an adequate airway. In contrast, the head, and thus the visual axis, was maintained in its original orientation in relation to the true vertical. Consistent with these findings, subjects with OSAS in the present study showed significantly more extended cranio-cervical angulation (<C2C4-SN) and a tendency toward significance in <C2-SN. Surprisingly, their visual axis indicated by <FH-True Horizon and Head Posture relative to the true Horizon (recorded from a fluid level device) was not significantly different from the snoring group. Although in the present study the true horizontal line was used as a reference, it could be transformed to the true vertical reference as used in Tallgren and Solow's study. Thus, this observation may provide support for the postulation that inferior hyoid bone position in OSAS patients may be a secondary effect due to an attempt to maintain patency of the upper airway passage.

A review of growth of the pharynx and its physiologic adaptation was recently presented by Tourne[113]. He concluded that adult nasopharyngeal depth dimensions are established in early life, thus, the pharynx increases its capacity predominantly by a vertical expansion at the lower level. He postulated that a drop in hyoid position relative to the mandible represents an attempt to secure a relatively constant anteroposterior diameter of the airway. Bench[114] also reported physiologic adaptation behavior of the hyoid bone. He described a dramatic descent of the hyoid in the late stages of development, especially in males. His finding was consistent to what Cohen and Vig[115] reported. They stated that the tongue, especially in the males, increases in bulk until maturity, and the tongue then becomes relatively larger in relation to the intermaxillary space with increasing age. The fact that the hyoid and thus the tongue drop considerably at a later age would compensate for this increase in bulk and would maintain function during growth.

There have been very few studies of cephalometric evaluation in OSAS patients concerning subjects' head posture when cephalographs were taken. Most of the studies used subjects' natural head position obtaining by visual feed back when gazing horizontally. Some studies used an upright position with the Frankfort Horizontal plane parallel to the floor.[72,116] However, some studies did not mention the method used to position the subjects' head.[59-61,69,97] According to our findings, head position affects a number of craniofacial measurements related to the airway passage and the hyoid bone. Thus it is important to be cautious when

evaluating cephalometric variables intended to measure the upper airway and the hyoid bone. The lack of careful control of head position in many reported studies in the literature makes comparisons of measurements among studies problematic. In addition, control of head position is critical when evaluating invasive treatment modalities such as surgery.

The present study used both polysomnography and/or home monitoring oximetry as diagnostic tests. Neither of these tests is universally accepted as the "gold standard" for diagnosis of OSAS. Some clinicians and researchers recommended the overnight polysomnography as a standard procedure for assessment of apneic activity. The advantages of polysomnography over oximetry are its ability to assess apneic severity in terms of frequency, and to identify subtypes of sleep apnea, i.e. central, obstructive or mixed. Although polysomnography can quantitate sleep stages and sleep efficiency, such information does not significantly contribute to the treatment options for the patients. In addition to its limitation of cost and time expense, a "first-night effect" commonly occurs, and consequently, insufficient sleep on the first night gives falsely negative results or necessitates a second night in the hospital.

Redline and coworkers[117] have demonstrated that measurement with a portable home monitoring (Edentec Monitoring System, model 4700 Scanner, Eden Prairie, MN) provides a valid and highly reproducible index for assessment of sleep-related breathing disturbances. While signals to examine sleep stages are not recorded, there is, nevertheless, a high level

of agreement between the RDI recorded with overnight hospital polysomnography and the portable monitor (r=0.96). Based on Redline's results, the present study used an RDI of 20 measured by the portable home monitoring or overnight polysomnography to discriminate between snorers and OSAS subjects.

A home monitoring pulse oximeter is also used as a screening device for OSAS. It has been reported that the sensitivity of the clinical diagnosis after inspection of the oximetry results was 72% and the specificity was 88%.[118] Gyulay and coworkers[118] demonstrated that when using the percentage of time spent more than 1% at SaO2 below 90%, a home oximetry could practically exclude clinically significant OSAS. They concluded that highly specific indicators of OSAS can be derived from home oximetry, however, the sensitivity of the test is also reduced. The specificity and sensitivity of the pulse oximeter for detecting apneas is not as high as overnight polysomnography. However, our intent was to use pulse oximetry along with the physicians physical assessment of the subject to differentiate those with multiple apneas (RDI≥20) from habitual snorers (RDI<20) who presented with few or no signs and clinical symptoms of OSAS. The selection criteria relied on oxygen desaturations per hour of sleep rather than an assessment of sleep efficiency, and thus the criteria is analogous to portable studies. Nevertheless, sleep efficiency may have been adequately assessed since subjectively daytime sleepiness reported by the heavy snorers was mild or non-existent. The cost of obtaining overnight

polysomnography, when not clinically indicated, was also taken into consideration.

The present study used a number of clinically useful methods to evaluate apnea and hypopnea activity. The methods are used in clinical practice to practically discriminate between habitual snorers and potential OSAS patients. In addition, to avoid the sample selection bias, the present study recruited snoring subjects either with or without OSAS by all the previously mentioned methods .

