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Measurements of the Pharyngeal Airway Using Whole Head 3T MRI and CBCT

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LOMA LINDA UNIVERSITY
School of Dentistry
in conjunction with the
Faculty of Graduate Studies

Measurements of the Pharyngeal Airway Using Whole Head 3T MRI and CBCT

by

Victoria Geren

A Thesis submitted in partial satisfaction of
the requirements for the degree
Master of Science in Orthodontics and Dentofacial Orthopedics

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September 2019

Each person whose signature appears below certifies that this thesis in his/her opinion is adequate, in scope and quality, as a thesis for the degree Master of Science.

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ABBREVIATIONS

SDB	Sleep-Disordered Breathing
OSA	Obstructive Sleep Apnea
ADHD	Attention-Deficit/Hyperactivity Disorder
CBCT	Cone Beam Computed Tomography
MRI	Magnetic Resonance Imaging
PPW	Posterior Pharyngeal Wall
APW	Anterior Pharyngeal Wall
3D	Three-dimensional
CBCT	Cone Beam Computed Tomography
MR	Magnetic Resonance
TMJ	Temporomandibular Joint
3T	3-Tesla
2D	Two-dimensional
CT	Computed Tomography
ALARA	As Low As Reasonably Achievable
IRB	Institutional Review Board
LLUSD	Loma Linda University School of Dentistry
FOV	Field of View
DICOM	Digital Imaging and Communications in Medicine

PNS	Posterior Nasal Spine
ICC	Intraclass Correlation Coefficient

ABSTRACT OF THE THESIS

Measurements of the Pharyngeal Airway Using Whole Head 3T MRI and CBCT

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Victoria Geren

Master of Science, Graduate Program in Orthodontics and Dentofacial Orthopedics
Loma Linda University, September 2019
Dr. V. Leroy Leggitt, Chairperson

Objective: This study compared pharyngeal airway measurements (volume, linear, area) made using whole head Cone-Beam Computed Tomography (CBCT) and 3T Magnetic Resonance Imaging (MRI) methods.

Methods: Eleven subjects (mean age 15y11m) received whole head CBCT (NewTom5G, AFP Imaging, USA) and 3T MRI (Siemens Medical Solutions, DE). Each subject received both scans within a one-month period of time. CBCT images were made with an 18x16 inch field of view, exposure time of 5.4s, and resolution of 0.3x0.3x0.3mm. 3T MR images were captured as contiguous sagittal images of the whole head with a T1-weighted 3D imaging sequence (Magnetization Prepared Rapid Acquisition by Gradient Echo (MP-RAGE), TP/TE = 1950/2.26ms) and resolution of 1.0x1.0x1.0mm. Simpleware Scan IP (v.M-2018.03) imaging software was used to process the images in the following order: 1) registration 2) airway segmentation, 3) volume measurement, 4) linear measurement, and 5) cross-section area measurement. Agreement between CBCT and MRI measurements was evaluated with an Intraclass Correlation Coefficient (ICC). Intra-rater reliability (after a 1-week washout period) was also evaluated with an ICC. A

Bland-Altman test was used to determine whether systematic or proportional bias was present.

Results: Excellent agreement between CBCT and MRI measurements of the pharyngeal airway was observed. Mean ICC was 0.982 (CI 0.975 - 0.986). Reliability was demonstrated with an ICC of 0.999 (CI 0.998 - 0.999) for MRI and an ICC of 0.998 (CI 0.997 - 0.999) for CBCT measurements. The degree of bias ranged from -0.16-0.96mm. No statistically significant systematic ($p>0.05$) or proportional ($p>0.05$) bias was observed.

Conclusion: MRI and CBCT give similar linear, cross-section area, and volumetric measurements of the pharyngeal airway. These results indicate that further studies are warranted to characterize the interchangeability of CBCT and MRI for the purpose of airway analysis.

CHAPTER ONE

REVIEW OF THE LITERATURE

The morphology of the pharyngeal airway influences craniofacial and occlusal development.[1-6] Pharyngeal restriction during growth and development may affect occlusion, speech and craniofacial morphology.[1-3] A number of orthodontic treatment modalities, such as headgear,[7-9] functional appliances[10] and orthognathic surgery[11] may affect the morphology of upper airway. Orthodontists are in a primary position to screen patients for clinical and radiographic signs of upper airway obstruction and refer to otolaryngologist as needed.[12] Airway analysis may facilitate early diagnosis and treatment of abnormal pharyngeal anatomy, which may lead to improved craniofacial development.[1-6] Quantitative analysis may improve evaluation of orthodontic, orthopedic and surgical treatment of the size and shape of pharyngeal air space.[7-9,13]

Anatomy

The upper airway consists of the pharynx and nasal cavity. The pharynx is a 12-14 cm long, semicircular in cross section, muscular tube lined by mucous membrane. It is located directly anterior to the vertebral column. It starts from the cranial base and ends at the level of the sixth cervical vertebra and the lower border of the cricoid cartilage.[1]

The pharynx is divided into three parts: 1) nasopharynx, 2) oropharynx, and 3) laryngopharynx.

The nasopharynx is located posterior to the nasal cavity and above the level of the soft palate.[14] The nasopharynx is involved in breathing and speech.[14] A mass of lymphoid tissue, the pharyngeal tonsil is embedded in the mucous membrane of the posterior wall of the nasopharynx.[14] Enlarged pharyngeal tonsils are called “adenoids” and depending on the intensity of the enlargement may be a cause of respiratory obstruction.[15] Both nasopharynx and oropharynx contain lymphoid tissue which has an annular arrangement and is called Waldeyer’s tonsillar ring.[15]

The oropharynx is situated posterior to the oral cavity. It extends from the level of the soft palate to the level of the hyoid.[14] The laryngopharynx is positioned posterior to the larynx. It reaches from the hyoid bone to the lower border of the cricoid cartilage. The oropharynx and laryngopharynx are involved in breathing and swallowing.[14,15]

Potential Effect on Craniofacial Development

Pharyngeal airway morphology is clinically relevant because it may influence craniofacial growth and occlusal development.[1-5] McNamara reported a link between obstruction of upper airway and a steep mandibular plane.[1] Mouth breathing may be a result of pharyngeal airway constriction. Paul and Nanda reported that mouth breathing causes the collapse of the maxillary arch, increase in overbite and overjet, influences development of class II division 1 occlusion.[3] In a more recent study, Kyung-Min Oh et al., demonstrated that patients with a class II malocclusions have smaller and more posteriorly positioned upper airways compared to skeletal class I and III patients.[4] Other studies suggest that patients with partially obstructed nasal breathing exhibit posterior crossbite, anterior open bite, increase in anterior face height, and a lower tongue posture.[2,4,6]

Pharyngeal Airway Morphology and SDB

Upper airway morphology is also clinically relevant due to its reported relationship to sleep-disordered breathing (SDB).[16,17] Obstructive sleep apnea (OSA), obstructive hypopnea, upper airway resistance syndrome, and snoring represent a continuum of sleep-related breathing disorders.[16] SDB is an umbrella term for several chronic conditions in which partial or complete cessation of breathing occurs many times throughout the night, resulting in daytime sleepiness or fatigue that interferes with a person's ability to function and reduces quality of life.[16] OSA is by far the most common form of sleep-disordered breathing, is associated with many other adverse health consequences, such as hypertension, cardiovascular diseases, and stroke in adults.[18,19] OSA is also estimated to affect 1-4% of children in the United States.[20] In children, the disorder commonly correlates with lymphoid hyperplasia during childhood.[21] Other important factors effecting pharyngeal airway morphology and promoting OSA in children and adults include obesity, craniofacial anomalies and neuromuscular disorders that could affect the size, shape, and collapsibility of the upper airway during sleep.[22,23] Studies suggest that untreated SDB in children is associated with attention-deficit/hyperactivity disorder and low academic performance.[12,20,24]

