Title
Three-Dimensional Conebeam CT Analysis of Pharyngeal Airway Changes After Orthognathic Surgery

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Three-Dimensional Conebeam CT Analysis of Pharyngeal Airway Changes after Orthognathic Surgery

by

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THESIS

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[redacted]

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ABSTRACT

Three-Dimensional Conebeam CT Analysis of

Pharyngeal Airway Changes after Orthognathic Surgery

Michael K. Chang, DDS

OBJECTIVE: The purpose of this study was to examine volumetric changes of the airway with orthognathic surgery. Airway changes are described quantitatively as well as qualitatively through 3-D superimpositions.

METHODS: 45 total patients are in three groups: maxillary surgery only (n=17), mandibular surgery only (n=17), and two-jaw surgery (n=11). CBCTs were obtained pre-surgical, "immediate" post-surgical (median=19 days), and "long-term" post-surgical (median=203 days).

CONCLUSIONS: Maxillary surgery group-a 7mm surgical advancement looks to be the point at which the airway volume begins to decrease, but it was not supported by statistical tests. At 248 days on average after surgery (t2-t0), the nasopharynx appears to be affected the most by LeFort surgery. Mandibular surgery group-a 7-8mm advancement appears to be the point at which the airway stops increasing; this was not supported by statistical tests in this study. At about 248 days after surgery (t2), those subjects that had a mandibular advancement, had the greatest effect on the oropharynx. In the mandibular setback group at about 248 days after surgery, the nasopharynx slightly decreases and the oropharynx slightly increases. The hypopharynx does not seem to be affected. Two-jaw surgery group-the two-jaw surgery group has effects that are more complicated than in simply determining the distance it is moved or displaced. Color map-three-dimensional superimpositions provide a viable alternative for qualitatively describing changes between timepoints. Further works needs to be done to develop reproducible landmarks to reliably use color maps.

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INTRODUCTION

Premise

The airway is an area of research that is of interest to scientists and clinicians from diverse disciplines. Some authors are interested in the airway as a causative role in influencing facial growth. Other researchers are interested in the airway due to the high prevalence of obstructive sleep apnea syndrome (OSAS); 20 million adult Americans are affected by sleep apnea.[1] Some studies are conducted due to the apparent association between OSAS and vascular disorders with substantial cardiovascular morbidity and mortality.[1,2] Surgical treatments have been advocated to help treat the negative effects that an unfavorably constricted airway may have on facial growth, quality of life, and condition of the cardiovascular system.

Airway Anatomy

The pharyngeal airway is the negative air space that is created by the pharynx. The pharynx transports food to the esophagus and air to the larynx, trachea, and lungs. The wall of the pharynx is made up of mostly two layers of muscles. The external circular layer of muscles are comprised of three constrictor muscles.[3] The internal layer of muscles is oriented in a mostly longitudinal fashion.

The pharyngeal airway, the focus of this thesis, can be divided into three subsections: 1) nasopharynx — the region between the nasal turbinates and the hard palate; 2) oropharynx — containing the retropalatal area (between the hard palate and tip of soft palate) and the retroglossal region (the caudal margin of the soft palate to the base of the epiglottis); and 3) the hypopharynx — the part from the base of the tongue to the cervical esophagus (Figure 1).[3] It is important to note that the exact determination of the pharyngeal airway varies greatly between individuals due to anatomic differences.

Figure 1. Sections of the Pharyngeal Airway

Facial and Dental Changes

"Adenoid facies" is a group of characteristics that describe an individual with a constricted airway.[5-8] Individuals have an appearance of a long face, pinched nose, difficulty in breathing, open mouth posture, and droopy eyes.[5-8] In addition to morphologic changes, dental changes associated with a constricted nasal airway have been reported in the literature.[9-13] These dental conditions include increased lower face height, retroclined incisors, anterior open bite, posterior cross bite, and/or high arched palatal vault. Together these dental characteristics make for some of the most difficult cases that orthodontists treat. In addition, failure to identify and address the etiology (*i.e.,* constricted nasal airway) can lead to relapse after orthodontic treatment is completed.[11]

Sleep Apnea

There are essentially two types of sleep apnea: 1) central apnea (CA) is thought to be caused by chemosensitivity to hypoxia or hypercapnia, and 2) OSAS is thought to be caused by recurrent physical occlusion of the upper airway during sleep.[14] Recently a combination of the two, termed complex sleep apnea syndrome, has been suggested.[14] This condition essentially starts as OSAS but transforms into central apnea even after the airway obstruction has been removed.[14]

OSAS is a chronic syndrome prevalent in middle-age populations, 30-60 years old, and evident in 4% of men and 2% of women. In elderly populations, it has been documented in 28-67% for men and 20-54% of women. [15] It is not the process of aging that leads to OSAS, but it is the simultaneous changes in the body that occur when getting older.

The hallmark finding of OSAS individuals is a collapse of the upper airway during inspiration while sleeping.[16] The airway collapses because the negative pressure in the pharynx exceeds the ability of the muscles in the pharyngeal wall to resist the pressure change. When this happens, airflow ceases and the patient has an apneic or hypopneic episode; the latter being less severe. An apneic/hypopneic episode is defined as a period of at least 10 seconds in which a patient's airway closes and prevents breathing. Sleep specialists then define sleep apnea as five or more apneic/hypopneic episodes per hour of sleep in a seven hour sleep period.[17] This is the apneic/hypopnea index (AHI) and is often used in diagnosing OSAS.[17]

Once the diagnosis is made, several treatment modalities are possible. Non-invasive medical treatments are prescribed first. These include weight loss, continuous positive airway pressure (CPAP), oral appliances, and medication.[18] The treatments have been found to be effective for some individuals, but, for others, these milder treatments are insufficient to correct the condition. For the more severe cases, more invasive surgery is necessary. Riley *et al.,* has proposed a two-phase surgical approach to treating OSAS.[19] This is also known as the Stanford Protocol. The first phase in their protocol involves uvulopalatopharyngoplasty (UPPP) and/or a genioglossus advancement with hyoid suspension to eliminate airway constriction at the base of the airway. This is the area of greatest constriction as reported by several authors.[19-22] If OSAS symptoms are not alleviated after this first phase of surgical intervention, the patient undergoes a polysomnogram. Confirmation of continued apnea by the polysomnogram is indicative of a second phase of surgery involving a maxillo-mandibular jaw advancement (Figure 2).[19,23] It seems intuitive that jaw advancement surgery would increase the airway size. However, studies by Riley *et al.,* in 1987 and Tselnik *et al.,* in 2000 have shown that the airway actually decreases, as measured on a lateral cephalogram, after maxillo-mandibular surgery.[24,25] Airway changes need to be confirmed using three-dimensional imaging tools.

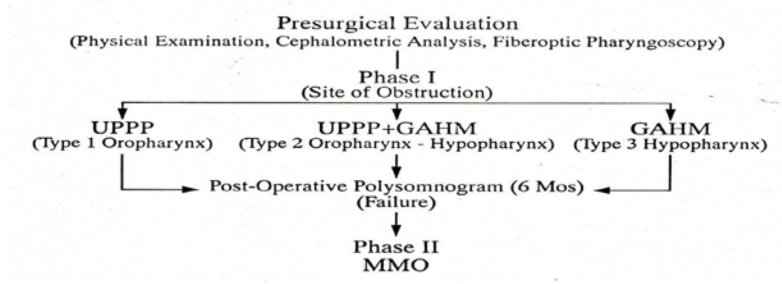


Figure 2. Stanford Protocol

Surgical treatments

As described in the Stanford Protocol, two phases of surgical treatments are indicated for OSAS individuals. UPPP removes or reduces the soft tissue that is obstructing the pharyngeal airway including the uvula, soft palate, pharyngeal tissues, tonsils, and adenoids (Figure 4).[19] Genioglossus advancement and hyoid suspension can also be performed. Genioglossus advancement is completed below the mandibular incisors where a wedge of bone containing the muscle attachments is advanced, turned, and held in place with a titanium screw (Figure 5). Hyoid suspension is accessed through a natural crease of the neck where the hyoid bone is immobilized by suturing it into place in front of and on top of the thyroid cartilage (Figure 6).

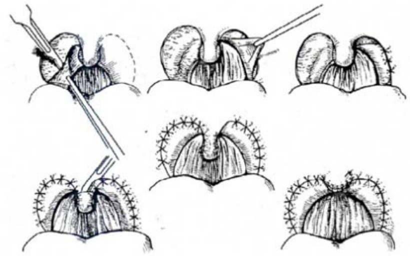


Figure 3. Uvulopalatopharyngoplasty indicating the stages of surgery

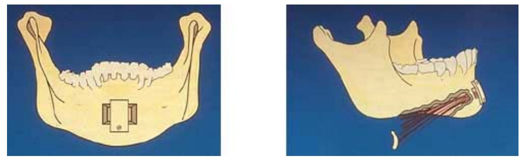


Figure 5. Genioglossus Advancement

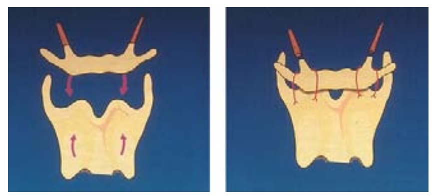


Figure 6. Hyoid Suspension

If these treatments are not effective, orthognathic surgery is recommended in the Stanford Protocol. Orthognathic surgery can markedly improve masticatory function, treat OSAS, and improve esthetics by moving the skeletal support for the soft tissue profile in three dimensions of space.

Orthognathic surgery involves moving the maxilla and/or mandible potentially in all three dimensions of space. Maxillary surgery is commonly completed utilizing a LeFort 1 technique described by Bell *et al.,* in 1975.[26] These techniques have stood the test of time in maximally preserving blood supply to the maxilla, maintaining vitality to the teeth, and producing a stable result when using rigid skeletal fixation. In the mandible, the bilateral sagittal split osteotomy (BSSO) technique was pioneered by Trauner and Obwegeser in 1957.[27,28] Since then the BSSO has been used routinely as a successful and predictable orthognathic surgical procedure.[29,30] However, changes in the spatial position of the maxilla and mandible have been shown to change the oropharyngeal complex.

The maxilla forms the anterior border of the oropharyngeal complex and, therefore, any movement of the maxilla is expected to change the surrounding soft tissue. Mandibular surgical changes affect the pharynx via numerous muscular attachments. The genioglossus muscle has its origin at the genial tubercle of the mandible and inserts into the tongue.[3] The geniohyoid muscle originates on the mylohyoid ridge of the mandible and inserts on the hyoid bone.[3] The genioglossus and the dorsal muscle fibers of the tongue work together to open the airway and allow patency.[12,31] The insertion areas of the geniohyoid and mylohyoid muscles move the hyoid bone whose position then alters the posterior airway space at the base of the tongue (Figure 7).[31]

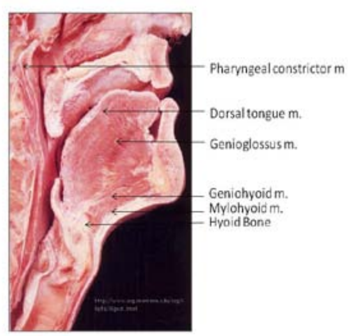


Fig 7. Structures of the oropharyngeal complex important to strategies in treating airway disorders

Many studies have confirmed the efficacy of orthognathic surgery on OSAS patients.[32,33] Hochban *et al.,* used a ten millimeter maxilla-mandibular advancement in their study, and since then, their protocol has become the standard treatment for OSAS patients.[32] This approach decreased the apnea-hypopnea index at a statistically significant level.[32] The Stanford Protocol has been reported as having a 61% success rate after only phase one, and a 100% success rate of phase one when followed by phase two.[23,34]

Respiratory Cycle and Head Position Effects

Numerous investigators have reported that swallowing most often occurs during expiration, and that expiration usually follows a swallow even if the swallow occurs during inspiration.[35] The act of swallowing involves the genioglossus muscle contracting to bring the tongue anterior. Since the tongue forms the anterior border of the airway, and the genioglossus protrudes the tongue, moving the tongue base would change the airway dimensions. EMG studies have suggested that the genioglossus muscle, when activated, moves the tongue anteriorly and dilates the airway during inspiration.[36] This appears to be a reflexive response as the negative pressure that is created in the pharynx during inspiration could collapse the airway except for the genioglossus.[36] Changes in the upper airway have been reported during CT imaging.[37] Schwab *et al.,* found that there was a 17% cross-sectional area change of the airway during quiet tidal breathing.[37]

Solow *et al.,* in 1984, looked at normal orthodontic patients who had constricted airways as determined by high nasal resistance as well as by measuring the anterior-posterior space of the airway on lateral cephalograms.[38] Solow *et al*., found significant associations in craniofacial morphology with retroclined maxillary incisors and retrognathic mandibles. He also found that smaller airways tended to have a larger craniocervical angulation.

Imaging the airway

Many studies have utilized two-dimensional technology to analyze the airway.[20,39-55 56,57] Lateral cephalogram is an example of two-dimensional technology that have been widely used. In addition, three-dimensional visualization of MRI and CT data have been created to analyze the airway.[21,55,58,59] Unfortunately, due to the amount of radiation with spiral CT and significant cost, this modality is difficult to justify for standard imaging protocol of the airway. More recently, an increasing number of authors have begun using 3-D cone beam computed tomography (CBCT) in their studies.[56,57,60-64]

The Hitachi MercuRay CBCT machine used in this study is a 12-bit gray scale machine.[65] The MercuRay provides three fields of view (FOV): 6-inch, 9-inch, and 12-inch.[66] The 6-inch FOV provides higher resolution while the 12-inch view allows viewing the entire craniofacial skeleton in one scan. The MercuRay takes 9.6 seconds to complete one image and one voxel is either 200, 300, or 376 um^3 depending on the field of view used.[65]

Based on the preceding information, a question can be posed: "What component of the respiration cycle is actually being captured by a CBCT machine that uses 9.6 seconds to take an image?" The airway can change in size and shape during different phases of quiet tidal breathing. The best way to approach this question would be to evaluate some of the studies that have validated CBCT as a research tool. In 2005, a landmark study was completed to validate the MercuRay as an accurate tool.[64] In Stratemann's study, he compared 120 linear measurements using chromium-steel fiducials on a human skull that were measured both with manual calipers as well as from the CBCT generated images. [64] He found the mean measurement error of the digital MercuRay measurements compared to the gold-standard (manual caliper measurement on the skull) was 0.01±0.06mm (mean±2SD).[64] Aboudara, in 2001, and Sears, in 2006 compared the MercuRay with traditional cephalograms to test if a CBCT is a valid tool for analyzing the airway.[63] They both found good to excellent correlations, depending on the subsection of the airway, between the two imaging techniques.[60,63] The hypophyarnx, in Sears' study, was found to have a Pearson's Correlation coefficient of 0.421 (p=.06); the oropharynx had a coefficient of 0.653 (p=.001), and the nasopharynx was 0.471 (p=.04).[63]

Superimpositions

Superimpositions have proven to be a valuable tool for evaluating changes in form and shape over a time period. Two-dimensional superimpositions of lateral cephalograms have been used as an important method to evaluate growth changes and orthodontic treatment. With the ability to now generate three-dimensional images of patients, analyzing changes in all dimensions enables the capacity to determine the true three-dimensional growth without image distortion. Bookstein and Dryden *et al.,* presented groundbreaking morphometric models.[67,68] Cevidanes *et al.,* applied this to orthodontic studies.[69-72] Her group has provided quantitative image analysis using three-dimensional superimpositions for skeletal structures.[69-72] Stratemann also used three-dimensional superimpositions to look at the maxilla, mandible, and airway differences in individuals with different facial patterns.[64] He used a series of bilateral landmarks that were visible only in three-dimensional images, on which the structures were superimposed.

To date, there have been no studies that examine the outcomes of orthgnathic surgery related to airway volume or attempt to localize the quantitative changes post-surgery. The purpose of this study was to analyze the airway changes that occur before, after, and long-term post-orthognathic surgery. The three-dimensional airways segmented out of the CBCT scans were then superimposed on one another to graphically demonstrate the location and magnitude of airway dimensional changes.

Specific Aims

- To correlate volumetric airway changes with magnitude and direction of surgical skeletal movement in healthy orthognathic surgery patients
- To correlate the level of jaw surgery with airway changes of the pharyngeal regions
- To determine if airway volume changes plateau despite increasing surgical repositioning
- To determine if volume changes from one-jaw surgery can predict volume changes in two-jaw surgeries

Hypotheses

- Airway volume changes will correspond with the amount, direction, and level of skeletal movement
- Airway volume change will correlate to the amount of surgical advancement however, the change will begin to plateau with increasing amount of skeletal movement
- Predicting volume changes in two-jaw surgeries will be multi-factorial and may not be extrapolated from one-jaw surgery analyses

MATERIALS AND METHODS

Study Design

This was a prospective study. The University of California, San Francisco (UCSF) Committee on Human Research approved the study protocol, and patients were recruited from the UCSF Orthodontic Clinic and from the Oral & Maxillofacial Surgery Clinic (OMFS). All the surgeries were done by one surgeon except for two procedures performed by other OMFS surgeons at UCSF. Informed consent was obtained by the authors of this study.

All of the patients involved in the study were treated surgically by the UCSF Oral and Maxillofacial Surgery team, and orthodontically by UCSF Division of Orthodontics residents or private orthodontists in the San Francisco Bay Area. Enrollment for this study was open for approximately three years, and patients are continuously being recruited for future research projects. This study increased the patient pool from the previous thesis by Sears *et al.*[63]

Each enrolled patient was assigned a number to anonymize his/her identity. Based on their diagnosis and indicated treatment patients were categorized into three groups: 1) maxillary surgery only, 2) mandibular surgery only, or 3) both maxillary and mandibular surgery. The amount of surgical movement was documented for each patient. Those patients that had an anterior repositioning of the craniofacial skeleton, in the sagittal dimension, were denoted with a positive number while posterior movement was assigned a negative number.

The maxillary-only surgical group had 17 subjects.(Table 1)

Table 1. Maxillary-only group demographics

Pt. ID	Sex	Age at surgery	Surgical Movement (mm)
1	F	28Y 5M	-3
2	F	31Y 0M	3
3	F	20Y 6M	4
4	F	15Y 2M	4
5	F	18Y 11M	4
6	M	20Y 11M	5
7	M	34Y 8M	5
8	F	20Y 8M	5
9	M	43Y 11M	5
10	M	23Y 10M	5
11	F	17Y 5M	5
12	M	25Y 4M	6
13	F	17Y 1M	6
14	F	34Y 3M	6
15	F	16Y 7M	7
16	M	16Y 10M	8
17	M	28Y 1M	8
age range: 15Y 2M-43Y 11M			
median age: 20Y 11M			

The mandibular-only surgical group had 17 subjects.(Table 2)

Table 2. Mandibular-only group demographics

Pt. ID	Sex	Age at surgery	Surgical Movement (mm)
18	F	18Y 6M	-4
19	M	29Y 8M	-4
20	M	31Y 0M	-4
21	M	37Y 1M	-4
22	F	32Y 6M	5
23	F	31Y 10M	6
24	F	43Y 4M	6
25	F	27Y 10M	6
26	F	19Y 5M	7
27	F	27Y 8M	7
28	F	18Y 4M	8
29	F	18Y 5M	8
30	F	20Y 10M	8
31	F	16Y 8M	8
32	F	17Y 8M	10
33	F	15Y 8M	10
34	M	20Y 11M	15
age range: 15Y 8M-43Y 4M			
median age: 20Y 11M			

The two-jaw surgical group had 11 subjects.(Table 3)

Table 3. Two-jaw surgery group demographics

Pt. ID	Sex	Age at surgery	Maxillary Movement (mm)	Mandibular Movement (mm)
35	M	28y 8m	10	-14
36	M	19y 0m	6	-7
37	F	37y 1m	3	-3
38	F	31y 2m	3	-3
39	M	27y 8m	5	-4
40	M	20y 11m	5	-3
41	F	37y 6m	1	1
42	L	18y 8m	4	2
43	F	18y 6m	1	8
44	F	14y 7m	4	6
45	F	43y 10m	10	10

Inclusion criteria for this study included patients that were selected for orthognathic surgery as part of their comprehensive treatment plan, had informed consent, and completed a pre-surgical CBCT scan and had at least one post-surgical CBCT scan available. Exclusion criteria included failure to obtain informed consent, maxillary widening surgery only, maxillary vertical surgery only, genioplasty surgery only, or the lack of appropriate CBCT scans as defined in the inclusion criteria. CBCT scans were obtained at three time points: t_0 is defined as pre-surgery, t_1 is “immediate” post surgery, and t_2 is long-term post surgery. Time from surgery to t_1 is described in (Figure 7) (mean=17.6 days, range=3-46 days). Time from surgery to t_2 had a mean of 248.4 days and range of 97-850 days.