Limitations of the study

The sample size is still small in the present study. Greater variability in structural abnormalities may have been demonstrated if a larger and more heterogenous group of OSAS patients were studied. In addition, there might be some sample selection bias due to differential diagnostic tests using in the present study, and bias introduced by using some of the controls who were potential OSAS cases.

It is important to emphasize that cephalometric radiographs provide only a two-dimensional static image. Information derived from a lateral cephalometric radiograph cannot be extrapolated to the three-dimensional anatomical structures. So far cephalometry has been introduced primarily to study awake subjects. Thus, information from cephalometric radiographs

cannot be used to identify potential sites of upper airway obstruction during sleep.

Although published studies using computerized tomography, magnetic resonance image and cephalography have demonstrated that patients with OSAS have structural narrowing of the upper airway. It must be kept in mind that such observations do not prove the existence of a causal relationship between craniofacial anatomy and OSAS. Anatomical aberrations associated with OSAS may be the result of physiologic compensations to clinical disease. On the other hand, craniofacial anatomy may be an underlying factor that contributes to the development of clinical illness. Cephalometry is a widely available and inexpensive test. Valuable information has been derived from a number of studies concerning cephalometric assessment in snorers and OSAS patients. However, it is essential to critically evaluate the validity of cephalometry in identifying subjects at risk for developing Obstructive Sleep Apnea. The present study is only the first step in testing the utility of using cephalometrics as a diagnostic test for OSAS and a larger study is planned to more fully address this question. Constructing a cephalometric index to differentiate patients at risk of OSAS is as important as testing the index in the general population.

SUMMARY AND CONCLUSIONS

This cross-sectional study attempted to test the hypothesis that some specific craniofacial structures are associated with subjects at risk for developing Obstructive Sleep Apnea Syndrome (OSAS). A craniofacial index score (CIS) was developed and used to differentiate subjects with OSAS from snorers. Over a period of two years, cephalometric and anthropometric measurements were collected on twenty eight OSAS patients and thirty self-reported habitual snorers over a period of two years. The cephalometric and anthropometric variables between the two groups were compared. Discriminant analysis was used to derive a Craniofacial Index Score using both a stepwise procedure , and a forced-entry method to determine the best predictor variables.

Analysis of the data yielded the following results:

1. Comparison of equality of means of the cephalometric and anthropometric variables indicated that the position of the hyoid bone was

hyoid bone of the OSAS patients was positioned more inferiorly relative to the mandibular plane.

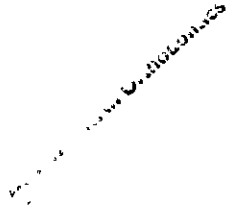
2. The cranio-cervical angulation of the OSAS patients was significantly more extended as compared to the snorers. However, OSAS subjects' head posture and the Frankfort plane relative to the true Horizon were not significantly different from the snorers.

3. The craniofacial index score derived using the discriminant analysis could be used to differentiate subjects at risk for developing obstructive sleep apnea syndrome.

4. When using the stepwise procedure, the position of the hyoid bone relative to the mandibular plane, the body mass index , and the soft palate length were the most important discriminant variables, respectively. The stepwise method correctly classified 67.9% of OSAS cases and 83.3% of snoring cases.

5. When all predictor variables were forced into the discriminant function, 82.1% of cases were correctly classified in the OSAS group whereas 86.7% of cases were correctly classify in the snoring group. The effectiveness of CIS derived using the forced-entry method was superior to that derived using the stepwise method. This was true based on the classification rate, the eigenvalue, and the canonical discriminant correlation.

In conclusion, findings from the present study indicated that cephalometric and anthropometric variables may be associated with the risks of developing obstructive sleep apnea. The present study demonstrated the utility of a statistical methodology additionally with valuable information from the cephalometric radiographs in identifying individuals predisposed to OSAS. The derived discriminant model using all of the possibly predictive cephalometric and anthropometric variables may be speculatively used to identify OSAS subjects from the snoring population. It is hoped that the craniofacial index derived from the present study will be validated, and subsequently applied as a practical diagnostic test for Obstructive Sleep Apnea Syndrome.



Appendix A

Correlation Matrix

- - Correlation Coefficients - -

	@ARN_PM	@BASN	@C2C4TGS	@C2TGSN	@SNA	@SNB
@ARN_PM	1.0000	-.0138	-.2161	-.1707	.3924	.4162
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .	P= .918	P= .103	P= .200	P= .002	P= .001
@BASN	-.0138	1.0000	.1203	.0856	-.4331	-.2422
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .918	P= .	P= .368	P= .523	P= .001	P= .067
@C2C4TGS	-.2161	.1203	1.0000	.8235	-.4433	-.4741
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .103	P= .368	P= .	P= .000	P= .000	P= .000
@C2TGSN	-.1707	.0856	.8235	1.0000	-.3995	-.4140
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .200	P= .523	P= .000	P= .	P= .002	P= .001
@SNA	.3924	-.4331	-.4433	-.3995	1.0000	.6226
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .002	P= .001	P= .000	P= .002	P= .	P= .000
@SNB	.4162	-.2422	-.4741	-.4140	.6226	1.0000
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .001	P= .067	P= .000	P= .001	P= .000	P= .
A_PNS	.0674	-.0084	-.1806	-.2361	.4200	.2319
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .615	P= .950	P= .175	P= .074	P= .001	P= .080
ARA_ARB	-.1981	.0784	.1249	.0592	.1274	-.3402
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .136	P= .558	P= .350	P= .659	P= .341	P= .009
BA_C4_VE	-.1472	-.3353	-.1104	.0999	-.0056	.0010
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .270	P= .010	P= .409	P= .455	P= .967	P= .994
BMI1	.2175	.2106	.3939	.3027	-.0889	.0085
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .101	P= .113	P= .002	P= .021	P= .507	P= .950
CI_FI	.0179	.0167	-.1870	-.2019	.1190	.0992
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .894	P= .901	P= .160	P= .128	P= .374	P= .459