Possible Effects of Treatment

A number of studies have shown that several of orthopedic, orthodontic and surgical treatment modalities, including headgear,[7-9] orthodontic extractions,[25] class II functional appliances,[10] bilateral sagittal split osteotomy[11] and distraction osteogenesis[11], may influence the shape of pharyngeal airway space. However, randomized controlled studies are needed to be able to draw evidence-based conclusions.[13]

Pharyngeal Airway Imaging Modalities

Several diagnostic imaging techniques have been used for evaluation of upper airway morphology, such as cephalometric radiography, acoustic reflection, fluoroscopy, MRI, computed tomography, CBCT, and nasopharyngoscopy.[13] Cephalometric radiography is widely available and is the most common imaging method used for airway evaluation. Despite its widespread use, cephalometric radiography cannot evaluate the three-dimensional shape of the airway.[26] Currently, several 3D imaging modalities are frequently used in orthodontics: 1) CBCT, 2) MRI, and 3) CT

CBCT

CBCT is the most popular form of 3D imaging technology in orthodontics.[27] It has been used to evaluate skeletal structures of the orofacial region, teeth, TMJ and the anatomy of the upper airway.[28,29,30] Because of its increased popularity over the last twenty years, the number of studies evaluating CBCT has increased.[31] The benefits of CBCT include: 1) dimensionally accurate imaging, 2) lower radiation compared to multidetector computed tomography, 3) fast image acquisition, 4) greater availability, and 5) lower cost compared to MRI.[32,33] Despite all these benefits, CBCT has one significant disadvantage: it exposes patients to ionizing radiation.[33] The exact dose of the radiation that the patients are exposed to during CBCT image acquisition varies and depends on the manufacturer and the setting used.[34] The diagnostic value of radiographs and CBCT images cannot be underestimated, however, the use of ionizing radiation should be based on the “As Low As Reasonably Achievable” principle.[33] Several studies assessed the amount of an effective radiation dose delivered to patients during CBCT scans and the cumulative range was 58.9 to 1073 microsieverts.[33] The effects of ionizing radiation are stochastic and cumulative in nature, leading to the fact that there is no such concept as “safe radiation”.[35] In 2013, a joint statement was released by The American Association of Orthodontists and the American Association of Oral and Maxillofacial Radiology. It highlighted the fact that CBCT examination is only a supplemental diagnostic modality and should not be conducted prior to a thorough clinical examination.[36]

Several studies have evaluated the accuracy of the pharyngeal airway analysis using CBCT as a diagnostic modality.[29,37,38,39] de Water et al., measured upper airway volume using Dolphin 3D and compared it to a manual segmentation method. They concluded that the airway analysis tool in Dolphin 3D is not accurate enough and further software improvement was recommended .[38] Alves et al., evaluated the airway volume analysis tool in Dolphin 3D software. They concluded that Dolphin 3D gives bettr control because it allows the user to increase or decrease the threshold value, however, it can be misleading. They determined that the threshold value of 73 used in Dolphin 3D software was the most accurate to measure airway volume.[39]

A study performed by Mattos et al., showed that a CBCT evaluation of the airway can accurately be made by a resident, orthodontist, or an oral radiologist. Using Dolphin software, they found that the most reliable measurements were: 1) anteroposterior linear measurements, 2) cross- sectional areas at the levels of the palatal plane, soft palate and tongue, 3) sagittal area and 4) volume.[37]

Aboudara et al., compared imaging information about nasopharyngeal airway size between a lateral cephalometric head film and a 3D CBCT scan in adolescent subjects. They concluded that CBCT scan is a simple and effective method to accurately analyze the airway.[29]

MRI

An alternative 3D imaging modality that does not expose patients to harmful ionizing radiation is MRI.[40] It has been increasingly used for detection of soft tissue pathology, the examination and assessment of the articular disk, masticatory muscles conditions, and faces of patients with jaw deformity.[40] Compared with conventional radiographic imaging techniques, MRI is accurate and reproducible. It provides multiplanar imaging with no known side effects. [21,41,42] MRI has superior soft-tissue contrast compared to that of CBCT and several studies have reported the advantages of utilizing MR images for delineation of soft-tissue.[43,44]

Despite all the benefits, MRI technology also has several drawbacks such as : 1) lower access and availability, 2) higher cost, 3) greater time for image acquisition, 4) incompatibility with metal restorations and implants in the head and neck area, and 5) lack of image resolution of hard tissues.[24,45]

Welch et al., utilized novel three-dimensional volumetric analysis techniques with MRI to study the upper airway and surrounding soft-tissue structures. The results indicated that volumetric MRI is a powerful tool to study anatomic changes in the upper airway and surrounding soft-tissue structures and is sensitive enough to detect changes.[47]

MRI and CBCT are two most commonly used 3D imaging modalities that provide the highest level of diagnostic information in the field of orthodontics. CBCT should not be used on all orthodontic patients due to the risks associated with ionizing radiation. In contrast, MRI provides the benefits of 3D visualization of head and neck structures without the risk of radiation and might become the method of choice for 3D imaging in some patients.

CHAPTER TWO

MEASUREMENTS OF THE PHARYNGEAL AIRWAY USING WHOLE HEAD 3T MRI AND CBCT

Abstract

Objectives: This study compared pharyngeal airway measurements (volume, linear, area) made using whole head Cone-Beam Computed Tomography (CBCT) and 3T Magnetic Resonance Imaging (MRI) methods.

Methods: Eleven subjects (mean age 15y11m) received whole head CBCT (NewTom5G, AFP Imaging, USA) and 3T MRI (Siemens Medical Solutions, DE). Each subject received both scans within a one-month period of time. CBCT images were made with an 18x16-inch field of view, an exposure time of 5.4s, and a resolution of 0.3x0.3x0.3mm. 3T MR images were captured as contiguous sagittal images of the whole head with a T1-weighted 3D imaging sequence (Magnetization Prepared Rapid Acquisition by Gradient Echo (MP-RAGE), TP/TE = 1950/2.26ms) and a resolution of 1.0x1.0x1.0mm. Simpleware Scan IP (v.M-2018.03) imaging software was used to process the images in the following order: 1) registration 2) airway segmentation, 3) volume measurement, 4) linear measurement, and 5) cross-section area measurement. Agreement between CBCT and MRI measurements was evaluated with an Intraclass Correlation Coefficient (ICC). Intra-rater reliability (after a 1-week washout period) was also evaluated with an ICC. A Bland-Altman test was used to determine whether systematic or proportional bias was present.

Results: Excellent agreement between CBCT and MRI measurements of the pharyngeal airway was observed. Mean ICC was 0.982 (CI 0.975 - 0.986). Reliability was demonstrated with an ICC of 0.999 (CI 0.998 - 0.999) for MRI and an ICC of 0.998 (CI 0.997 - 0.999) for CBCT measurements. The degree of bias ranged from -0.16-0.96mm. No statistically significant systematic ($p>0.05$) or proportional ($p>0.05$) bias was observed.

Conclusion: MRI and CBCT give similar linear, cross-section area, and volumetric measurements of the pharyngeal airway. These results indicate that further studies are warranted to characterize the interchangeability of CBCT and MRI for the purpose of airway analysis.