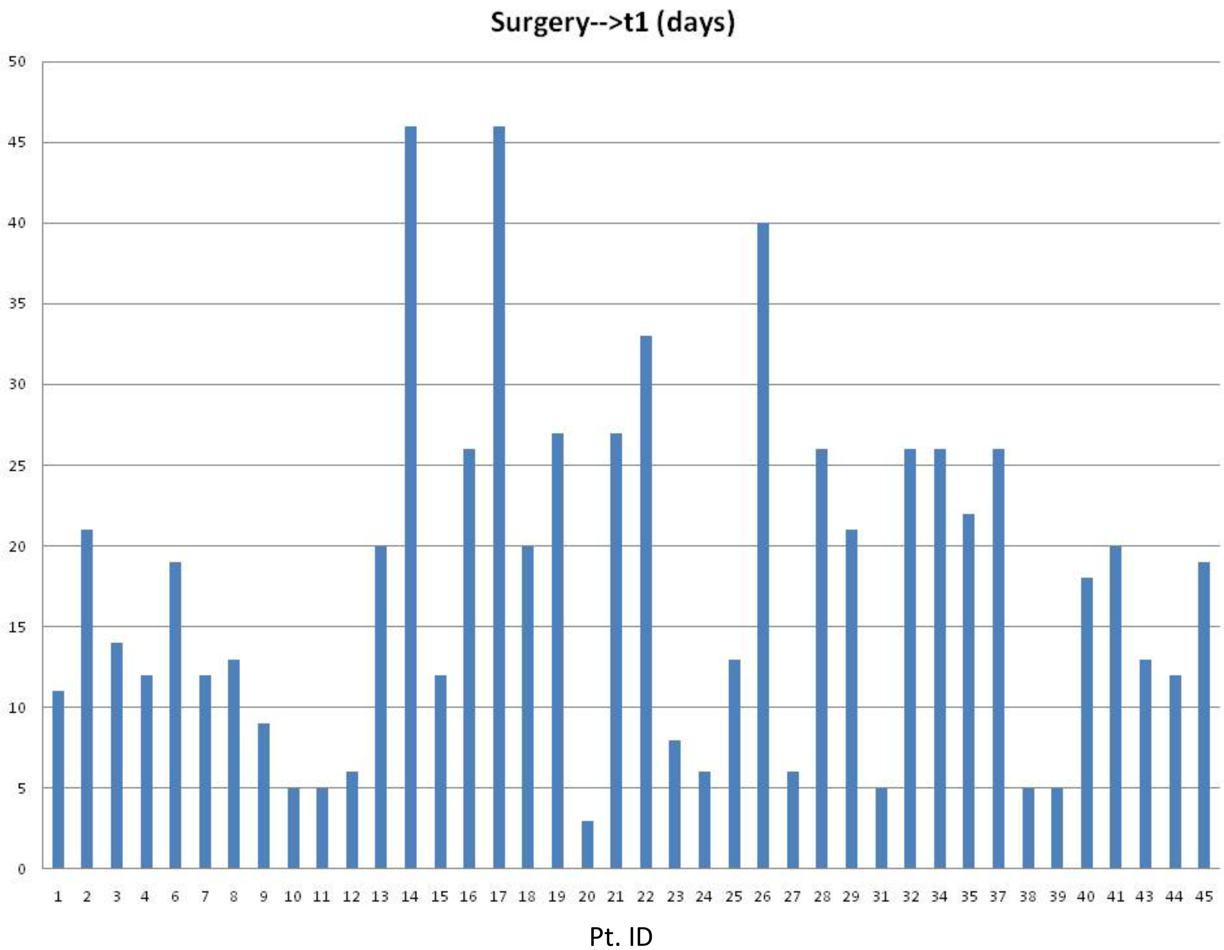


Figure 7. Time from surgery to the first post-surgical, t1, scan

All CBCT scans were obtained at UCSF on a CB MercuRay cone beam CT system (Hitachi Medical Corporation, Tokyo, Japan). The 12-inch field of view was required for this study in order to capture the entire length of the airway and was scanned at the manufacturer's recommended operating parameters of 10 mA and 100 kVp. The equivalent radiation dosage for each scan was 300 μSv. After the study had begun, the machine was modified to accommodate 2 mA for the same 12-inch field of view, reducing the equivalent radiation dosage for each scan to 132.3 μSv.

Each CBCT referral form had clearly written instructions for the patient to hold still, to not swallow, and maintain her or his tongue on the roof of the mouth. This would decrease the variation in airway size and shape changes due to the respiration cycle. Additionally, the technician ensured all patients kept their head in natural head position by having patients look into their own eyes by using a mirror that was placed directly in front of the CB MercuRay. Numerous studies have shown the mirror method to be a reliable technique for obtaining a consistent natural head position.[46,73]

Furthermore, to confirm the technician's instructions, head posture and airway position reproducibility, we randomly selected five non-growing and non-surgical patients for our pilot sample. All of these patients had two CBCT scans taken less than one year apart as part of their normal orthodontic treatment at the UCSF Orthodontic Clinic. These selection criteria for our pilot group allowed us to exclude the effect of weight gain on the airway volume.(**Table** 4)

Table 4. Pilot Group Demographics

ID	Sex	Age at 1st Timepoint	Days between timepoints		
Pilot Pt.1	M	20Y 8M	172		
Pilot Pt.2	M	19Y 8M	164	mean=	179.2
Pilot Pt.3	F	24Y 3M	184	median=	172
Pilot Pt.4	F	46Y 9M	356	range=	20-356
Pilot Pt.5	F	25Y 3M	20		

All CBCT scans were analyzed using CB Works 2.1 software (CyberMed Inc., Seoul, Korea). All three time points were viewed, with the airway segmented and measured in the exact same manner by one evaluator. The DICOM data were opened using the multi-planar reconstruction mode (Figure 8).

Figure 8. MPR mode of the CB Works software depicting the three planes of view: upper left is horizontal; upper right is midsagittal; and lower left is coronal

1. The airway was then visualized by a histogram setting that was applied consistently to every scan. Values of -1024 through -579 were created and utilized by the author.(Figure 9) These values were chosen as a compromise between optimally visualizing the airway, without excluding any part of the airway, and at the same time excluding structures not part of the airway.

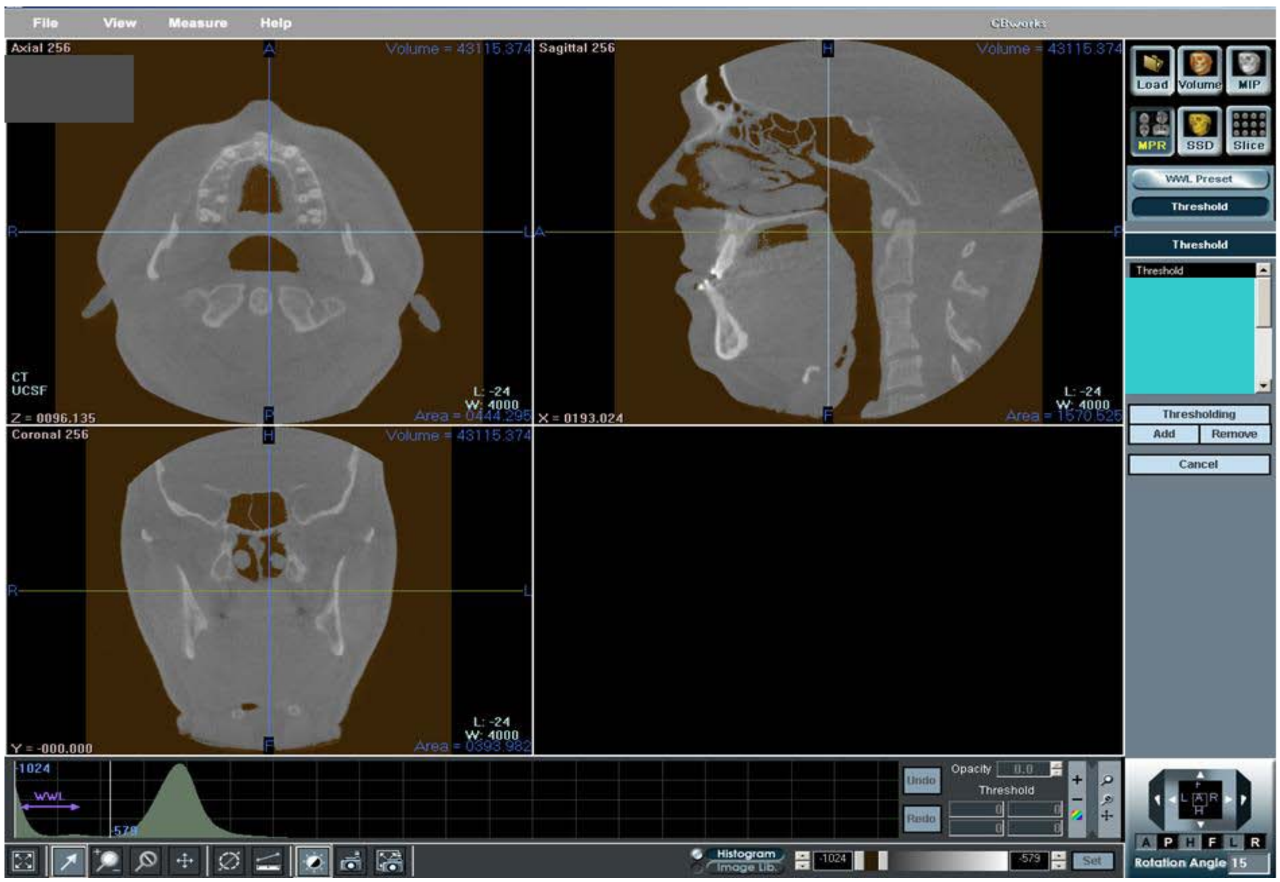


Figure 9. Voxels selected (brown) based on the CT numbers ranging from -1024 to -579 CT units

2. Meticulous segmentation techniques were utilized to extract the airway out of the surrounding craniofacial skeleton. First, the volume of interest was localized and then careful regional sculpting was completed to grossly remove all unintended negative airspace that was created by the threshold values. The three-dimensional airway with "noise" was then displayed (Figure 10). Next, further detailed segmentation was completed to remove all of the "noise;" this resulted in the final airway object (Figure 11). Once segmentation was complete, CB Works provided a volumetric value for the airway expressed as cubic millimeters.

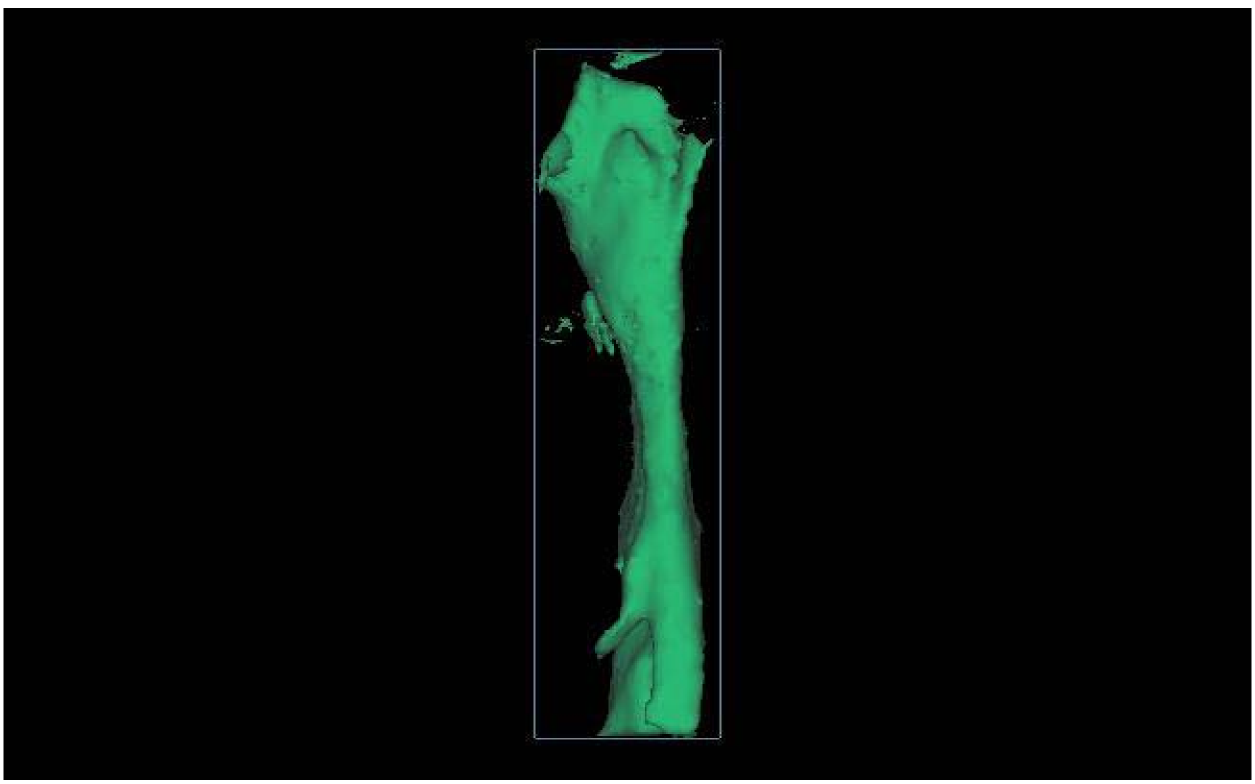


Figure 10. Three dimensional surface volume of one human airway showing some scattered "noise"

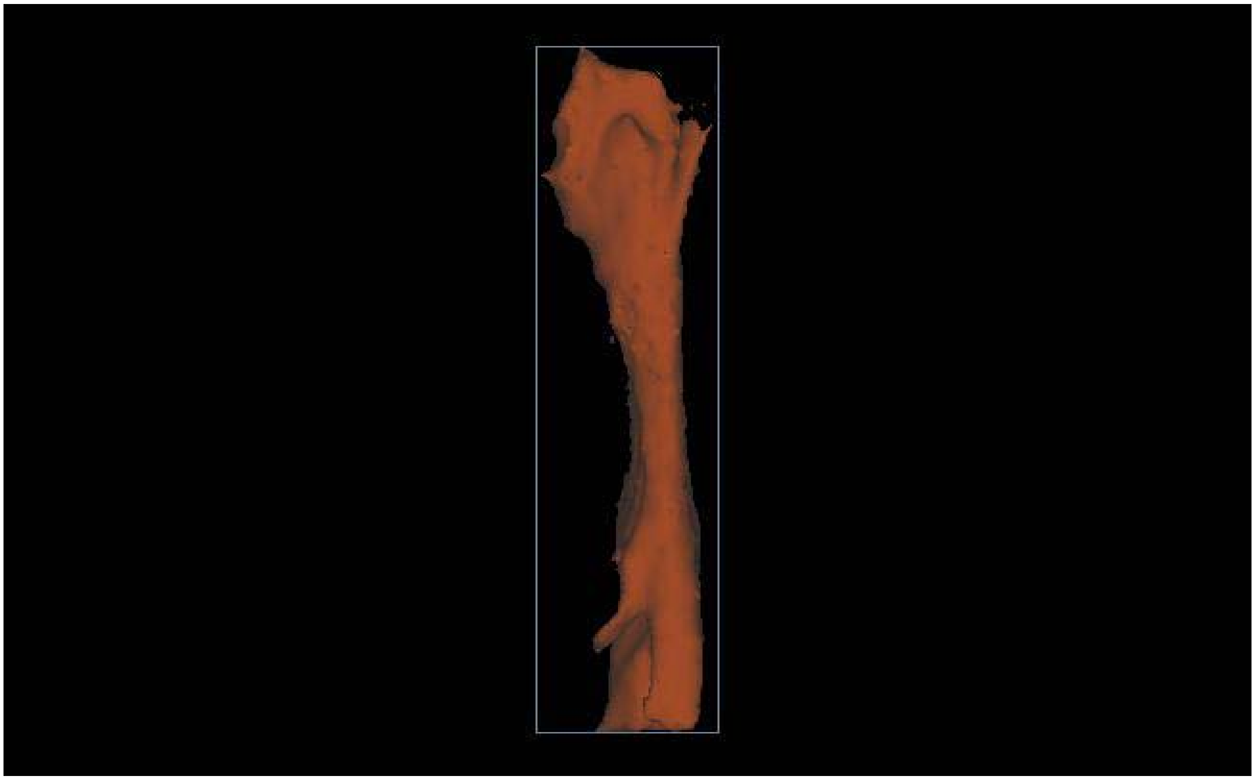


Figure 11. Final segmented three dimensional surface volume of one human airway without extraneous voxels being present

Airway Analysis

A number of airway analyses exist for studying cephalometric x-rays.[39-42,52,54] However, there is no consensus on an approach in the literature. There is no standard approach to analyzing the airway in three-dimensional CBCT scans. Selected anatomy textbooks were referenced and compared to the existing literature and their analyses (Figure 12).[74,75] The three levels of the airway in the anatomy texts defined as the nasopharynx, oropharynx, and hypopharynx (laryngopharynx), were found most closely, but not perfectly, to match the boundaries depicted in the study by Achilleos.[39]

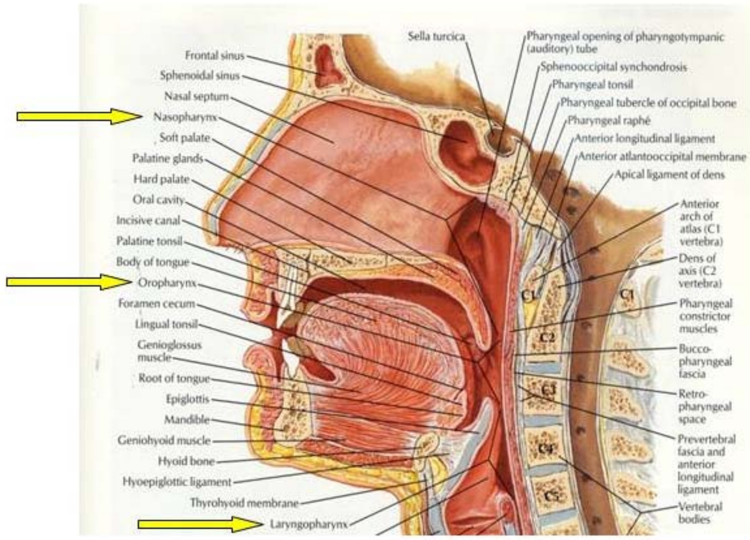


Fig 12. Schematic of the sagittal midline of an adult human depicting anatomical sites and landmarks

Once the entire airway could be visualized, boundaries were created. Using Achilleos as a guide, the superior boundary was defined as a straight line connecting sella and posterior nasal spine. The inferior boundary was drawn as a line perpendicular to the posterior pharyngeal wall at the level of the bifurcation of the trachea and esophagus. The entire airway was successfully segmented and could be visualized (Figure 13).

Fig. 13. Whole Airway shown in midsagittal view depicting the rostral and caudal boundaries

The whole airway was then subdivided, according to Achilleos, into nasopharynx, oropharynx, and hypopharynx. The inferior boundary of the nasopharynx was defined as a line drawn perpendicular to the posterior pharyngeal at the level of basion (Figure 14).

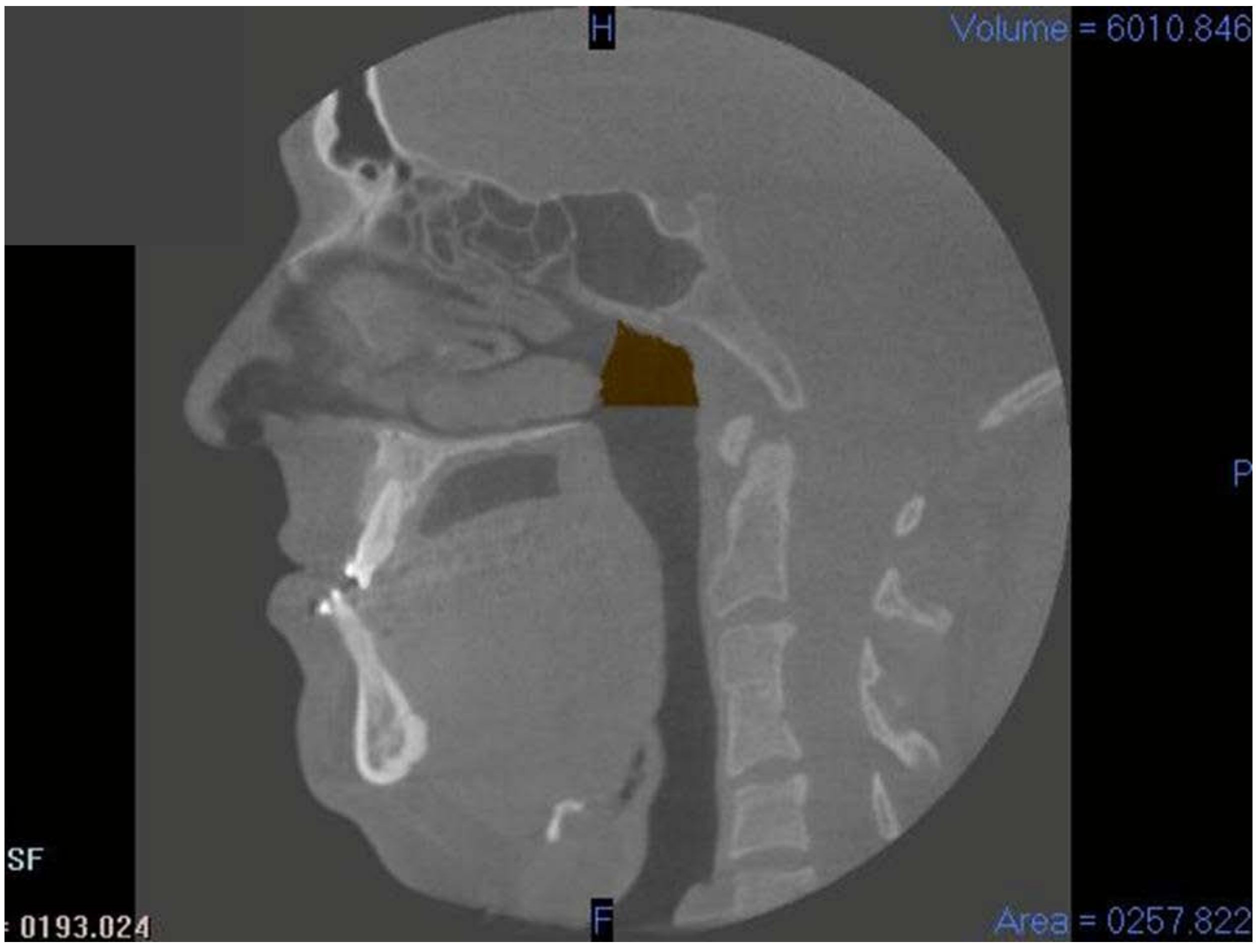


Figure 14. Nasopharynx

The inferior border of the oropharynx was at the level of the tip of the epiglottis line perpendicular to the posterior pharyngeal wall (Figure 15).