(Coefficient / (Cases) / 2-tailed Significance)

" . " is printed if a coefficient cannot be computed

- - Correlation Coefficients - -

@ARN_PM @BASN @C2C4TGS @C2TGSN @SNA @SNB

FH_HOR	-.2087	-.0283	.2727	.1408	-.2377	-.0869
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .116	P= .833	P= .038	P= .292	P= .072	P= .517
H_MP	-.2923	.0933	.5155	.3008	-.2841	-.3148
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .026	P= .486	P= .000	P= .022	P= .031	P= .016
H_VER	-.2426	-.1582	.3742	.2603	-.1891	-.2622
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .066	P= .236	P= .004	P= .048	P= .155	P= .047
HEAD_POS	.0166	.1350	.3716	.1760	-.0544	-.1907
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .901	P= .312	P= .004	P= .186	P= .685	P= .152
INMXLTH	.2457	.2543	-.1889	.0438	.1153	.3395
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .063	P= .054	P= .156	P= .744	P= .389	P= .009
MCF	.8107	.2710	-.2903	-.3019	.3908	.3687
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .000	P= .040	P= .027	P= .021	P= .002	P= .004
NECK_CM_	.0966	.0337	.3960	.4645	.0291	.1401
	(32)	(32)	(32)	(32)	(32)	(32)
	P= .599	P= .855	P= .025	P= .007	P= .874	P= .444
P_PNS	-.1540	-.0116	.1314	.2740	-.0837	-.0163
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .249	P= .931	P= .325	P= .037	P= .532	P= .903
PHW_PSP	.1692	-.0105	.0330	.1642	.0335	-.0346
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .204	P= .938	P= .806	P= .218	P= .803	P= .796
PNS_BA	.3965	.2411	-.2635	-.1254	.2660	.3439
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .002	P= .068	P= .046	P= .348	P= .044	P= .008
RAM_MCF	-.5041	-.0502	.3510	.3729	-.4126	-.3977
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .000	P= .708	P= .007	P= .004	P= .001	P= .002

(Coefficient / (Cases) / 2-tailed Significance)

" . " is printed if a coefficient cannot be computed

- - Correlation Coefficients - -

	@ARM_PM	@BASN	@C2C4TGS	@C2TGSN	@SNA	@SNB
T_INMX	-.0961	.1770	.3159	.1095	-.2609	-.1641
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .473	P= .184	P= .016	P= .413	P= .048	P= .218
TAREA	.0182	.1214	.2697	.2368	-.1347	.0071
	(58)	(58)	(58)	(58)	(58)	(58)

	P= .892	P= .364	P= .041	P= .073	P= .313	P= .958
TL	-.0960 (58) P= .474	-.0220 (58) P= .870	.5861 (58) P= .000	.5524 (58) P= .000	-.0479 (58) P= .721	-.1322 (58) P= .322

(Coefficient / (Cases) / 2-tailed Significance)

" . " is printed if a coefficient cannot be computed

- - Correlation Coefficients - -

	A_PNS	ARA_ARB	BA_C4_VE	BMI1	CI_FI	FH_HOR
@ARN_PM	.0674 (58) P= .615	-.1981 (58) P= .136	-.1472 (58) P= .270	.2175 (58) P= .101	.0179 (58) P= .894	-.2087 (58) P= .116
@BASN	-.0084 (58) P= .950	.0784 (58) P= .558	-.3353 (58) P= .010	.2106 (58) P= .113	.0167 (58) P= .901	-.0283 (58) P= .833
@C2C4TGS	-.1806 (58) P= .175	.1249 (58) P= .350	-.1104 (58) P= .409	.3939 (58) P= .002	-.1870 (58) P= .160	.2727 (58) P= .038
@C2TGSN	-.2361 (58) P= .074	.0592 (58) P= .659	.0999 (58) P= .455	.3027 (58) P= .021	-.2019 (58) P= .128	.1408 (58) P= .292
@SNA	.4200 (58) P= .001	.1274 (58) P= .341	-.0056 (58) P= .967	-.0889 (58) P= .507	.1190 (58) P= .374	-.2377 (58) P= .072
@SNB	.2319 (58) P= .080	-.3402 (58) P= .009	.0010 (58) P= .994	.0085 (58) P= .950	.0992 (58) P= .459	-.0869 (58) P= .517
A_PNS	1.0000 (58) P= .	.2694 (58) P= .041	.0403 (58) P= .764	-.0615 (58) P= .646	-.0666 (58) P= .619	-.2034 (58) P= .126
ARA_ARB	.2694 (58) P= .041	1.0000 (58) P= .	-.1169 (58) P= .382	-.1181 (58) P= .377	.0131 (58) P= .922	-.0284 (58) P= .832
BA_C4_VE	.0403 (58) P= .764	-.1169 (58) P= .382	1.0000 (58) P= .	-.3068 (58) P= .019	-.1426 (58) P= .286	.0831 (58) P= .535
BMI1	-.0615 (58) P= .646	-.1181 (58) P= .377	-.3068 (58) P= .019	1.0000 (58) P= .	-.0491 (58) P= .715	.1796 (58) P= .177
CI_FI	-.0666 (58) P= .619	.0131 (58) P= .922	-.1426 (58) P= .286	-.0491 (58) P= .715	1.0000 (58) P= .	-.1855 (58) P= .163