Introduction

Orthodontic and orthognathic surgical treatment have been associated with changes in the morphology of the upper airway.[7-11] Decreases in pharyngeal airway patency have been associated with negative effects on speech, occlusion, craniofacial development and breathing (SDB).[1,2,3,5] Early detection of airway problems may lead to improved management of pharyngeal airway morphology and allow for normal craniofacial development.[5] Orthodontists who use 3D imaging methods for orthodontic treatment planning are in an ideal position to evaluate and influence the morphology of the pharyngeal airway.[7-11]

Cephalometric radiography, acoustic reflection, fluoroscopy, MRI, computed tomography, CBCT, and nasopharyngoscopy are diagnostic imaging techniques used for the evaluation of upper airway morphology.[13] Cephalometric radiography is the most common imaging method used due to its availability and low cost. However, the quality of the image is affected by tissue overlapping, image magnification and distortion.[26] Additional distortion is introduced by converting a 3D object into a 2D image.[26] Because of these limitations, the popularity of 3D imaging modalities in orthodontics has increased.[27,32]

The popularity of CBCT has significantly increased over the last twenty years. It has been used to evaluate the skeletal structures of the orofacial region, teeth, TMJ and the anatomy of the upper airway.[27-30] Several studies have evaluated the accuracy and reliability of CBCT.[31,33,34,48,49]

Compared to other imaging modalities, CBCT has several benefits: 1) a dimensionally accurate image, 2) lower radiation compared to multidetector computed tomography, 3) fast image acquisition, 4) higher availability, and 5) lower cost compared to MRI.[32,33] CBCT, however, has one significant disadvantage: it exposes patients to ionizing radiation.[35]

There is no such concept as "safe radiation" because the effects of ionizing radiation are stochastic and cumulative in nature.[35,46] In 2013, The American Association of Orthodontists and the American Association of Oral and Maxillofacial Radiology released a joint statement highlighting the fact that CBCT examination is only a supplemental diagnostic modality and should not be conducted prior to a thorough clinical examination.[36,46]

An alternative 3D imaging modality that does not expose patients to harmful ionizing radiation is MRI.[40] There are several benefits to this technique. It provides multiplanar imaging with no known side effects.[40] Several studies have reported the advantages of using MR images for the delineation of soft-tissue.[41-45]

MRI technology has several drawbacks including less equipment access and availability, higher cost, longer image acquisition time, incompatibility with metal restorations and implants in the head and neck area, and lack of image resolution of hard tissues.[24,50, 51,52]

Both MRI and CBCT provide the most accurate diagnostic information in the field of orthodontics. Due to the risks associated with ionizing radiation, CBCT should not be used on all orthodontic patients. This is particularly relevant to the majority of orthodontic patients who are growing children and adolescents who exhibit increased sensitivity to ionizing radiation. In contrast, MRI provides the benefits of 3D visualization of head and neck structures without the risk of radiation and might become the method of choice for 3D imaging in orthodontics.

The purpose of this research was to compare the accuracy of pharyngeal airway measurements made on CBCT and MRI. This study tested the hypothesis that there are no statistically significant differences between volumetric, cross-sectional and linear measurements of the pharyngeal airways made on CBCT and MRI images. The potential significance of this study was to possibly be able to say that MRI and CBCT techniques give equal assessments of the pharyngeal airway space.

Materials and Methods

Patient Selection

Approval for this study was granted by the Institutional Review Board (IRB) of Loma Linda University. This was a retrospective study of the MRI and CBCT records of 11 subjects. Patients were excluded from the study based on several criteria: 1) metal dental restorations, 2) dental implants, 3) stainless steel fixed orthodontic appliances, 4) metal fixed orthodontic retainers, 5) pacemakers, 6) cochlear implants, 7) metal foreign bodies in the eyes, 8) aneurysm clips, 9) prosthetic metal implants, 10) pregnancy. Patients' age ranged from 12 years and 1 month to 31 years and 5 months, with the average age being 15 years and 11 months. Six subjects were male and five were female.

Image Acquisition

MRI and CBCT scans were preformed within two weeks of each other. One CBCT scan (NewTom5G, AFP Imaging, USA) and one 3T MR scan (Siemens Medical Solutions, DE) were performed on each subject. CBCT images were captured with an

18x16-inch field of view (FOV), an exposure time of 5.4 seconds and image resolution of 0.3x0.3x0.3 mm. Scans were taken with patients in a face-up supine position. Digital Imaging and Communications in Medicine (DICOM) formatted images were be created from axial slices 0.5 mm in thickness. MR scans were performed using 3T imaging system in a 12-channel head array coil (TIM/Trio, Siemens Medical Solutions, Erlangen Germany). Contiguous sagittal images of the whole head were created with a T1-weighted 3D imaging sequence (Magnetization Prepared Rapid Acquisition by Gradient Echo (MP-RAGE), TP/TE = 1950/2.26 ms) and isotropic resolution of 1.0x1.0x1.0 mm.

Captured images of the pharyngeal airway space were exported in Digital Imaging and Communications in Medicine (DICOM) format.

Data collection

Simpleware Scan IP (v. M-2018.03) imaging software (Synopsis, Mountain View, CA) was used for DICOM file registration, orientation, evaluation and measurement of the pharyngeal airway space.

To reduce measurement variability, CBCT and MRI images were registered (superimposed) in three planes using the following landmarks: 1) the root apex of the right maxillary central incisor, 2) the root apex of the left maxillary central incisor, 3) the root apex of the right maxillary canine, 4) the root apex of the left maxillary canine, and 5) the apex of the odontoid process of Axis. After the volume orientation was accomplished, CBCT and MRI images were segmented and measured separately.

Cephalometric landmarks were identified on each image (Table 1). These landmarks were used to identify the upper and lower limits of the airway space as well as for reference to the relevant planes for calculation of the cross-sectional area, length, and width at each plane (Table 2). Measurements were made on each patient's CBCT and MRI scan (Table 3). Figure 1 is a graphic representation of the landmarks and planes used in this study.[53]

Table 1. Cephalometric landmarks.

Cephalometric landmark	Abbreviation	Definition
Anterior nasal spine	ANS	The most anterior point of the anterior nasal spine
Posterior nasal spine	PNS	The most posterior point of the posterior nasal spine
Palate point	P	The most inferior point of the soft palate
Tip of epiglottis	Et	The most superior point of the epiglottis
Third cervical vertebra	V	The most anterior inferior point of the third cervical vertebrae

Table 2. Planes.

Planes	Definitions
Plane A	Plane extending from PNS to posterior pharyngeal wall, parallel to the palatal plane
Plane B	Plane extending between the anterior and posterior pharyngeal walls at the level of P point, parallel to the palatal plane
Plane C	Plane extending between the anterior and posterior pharyngeal wall at the level of Et point, parallel to the palatal plane
Plane D	Plane extending between the anterior and posterior pharyngeal wall at the level of V point, parallel to the palatal plane

Table 3. Measurements.

Measurements	Definition
Volume	The volume of the airway – the upper limit is defined at the level of plane A, the lower limit is defined at the level of plane D
Midsagittal Length A, B, C, D	The anterior posterior distance between the anterior and posterior pharyngeal walls in the midsagittal plane at the level of the respective planes (A, B, C, D)
Cross-Sectional Length A, B, C, D	The largest anteroposterior distance between the anterior and posterior pharyngeal walls parallel to the respective planes (A, B, C, D), parallel to the midsagittal plane
Cross-Sectional Width A, B, C, D	The greatest distance between the lateral pharyngeal walls along the respective planes (A, B, C, D) perpendicular to the midsagittal plane.
Cross-Sectional Area A, B, C, D	The cross-sectional area of the airway along the respective planes (A, B, C, D)