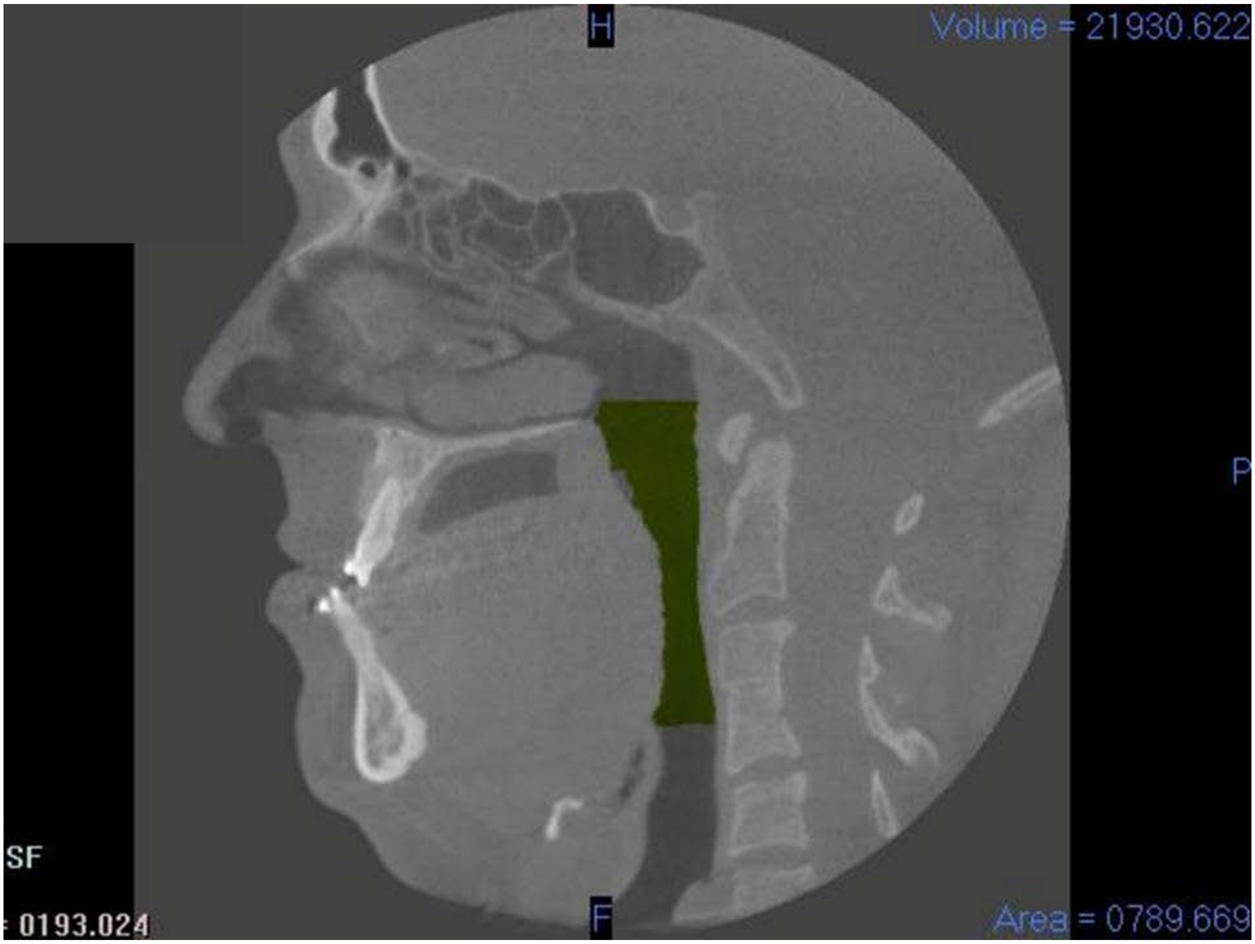


Figure 15. Oropharynx

The remaining part of the airway extends to the bifurcation of the esophagus and trachea (Figure 16).

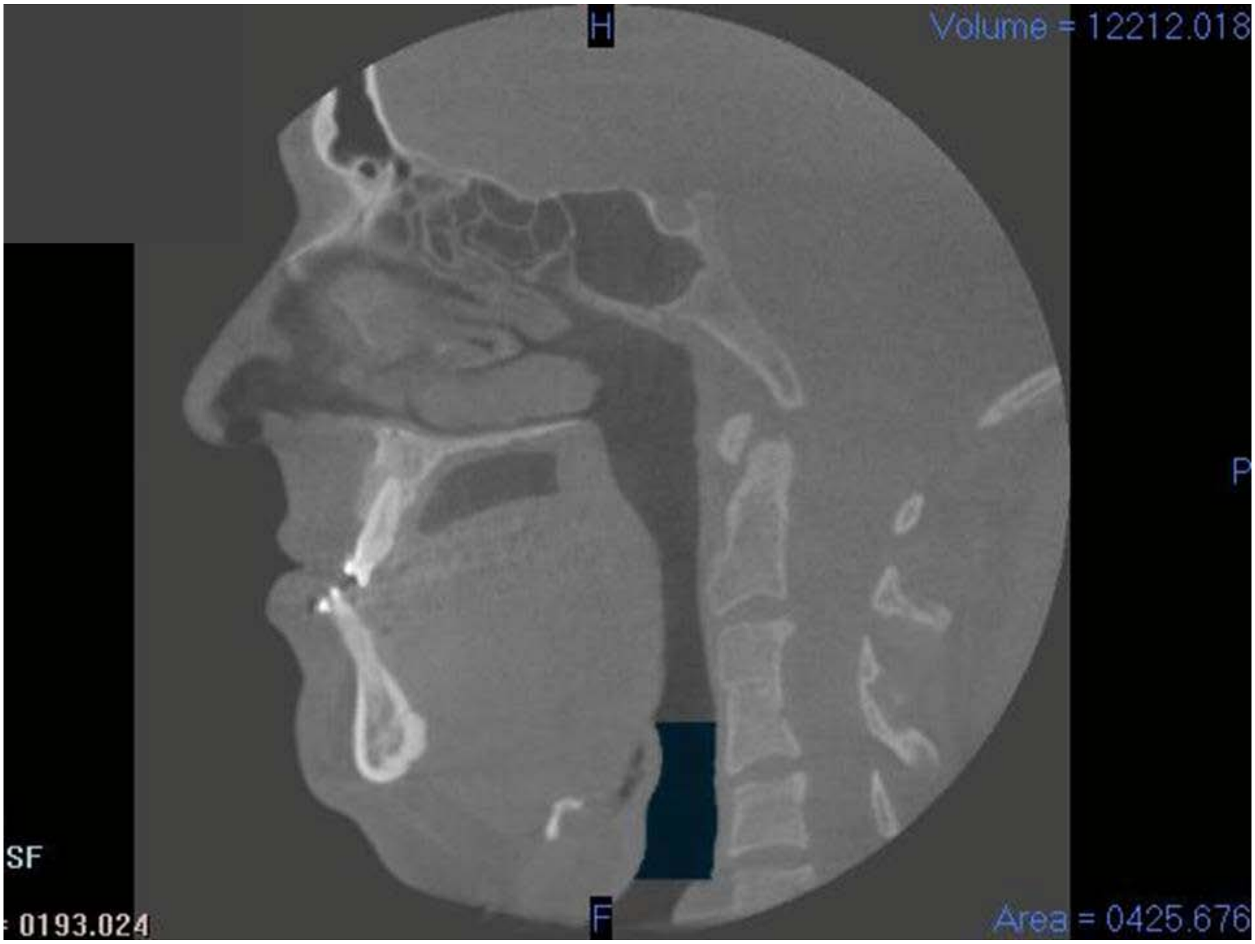


Figure 16. Hypopharynx

Airway Landmarks

Stratemann *et al.* described the use of airway landmarks that could be identified in three dimensions.[64] In addition to these structures, an anatomy textbook was consulted to aid in developing landmarks that could be with a 3-D CBCT image.[74] The landmarks used are described in figure 17.

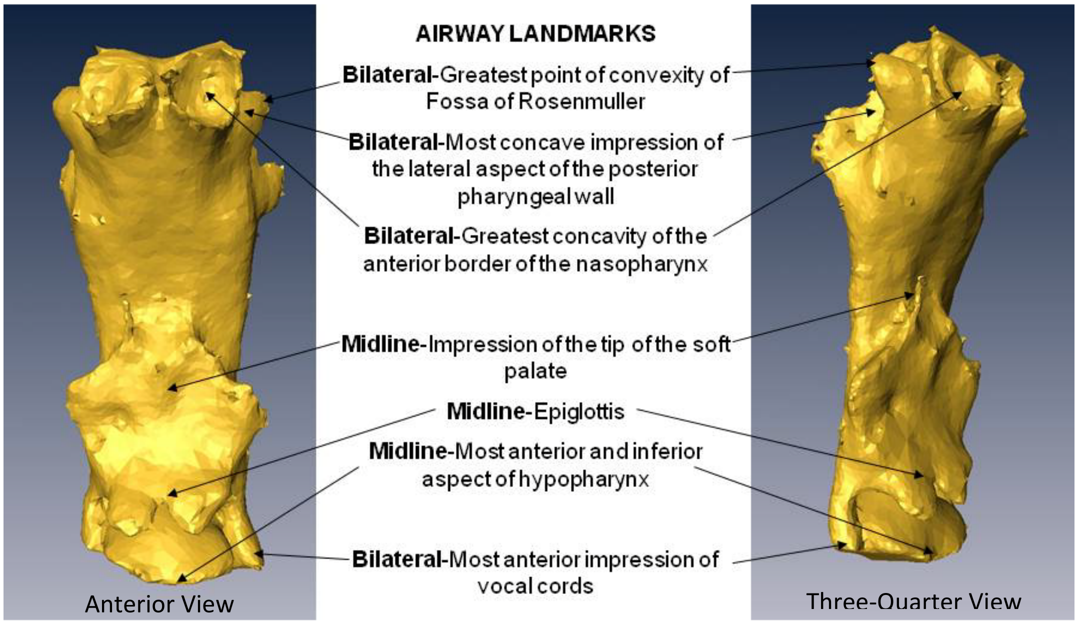


Figure 17: Airway landmarks depicted on an anterior (left) and oblique (right) view of the volumetrically rendered three dimensional surface of one human airway

Once these landmarks were identified, they were then used to superimpose airways from two different timepoints and create a color map of changes. This was done with Amira software (Amira 3.1, Mercury Computer Systems GmbH, Berlin, Germany) using a custom-programmed algorithim. A sample color map is seen in figure 18.

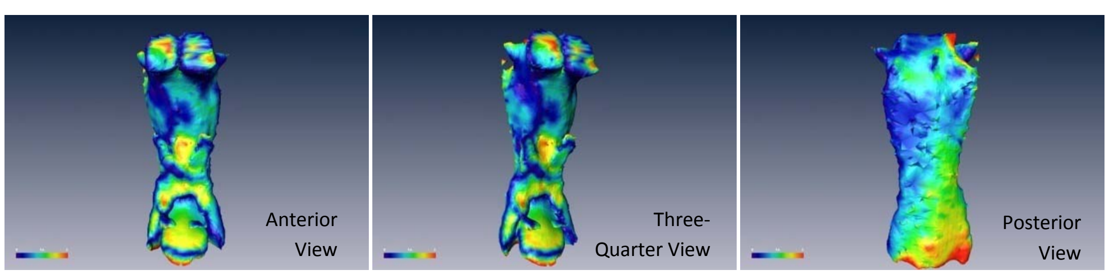


Figure 18: Color map of airway of one airway in which blue depicts least change between two superimpositions, and red indicates the most change for each voxel composing the surface rendered volumetric view

The scale was set so that “blue” represented the least amount of change (0 voxel) and “red” color showed the most amount of change (≥ 3 voxels). Voxels in our CB MercuRay system with a 12-inch field of view was equivalent to $0.376mm^3$.[64] Therefore, the range of change visible is 0-1.13mm.

STATISTICS

Comparison of means: Maxillary only group

A Kruskal-Wallis test was used to examine percent airway volume changes based on amount of maxillary changes. In the maxillary only group, the amount of surgical movement was subdivided as: slight maxillary advancement (1-4mm), moderate maxillary advancement (5-6mm), significant maxillary advancement (7mm +).

A Mann-Whitney statistical test was applied to examine if the change in the airway reached a maximum plateau with surgical movement in the maxilla. In other words, does the airway volume change begin to change direction (from positive to negative) or reach a maximum volume with increasing surgical movement? In order to examine this, <6mm and ≥6mm groups were compared.

Comparison of means: Mandibular only group

Similar to the maxillary only group, a Kruskal-Wallis test was used to examine percent airway volume changes based on amount of mandibular changes. The amount of surgical movement was broken down into: slight mandibular movement (1-5mm), moderate mandibular advancement (6-7mm), and severe mandibular advancement (8mm +).

A Mann-Whitney test was then utilized to examine if increasing surgical movment in the mandible began to actually decrease the airway volume or if a maximum volume is reached despite increasing mandibular movement. The groups of <7mm and ≥7mm were compared.

Correlation

A Spearman Signed Rank test was used to examine the correlation of percent volume change with the surgical movement performed in each of the three different groups.

Reliability

A "pilot group" of data was collected to test the repeatability of our patient instructions and airway segmentation techniques. We used a C*oefficient of Repeatability* (CR) test to analyze our methods. Since the same method was used, the mean difference should be zero. The CR can be calculated as 1.96 (or 2) times the standard deviations of the differences between the two measurements. This means that there was a 95% probability of repeated whole airway volume measurements differing by 241 mm^3. In addition, a paired t-test was done. Based on the results of this test (*p*=0.39) there was not a statistically significant difference between the measurements since the standard deviation is 123.2 mm^3. These tests can be seen in tables 5 and 6.

Pilot Group—Coefficient of Repeatability										
Difference	N	Lower CL Mean	Mean	Upper CL Mean	Lower CL Std Dev	Std Dev	Upper CL Std Dev	Std Err	Min.	Max.
Whole_Airway1 - Whole_Airway2	5	-206	-52.99	99.988	73.814	123.2	354.02	55.097	-236.1	100.63

Table 5. Pilot Group—Coefficient of Repeatability

Pilot group—T-Test			
Difference	DF	t Value	Pr > |t|
Whole_Airway1 - Whole_Airway2	4	-0.96	0.3907

Table 6. Pilot Group—T-test

Intra-rater variability

Coefficient of Repeatability was also used to analyze the measurements for subjects in the test group to determine any variability within the measurements by the same rater (principle investigator). The PI randomly chose six airways to be repeated one week after the initial airway measurement. The resulting coefficient of repeatability was 876.77 mm^3. This means that there is a 95% probability of repeated airway volume measurements differing by about 877 mm^3. In other words, a difference greater than 877 mm^3 would be greater than that expected by chance ($p<0.05$). Also, a paired t-test was done and, again, the results did not indicate that there is a statistically significant change in the measurement of these airway volumes (*p*=0.52). These tests are shown in table 7.

Repeated Measurements—Coefficient of Repeatability										
Difference	N	Lower CL Mean	Mean	Upper CL Mean	Lower CL Std Dev	Std Dev	Upper CL Std Dev	Std Err	Min.	Max.
Measurement1 - Measurement2	6	-342.6	126.85	596.29	279.23	447.33	1097.1	182.62	-397.5	807.81

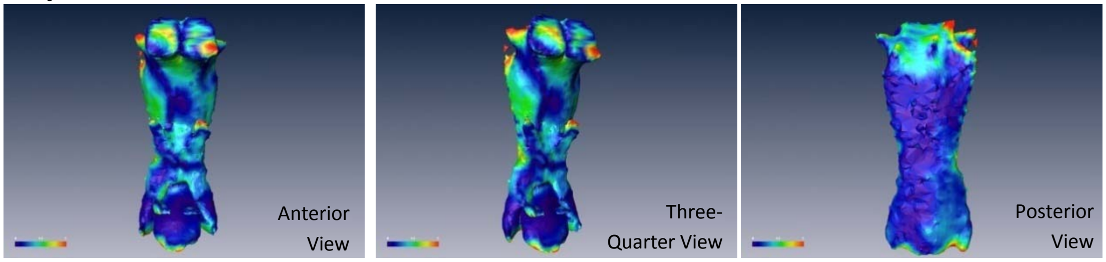
Repeated Measurements—T-Test			
Difference	DF	t Value	Pr > |t|
Measurement1 - Measurement2	5	0.69	0.5183

Table 7. Repeated Measurements—Coefficient of Repeatibility and T-test

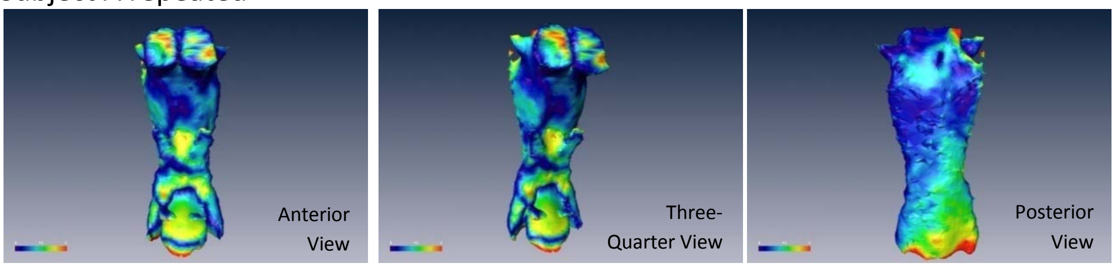
Repeatability of airway color maps

Five random subjects were selected to have their color maps repeated, one week after the initial color map, to assess repeatability in the creation of the images. This can be seen in figure 19.