(Coefficient / (Cases) / 2-tailed Significance)

" . " is printed if a coefficient cannot be computed

- - Correlation Coefficients - -

	A_PNS	ARA_ARB	BA_C4_VE	BMI1	CI_FI	FH_HOR
FH_HOR	-.2034	-.0284	.0831	.1796	-.1855	1.0000
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .126	P= .832	P= .535	P= .177	P= .163	P= .
H_MP	-.0687	.1485	-.0591	.3407	-.0667	.3387
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .608	P= .266	P= .660	P= .009	P= .619	P= .009
H_VER	-.0298	.2553	.2824	.0808	-.4060	.3481
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .824	P= .053	P= .032	P= .547	P= .002	P= .007
HEAD_POS	.1465	.1200	-.0472	.3352	-.0969	.2459
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .272	P= .370	P= .725	P= .010	P= .469	P= .063
INMXLTH	.1761	-.1965	.1882	-.1045	-.3228	-.0819
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .186	P= .139	P= .157	P= .435	P= .013	P= .541
MCF	.1693	-.0202	-.2897	.2519	.0234	-.2185
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .204	P= .881	P= .027	P= .056	P= .861	P= .099
NECK_CM_	.1534	.0409	.2004	.6687	-.3719	.1670
	(32)	(32)	(32)	(32)	(32)	(32)
	P= .402	P= .824	P= .271	P= .000	P= .036	P= .361
P_PNS	-.1016	.1761	.3484	.0629	-.1963	.2465
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .448	P= .186	P= .007	P= .639	P= .140	P= .062
PHW_PSP	-.0344	-.0306	.0734	-.0609	-.2133	-.0932
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .798	P= .820	P= .584	P= .650	P= .108	P= .486
PNS_BA	.1266	.0193	-.0185	.0311	-.2359	-.0446
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .346	P= .886	P= .891	P= .816	P= .075	P= .740
RAM_MCF	-.2246	.1659	.0476	-.0902	.1181	.1860
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .090	P= .213	P= .723	P= .501	P= .377	P= .162

(Coefficient / (Cases) / 2-tailed Significance)

" . " is printed if a coefficient cannot be computed

- - Correlation Coefficients - -

A_PNS	ARA_ARB	BA_C4_VE	BMI1	CI_FI	FH_HOR

	P= .009	P= .547	P= .010	P= .435	P= .056	P= .000
CI_FI	-.0667	-.4060	-.0969	-.3228	.0234	-.3719
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .619	P= .002	P= .469	P= .013	P= .861	P= .036

(Coefficient / (Cases) / 2-tailed Significance)

" . " is printed if a coefficient cannot be computed

- - Correlation Coefficients - -

	H_MP	H_VER	HEAD_POS	INMXLTH	MCF	NECK_CM_
FH_HOR	.3387	.3481	.2459	-.0819	-.2185	.1670
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .009	P= .007	P= .063	P= .541	P= .099	P= .361
H_MP	1.0000	.7066	.4162	-.3827	-.2596	.4963
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .	P= .000	P= .001	P= .003	P= .049	P= .004
H_VER	.7066	1.0000	.2895	-.1546	-.3525	.6146
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .000	P= .	P= .027	P= .247	P= .007	P= .000
HEAD_POS	.4162	.2895	1.0000	-.2210	.0458	.3671
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .001	P= .027	P= .	P= .095	P= .733	P= .039
INMXLTH	-.3827	-.1546	-.2210	1.0000	.2943	.1206
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .003	P= .247	P= .095	P= .	P= .025	P= .511
MCF	-.2596	-.3525	.0458	.2943	1.0000	.1304
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .049	P= .007	P= .733	P= .025	P= .	P= .477
NECK_CM_	.4963	.6146	.3671	.1206	.1304	1.0000
	(32)	(32)	(32)	(32)	(32)	(32)
	P= .004	P= .000	P= .039	P= .511	P= .477	P= .
P_FNS	.2540	.5001	.0020	.2029	-.1193	.6683
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .054	P= .000	P= .988	P= .127	P= .372	P= .000
PHN_PSP	-.1495	-.1274	.0423	.2403	.0548	-.2454
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .263	P= .341	P= .752	P= .069	P= .683	P= .176
PNS_BR	-.0450	.1356	.0405	.4402	.4874	.4390
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .737	P= .310	P= .763	P= .001	P= .000	P= .012
RAM_MCF	.3877	.3006	.1019	-.3018	-.5833	.0250
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .003	P= .022	P= .447	P= .021	P= .000	P= .892