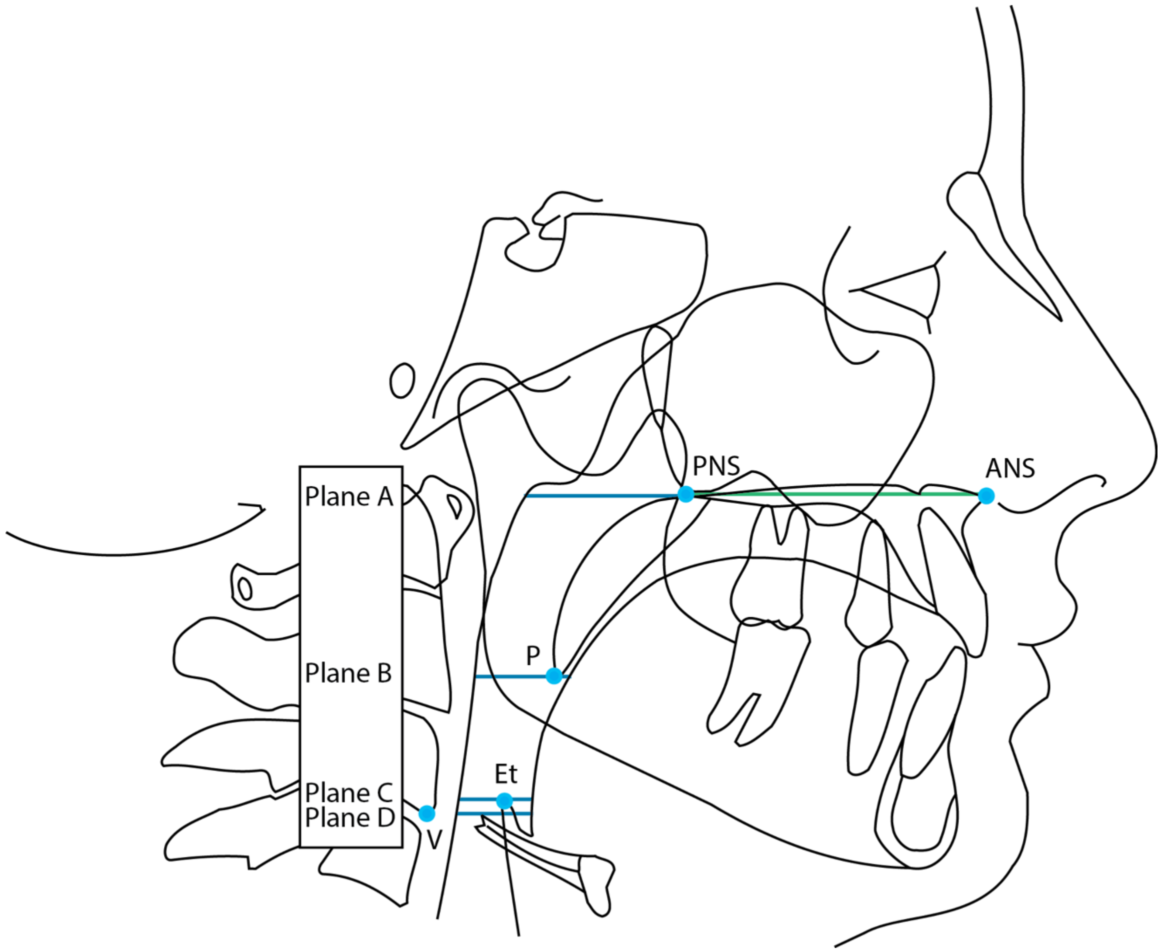

Figure 1. Pharyngeal airway measurement planes. Airway measurement planes A-D (blue) are parallel to the palatal plane, ANS-PNS (green). Plane A is at the level of PNS. Plane B is at the level of P point. Plane C is at the level of Et point. Plane D is at the level of V point.

The images were processed in the following order: 1) airway segmentation, 2) volume determination, 3) linear measurements, 4) cross sectional measurements.

Segmentation

A threshold tool was used to define the location of the segmentation. To maintain the consistency of the segmentation, a mask was created and used throughout the segmentation process. The pharyngeal airway was isolated using the “paint” tool. All structures that were not pharyngeal airway were removed using the “un-paint” tool, the “ungroup mask” tool and the “smoothing” tool. A 3D model of the pharyngeal airway was generated.

Volume Calculation

The volume of the pharyngeal airway was determined as follows. The upper limit was defined by plane A and the lower limit by plane D. The lateral limits were defined by the interior soft tissue wall of the pharynx. The volume was calculated using the “general statistics” tool.

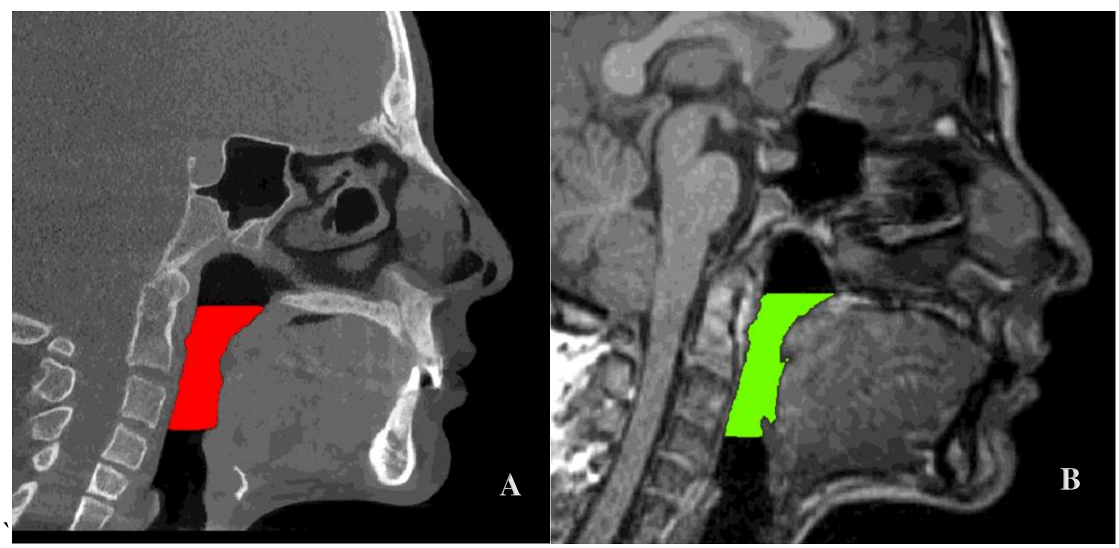

Figure 2. Segmented pharyngeal airway for volume analysis. A) CBCT and B) MRI. The superior limit is plane A, the inferior limit is plane D. Images are shown in two dimensions to illustrate the limits of the 3D volumes.

Midsagittal Linear Measurements

The image was displayed in a multiplanar view. The midsagittal cut was made through the ANS (anterior nasal spine). The linear measurements were performed in the midsagittal view along planes A, B, C, and D using the “measurements” tool.

Cross Sectional Measurements

For each plane, cross-sectional area, length and width were measured. The cross-sectional area of the airway at each plane was limited by the interior soft tissue of the pharynx and the airway space. The cross-sectional measurements were performed in the axial view of the image using the “magnetic lasso” tool and the “mask statistics” tool. A point was placed along the border of the radiolucent pharyngeal airway and the boundary was outlined in a continuous series of points until the first initial point was reached and the area calculated in mm^2 (Figure 3). The same steps were carried out for each of the plane areas A, B, C, and D. The length of the cross-section at each plane was defined as the longest anteroposterior distance along the plane parallel to the midsagittal plane. The width was defined as the largest distance between the lateral pharyngeal walls along the plane perpendicular to midsagittal plane (Figure 3).[56]