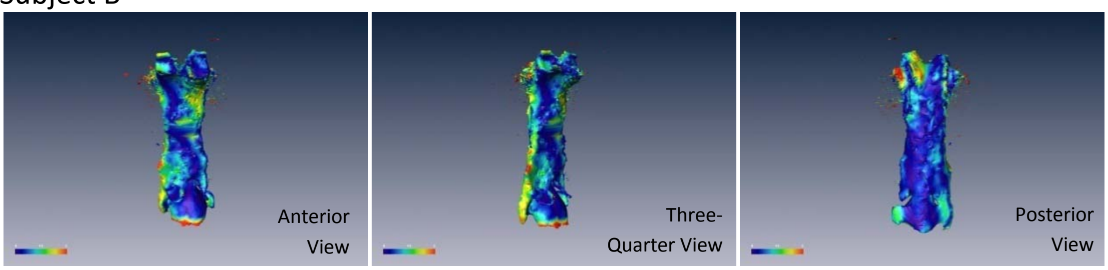
Subject A



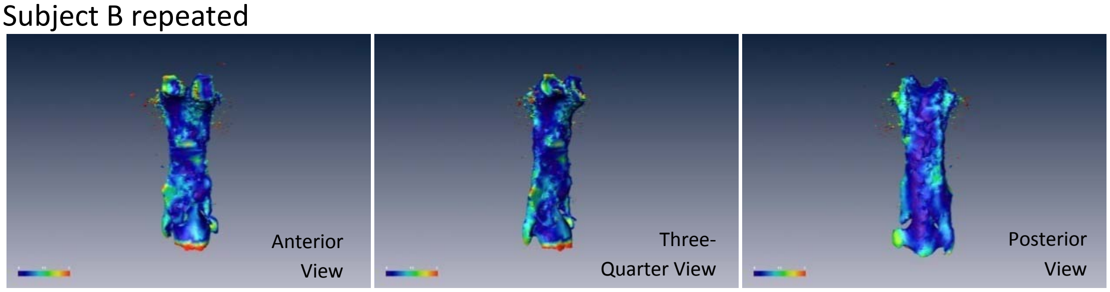
Subject A repeated



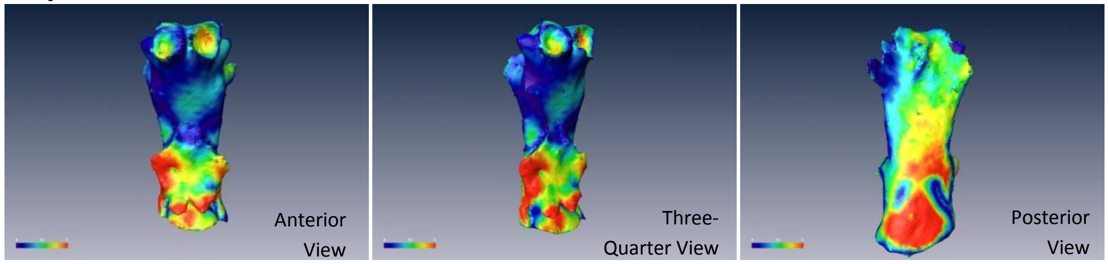
Subject B



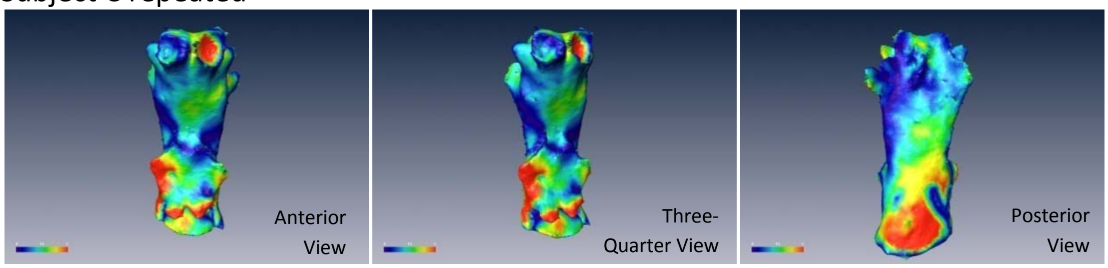
Subject B repeated



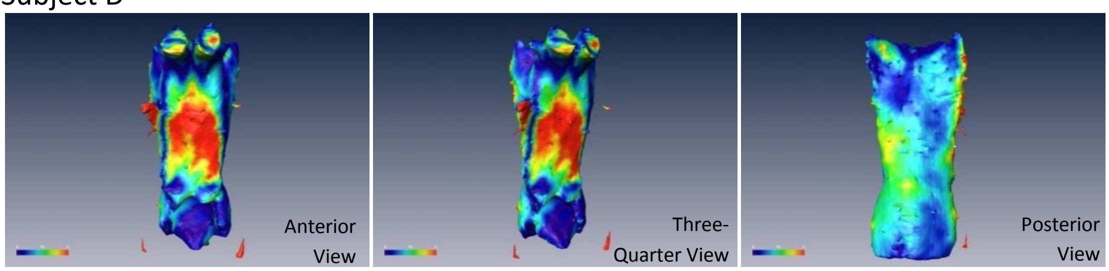
Subject C



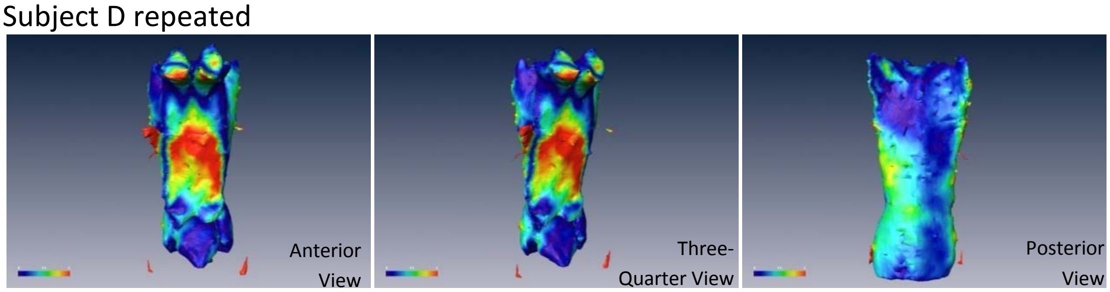
Subject C repeated



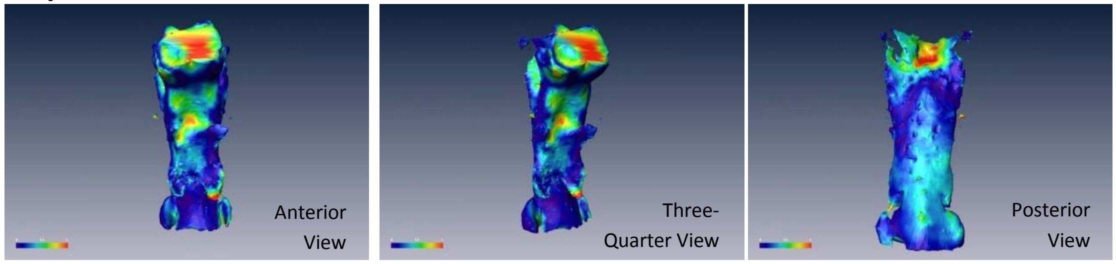
Subject D



Subject D repeated



Subject E



Subject E repeated

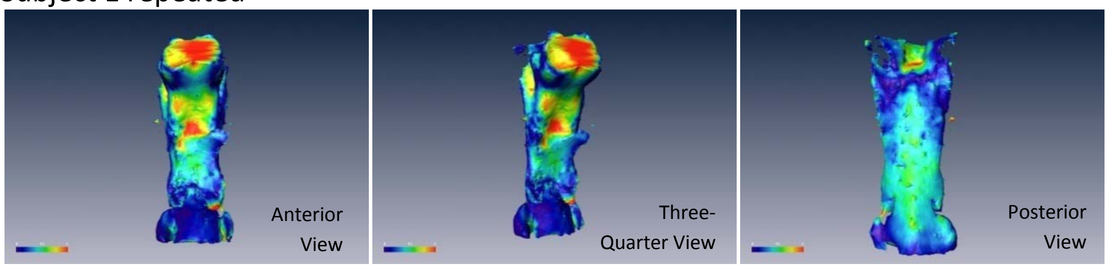


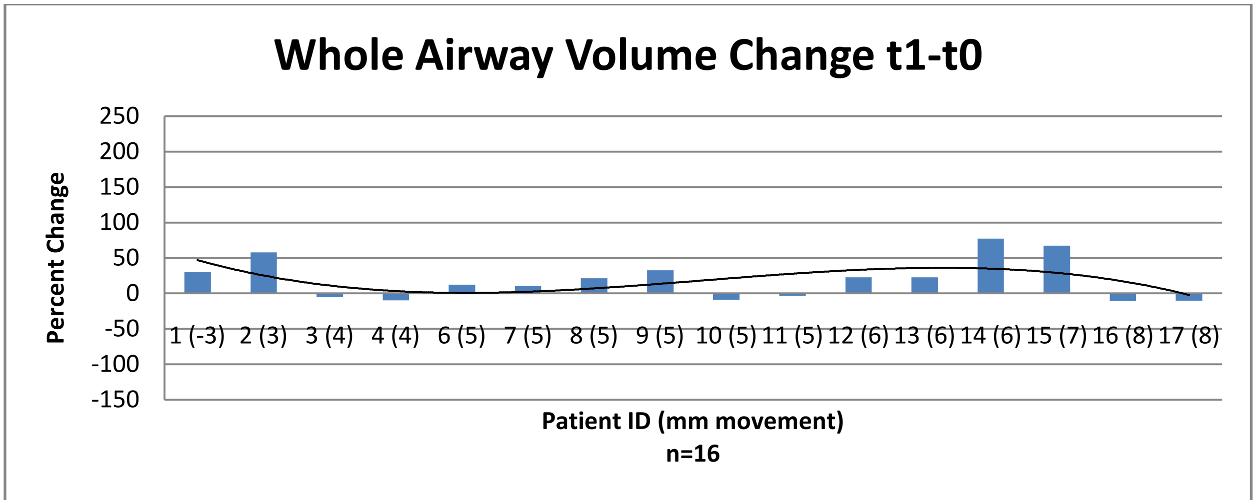
Figure 19. Color maps repeated for five patients using an anterior (left), oblique (middle), and posterior view (right) showing differences ranging from blue (0) to red (1.3mm)

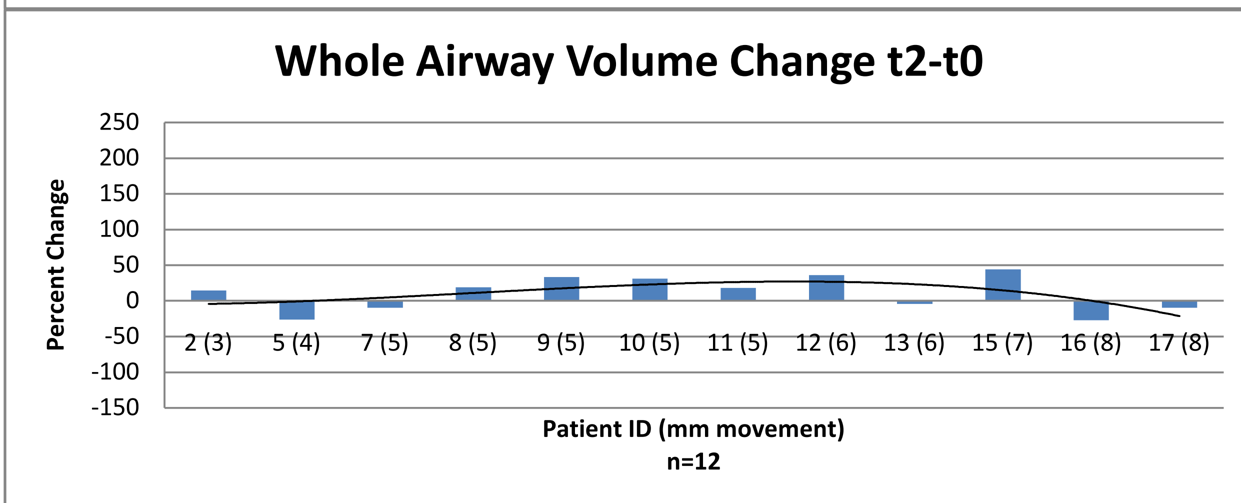
Qualitatively, it can be seen that while most of the repeated color maps are close, none are identical between the first and second images. In particular it seems that Subject A had the greatest differences between the two color maps and Subject D has the least difference.

RESULTS

Individual effects of surgery on airway volume—Maxillary Only Group

The effects of surgical *maxillary* movement on the whole airway can be seen in Figure 20 with an order 3 polynomial trendline. The airway volume changes, as defined by percentage change between any of the three timepoints, and ranked by increasing maxillary displacement. When comparing t2 to t0, it appears that the airway actually begins to decrease as the maxilla is advanced 7mm and more.





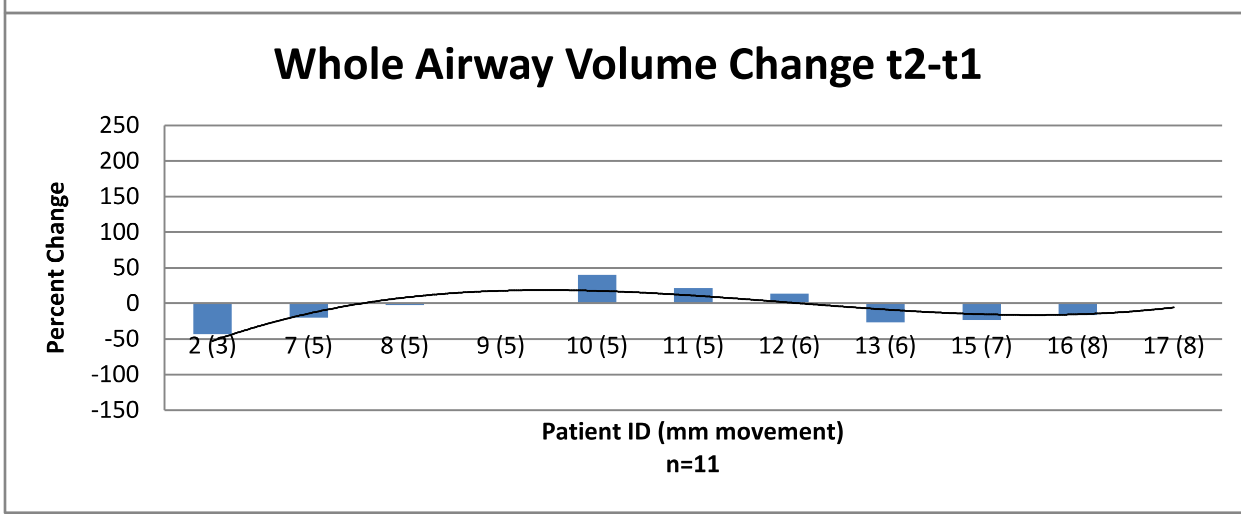


Figure 20. Maxillary Only group-Whole Airway: Change in the volume of the total airway for each subject that had maxillary surgery, ranked by the amount of change in position for the maxilla, and defined as a percentage change when comparing the actual volumes at the three timepoints, t0=pre-surgical; t1="immediate post-surgical;" t2="long-term" post-surgical

The effects of surgical *maxillary* movement on the nasopharynx can be seen in Figure 21 with an order 3 polynomial trendline. There does not appear to be a clear trend showing that the nasopharynx increases in volume as the maxilla is advanced. However, there is considerable individual variation where some patients' nasopharynx volumes actually decreased with maxillary advancement of 7mm or more.

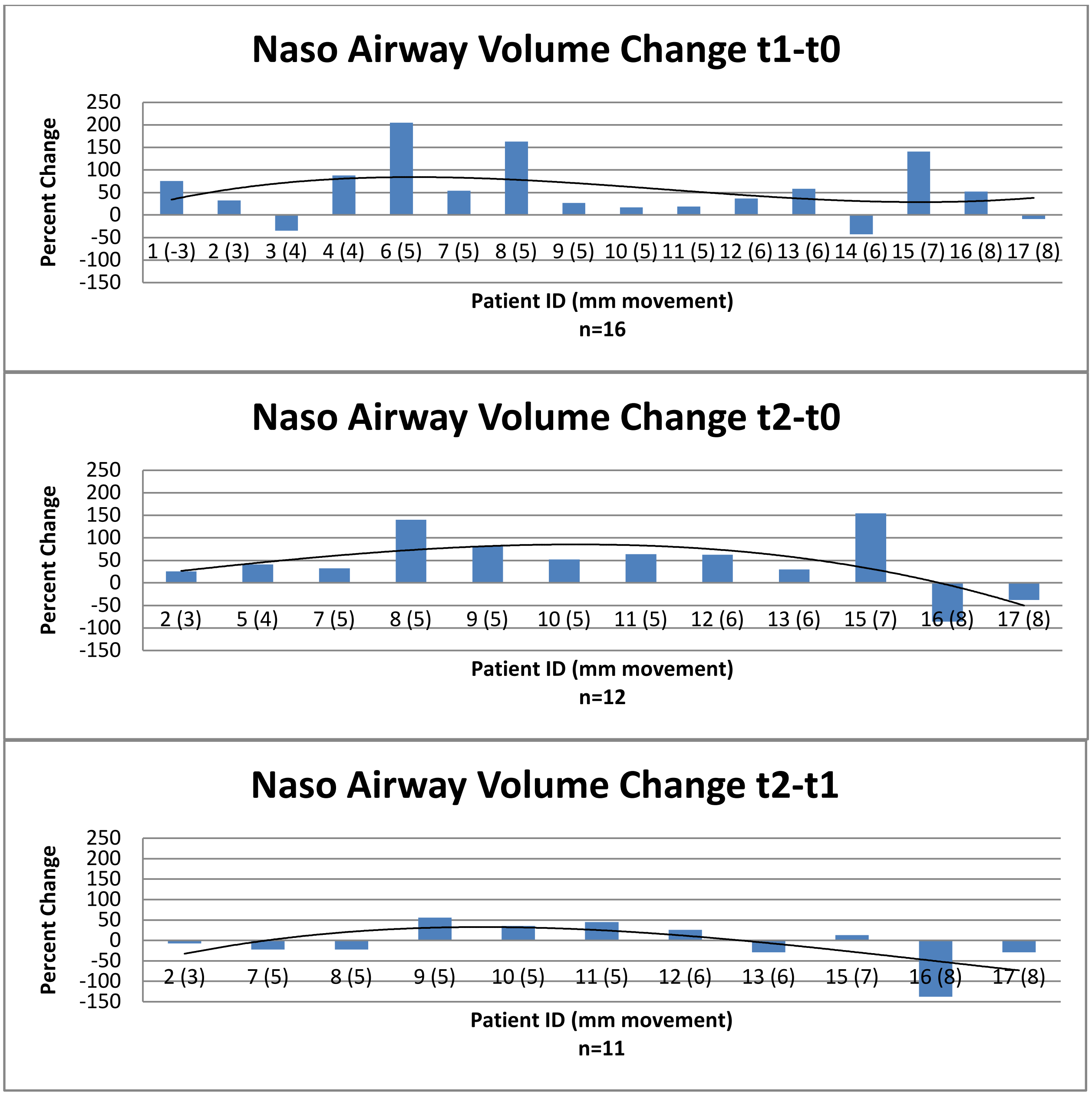


Figure 21. Maxillary group—nasopharynx

The effects of surgical *maxillary* movement on the oropharynx are seen in Figure 22. An order 3 polynomial trendline can be seen. The displacement of the maxilla has less effect on the oropharynx volume than the nasopharynx, without a clear trend that more surgical displacement of the maxilla leads to increased volume of the oropharynx.

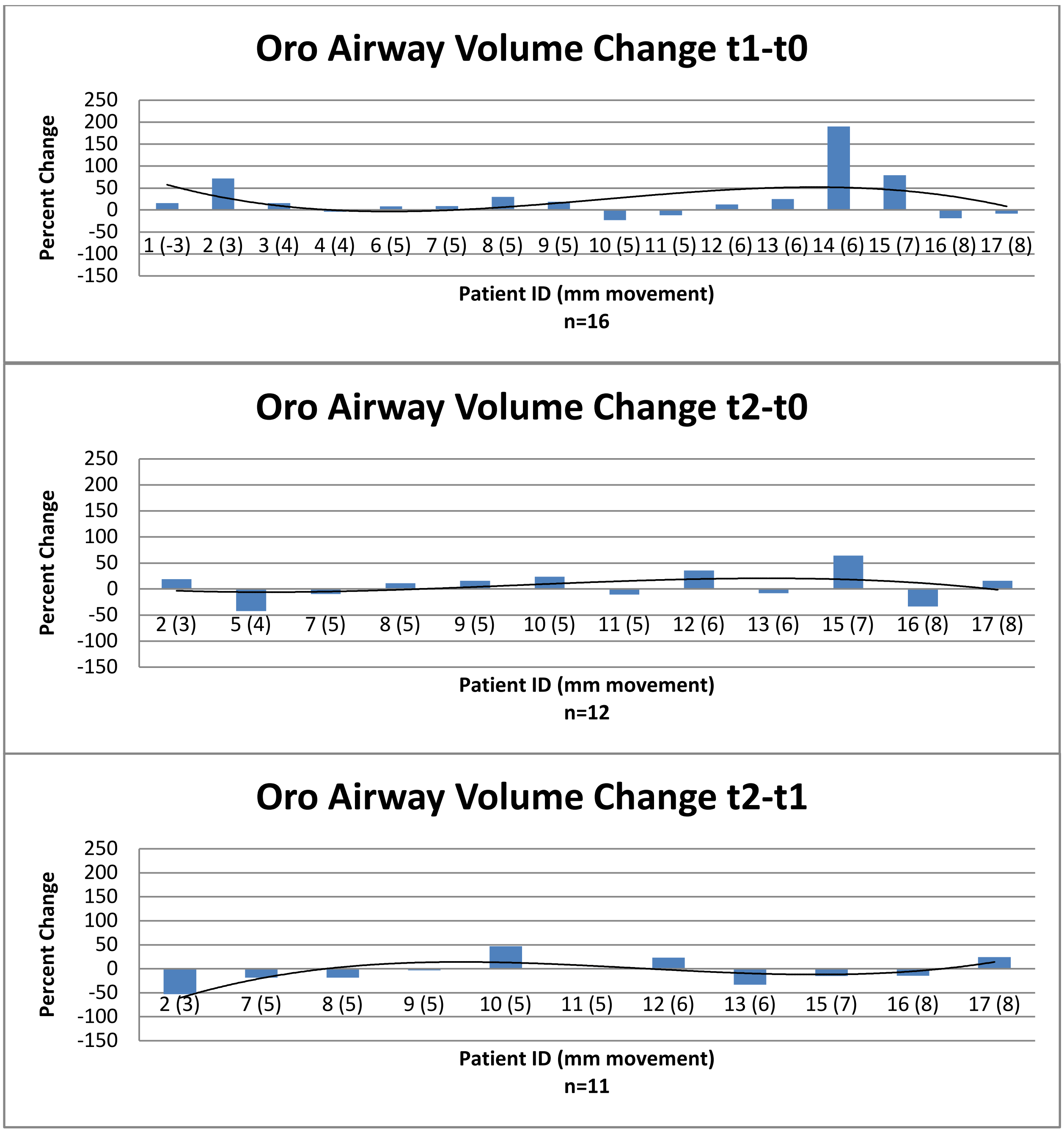


Figure 22. Maxillary group—oropharynx

The effects of surgical *maxillary* movement on the hypopharynx can be seen in Figure 23 with an order 3 polynomial trendline. Displacement of the maxilla does not have a trend in how it affects the hypopharynx with some patients demonstrating a decrease in the hypopharynx around 6-7mm.

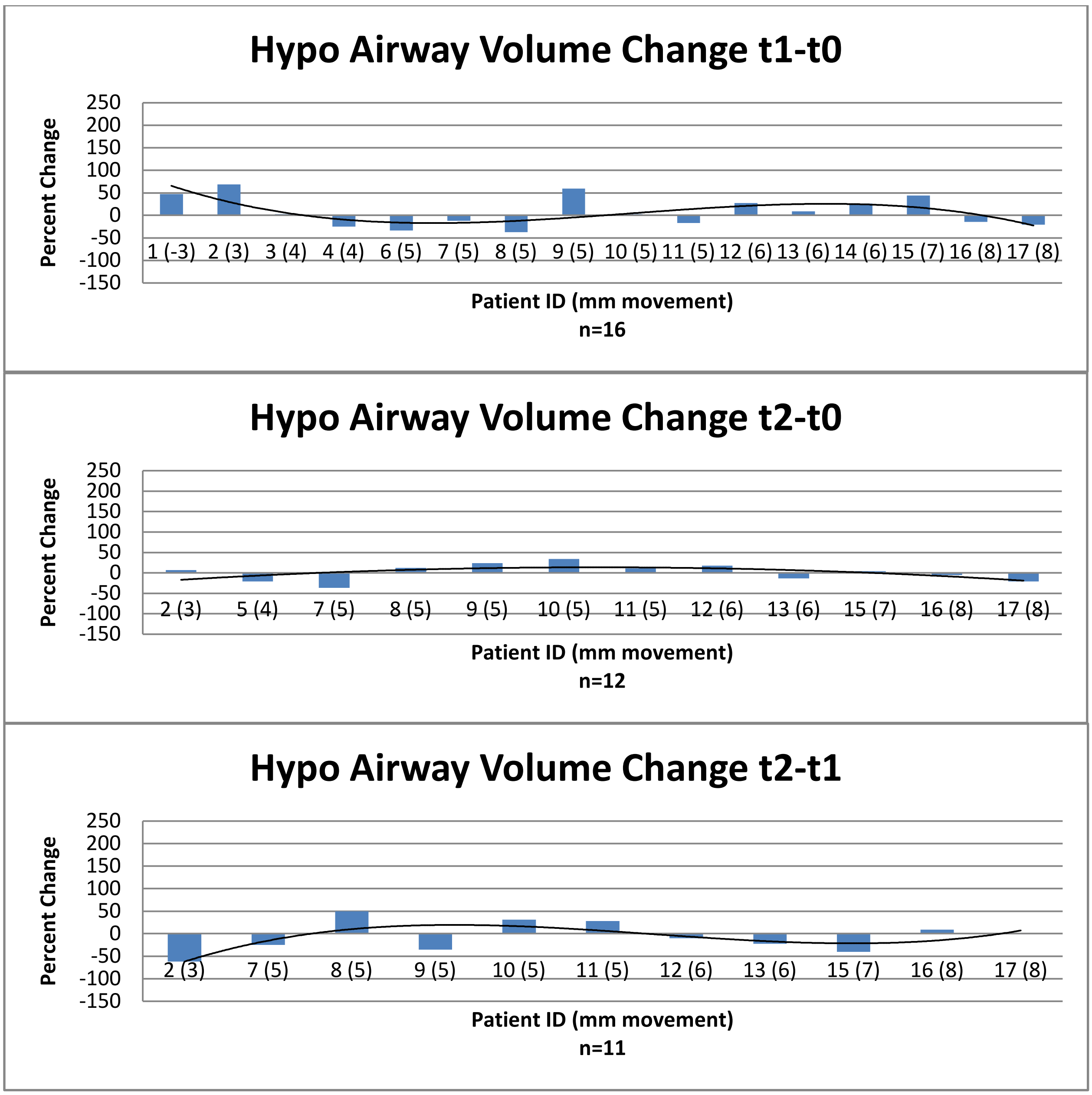


Figure 23. Maxillary group—hypopharynx

MANDIBULAR ONLY GROUP

The effects of surgical *mandibular* movement on the whole airway is seen in Figure 24 with an order 4 polynomial trendline. There appears to be a slight but minimal effect of the amount/direction of mandibular displacement by surgery on the total airway volume.