T_INMX	.0294	.0675	-.2091	.4273	.1824	.2109
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .826	P= .615	P= .115	P= .001	P= .171	P= .112
TAREA	.2396	.1047	.2109	.3349	-.3643	.2317
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .070	P= .434	P= .112	P= .010	P= .005	P= .080
TL	.1703	.2817	.1800	.2728	-.4488	.3096
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .201	P= .032	P= .176	P= .038	P= .000	P= .018

(Coefficient / (Cases) / 2-tailed Significance)

" . " is printed if a coefficient cannot be computed

- - Correlation Coefficients - -

	H_MP	H_VER	HEAD_POS	INMXLTH	MCF	NECK_CM_
@ARN_PM	-.2923	-.2426	.0166	.2457	.8107	.0966
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .026	P= .066	P= .901	P= .063	P= .000	P= .599
@BASN	.0933	-.1582	.1350	.2543	.2710	.0337
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .486	P= .236	P= .312	P= .054	P= .040	P= .855
@C2C4TGS	.5155	.3742	.3716	-.1889	-.2903	.3960
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .000	P= .004	P= .004	P= .156	P= .027	P= .025
@C2TGSN	.3008	.2603	.1760	.0438	-.3019	.4645
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .022	P= .048	P= .186	P= .744	P= .021	P= .007
@SNA	-.2841	-.1891	-.0544	.1153	.3908	.0291
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .031	P= .155	P= .685	P= .389	P= .002	P= .874
@SNB	-.3148	-.2622	-.1907	.3395	.3687	.1401
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .016	P= .047	P= .152	P= .009	P= .004	P= .444
A_PNS	-.0687	-.0298	.1465	.1761	.1693	.1534
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .608	P= .824	P= .272	P= .186	P= .204	P= .402
ARA_ARB	.1485	.2553	.1200	-.1965	-.0202	.0409
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .266	P= .053	P= .370	P= .139	P= .881	P= .824
BA_C4_VE	-.0591	.2824	-.0472	.1882	-.2897	.2004
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .660	P= .032	P= .725	P= .157	P= .027	P= .271
BMI1	.3407	.0808	.3352	-.1045	.2519	.6687
	(58)	(58)	(58)	(58)	(58)	(32)

(Coefficient / (Cases) / 2-tailed Significance)

" . " is printed if a coefficient cannot be computed

- - Correlation Coefficients - -

	H_MP	H_VER	HEAD_POS	INMXLTH	MCF	NECK_CM_
T_INMX	.7033	.2649	.3120	-.4661	-.0301	.3211
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .000	P= .044	P= .017	P= .000	P= .822	P= .073
TAREA	.4276	.5853	.1090	.2806	.0289	.7287
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .001	P= .000	P= .415	P= .033	P= .829	P= .000
TL	.4859	.6391	.2458	.2568	-.0992	.7935
	(58)	(58)	(58)	(58)	(58)	(32)
	P= .000	P= .000	P= .063	P= .052	P= .459	P= .000

(Coefficient / (Cases) / 2-tailed Significance)

" . " is printed if a coefficient cannot be computed

- - Correlation Coefficients - -

	P_PNS	PHW_PSP	PNS_BA	RAM_MCF	T_INMX	TAREA
@ARN_PM	-.1540	.1692	.3965	-.5041	-.0961	.0182
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .249	P= .204	P= .002	P= .000	P= .473	P= .892
@BASN	-.0116	-.0105	.2411	-.0502	.1770	.1214
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .931	P= .938	P= .068	P= .708	P= .184	P= .364
@C2C4TGS	.1314	.0330	-.2635	.3510	.3159	.2697
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .325	P= .806	P= .046	P= .007	P= .016	P= .041
@C2TGSN	.2740	.1642	-.1254	.3729	.1095	.2368
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .037	P= .218	P= .348	P= .004	P= .413	P= .073
@SNA	-.0837	.0335	.2660	-.4126	-.2609	-.1347
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .532	P= .803	P= .044	P= .001	P= .048	P= .313
@SNB	-.0163	-.0346	.3439	-.3977	-.1641	.0071
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .903	P= .796	P= .008	P= .002	P= .218	P= .958
A_PNS	-.1016	-.0344	.1266	-.2246	.0294	.2396
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .448	P= .798	P= .344	P= .090	P= .826	P= .070
ARA_ARB	.1761	-.0306	.0193	.1659	.0675	.1047
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .186	P= .820	P= .886	P= .213	P= .615	P= .434