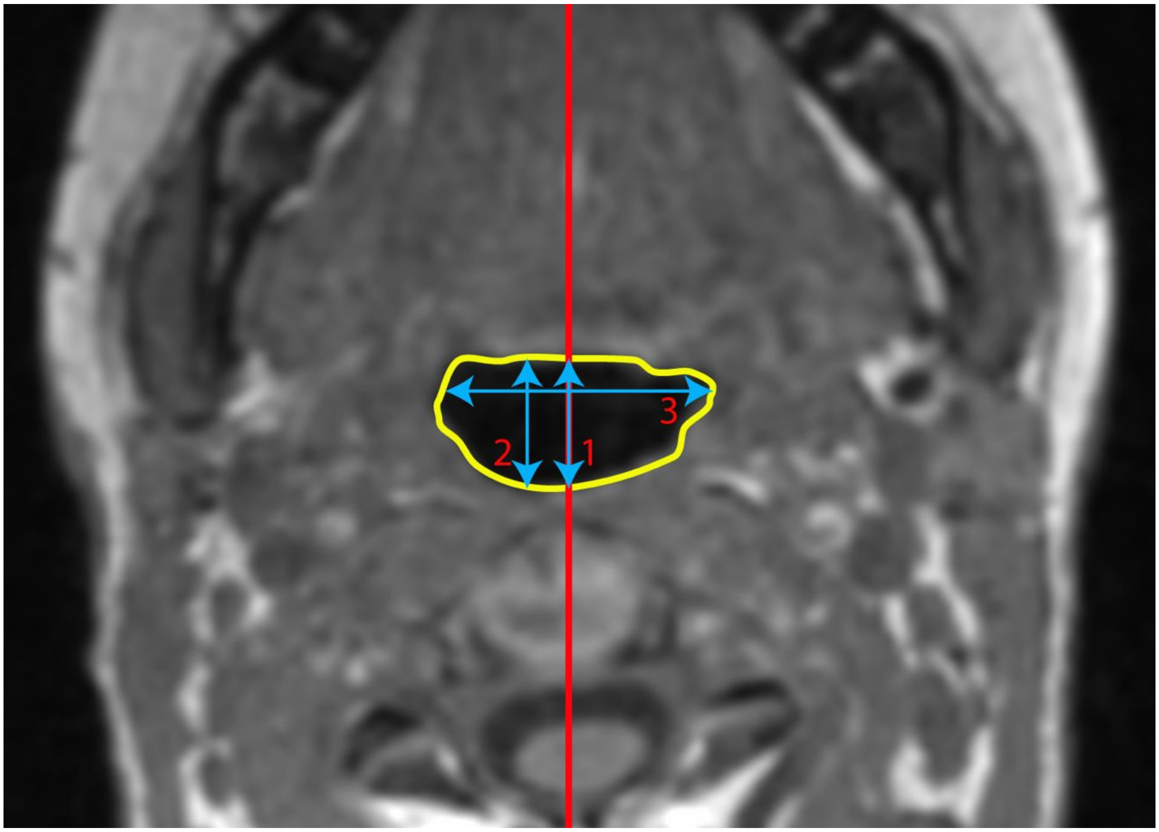

Figure 3. Axial view of a measurement plane. The red line is midsagittal plane. The yellow line is the outline of the airway space. 1= midsagittal linear measurement. 2 = cross-sectional length measurement. 3 = cross-sectional width measurement.

Statistical Analysis

SPSS™ (23.0) software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. In each group (CBCT and MRI), the means and standard deviations of the volumetric, area, and linear measurements were recorded and rounded to the nearest 0.1 mm. One examiner performed all measurements. To determine agreement between CBCT and MRI measurements, an interclass correlation coefficient statistic (ICC) was performed at an alpha level of 0.05. A 30% random sample of the study's measurements (four sets of airway measurements) were remeasured by the same operator two weeks after the initial measurements to determine intra-rater reliability.

Bland-Altman plots were created to determine whether the error in the delta was random or whether a systematic or proportional bias exists. One Sample Wilcoxon test and Kendall's tau correlation were conducted to test for presence of a systematic and proportional bias.

Results

Excellent agreement between CBCT and MRI volumetric, linear and cross-sectional measurements of the pharyngeal airway was observed using Intraclass Correlation Coefficient (ICC).

Overall agreement between the pharyngeal airway measurements made on CBCT and MRI was very high with an ICC of 0.982 (CI 0.975 to 0.986). All individual measurement types (volume, linear midsagittal, linear cross-sectional length and width, cross-sectional area) showed a very high agreement (Table 4).

Table 4. Stratified Intraclass Correlation Coefficient with 95% confidence level.

Category	ICC	Lower Bound	Upper Bound	p-Value ($\alpha = 0.05$)
All measurements	0.982	0.975	0.986	0.001
Volume	0.816	0.442	0.947	0.001
Linear Midsagittal	0.912	0.844	0.951	0.001
Cross-Sectional Length	0.929	0.873	0.960	0.001
Cross-Sectional Width	0.917	0.854	0.954	0.001
Cross-Sectional Area	0.887	0.803	0.937	0.001

The CBCT-MRI mean differences were calculated for each measurement type (Table 5). No statistically significant differences were observed. The positive mean difference indicated higher values for CBCT measurements on average. The negative mean difference was indicative of higher MRI values.

Table 5. Mean difference (mm) of MRI-CBCT airway measurements with 95% confidence level.

Category	Mean Difference (mm)	SD (mm)
Volume	965	1813.99
Linear Midsagittal	-0.16	1.92
Cross-Sectional Length	0.42	2.21
Cross-Sectional Width	0.34	2.58
Cross-Sectional Area	10.54	102.08

Bland-Altman plots were used to detect bias and confirm the degree of agreement between the CBCT and MRI measurements (Figure 4-8). The mean difference (solid red line) is the estimated bias. Standard deviation lines (dashed blue) demonstrate what should be a random variation around the mean. The heteroscedasticity of the data with values both above and below the delta line confirms the absence of the systematic bias in all types of measurements. The lack of a slope formed by the values confirms the absence of the proportional bias. The differences between the two imaging modalities were minimal.

The mean difference in volume measurements when comparing imaging modalities was 965 mm^3 (Figure 4).

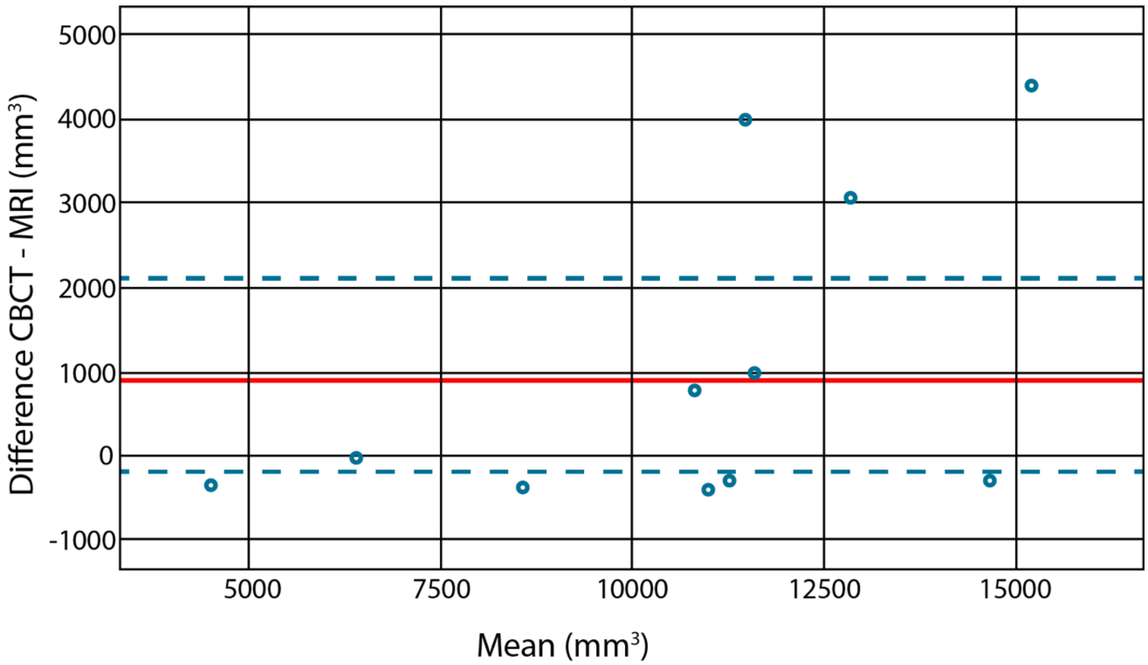

Figure 4. A Bland-Altman plot comparing CBCT and MRI pharyngeal airway volumes. The horizontal lines (dashed blue) represent the 95% confidence interval for the difference between CBCT and MRI measurements.

The mean difference in linear measurements made in mid sagittal plane along planes A-D was -0.16 mm (Figure 5), indicating slightly higher MRI values on average in this category.