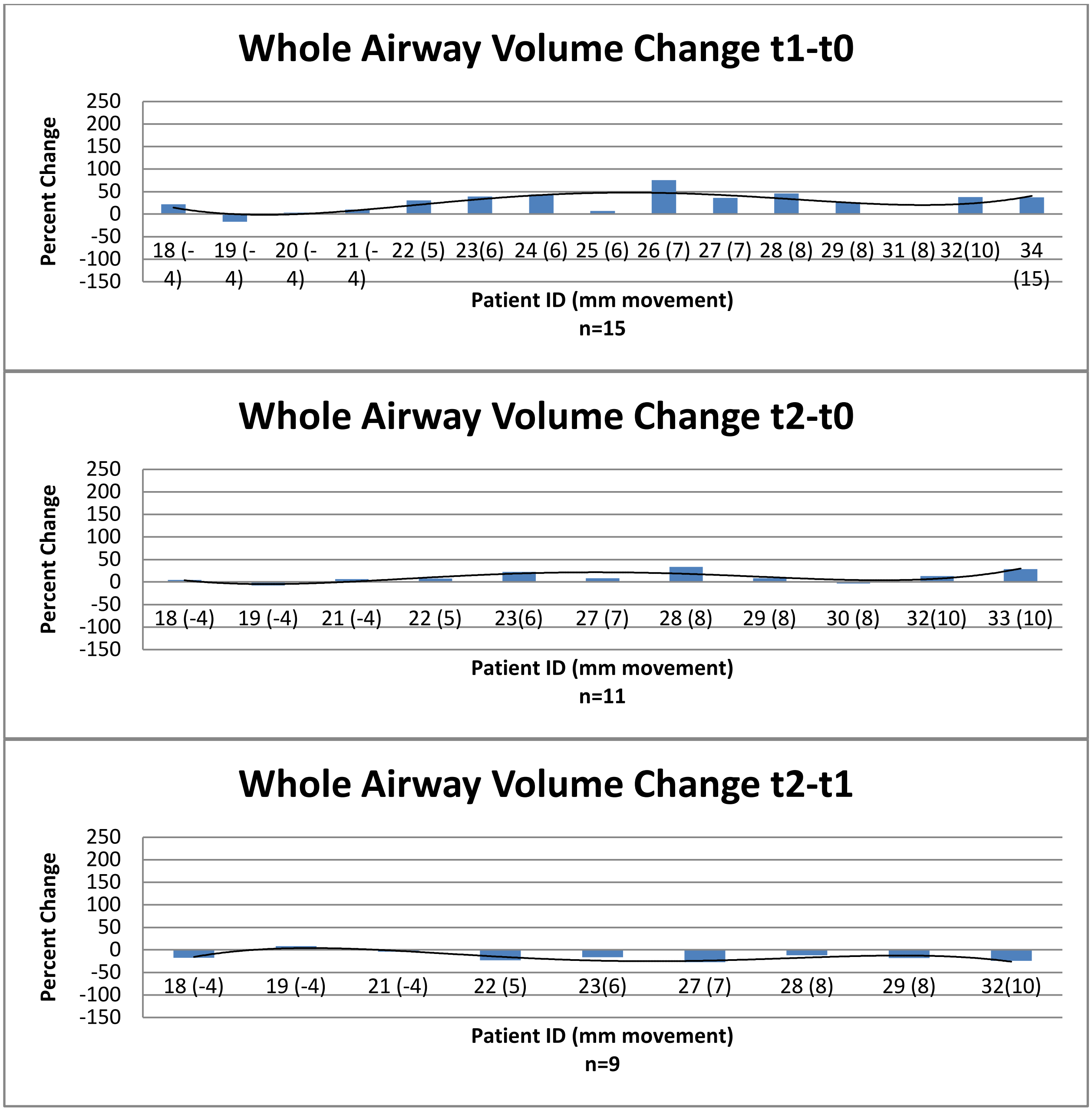


Figure 24. Mandibular group—whole airway

The effects of surgical *mandibular* movement on the nasopharynx airway can be seen in Figure 25. An order 4 polynomial trendline can be seen drawn over the charts. Comparing the percentage change from the “long-term” post-surgical to the pre-surgical CBCT scan (t2-t0) shows that the nasopharynx airway volume actually decreases with surgical advancement of 8-10mm.

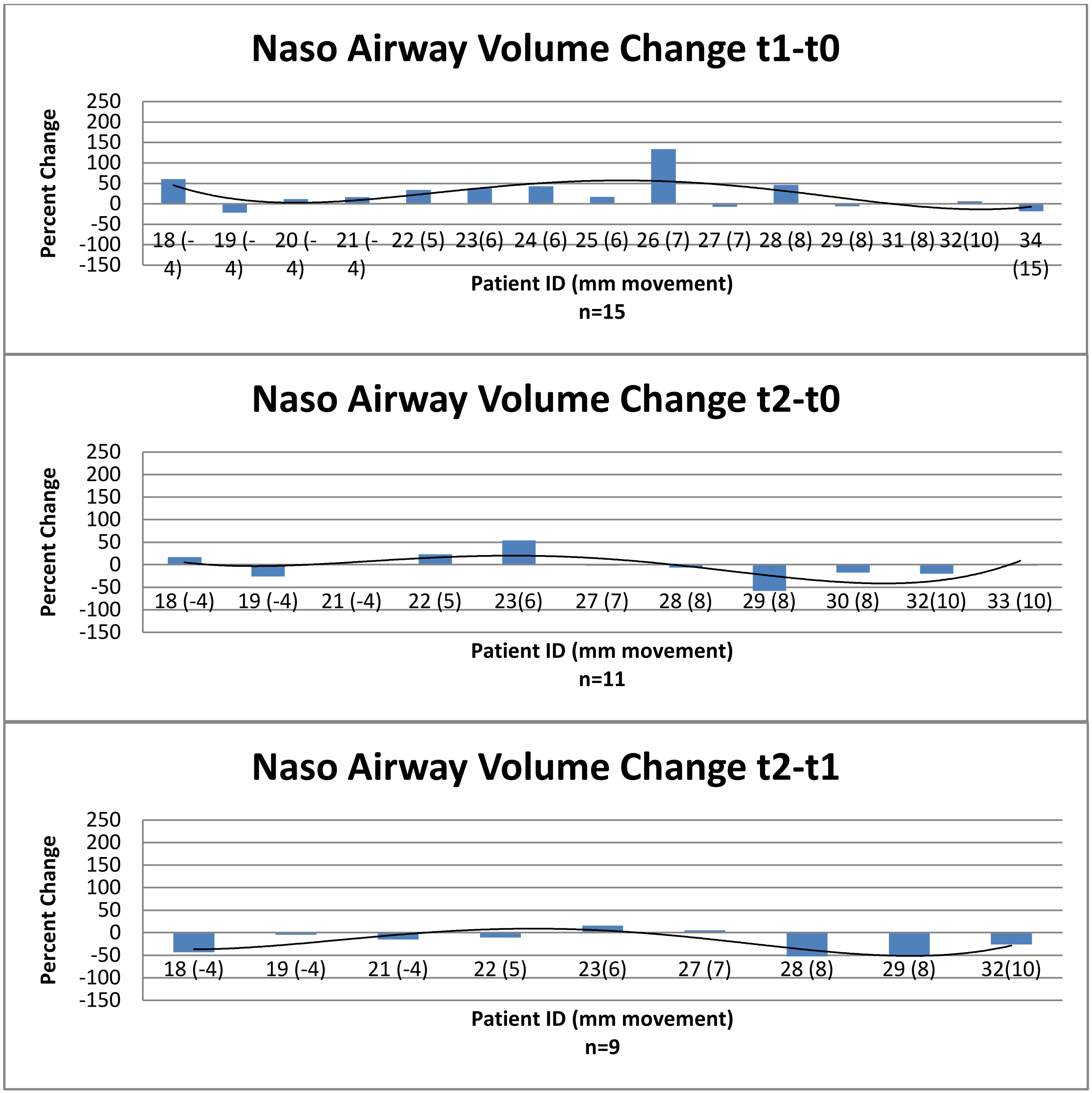


Figure 25. Mandibular group--nasopharynx

The effects of surgical *mandibular* movement on the oropharynx airway are seen in Figure 26. An order 4 polynomial trendline shows that the volume of the oropharynx changes with mandibular advancement and it occurs more markedly when the mandible is advanced by surgery >5mm. However, some relapse does occur as evident when comparing the percentage change between the two post-surgical timepoints (t2-t0).

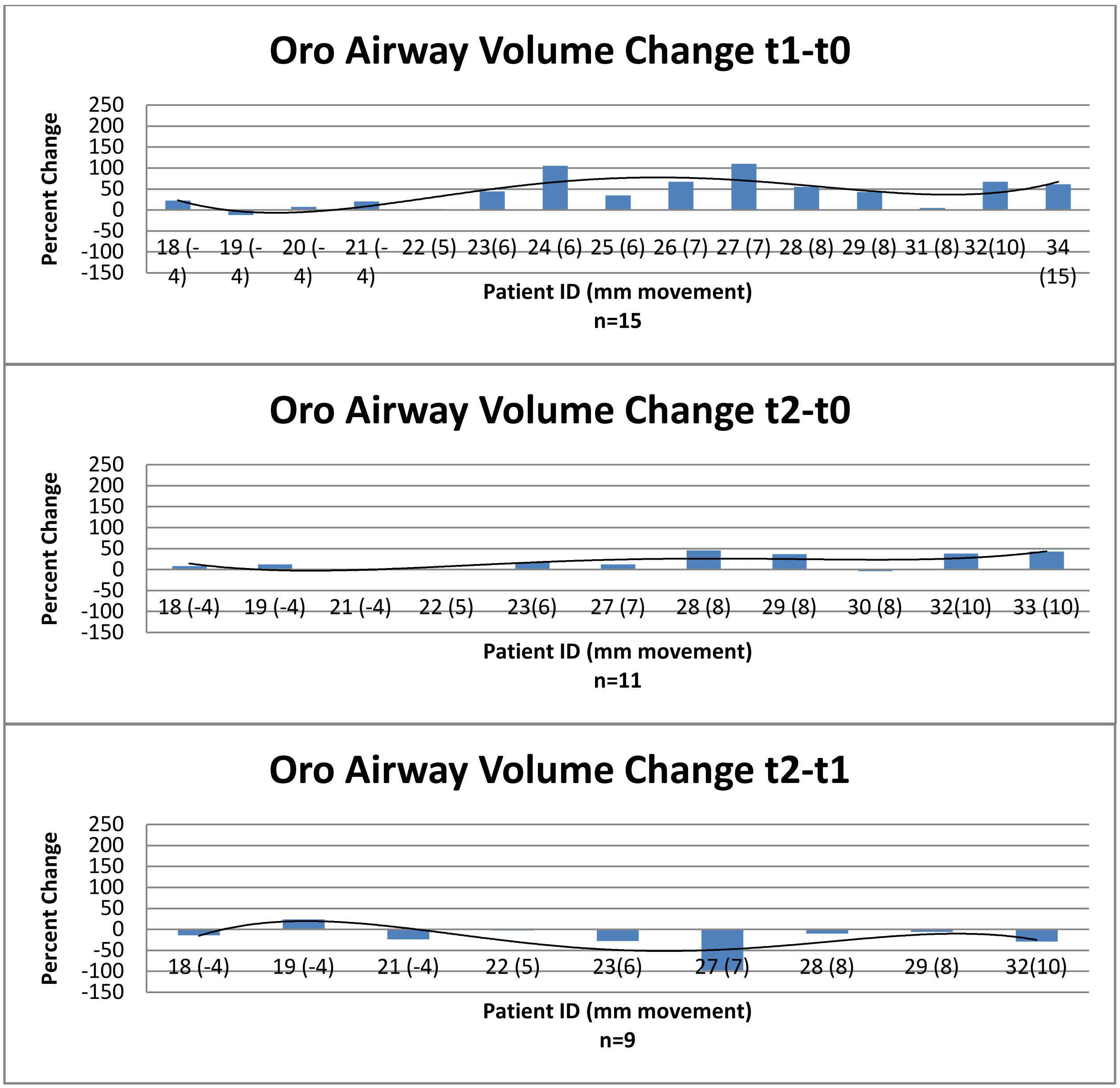


Figure 26. Mandibular group—oropharynx

The effects of surgical *mandibular* movement on the hypopharynx airway can be seen in Figure 27. An order 4 polynomial trendline can be seen drawn over the charts. Mandibular advancement seems to have little effect on the hypopharynx.

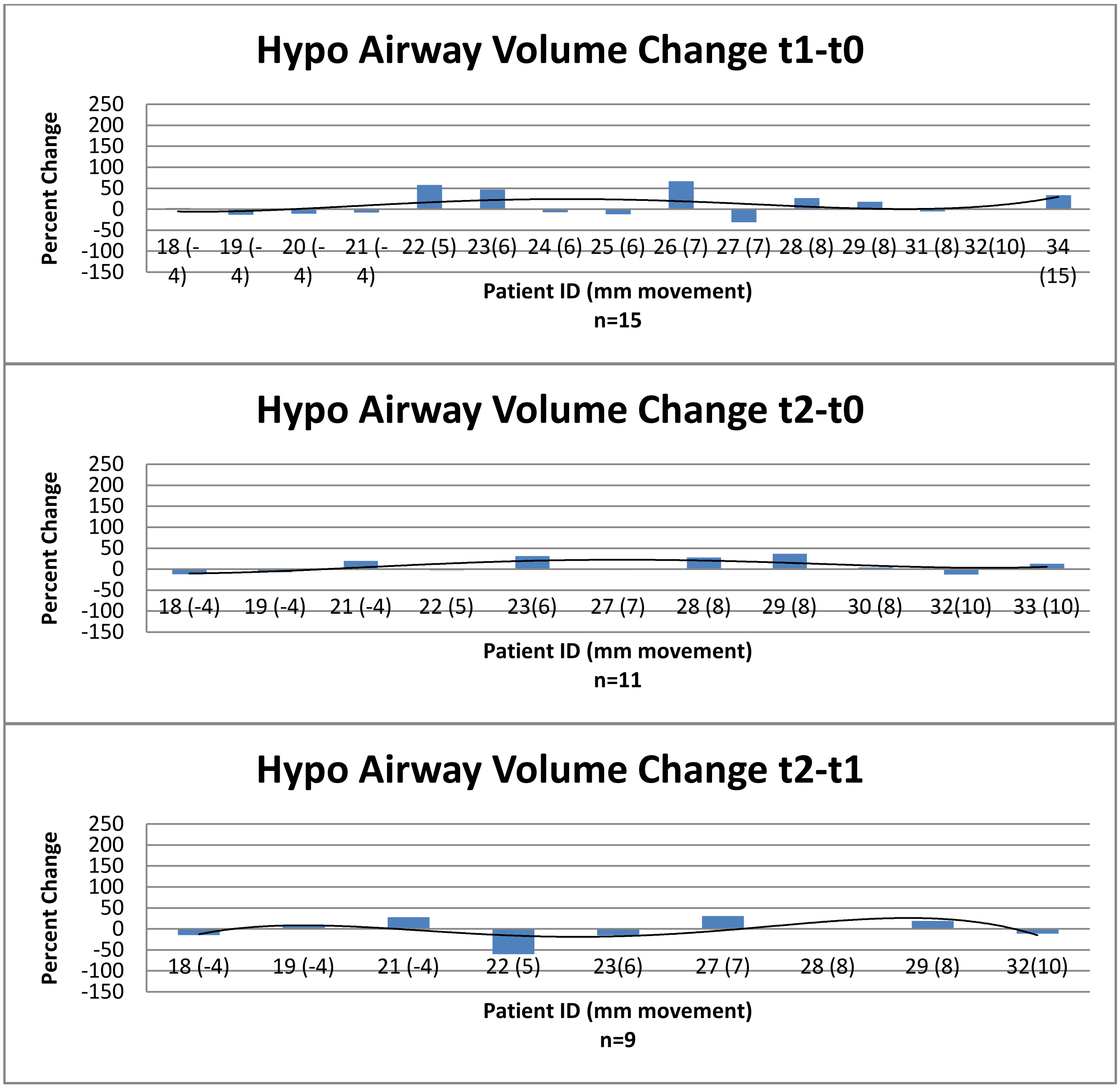


Figure 27. Individual effects of surgery on airway volume—Maxillary and Mandibular Surgery Group

The effects of surgical movement of both jaws on the whole airway are seen in Figure 28 with an order 4 polynomial trendline. The data show that despite extensive surgery manipulating both jaws, the effect on the airway is not predictable or extensive.

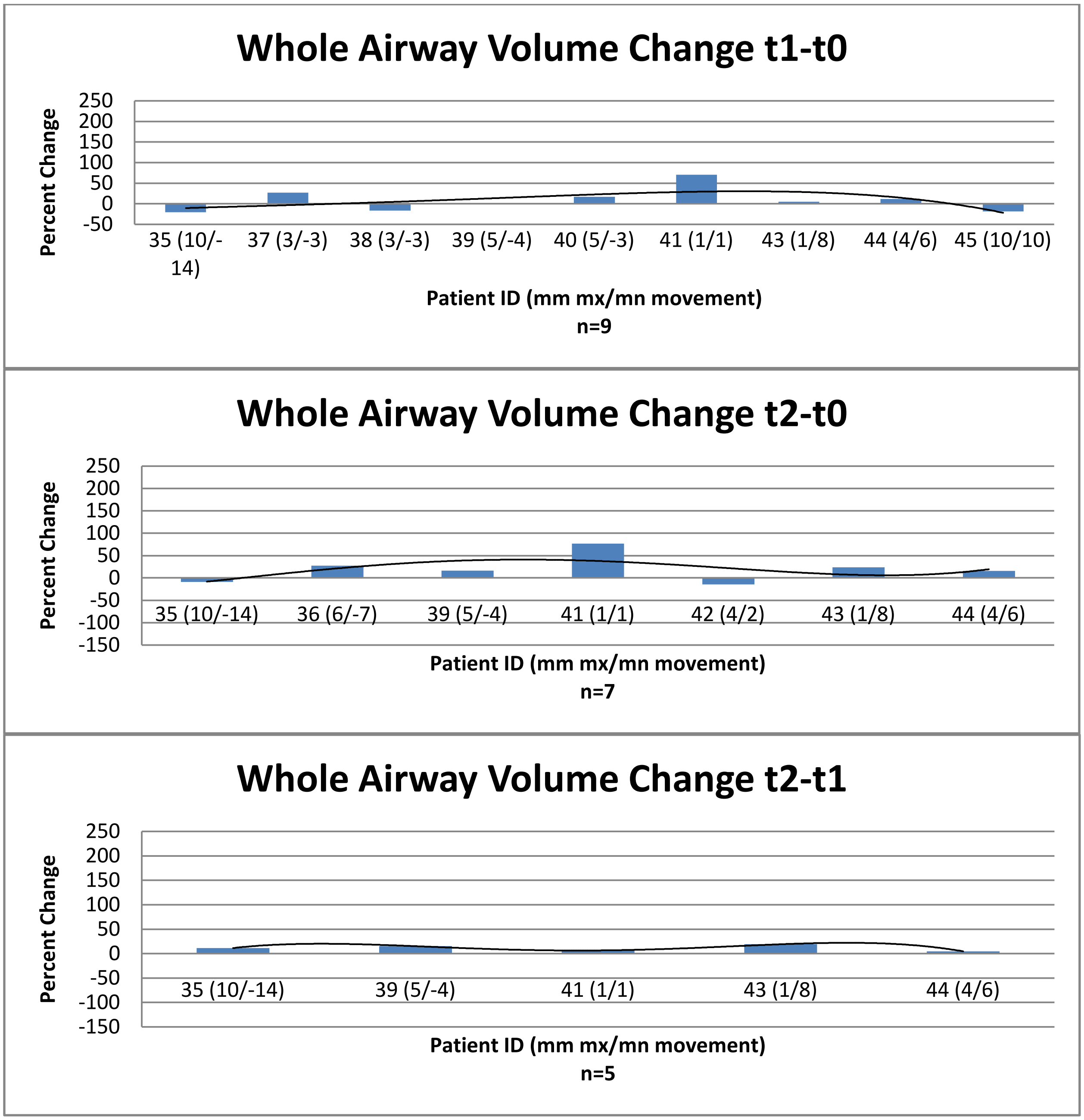


Figure 28. Two-jaw surgery group—Whole Airway: The displacement of the maxilla (left number) and mandible (right number) are shown for each patient starting with patients that have maxillary advancement with mandibular set-back and proceeding to patients that have both maxillary and mandibular advancement.