BA_C4_VE	.3484	.0734	-.0185	.0476	-.2091	.2109
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .007	P= .584	P= .891	P= .723	P= .115	P= .112
BMI1	.0629	-.0609	.0311	-.0902	.4273	.3349
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .639	P= .650	P= .816	P= .501	P= .001	P= .010
CI_FI	-.1963	-.2133	-.2359	.1181	.1824	-.3643
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .140	P= .108	P= .075	P= .377	P= .171	P= .005

(Coefficient / (Cases) / 2-tailed Significance)

" . " is printed if a coefficient cannot be computed

- - Correlation Coefficients - -

	P_PNS	PHW_PSP	PNS_BA	RAM_MCF	T_INMX	TAREA
FH_HOR	.2465	-.0932	-.0446	.1860	.2109	.2317
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .062	P= .486	P= .740	P= .162	P= .112	P= .080
H_MP	.2540	-.1495	-.0450	.3877	.7033	.4276
	(58)	(58).	(58)	(58)	(58)	(58)
	P= .054	P= .263	P= .737	P= .003	P= .000	P= .001
H_VER	.5001	-.1274	.1356	.3006	.2649	.5853
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .000	P= .341	P= .310	P= .022	P= .044	P= .000
HEAD_POS	.0020	.0423	.0405	.1019	.3120	.1090
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .988	P= .752	P= .763	P= .447	P= .017	P= .415
INMXLTH	.2029	.2403	.4402	-.3018	-.4661	.2806
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .127	P= .069	P= .001	P= .021	P= .000	P= .033
MCF	-.1193	.0548	.4874	-.5833	-.0301	.0289
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .372	P= .683	P= .000	P= .000	P= .822	P= .829
NECK_CM_	.6683*	-.2454	.4390	.0250	.3211	.7287
	(32)	(32)	(32)	(32)	(32)	(32)
	P= .000	P= .176	P= .012	P= .892	P= .073	P= .000
P_PNS	1.0000	-.2825	.3040	.1379	.0928	.5398
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .	P= .032	P= .020	P= .302	P= .488	P= .000
PHW_PSP	-.2825	1.0000	.0950	-.1714	-.3314	-.2039
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .032	P= .	P= .478	P= .198	P= .011	P= .125
PNS_BA	.3040	.0950	1.0000	-.2116	-.1402	.2646
	(58)	(58)	(58)	(58)	(58)	(58)

	P= .020	P= .478	P= .	P= .111	P= .294	P= .045
RAM_MCF	.1379	-.1714	-.2116	1.00.	.3449	.1012
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .302	P= .198	P= .111	P= .	P= .008	P= .450

(Coefficient / (Cases) / 2-tailed Significance)

" . " is printed if a coefficient cannot be computed

- - Correlation Coefficients - -

	P_PNS	PHW_PSP	PNS_BA	RAM_MCF	T_INMX	TAREA
T_INMX	.0928	-.3314	-.1402	.3449	1.0000	.4407
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .488	P= .011	P= .294	P= .008	P= .	P= .001
TAREA	.5398	-.2039	.2646	.1012	.4407	1.0000
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .000	P= .125	P= .045	P= .450	P= .001	P= .
TL	.5196	-.0349	.2097	.2035	.1615	.6906
	(58)	(58)	(58)	(58)	(58)	(58)
	P= .000	P= .795	P= .114	P= .125	P= .226	P= .000

(Coefficient / (Cases) / 2-tailed Significance)

" . " is printed if a coefficient cannot be computed

- - Correlation Coefficients - -

	TL
@ARN_PM	-.0960
	(58)
	P= .474
@BASN	-.0220
	(58)
	P= .870
@C2C4TGS	.5861-
	(58)
	P= .000
@C2TGSB	.5524-
	(58)
	P= .000
@SNA	-.0479
	(58)
	P= .721
@SNB	-.1322
	(58)
	P= .322

Appendix B

Human Investigation Consent Form

Human Investigation Consent Form

Consent to Participate in Research Study

I have been asked to participate in a research study entitled: Cephalometric Assessment in Obstructive Sleep Apnea

by:		
	Nonglak Pracharktam, D.D.S.	Principal Invesitgator
	Mark G. Hans, D.D.S. M.S.D.	Coinvestigator
	Kingman P. Strohl, M.D.	Coinvestigator
	Suchitra Nelson, M.S., Ph.D.	Coinvestigator

I understand that this study involves:

A) Lateral and frontal cephalometric radiographs while sitting.
B) Polysomnographic testing (Sleep monitoring) for diagnosis of Obstructive Sleep Apnea Syndrome.

I further understand that:

1. The cephalometric radiographs will be taken using the effective minimum X-ray dosage, and a lead apron will be used to further reduce radiation exposure. A spoon of radiographic contrast media (Esophotrast, Rorer Pharmaceutical Corp.) will be required to be swallowed prior the radiograph taken.

2. Polysomnographic testing (Sleep Monitoring) will be used to accurately diagnose Obstructive Sleep Apnea Syndrome (OSAS).