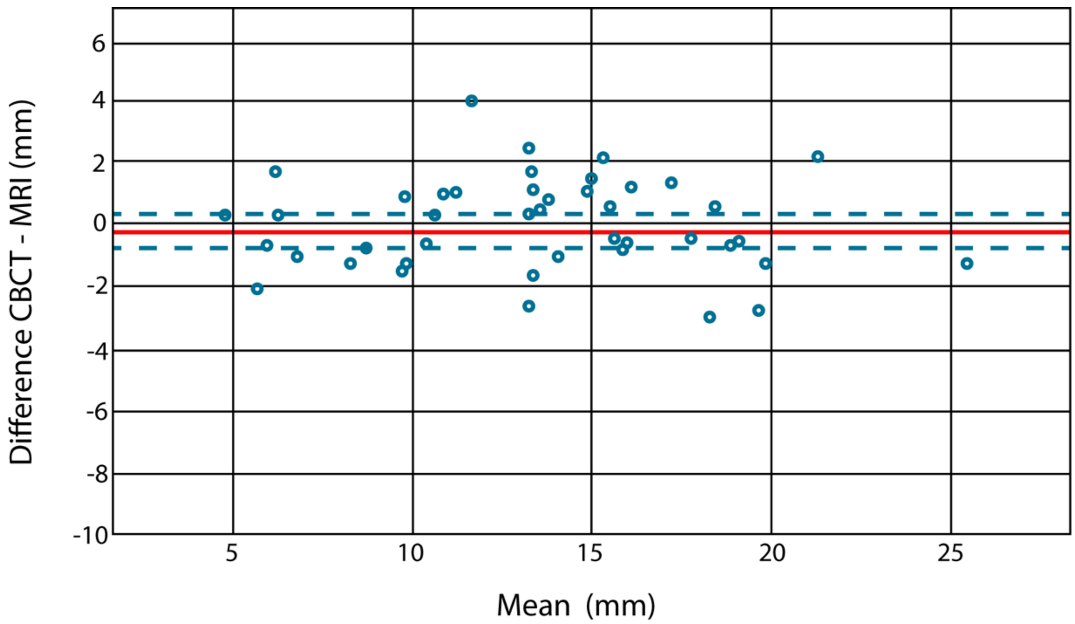

Figure 5. A Bland-Altman plot comparing CBCT and MRI pharyngeal airway linear measurements in the midsagittal plane. The horizontal lines (dashed blue) represent the 95% confidence interval for the difference between CBCT and MRI measurements.

When comparing cross-sectional widths in planes A-D, the mean CBCT-MRI difference was 0.34 mm indicating slightly higher CBCT values (Figure 6).

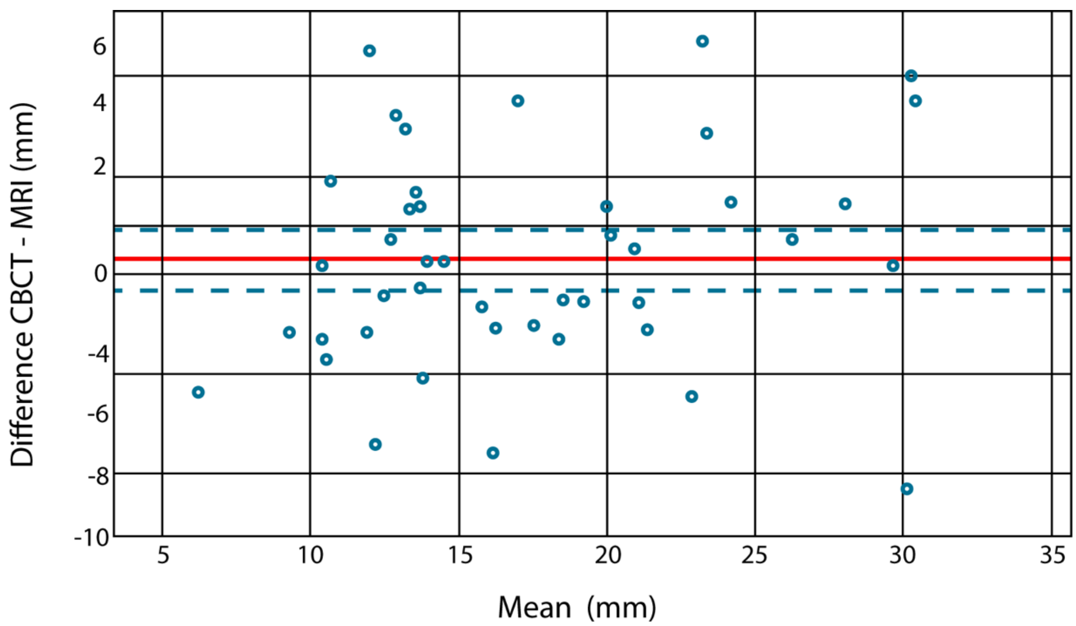

Figure 6. A Bland-Altman plot comparing CBCT and MRI pharyngeal airway cross-sectional widths. The horizontal lines (dashed blue) represent the 95% confidence interval for the difference between CBCT and MRI measurements.

The mean CBCT-MRI difference for cross-sectional lengths along planes A-B was determined to be 0.42 mm (Figure 7).

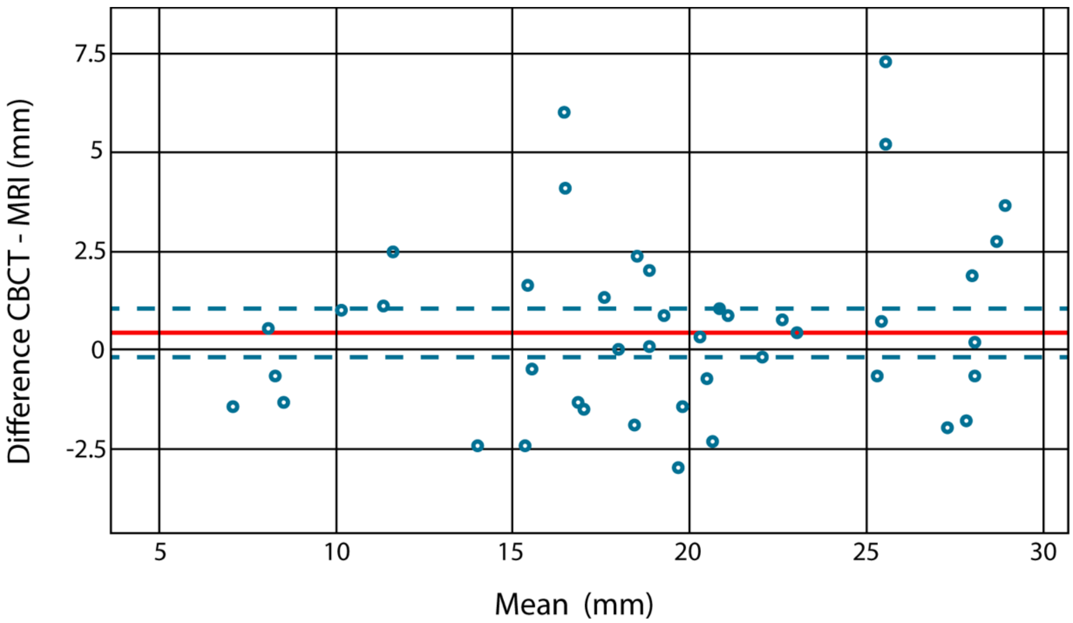

Figure 7. A Bland-Altman plot comparing CBCT and MRI pharyngeal airway cross-sectional lengths. The horizontal lines (dashed blue) represent the 95% confidence interval for the difference between CBCT and MRI measurements.

The mean CBCT-MRI difference of cross-sectional areas along planes A-B was 10.54 mm^2 (Figure 8).