The effects of surgical movement of both jaws on the nasopharynx are seen in Figure 29. An order 4 polynomial trendline is seen drawn over the charts. A clear trend is not evident; some patients increase and some decrease in their nasopharynx volume.

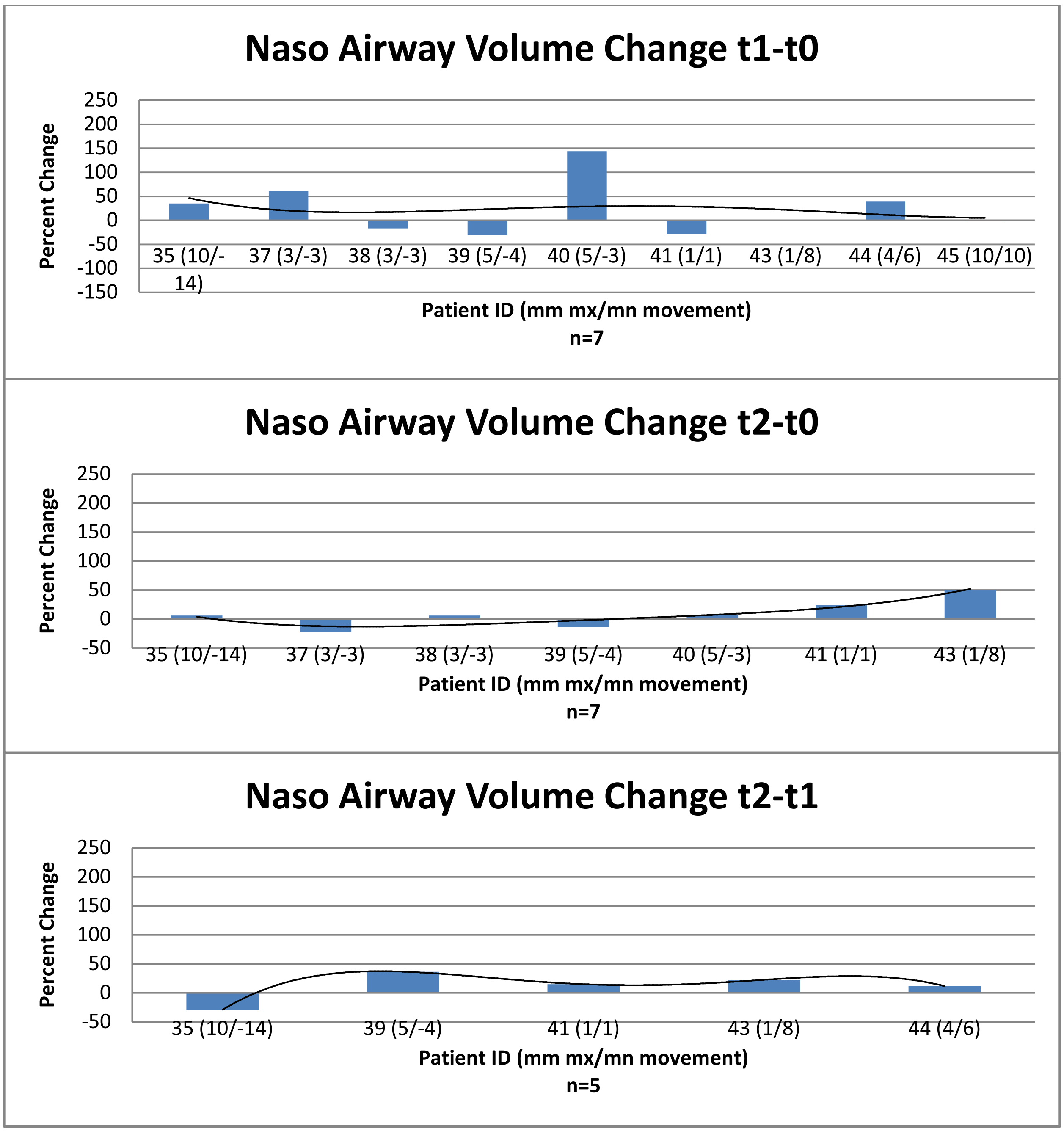


Figure 29. Two-jaw group—nasopharynx

The effects of surgical movement of both jaws on the oropharynx can be seen in Figure 30. An order 4 polynomial trendline can be seen drawn over the charts.

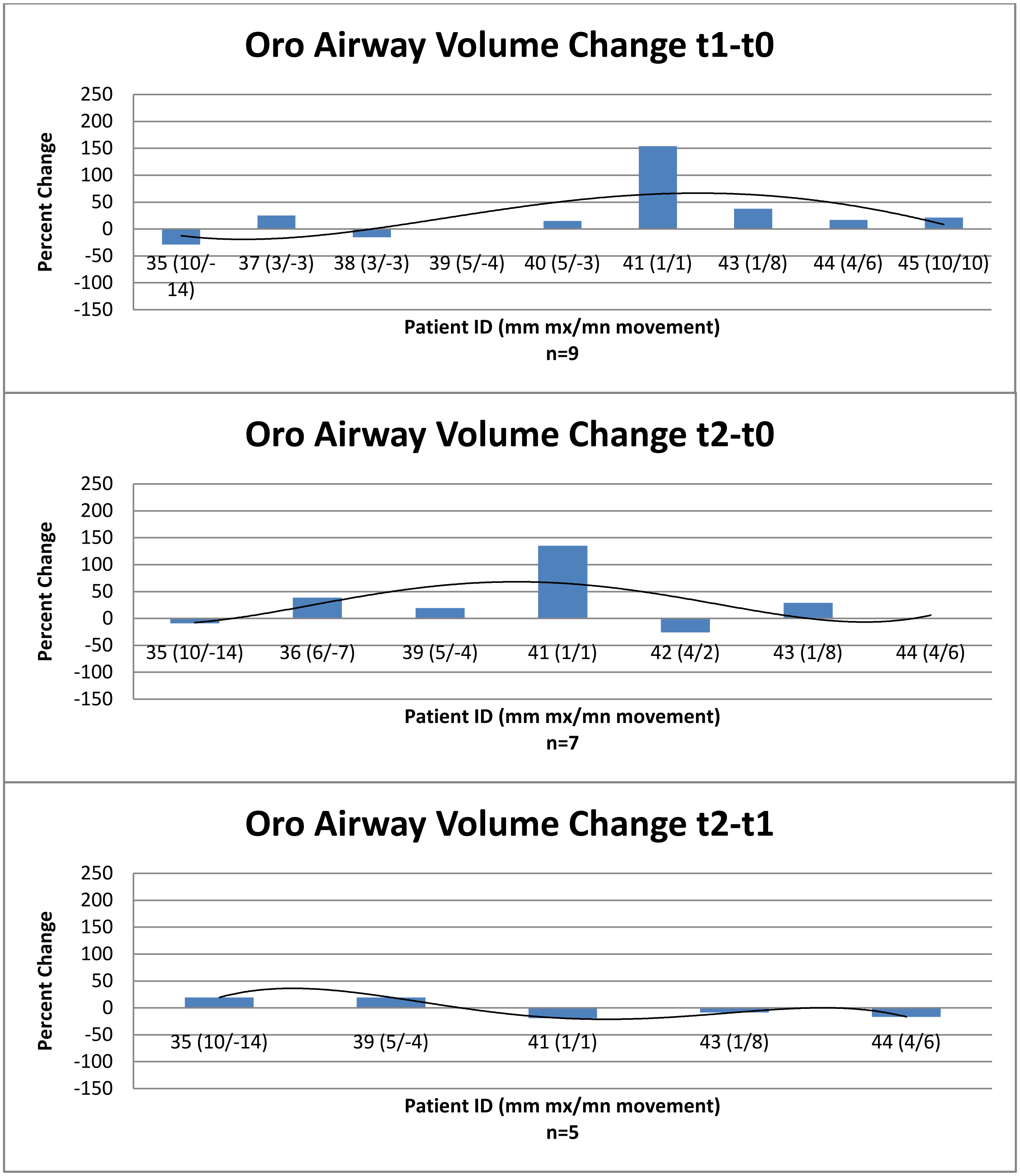


Figure 30. Two-jaw group—oropharynx

The effects of surgical movement of both jaws on the hypopharynx can be seen in Figure 31. An order 4 polynomial trendline can be seen drawn over the charts.

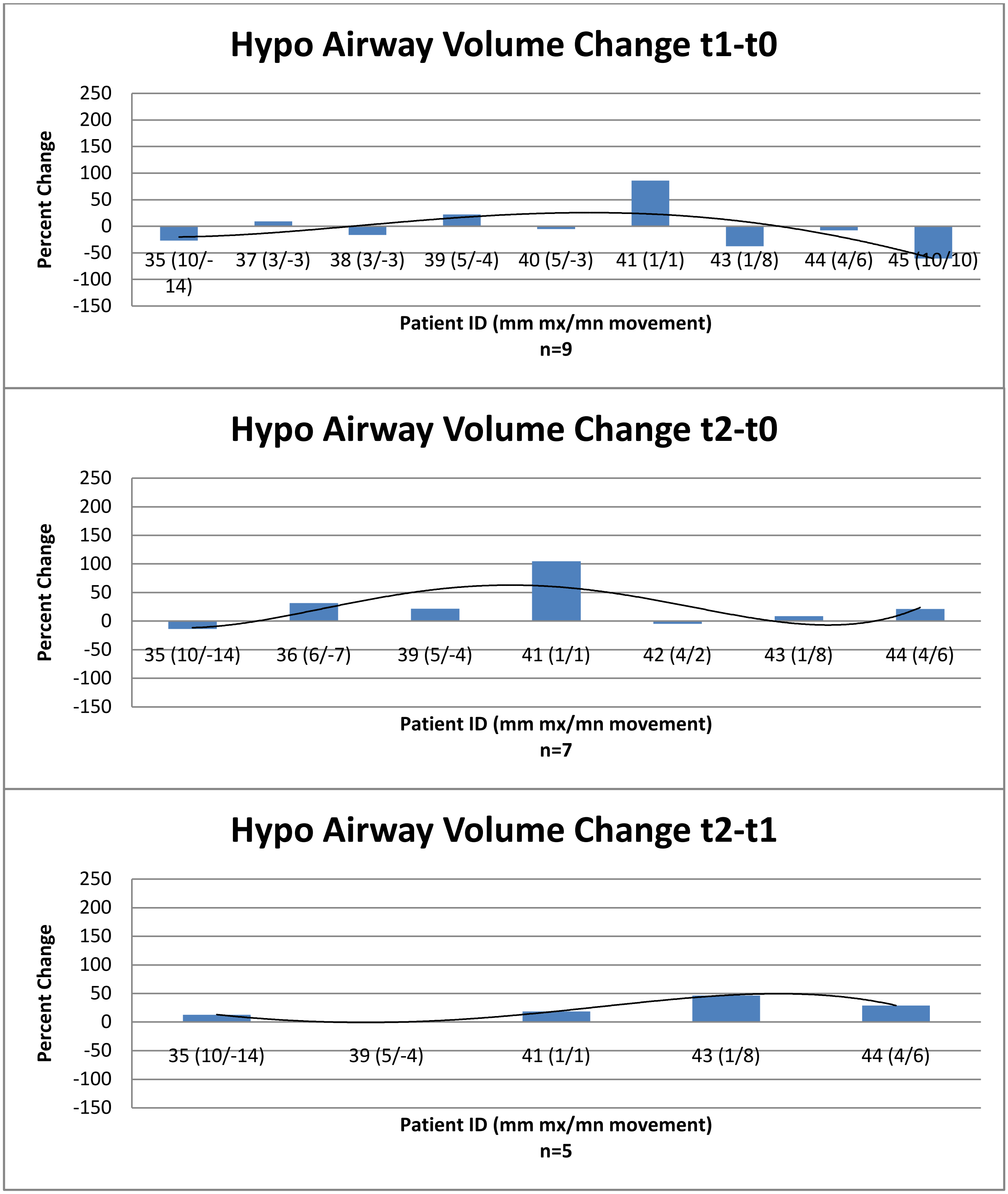


Figure 31. Two-jaw group--hypopharynx

Average airway volume change between timepoints

The mean effect of surgical movement of the maxilla is seen in Figure 32 depicting the average effect in all patients receiving this surgery. It is seen that maxillary advancement has the greatest long-term effect on the nasopharynx volume. Its greatest effect is an increase in nasopharynx volume (60%) and less with the oropharynx. 16 subjects are included in each of these graphs

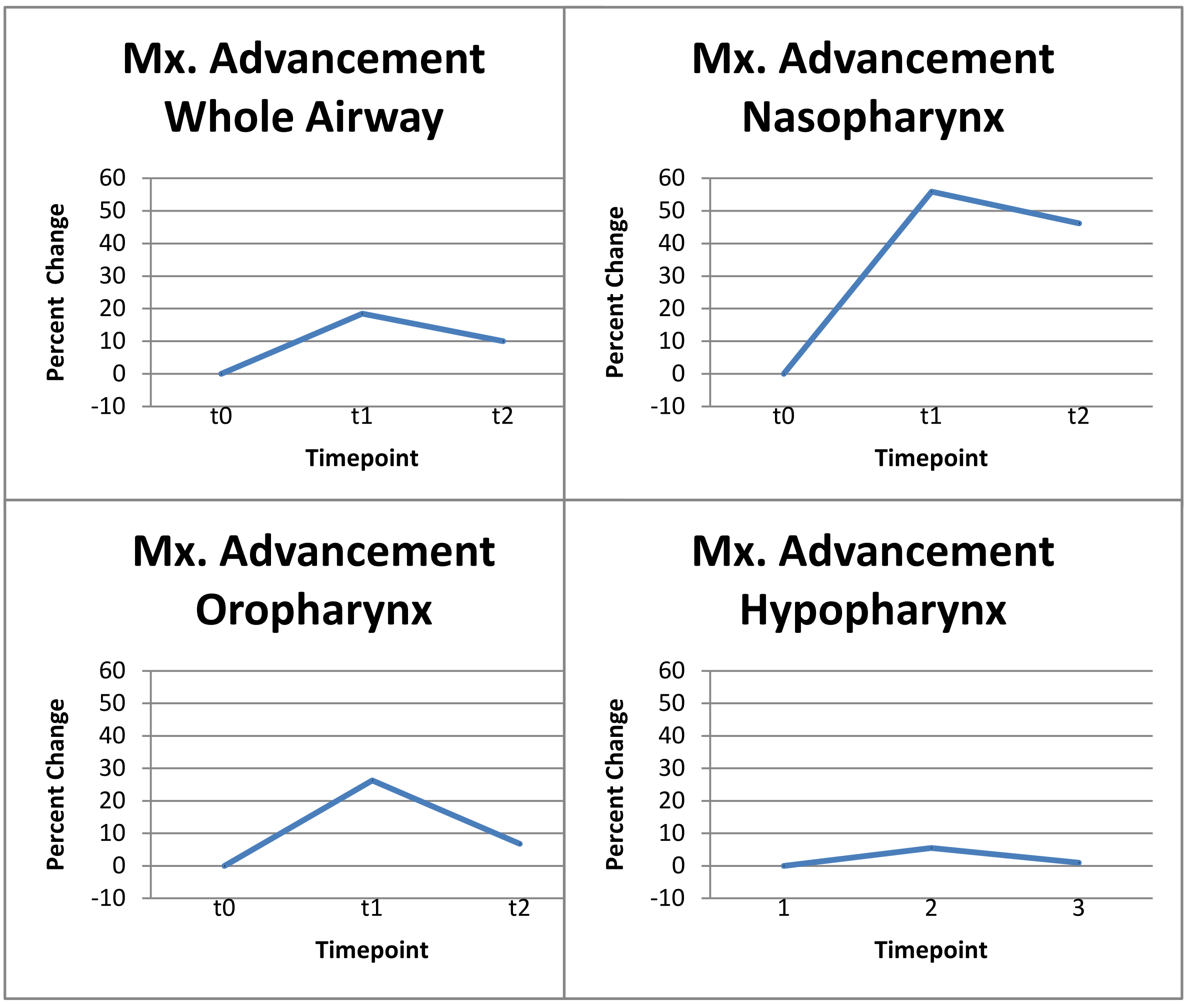


Figure 32. Maxillary only group volume changes between timepoints: The percentage change in volume for the airway as an average for the patients that had surgery to advance only their maxilla is depicted for the total airway and the three subdivisions at three timepoints depicting pre-surgery (t0), "immediate" post-surgical, and "long-term" post-surgical.

The mean effect of surgical *advancement* on the mandible is seen in Figure 33. Mandibular advancement has the greatest long-term effect on the oropharynx (50%) and to a lesser extent, on the total airway.

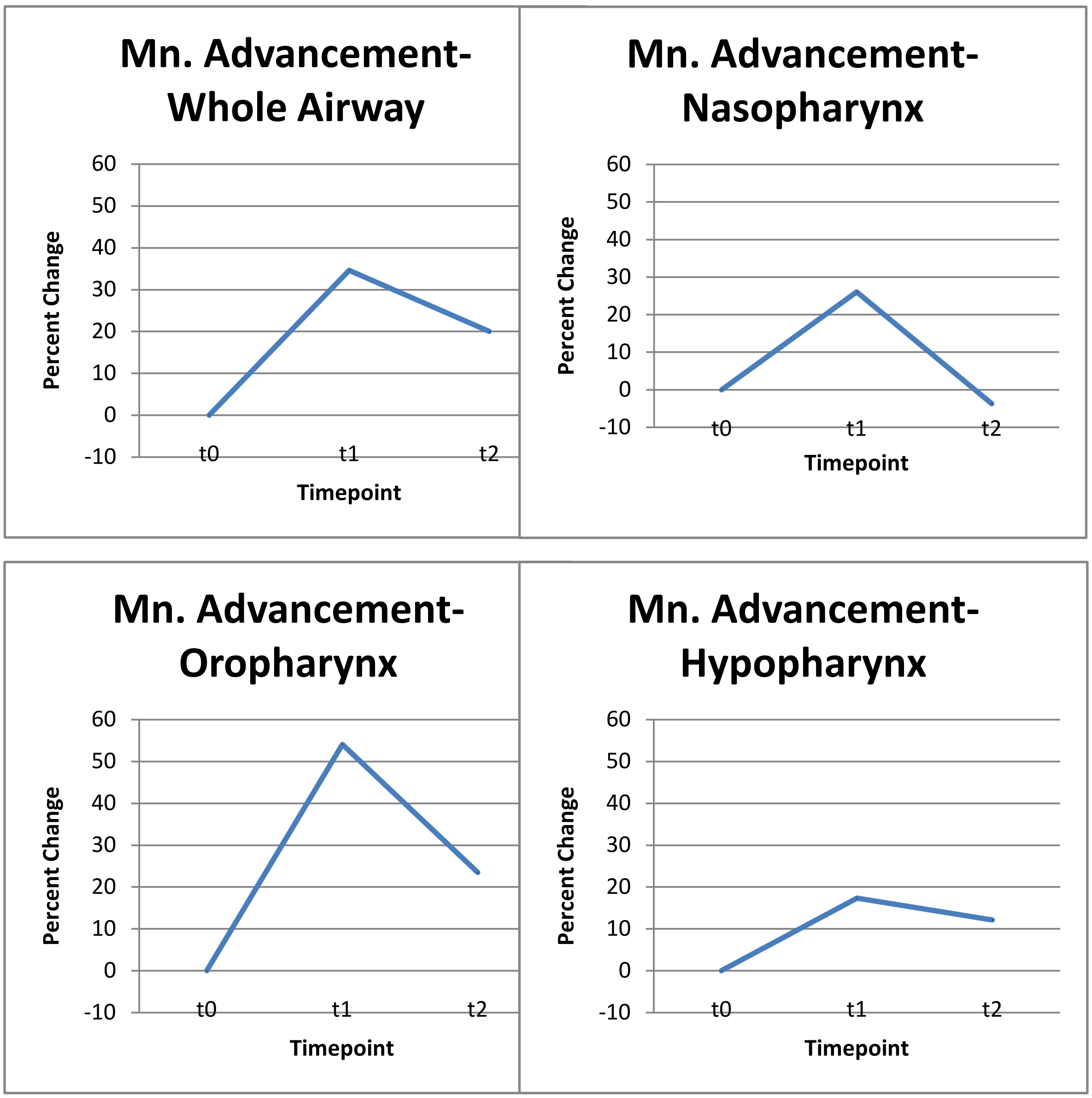


Figure 33. Mandible advancement only group showing volume changes between timepoints.

The mean effect of surgical setback on the mandible is seen in Figure 34. Mandibular setback seems to have a very minimal effect on the airway with the nasopharynx slightly decreasing, oropharynx slightly increasing, and no long-term effect on the hypopharynx.