3. I will not be required to pay any cost for the cephalograph. All radiographs will be taken in the Bolton-Brush Growth Study Center, School of Dentistry, Case Western Reserve University, Cleveland.

4. The information from the study is confidential and will be contained in a data base for future study.

5. Dr. Hans, Dr. Nelson, Dr. Pracharktam and Dr. Strohl will be coordinating this study and will be available to answer any questions about the study. The telephone numbers in the department of orthodontics are (216) 368-3469, 368-4649. Dr. Strohl's office phone number is (216) 844-8675.

6. I have the right to refuse to participate in this study. In this case, my refusal will not affect the medical or dental care I can receive at the dental school of Case Western Reserve University, University Hospitals or the V. A. Hospital.

I have read the above information and understand the risks and benefits involved in participation in this study.

_____ _____

Date Subject/Patient

Appendix C

Approval of the University Review Committee for Human Studies

To: Dr. Mark Hans/Dr. N. Pracharktam Dept/School: Orthodontics/Denistry

Subject: Notice of [X] Review and approval
[ ] Exemption

The Committee has reviewed your proposal entitled: Craniofacial Evaluation and Effect of a Modified Functional Appliance in Obstructive Sleep Apnea Syndrome: A Pilot Study

Please be advised that with respect to: (1) the rights and welfare of the individual(s) involved, (2) the appropriateness of the methods to be used to secure informed consent, and (3) the risks and potential benefits of the investigation, the Committee considers your project:

[ ] Exempt
[X] Fully acceptable
[ ] Acceptable with reservations noted
[ ] Not acceptable for reasons noted

Followup: The Committee wishes to have a status report on this project on October 2, 1992 (date).

SIGNED FOR THE COMMITTEE BY:

Sonia A. Alemagno
(Signature)
Sonia A. Alemagno, Ph.D.
Assistant Director
(Title)

October 3, 1991
(Date)

Remarks:

*ORA USE ONLY***

Type Project: [ ] New [ ] Renewal Human Risk: [ ] Yes [ ] No

Source of Support: [ ] Outside Funding [ ] Department or Other

Agency (Potential): Agency No.

Are any of the following involved: [ ] Yes [ ] No
If yes, which category(ies):

[ ] Minors [ ] Fetuses [ ] Abortuses [ ] Pregnant Women
[ ] Prisoners [ ] Mentally Retarded [ ] Mentally Disabled
****

cc: Faculty Advisor
Dean
Department Chairman (or Investigator)

Title change only. New title is: CEPHALOMETRIC ASSESSMENT IN OBSTRUCTIVE SLEEP APNEA

GLOSSARY

Definitions of Anatomic Landmarks

Point/Line	Definition
A	Subspinale : Point in the median sagittal plane where the lower front edge of the anterior nasal spine meets the front wall of the maxillary alveolar process (Downs Point A).
ANS	Anterior nasal spine: Sharp Median Process formed by the forward prolongation of the two maxillae at the lower margin of the anterior aperture of the nose.
Ar	Articulare (Bjork) : Intersection of the lateral radiographic image of the posterior border of the ramus with the base of the occipital bone.
ARa	Anterior Ramus plane, a line from the intersection of the functional occlusal plane (FOP) and the anterior border of the ramus drawn parallel to PRa up to the reference line.
B	Supramentale : Deepest midline point on the mandible between infradentale and pogonion (Downs point B).
Ba	Basion point : The most postero-inferior point on the clivus.
C2	The most posterior-inferior point on the corpus of the second cervical vertebrae.
C2tg	The tangent point of which a line from C2 passes through the odontoid process.

GLOSSARY (Continued)

Definitions of Anatomic Landmarks

Point/Line	Definition
C4	The most posterior-inferior point on the corpus of the fourth cervical vertebrae.
Eb	Base of Epiglottis : The deepest point of the epiglottis.
Et	Tip of the Epiglottis : The most superior point of the epiglottis.
FOP	Functional Occlusal plane : A line from the most posterior occlusal contact point to the last fully erupted maxillary and mandibular molars to the most anterior maxillary-mandibular first premolar occlusal contact.
Go	Gonion : External angle of mandible, located on the lateral radiograph by bisecting the angle formed by tangents to posterior border of ramus and the mandibular plane.
H	Hyoidale : The most superior-anterior point on the body of hyoid bone.
H'	Hyoidale Projection : The projection from H to mandibular plane.
MCF	Middle Cranial Fossa : Represented by a line from Bjork's articulare (Ar)to SE.

GLOSSARY (Continued)

Definitions of Anatomic Landmarks

Point/Line	Definition
Me	Menton : The most inferior point on the symphysis of the mandible in the median plane. Seen in the lateral radiograph as the most inferior point on the symphysial outline when the head is oriented in Frankfort relation.
N	Nasion : Craniometric point where the mid sagittal plane intersects the most anterior point of the naso-frontal suture.
O	Orbitale : The lowest point on the inferior margin of the orbit.
P	Tip of the soft palate.
Phw	Posterior Pharyngeal wall at the level of posterior superior airway space.
PNS	Posterior nasal spine : Process formed by the united projecting medial ends of the posterior borders of the two palatine bones.
PM	Vertical PM : A line from SE through the averaged inferior-most points of the left and right pterygomaxillary fissure.
Po	Anatomic Porion : Point on the upper margin of the porus acusticus externus.