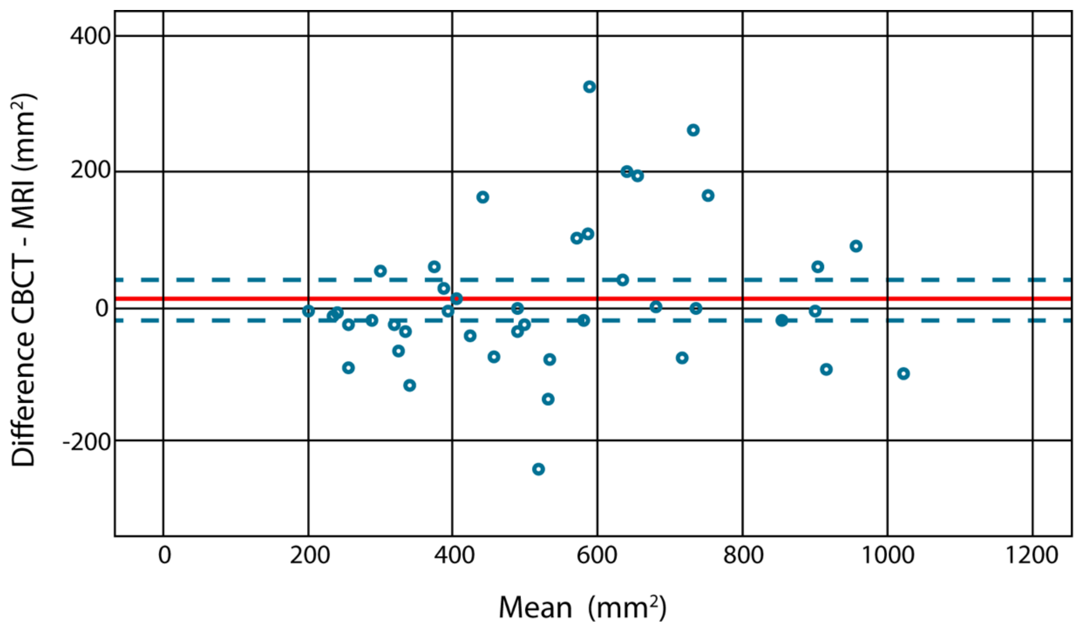

Figure 8. A Bland-Altman plot comparing CBCT and MRI pharyngeal airway cross-sectional areas. The horizontal lines (dashed blue) represent the 95% confidence interval for the difference between CBCT and MRI measurements.

Reliability was tested by repeating the measurements for four subjects on CBCT and MRI images after a two-week wash-out period. Reliability was very high for both imaging modalities. For CBCT, ICC was 0.998 (CI 0.997 - 0.999). MRI had an ICC of 0.999 (CI 0.998 - 0.999).

The bias was assessed using the One Sample Wilcoxon test and Kendall's tau correlation. The One Sample Wilcoxon test was performed to determine whether the mean difference between the CBCT and MRI measurements were significantly different from 0. The degree of bias ranged from -0.16-0.96mm. Kendall's tau correlation was also conducted to determine whether the CBCT and MRI modalities do not agree equally through the range of measurements. No statistically significant systematic ($p>0.05$) or proportional ($p>0.05$) bias was observed.

Raw data can be found in appendices A-D.

Discussion

Orthodontists and other clinicians should feel confident when using an MRI for pharyngeal airway measurements. Welch et al., validated MRI techniques on a phantom and determined that MRI is a powerful tool to study upper airway volume.[47] The use of CBCT is more widely evaluated and documented. Yamashina et al, concluded that the measurement of the volume acquired from CBCT is accurate.[44] However, a lack of standardized volumetric, linear and crow-sectional measurements continues to make comparisons challenging.

Taylor and Piano compared the agreement of tooth length measurements made on CBCT and MRI.[54,55] Those studies showed a high degree of agreement between CBCT and MRI measurements. The mean difference in the linear measurements reported by Taylor was 0.03mm +/- 0.11 mm with an ICC of 0.956.[56] Piano reported a mean difference of 0.04 mm +/- 0.77 with an ICC of 0.981 (CI 0.976 – 0.984).[57] These published linear tooth length differences are comparable with the mean differences in pharyngeal airway linear measurements reported in this paper (mean differences of 0.1-0.4 mm and ICC of 0.982 (CI 0.975-0.986)).

Flugge et al., compared the dimensional accuracy of measurements made on MRI and CBCT images to a histological section of the mandible ex vivo.[56] In vivo CBCT and MRI images were also compared. Both hard and soft tissues were evaluated, however only linear measurements were made. A high congruence between CBCT, MRI and histologic specimens was demonstrated. The ICC for the MRI and CBCT images made ex vivo was reported to be 0.993 (CI 0.986-0.997).[56] The ICC between the histological section and CBCT was 0.987 (CI 0.974– 0.994). The ICC between the MRI images and the histological section was 0.990 (CI 0.979-0.995). In vivo linear measurements of CBCT and MRI images had an ICC of 0.990 (CI 0.952-0.997). These results are similar to the results in this study where the ICC for linear measurements ranged between 0.912 (CI 0.844-0.951) and 0.929 (CI 0.873-0.960). In the study by Flugge et al., an intraoral coil and FLASH sequences were used to obtain MRI images, only linear measurements were made and only two subjects were used for the in vivo portion of the study.[56] Routine use of an MRI for orthodontic purposes is limited because of its greater cost, the limited availability of the equipment, the long imaging acquisition time, the metal induced image distortion and the inferior visualization of the teeth and the hard tissue.[24] Advancing MRI technology will continue to address these limitations. For example, recent software development allows clinicians to obtain multi-contrast MR images from a single acquisition, which improves image quality and reduces image acquisition time.[57] Additionally, ceramic brackets allow MR image acquisition without clinically significant distortion.[58] Another study shows that, as the availability of MR scanners is increasing, the cost is decreasing.[59] The visualization of the dentition and other hard tissue continues to be problematic.[40] Several studies have been conducted to develop topical oral contrast media that may lead to improved identification of teeth on MR scans.[60,61]

Further studies are warranted to characterize the interchangeability of CBCT and MRI for the purpose of airway analysis. The evaluation of the smallest cross-sectional area probably has the highest clinical significance. Color mapping of the pharyngeal airway will facilitate better visualization of the differences it the cross-sectional dimensions. The accuracy of measurements can be validated against an experimental model or by comparing measurement to the external soft tissues and dental casts. Further research is needed to determine the clinical significance of the difference in measurements made on CBCT and MRI scans.

Conclusion

MRI and CBCT give similar linear, cross-section area, and volumetric measurements of the pharyngeal airway.

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CHAPTER THREE

EXTENDED DISCUSSION

Limitations of the Study

This study had several limitations. The most significant limitation was the sample size. Only eleven sets of CBCT and MRI records were available. The second limitation was the difficulty in determining the difference between tissue and air when using the software threshold tool. The airway space-filling was subjective because it relied on a visual inspection of the examiner. At this time there is no standardization of the threshold value to achieve the actual volume. Another limitation was the complexity of the software. Extensive training in the software use was required and the learning curve was evident in the statistical analysis. Agreement between CBCT and MRI was markedly improved for the repeated subsample compared to the original sample. The level of improvement suggests the presence of the learning curve in the software use and MRI image recognition. Excellent intra rater reliability measures suggested that an effective calibration had taken place.

Recommendation for Future Studies

The results of this study indicate that further studies are warranted to characterize the interchangeability of CBCT and MRI for the purpose of airway analysis. The sample size should be expanded to increase the power to 95% or 99%. Classification of the sample size by facial types (mesiofacial, brachyfacial, dolichofacial) should be performed in a larger sample size to determine whether any trends exist. The accuracy of MRI and

CBCT measurements of the pharyngeal airway can be confirmed using different software (Scan IP, Anatomage, Quickceph, Dolphin 3D^{TM}, etc). The accuracy of data can also be validated against an experimental model or by comparing MRI and CBCT measurements to the external soft tissue landmarks and dental casts.