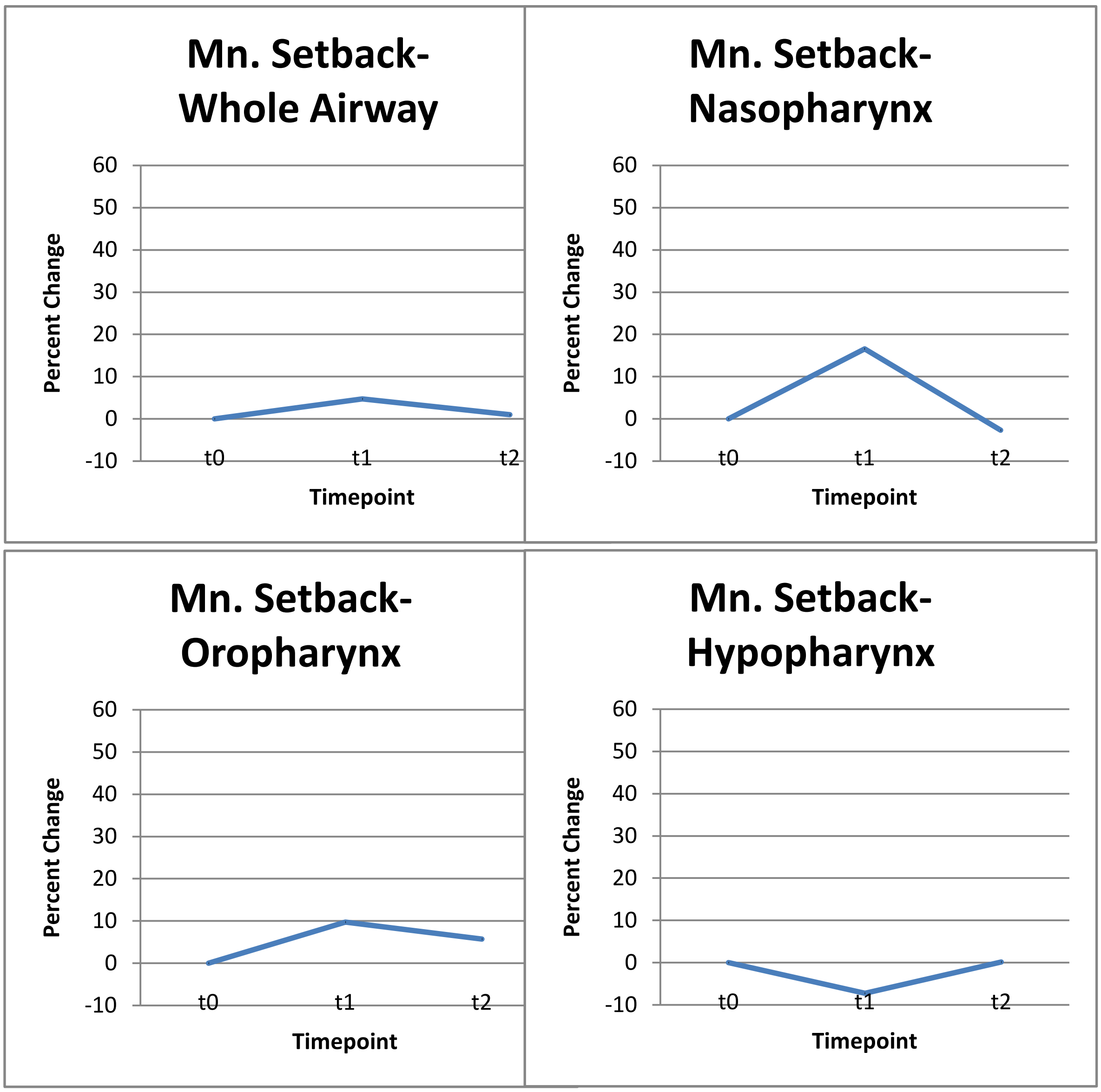


Figure 34. Mandible setback only group showing volume changes between timepoints.

Comparison of means—maxillary only group.

The Kruskal-Wallis test to examine significant changes of the airway between the three timepoints in patients who had only a maxillary advancement revealed no significance (table 8).

Variable	MAXMOVEMENT = slight (1-4mm) (N=4)	MAXMOVEMENT = moderate (5-6mm) (N=9)	MAXMOVEMENT = severe (7+mm (N=3)	P-Value
Whole Change t1t0p (Median (min-max))	-5.2 (-9.7 to 57.9)	21.3 (-9.0 to 77.3)	-10.0 (-10.6 to 67.4)	0.47
Whole Change t2t0p (Median (min-max))	-5.9 (-26.1 to 14.4)	19.1 (-9.5 to 36.2)	-9.5 (-27.0 to 44.4)	0.42
Whole Change t2t1p (Median (min-max))	-43.5 (-43.5 to -43.5)	0.6 (-26.9 to 40.3)	-16.3 (-23.1 to 0.6)	0.18
Naso Change t1t0p (Median (min-max))	32.7 (-34.9 to 87.9)	36.7 (-42.8 to 205.3)	52.0 (-8.6 to 141.1)	0.91
Naso Change t2t0p (Median (min-max))	33.3 (25.6-41.1)	62.4 (29.7-140.3)	-38.0 (-85.7 to 154.4)	0.38

Naso Change t2t1p (Median (min-max))	-7.1 (-7.1 to -7.1)	25.7 (-28.8 to 56.0)	-29.4 (-137.7 to 13.3)	0.25
Oro Change t1t0p (Median (min-max))	15.7 (-3.8 to 71.7)	12.5 (-23.2 to 190.4)	-8.4 (-18.8 to 79.2)	0.81
Oro Change t2t0p (Median (min-max))	-11.8 (-42.5 to 18.9)	11.4 (-10.6 to 35.9)	15.7 (-33.6 to 64.1)	0.81
Oro Change t2t1p (Median (min-max))	-52.8 (-52.8 to -52.8)	-3.3 (-33.3 to 46.9)	-14.7 (-15.2 to 24.1)	0.27
Hypo Change t1t0p (Median (min-max))	3.1 (-24.8 to 68.8)	2.7 (-37.4 to 59.3)	-14.3 (-20.3 to 44.1)	0.91
Hypo Change t2t0p (Median (min-max))	-7.0 (-21.1 to 7.0)	12.3 (-36.8 to 33.9)	-5.5 (-21.0 to 3.9)	0.30
Hypo Change t2t1p (Median (min-max))	-61.8 (-61.8 to -61.8)	-10.2 (-35.4 to 49.8)	-0.7 (-40.2 to 8.8)	0.25

Table 8. Kruskal-Wallis test. Maxillary only group

A Mann-Whitney test was then used to see there was a significant difference in the airway between subjects that had <6mm and ≥6mm maxillary movement. No significant changes were seen (table 9).

Variable	MAXMOVEMT = < 6mm (N=10)	MAXMOVEMT = ≥ 6mm (N=6)	P-Value
Whole Change t1t0p (Median (min-max))	10.6 (-9.7 to 57.9)	22.6 (-10.6 to 77.3)	0.60
Whole Change t2t0p (Median (min-max))	18.0 (-26.1 to 33.4)	-4.3 (-27.0 to 44.4)	1.00
Whole Change t2t1p (Median (min-max))	-0.8 (-43.5 to 40.3)	-16.3 (-26.9 to 13.6)	0.52
Naso Change t1t0p (Median (min-max))	32.7 (-34.9 to 205.3)	44.4 (-42.8 to 141.1)	0.77
Naso Change t2t0p (Median (min-max))	52.0 (25.6-140.3)	29.7 (-85.7 to 154.4)	0.42
Naso Change t2t1p (Median (min-max))	14.1 (-22.6 to 56.0)	-28.8 (-137.7 to 25.7)	0.12
Oro Change t1t0p (Median (min-max))	8.9 (-23.2 to 71.7)	18.8 (-18.8 to 190.4)	0.52
Oro Change t2t0p (Median (min-max))	11.4 (-42.5 to 23.7)	15.7 (-33.6 to 64.1)	0.52

Oro Change t2t1p (Median (min-max))	-10.8 (-52.8 to 46.9)	-14.7 (-33.3 to 24.1)	0.78
Hypo Change t1t0p (Median (min-max))	-11.8 (-37.4 to 68.8)	17.6 (-20.3 to 44.1)	0.38
Hypo Change t2t0p (Median (min-max))	11.0 (-36.8 to 33.9)	-5.5 (-21.0 to 17.6)	0.52
Hypo Change t2t1p (Median (min-max))	1.4 (-61.8 to 49.8)	-10.2 (-40.2 to 8.8)	0.78

Table 9. Mann-Whitney test. Maxillary only group

Comparison of means—mandibular only group.

The Kruskal-Wallis test to examine significant changes of the airway between the three timepoints with the patients that only had mandibular advancement showed no significance (table 10).

Variable	MANMOVEMENT = slight (1-5mm) (N=1)	MANMOVEMENT = moderate (6-7mm) (N=5)	MANMOVEMENT = severe (8+mm (N=7)	P-Value
Whole Change t1t0p (Median (min-max))	30.5 (30.5-30.5)	39.2 (7.0-75.8)	37.4 (1.4-45.7)	0.61

Whole Change t2t0p (Median (min-max))	7.8 (7.8-7.8)	15.7 (8.6-22.8)	13.4 (-3.4 to 33.8)	0.55
Whole Change t2t1p (Median (min-max))	-22.7 (-22.7 to -22.7)	-21.8 (-27.3 to -16.4)	-17.9 (-24.3 to -11.9)	0.81
Naso Change t1t0p (Median (min-max))	33.9 (33.9-33.9)	38.2 (-7.6 to 133.6)	0.8 (-18.5 to 46.3)	0.44
Naso Change t2t0p (Median (min-max))	23.3 (23.3-23.3)	25.9 (-2.3 to 54.2)	-17.7 (-58.4 to -1.9)	0.15
Naso Change t2t1p (Median (min-max))	-10.6 (-10.6 to -10.6)	10.6 (5.4-15.9)	-52.4 (-52.9 to -26.4)	0.12
Oro Change t1t0p (Median (min-max))	2.1 (2.1-2.1)	67.6 (34.7-109.9)	55.2 (4.9-67.0)	0.17
Oro Change t2t0p (Median (min-max))	-0.4 (-0.4 to -0.4)	14.5 (12.4-16.6)	37.8 (-4.0 to 45.4)	0.36
Oro Change t2t1p (Median (min-max))	-2.5 (-2.5 to -2.5)	-62.5 (-97.5 to -27.5)	-9.8 (-29.2 to -5.7)	0.21
Hypo Change t1t0p (Median (min-max))	57.5 (57.5-57.5)	-7.6 (-31.4 to 66.5)	17.7 (-5.2 to 33.4)	0.42

Hypo Change t2t0p (Median (min-max))	-2.7 (-2.7 to -2.7)	15.3 (-0.9 to 31.6)	13.0 (-12.7 to 36.7)	0.55
Hypo Change t2t1p (Median (min-max))	-60.2 (-60.2 to -60.2)	7.5 (-15.4 to 30.5)	1.5 (-11.5 to 19.1)	0.34

Table 10. Kruskal-Wallis test. Maxillary only group.

A Mann-Whitney test was then used to see if there was a significant difference in the airway between subjects that had <7mm and≥ 7mm maxillary movement. No significant changes were seen (table 11).

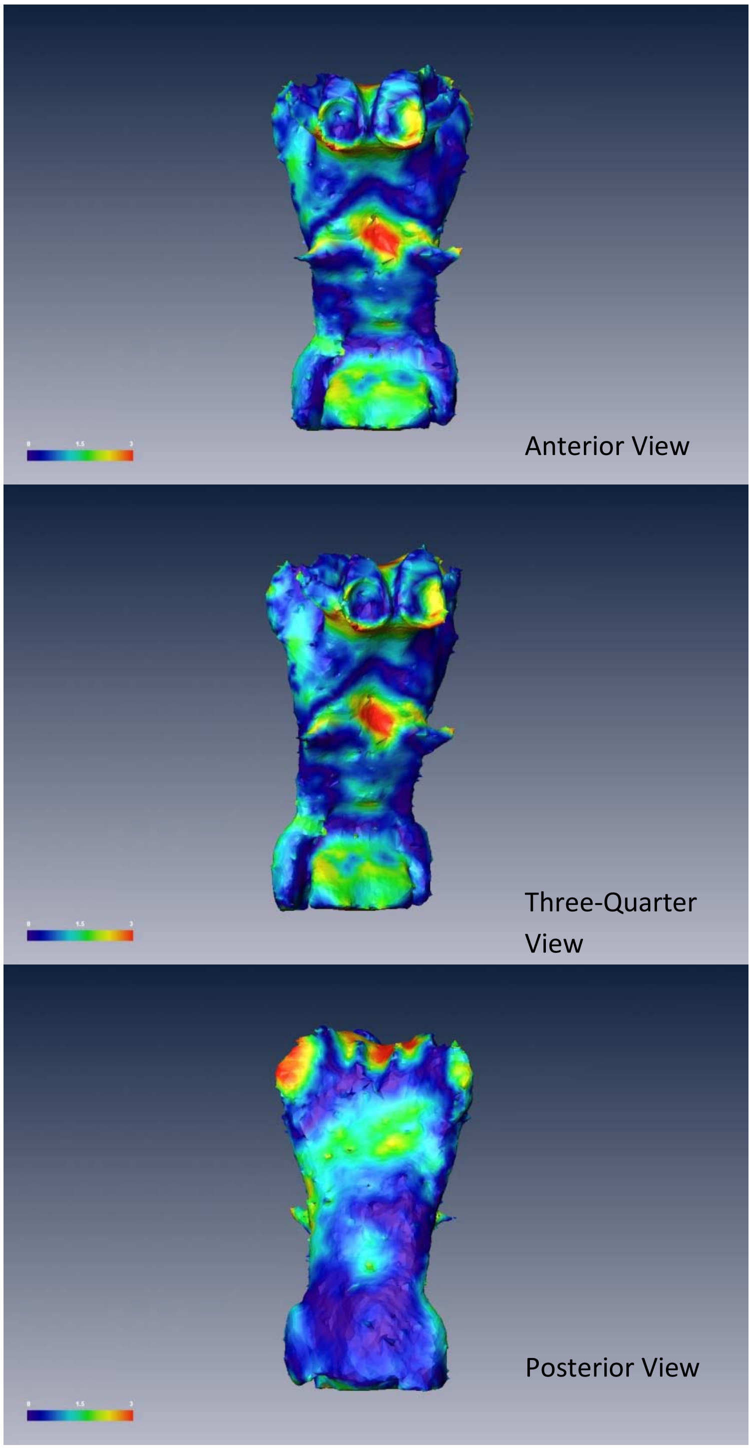
Variable	MANMOVEMT = < 7mm (N=4)	MANMOVEMT = ≥7mm (N=9)	P-Value
Whole Change t1t0p (Median (min-max))	34.8 (7.0-43.7)	37.4 (1.4-75.8)	0.92[1]
Whole Change t2t0p (Median (min-max))	15.3 (7.8-22.8)	11.0 (-3.4 to 33.8)	0.87[1]
Whole Change t2t1p (Median (min-max))	-19.6 (-22.7 to -16.4)	-21.1 (-27.3 to -11.9)	0.82[1]
Naso Change t1t0p (Median (min-max))	36.1 (17.2-42.8)	0.8 (-18.5 to 133.6)	0.30[1]
Naso Change t2t0p (Median (min-max))	38.7 (23.3-54.2)	-12.2 (-58.4 to -1.9)	0.067[1]

Naso Change t2t1p (Median (min-max))	2.7 (-10.6 to 15.9)	-39.4 (-52.9 to 5.4)	0.25[1]
Oro Change t1t0p (Median (min-max))	39.4 (2.1-105.5)	61.2 (4.9-109.9)	0.40[1]
Oro Change t2t0p (Median (min-max))	8.1 (-0.4 to 16.6)	37.4 (-4.0 to 45.4)	0.40[1]
Oro Change t2t1p (Median (min-max))	-15.0 (-27.5 to -2.5)	-19.5 (-97.5 to -5.7)	0.49[1]
Hypo Change t1t0p (Median (min-max))	19.7 (-12.2 to 57.5)	17.7 (-31.4 to 66.5)	1.00[1]
Hypo Change t2t0p (Median (min-max))	14.5 (-2.7 to 31.6)	8.4 (-12.7 to 36.7)	1.00[1]
Hypo Change t2t1p (Median (min-max))	-37.8 (-60.2 to -15.4)	10.3 (-11.5 to 30.5)	0.11[1]

Table 11. Mann-Whitney test. Mandibular only group.

Three-dimensional superimpositions of the pharyngeal airway

We were able to successfully superimpose two surface rendered airway volumes from the same patient, comparing one of the two post-surgical volumes (t2 or t1) to the pre-surgical (t0) using color maps. Figure 35 shows the whole airway and the color map offers an alternative method to see what part of the airway change and by what degree. Dark blue represents no difference between the two airways and red which represents a greater than 3 voxel change of the airway. Since 1 voxel equals 0.376mm^3, the range of change visible is at least 0-1.128mm. [64] For purposes of comparison, the quantitative changes are shown next to the color map. Color maps for all patients in the study are available in the Appendix.



3mm maxillary advancement	t2-t0 (%)
Whole Airway	14.37
Nasophyarnx	25.57
Oropharynx	18.91
Hypophyarnx	6.95

Figure 35. Color map of patient with 3mm maxillary advancement

DISCUSSION

The purpose of this study was to better understand the effect of orthognathic surgery on the airway. Previous studies have used predominantly two-dimensional analyses, particularly with lateral cephalograms. Although limited in information, the use of lateral cephalograms was a convenient method for looking at a three-dimensional structure such as the pharyngeal airway. Furthermore, with the widespread adoption of three-dimensional conebeam computed tomography technology, it is a natural progression to look at the airway using 3-D CBCT. For example, one recently published article used CBCT images to examine airway shape and size differences between a group of patients that have OSAS and a control group.[56] Another article used CBCT to draw a correlation between a specific airway cross-sectional area with a subject's body-mass index. However, the scope of this study will go beyond any publication to date, while adding to the pioneering work of Sears *et al.,* in 2006, in analyzing the surgical effects of the airway using CBCT.[63] Specifically, we have closely examined the effect of orthognathic surgery on the three sub-sections of the pharyngeal airway, and have developed a method to three-dimensionally superimpose the airway.

Obtaining the 3-D CBCT image and segmentation technique

The method by which the CBCT scans and images are obtained can be a source of variability. The number of radiology technicians taking each image was limited to minimize differences in patient instructions. One technician took approximately 85% of the images, and a second technician took the last 15% of the images. In addition to consistent and precise instructions that were given to each patient, efforts were made to ensure that the actual image captured of the airway was reproducible to validate the airway segmentation techniques. Our statistical tests show that we were consistent in both aspects and we felt comfortable continuing the study with our method of taking a CBCT and our 3-D airway segmentation technique. However, further study needs to be conducted to directly answer the question of what "phase" of the respiratory cycle is captured in this 9.6 second scan.

Airway changes dependent on the amount of maxillary movement

The pharyngeal airway was subdivided using a modified protocol of work done by previous authors.[39] As a result, we were able to learn how the airway volume changed at three subdivisions of the airway: nasopharynx, oropharynx, and hypopharynx. The percent of airway volume increase for the nasopharynx was relatively consistent with all three surgical groups. Looking at long-term post-surgical versus pre-surgical airway volume, a trend is seen; the airway volume gradually increases up until approximately 6mm advancement. It appears that there is a "morphological tolerance" of how much the airway volume can be increased. This limit, approximately a doubling in size of the nasopharynx volume, appears to be reached around 6-7mm of maxillary jaw advancement. Once this natural limit is exceeded, the nasopharynx reacts by decreasing in volume. Lastly, it is seen that the amount the airway relapses post-surgically, and that there is more relapse with a 5 and 6mm maxillary advancement than at larger maxillary advancements of 7 and 8mm.

In the oropharynx, an interesting phenomenon is seen which seems to "compensate" for the changes in the nasopharynx. This makes intuitive sense, since 1) the naso- and oropharynx are in closest physical proximity to the physical changes in the maxilla. Secondly, it is not surprising that the oropharynx compensates for changes in the nasopharynx if we again think about the concept of a "physiologic limit" for the airway. The airway wants to be at its "natural" size and it will adapt as needed to maintain this volume. In this study, it seems that the oropharynx and nasopharynx work in concert with one another to maintain this.

Since the upper two levels of the airway have compensated for one another, it makes sense that the hypopharynx does not appreciably change; which was observed in this study.

While the graphs suggest significance, our statistical results do not support this observation. One possible reason is that our sample size was too small for statistical significance to be established. Another reason is that not all of the subjects in the maxillary only group had a purely anterior-posterior surgical change nor were they all one piece LeFort I surgeries. Some patients had two piece LeFort surgery due to hypoplasia in the transverse dimension. Others were disimpacted while a few were impacted. These differences in surgical procedure modify the end result of the maxillary surgery. However, a decision was made to keep these patients in the study, since excluding them would have resulted in such a small sample that any worthwhile analysis would become extremely difficult. Lastly, another reason that no statistically significant changes were detected could be because of the number of subdivisions of the airway which were analyzed. It might be that having three subdivisions broke-up a larger segment of the airway that would have shown statistical significance. Dividing the pharyngeal airway into two subdivisions at the level of the tip of the soft palate, a naso-oropharynx and an oro-hypopharynx may address this issue in future studies.

Airway changes dependent on the amount of mandibular surgical change

Studying the graphs of the mandibular-only group reveal that three factors seem to be important with differing amounts and/or directions of movement. When the mandible is set-back, very little, if any, negative percent volume changes occur. Mandibular advancements in the range of 1-6mm show a slight increase in airway volume while larger advancements of 7mm+ show minimal changes. In fact, in some instances an actual decrease of the volume was seen at such large movements.

The nasopharynx shows this trend at all three timepoint comparisons. However, looking at the t1-t0 comparison, patient #18 appears to be an outlier. This subject had >50% increase in volume even though other subjects who received setbacks demonstrated minimal to very slight airway changes. Subject 18 was unique in that he received a rotational setback of the mandible. Since the setback was not purely in an antero-posterior plane like the setback subjects, his outlier number is justified.

The oropharynx results for t2-t0, show an overall slight but steady increase of the airway volume ranging from a 4mm set-back to larger advancements of 10mm. It is not completely clear why subject #30 did not show a corresponding increase in the airway volume that was noted in other subjects with larger advancements. However, it can be seen that subject #30 had minimal changes at any pharyngeal sub-area. It appears that this patient's airway was less affected by orthognathic surgery than the rest of the sample group.

The mandible only group did not show statistical difference for many of the same reasons as the maxillary only group. Surgery has such a multi-factorial effect on the airway that this study is not able to adequately differentiate what exactly causes the airway changes. In order to do so, a multi-center study would likely be needed with extremely tight inclusion criteria so that solely AP movements can be examined.

Airway changes of the pharyngeal subareas, over timepoints for the maxillary only surgical group

Maxillary surgery had its largest effect in the nasopharynx. There was a 50% increase in volume indicating that the nasopharynx, as defined in this study, was most effected by LeFort surgery. With the nasopharynx being at the same superior/inferior level as the maxilla it seems to make sense that this would happen. Similarly, as the segment of the airway gets farther from the maxilla, less airway changes are seen.