GLOSSARY (Continued)

Definitions of Anatomic Landmarks

Point/Line	Definition
Psp	The most superior-posterior point of the soft palate.
PRa	Posterior Ramus : A line from Ar to the intersection of the posterior border of the ramus with FOP.
REF	Reference line : A line parallel to FOP from Ar anteriorly.
Rgn	Retrognathion : The most inferior-posterior point of the symphysis.
S	Sella Turcica : The center of the hypophyseal fossa, lodging the pituitary body.
SE	Sphenoethmoidal junction : The point at which the floor of the anterior cranial fossa intersects the averaged image left and right of the great wings of the sphenoid bone.
Tb	The dorsum of the tongue on a line joining the gonion (Go) and the supramentale(B).
Tt	Tongue tip: The most anterior point of the tongue which touches the lingual surface of the mandibular incisor.

GLOSSARY (Continued)

Lateral Cephalometric Measurements

Variables	Interpretation
Cranial Base :	
< BaSN	Cranial Base Angulation in mid sagittal plane.
MCF.	Middle cranial fossa and posterior maxillary relative alignment (MCF./PM). A neutral MCF/PM is an internal angle of 40.3 degree. When a subject's PM is forward the neutral PM, a clockwise(+) results. This forward (+) alignment of the MCF results in a mandibular retrusive effect (fig.4). When a subject's PM is behind the neutral PM, a counter- clockwise(-) results. The backward (-) alignment of the MCF results in a mandibular protrusive effect. If the neutral MCF plane coincides with the individual's own MCF, a neutral effect(0) is present.
Maxilla :	
<SNA	Anteroposterior position of the maxilla relative to the anterior cranial base.
<ArN-PM	Posterior wall of the maxilla relative to the a constructed cranial base (Ar-N).
A-PNS	Effective antero-posterior dimension of the maxilla when project to a line which is perpendicular to PM and passes point SE.
PNS-Ba	Horizontal position of PNS to Basion.

GLOSSARY (Continued)

Lateral Cephalometric Measurements

Variables	Interpretation
Mandible :	
<SNB cranial	Anteroposterior position of the mandible relative to the anterior base.
Ram/MCF	Ramus width relative to middle cranial fossa horizontal dimension. The measurement of ramus width is made at the level of REF by comparing to the horizontal dimension of the MCF. along this line. The distance from Ar to ARa and Ar to neutral PM are measured along the reference line. A (+) effect occurs when the ramus width is less than Ar to PM neutral, and (-) effect when greater (fig 5).When the measurements are the same, a neutral (0) effect results.
ArA-ArB	Relative comparison of cumulative maxillary length from Ar to A point with cumulative mandibular point from Ar to B point. The measurements are made along the Reference line.
Head Position:	
FH-Hor	Head position interpreted by an angle formed by the Frankfort Horizontal plane and the True Horizontal (recorded from a fluid level device).
Soft Tissues:	
Soft palate and Oropharynx	
P-PNS	Soft Palate Length.
Phw-Psp	Superior Posterior Airway Space (Distance measured along a line parallel to B-Go).

GLOSSARY (Continued)

Lateral Cephalometric Measurements

Variables	Interpretation
Tongue	
TI	Tongue length: Length of the tongue measured from Tt-Eb.
T area	Area of the tongue (Outline from Tt along retrognathion surface to menton, Eb and dorsum of the tongue).
Hyoid Bone:	
H-H'	Vertical position of the Hyoid relative to the mandibular plane.
H-Ver	Vertical position of the Hyoid relative to a line which is perpendicular to PM and passes point SE.
Neck:	
<C2C4-SN	A craniocervical angle formed by a line from C2 to C4 and S-N plane.
<C2-SN	A craniocervical angle formed by a line from C2 to C2tg and S-N plane.
Intermaxillary dimension:	
AntrMxHt.	Anterior intermaxillary space height: The length of a perpendicular from the maxillary plane to menton.

GLOSSARY (Continued)

Lateral Cephalometric Measurements

Variables	Interpretation
PostMx Ht.	Posterior intermaxillary space height: The length of a perpendicular from the maxillary plane to the mandibular plane which passes through the point where the FOP intersects the Phw.
In Mx Lth.	Length of the Intermaxillary space: Linear distance measured along the FOP from the point where it intersects the Tt anteriorly, to where it intersects the Phw posteriorly.
In Mx Area	Intermaxillary area: calculated by the average of anterior and posterior intermaxillary space height multiply by intermaxillary length.

Skeleton and soft tissue relationship:

T/In Mx area	Ratio between tongue area to Intermaxillary area in midsagittal plane.

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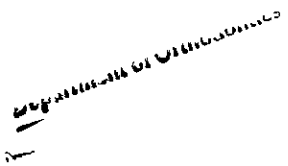
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