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APPENDIX A
AIRWAY MEASUREMENTS (MM) MADE ON MRI SCANS

Subject	1	2	3	4	5	6	7	8	9	10	11
Volume (mm^3)	11300	14800	11200	11100	9480	10400	13000	8760	6390	4640	11400
Midsagittal Plane A (mm)	13.44	6.34	14.38	19.38	20.48	26.03	15.18	16.54	10.52	4.68	21.08
Midsagittal Plane B (mm)	14.23	16.31	6.71	12.01	18.00	19.16	9.13	14.56	15.47	5.39	8.85
Midsagittal Plane C (mm)	15.85	18.10	10.38	12.83	13.33	19.48	12.44	9.36	14.24	7.36	6.13
Midsagittal Plane D (mm)	16.26	14.21	9.71	13.11	10.54	19.78	20.17	14.56	10.59	10.71	10.68
Cross-Sectional Area Plane A (mm^2)	423	356	678	1070	912	902	872	735	375	203	964
Cross-Sectional Area Plane B (mm^2)	349	398	298	522	488	374	514	265	239	333	342
Cross-Sectional Area Plane C (mm^2)	540	864	273	611	600	599	668	492	398	243	298
Cross-Sectional Area Plane D (mm^2)	636	588	357	529	574	507	555	493	400	445	754
Cross-Sectional Lengths Plane A (mm)	13.51	9.13	17.37	18.01	20.55	25.09	17.87	20.84	10.84	7.80	19.46
Cross-Sectional Widths Plane A (mm)	14.26	12.52	7.68	12.83	12.62	18.82	16.86	11.62	16.18	11.22	10.22
Cross-Sectional Lengths Plane B (mm)	14.66	16.92	9.69	10.37	14.38	19.48	18.88	15.23	16.59	8.60	7.82

AIRWAY MEASUREMENTS (MM) MADE ON MRI SCANS (CONTINUED)

Subject	1	2	3	4	5	6	7	8	9	10	11
Cross-Sectional Widths Plane B (mm)	18.33	10.84	9.08	12.55	13.81	19.19	19.18	14.22	10.02	12.71	18.08
Cross-Sectional Lengths Plane C (mm)	20.62	17.59	27.08	27.31	22.93	21.14	22.26	21.84	22.22	15.79	27.97
Cross-Sectional Widths Plane C (mm)	11.34	15.11	14.70	21.57	20.25	13.90	19.56	12.26	9.48	20.56	21.40
Cross-Sectional Lengths Plane D (mm)	21.97	28.42	25.72	27.04	28.75	20.14	28.33	22.83	17.70	18.79	20.42
Cross-Sectional Widths Plane D (mm)	27.17	32.81	27.73	29.48	25.83	19.48	23.27	21.98	27.11	24.43	28.18

APPENDIX B
REPEATED AIRWAY MEASUREMENTS (MM) MADE ON MRI SCANS.

Subject	8	9	10	11
Volume (mm^3)	8470	6360	4940	10700
Midsagittal Plane A (mm)	18.20	10.83	14.38	19.24
Midsagittal Plane B (mm)	8.61	17.63	5.19	8.86
Midsagittal Plane C (mm)	11.91	14.23	6.15	6.72
Midsagittal Plane D (mm)	14.56	9.30	10.87	11.90
Cross-Sectional Area Plane A (mm^2)	809	338	196	928
Cross-Sectional Area Plane B (mm^2)	291	214	302	348
Cross-Sectional Area Plane C (mm^2)	459	340	247	290
Cross-Sectional Area Plane D (mm^2)	509	378	408	782
Cross-Sectional Lengths Plane A (mm)	23.95	10.92	8.46	19.00
Cross-Sectional Widths Plane A (mm)	12.70	15.59	10.39	9.50
Cross-Sectional Lengths Plane B (mm)	13.90	15.10	8.83	7.23
Cross-Sectional Widths lane B (mm)	15.21	9.75	12.70	18.74
Cross-Sectional Lengths Plane C (mm)	21.93	20.89	15.55	28.45
Cross-Sectional Widths Plane C (mm)	12.42	9.12	20.42	20.22
Cross-Sectional Lengths Plane D (mm)	23.17	18.83	18.16	21.70
Cross-Sectional Widths Plane D (mm)	22.73	27.68	25.34	30.22

APPENDIX C
AIRWAY MEASUREMENTS (MM) MADE ON CBCT SCANS.

Subject	1	2	3	4	5	6	7	8	9	10	11
Volume (mm^3)	14400	14500	10800	12100	13500	11200	17400	8380	6370	4300	11100
Midsagittal Plane A (mm)	14.23	5.73	15.38	18.83	19.25	24.78	15.80	17.87	8.99	5.03	18.31
Midsagittal Plane B (mm)	12.60	15.70	4.68	14.46	17.52	18.50	8.40	11.93	16.70	7.05	7.64
Midsagittal Plane C (mm)	15.45	18.71	11.36	13.92	13.88	10.54	14.14	10.26	16.39	6.35	6.44
Midsagittal Plane D (mm)	15.45	15.69	13.73	13.42	10.86	16.84	22.38	13.57	9.28	11.71	10.071
Cross-Sectional Area Plane A (mm^2)	749	288	679	970	1000	894	931	731	403	196	870
Cross-Sectional Area Plane B (mm^2)	317	282	210	622	484	401	486	242	228	307	402
Cross-Sectional Area Plane C (mm^2)	737	842	327	651	862	462	833	485	391	235	280
Cross-Sectional Area Plane D (mm^2)	396	568	522	635	494	472	750	418	411	401	678

AIRWAY MEASUREMENTS (MM) MADE ON CBCT SCANS. (CONTINUED)

Subject	1	2	3	4	5	6	7	8	9	10	11
Cross-Sectional Lengths Plane A (mm)	19.52	7.81	19.72	18.01	19.08	25.75	19.90	20.12	11.92	8.34	17.51
Cross-Sectional Widths Plane A (mm)	9.99	14.55	4.69	14.50	11.15	18.16	15.52	9.45	15.36	9.58	10.46
Cross-Sectional Lengths Plane B (mm)	16.26	18.26	10.70	12.85	18.48	17.50	18.90	12.77	14.12	7.94	6.37
Cross-Sectional Widths Plane B (mm)	13.83	14.88	14.74	14.19	14.09	17.51	20.87	14.56	8.56	12.17	16.78
Cross-Sectional Lengths Plane C (mm)	21.55	16.24	30.74	30.05	28.17	18.16	22.97	19.54	22.03	15.27	28.21
Cross-Sectional Widths Plane C (mm)	14.98	12.52	19.09	25.13	26.12	13.54	20.62	13.17	11.78	21.17	20.68
Cross-Sectional Lengths Plane D (mm)	29.27	27.74	25.05	28.93	26.99	20.47	26.30	23.31	16.20	19.70	21.40
Cross-Sectional Widths Plane D (mm)	28.87	27.39	32.75	29.75	26.72	18.83	25.03	20.56	28.88	21.28	32.55

APPENDIX D
REPEATED AIRWAY MEASUREMENTS (MM) MADE ON CBCT SCANS

Subject	8	9	10	11
Volume (mm^3)	8280	6130	4770	10400
Midsagittal Plane A (mm)	17.87	9.28	4.88	19.23
Midsagittal Plane B (mm)	8.41	16.70	5.54	7.96
Midsagittal Plane C (mm)	11.25	17.04	6.22	7.33
Midsagittal Plane D (mm)	13.57	9.59	10.67	10.99
Cross-Sectional Area Plane A (mm^2)	800	343	188	892
Cross-Sectional Area Plane B (mm^2)	254	206	316	412
Cross-Sectional Area Plane C (mm^2)	465	418	229	288
Cross-Sectional Area Plane D (mm^2)	443	373	403	704
Cross-Sectional Lengths Plane A (mm)	21.60	11.18	8.90	18.25
Cross-Sectional Widths Plane A (mm)	11.27	14.45	10.03	10.22
Cross-Sectional Lengths Plane B (mm)	13.65	16.22	7.94	6.90
Cross-Sectional Widths Plane B (mm)	13.90	8.28	11.92	16.85
Cross-Sectional Lengths Plane C (mm)	20.19	21.81	15.29	29.70
Cross-Sectional Widths Plane C (mm)	14.23	10.29	20.40	21.92
Cross-Sectional Lengths Plane D (mm)	23.40	17.00	19.03	21.70
Cross-Sectional Widths Plane D (mm)	20.52	28.53	22.72	32.22