Airway changes over timepoints in the mandibular-only surgical group

In cases of mandibular advancement, a BSSO procedure most affects the oropharynx. Similar to the maxillary advancement subjects, the area closest to the level of the surgery was affected the most. The nasopharynx decreased by nearly 5% at t2, the oropharynx showed an increase of approximately 25%, and the hypopharynx increased by approximately 10%. The area of greatest constriction, which is commonly in the retropalatal area[22], was increased with mandibular surgery.

Subjects with mandibular setbacks showed unique results. None of the pharyngeal subvolumes showed a larger than 10% change of their respective area. The largest change was in the oropharynx, followed by the nasopharynx, and then the hypopharynx.

Two-jaw surgical group

The two-jaw surgery group proved to be challenging to study since this one group could actually be further divided into: two-jaw setback, two-jaw advancement, maxillary advancement/mandibular setback, and maxillary setback/mandibular advancement. With only 11 subjects in the larger "two-jaw surgical" group, there was an extremely small sample when further divided into the subgroups. Consequently, summaries of this data and derived conclusions would be imprecise and stepping beyond the scope of this study.

Airway volume relapses between t1 and t2

Relapse occurred between immediate post-operative CBCT scan (t1) and long-term post-operative scan (t2). The maxillary only group showed the most amount of relapse was in the oropharynx, followed by the nasopharynx, and then the hypopharynx. The mandibular advancement group had similar amounts of relapse in the naso- and oropharynx while the hypopharynx had the least amount of relapse.

Lastly the mandibular setback group had the most relapse in the nasopharynx and the least in the hypopharynx group. In all three groups, the hypopharynx had the least amount of relapse. This is possibly because it had the smallest percent of volume change from t2-t0. The hypopharynx was the most stable airway volume.

We believe that the primary cause of this relapse is the body's natural tendency to want to return back towards "baseline" dimensions dictated by its skeletal form, elasticity within the soft tissue, and active tone in the muscles. Since rigid fixation, with extremely stable post-surgery results was used in all cases, skeletal relapse does not seem to be a primary cause.[32,76] However, this is an aspect of the project that should be confirmed using three dimensional volumetric imaging with CBCT.

Three-dimensional superimposition of the airways

The diagnostic value of superimposing 2-D images has been advocated as an essential tool since its introduction by Broadbent in 1913.[77]. It has been used for longitudinal growth studies[78], for evaluation of treatment outcomes, and for a myriad of other purposes. The natural progression is to superimpose structures in 3-D using CBCT data. The technique of Cevidanes *et al*. has been described.[70] We wanted to develop a technique that was increasingly user friendly and applicable in daily orthodontic and surgical care. The re-programming of Amira was required because at the start of this project there were few alternatives. Additionally, Stratemann *et al.,* [64] demonstrated the capability of Amira to superimpose three-dimensionally. A customized script for Amira automated many of the steps that Dr. Stratemann had to do manually. We were able to superimpose the three-dimensional airways using landmarks that we felt were readily and reproducibly located.

An extensive process of trial and error was involved before accepting the landmarks that were used for this study. Two clinicians then proceeded to superimpose the airway on 13 landmarks. Five superimpositions were then randomly repeated, one week after the initial superimposition, to test reliability. In looking at these repeated analyses, there is some variability. This variability was largely expected due to the difficulty in landmark identification that has been thoroughly discussed in the scientific literature. Reproducibility of three-dimensional landmark identification should be further studied before it can be reliably used to assist in making clinical decisions.

Three-dimensional superimpositions seem to be the logical successor for current techniques using lateral cephalometric film tracings. Future uses include studying growth, evaluating treatment outcomes, and to assess disease processes of the craniofacial skeleton and soft tissue. We believe that color maps are a useful method of semi-quantitatively demonstrating change between at least two timepoints.

CONCLUSION

Maxillary surgery group

-A 7mm surgical advancement looks to be the point at which the airway volume begins to decrease, but it was not supported by statistical tests.

-At 248 days on average after surgery (t2-t0), the nasopharynx appears to be affected the most by LeFort surgery.

Mandibular surgery group

-A 7-8mm advancement appears to be the point at which the airway stops increasing. However, this was not supported by statistical tests in this study.

-At about 248 days after surgery (t2), those subjects that had a mandibular advancement, had the greatest effect on the oropharynx.

-In the mandibular setback group at about 248 days after surgery, the nasopharynx slightly decreases and the oropharynx slightly increases. The hypopharynx does not seem to be affected.

Two-jaw surgery group

-The two-jaw surgery group has effects that are more complicated than simply determining the distance it was moved or displaced.

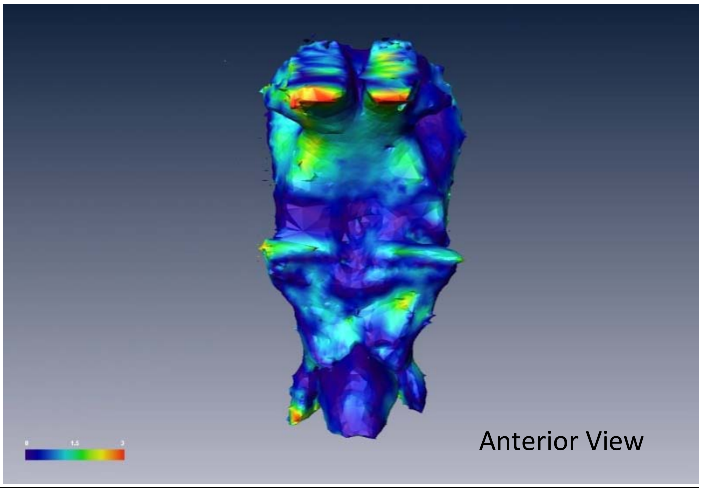
Color map

-Three-dimensional superimpositions provide a viable alternative for qualitatively describing changes between timepoints.

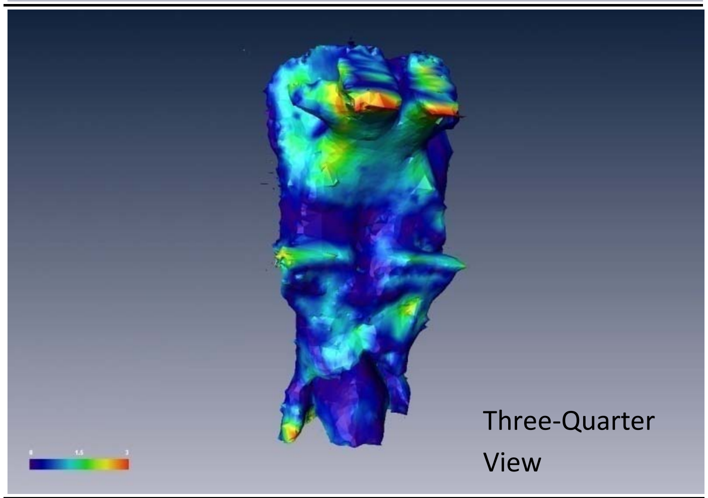
-Further works needs to be done to develop reproducible landmarks to reliably use color maps.

APPENDIX

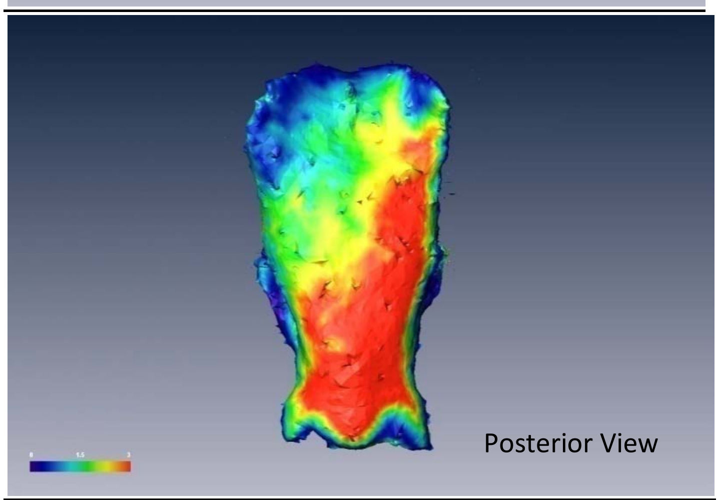
Subject 1



Anterior View



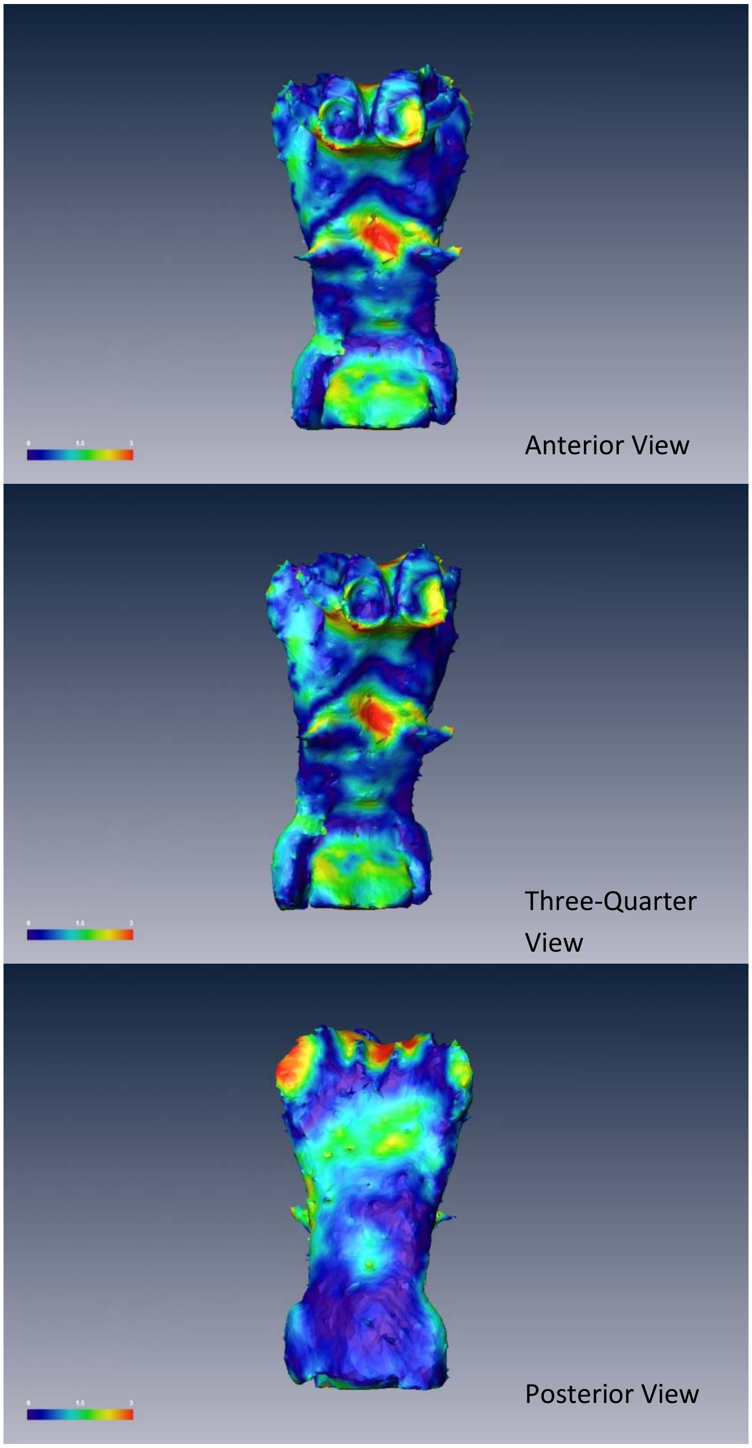
Three-Quarter View



Posterior View

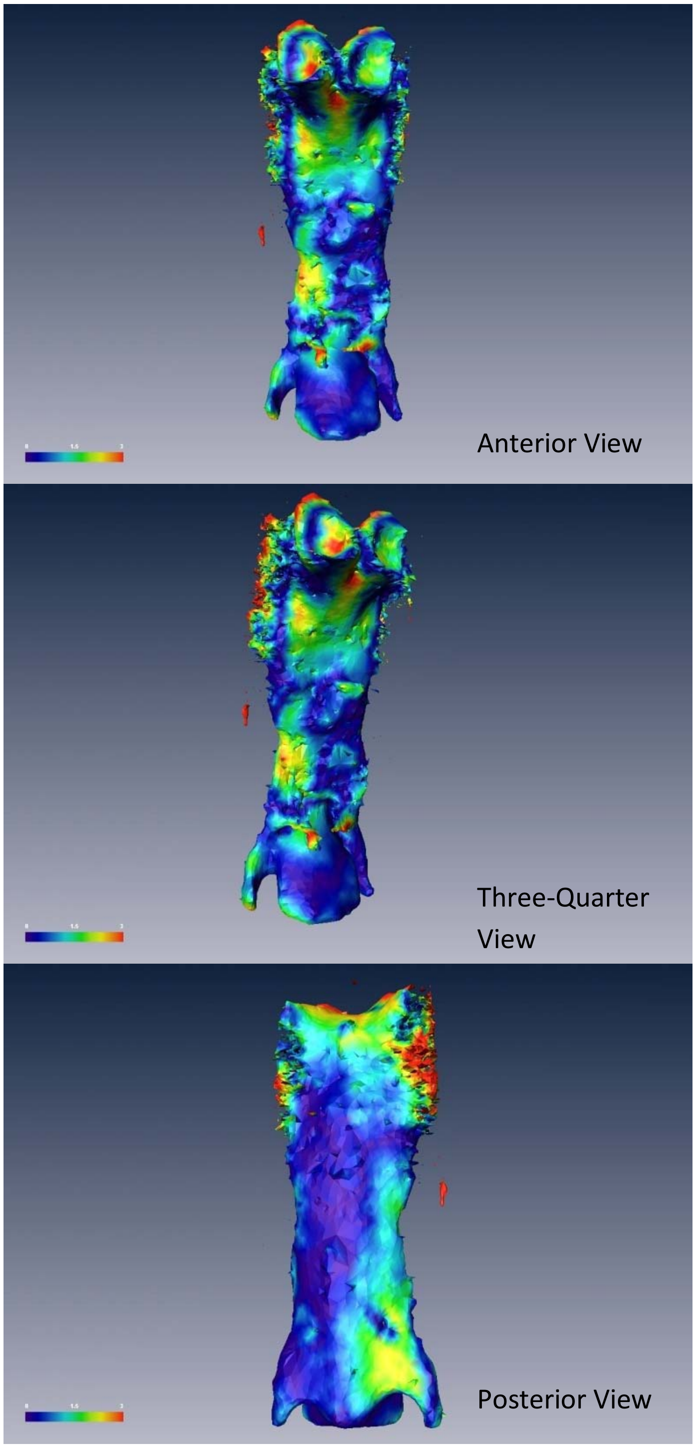
3mm maxillary setback	t1-t0 (%)
Whole Airway	29.93
Nasophyarnx	75.33
Oropharynx	15.84
Hypophyarnx	47.02

Subject 2



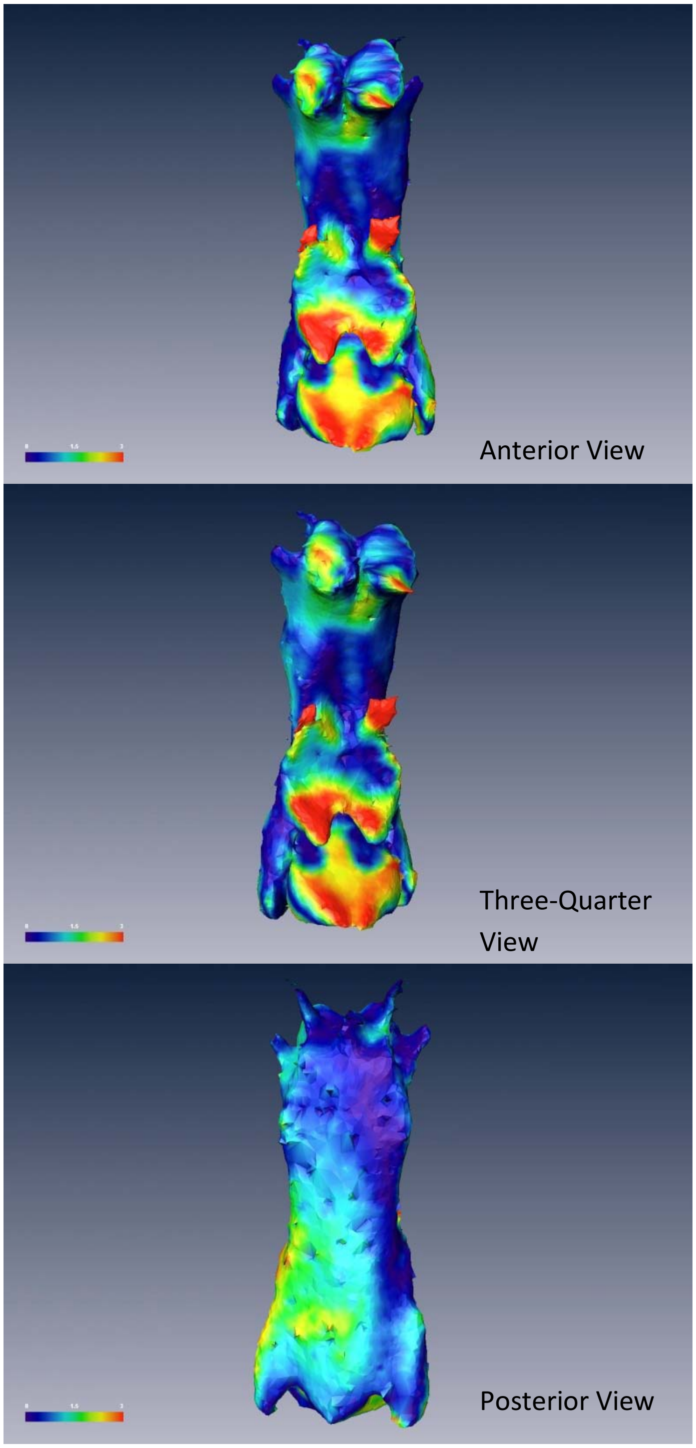
3mm maxillary advancement	t2-t0 (%)
Whole Airway	14.37
Nasophyarnx	25.57
Oropharynx	18.91
Hypophyarnx	6.95

Subject 3



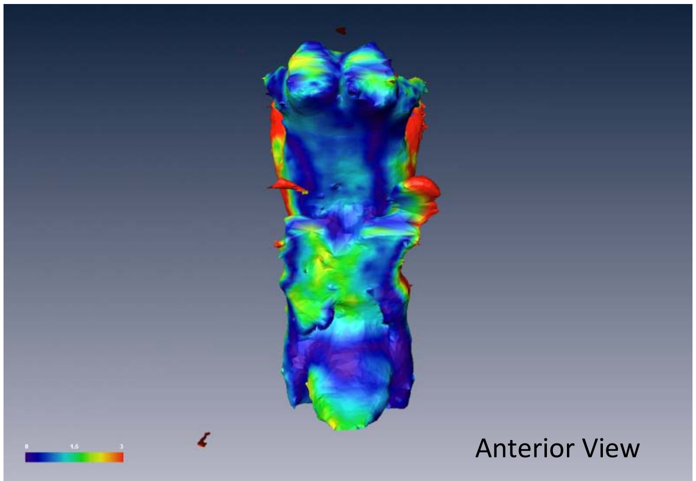
4mm maxillary advancement	t1-t0 (%)
Whole Airway	-5.18
Nasophyarnx	-34.89
Oropharynx	15.65
Hypophyarnx	3.09

Subject 4

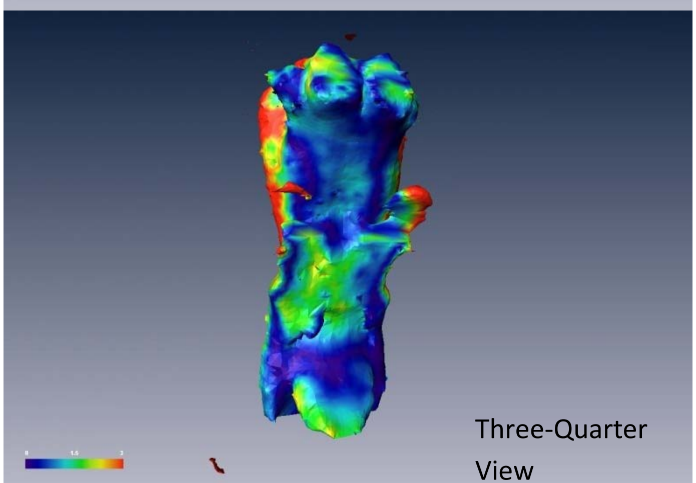


4mm maxillary advancement	t1-t0 (%)
Whole Airway	-9.74
Nasophyarnx	87.86
Oropharynx	-3.8
Hypophyarnx	-24.82

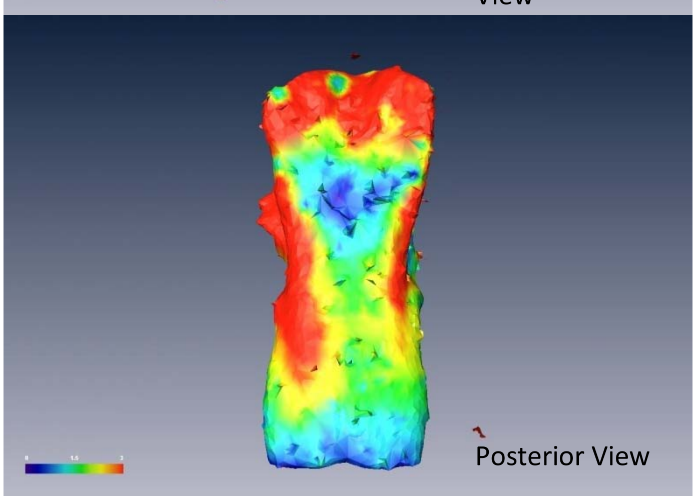
Subject 5



Anterior View



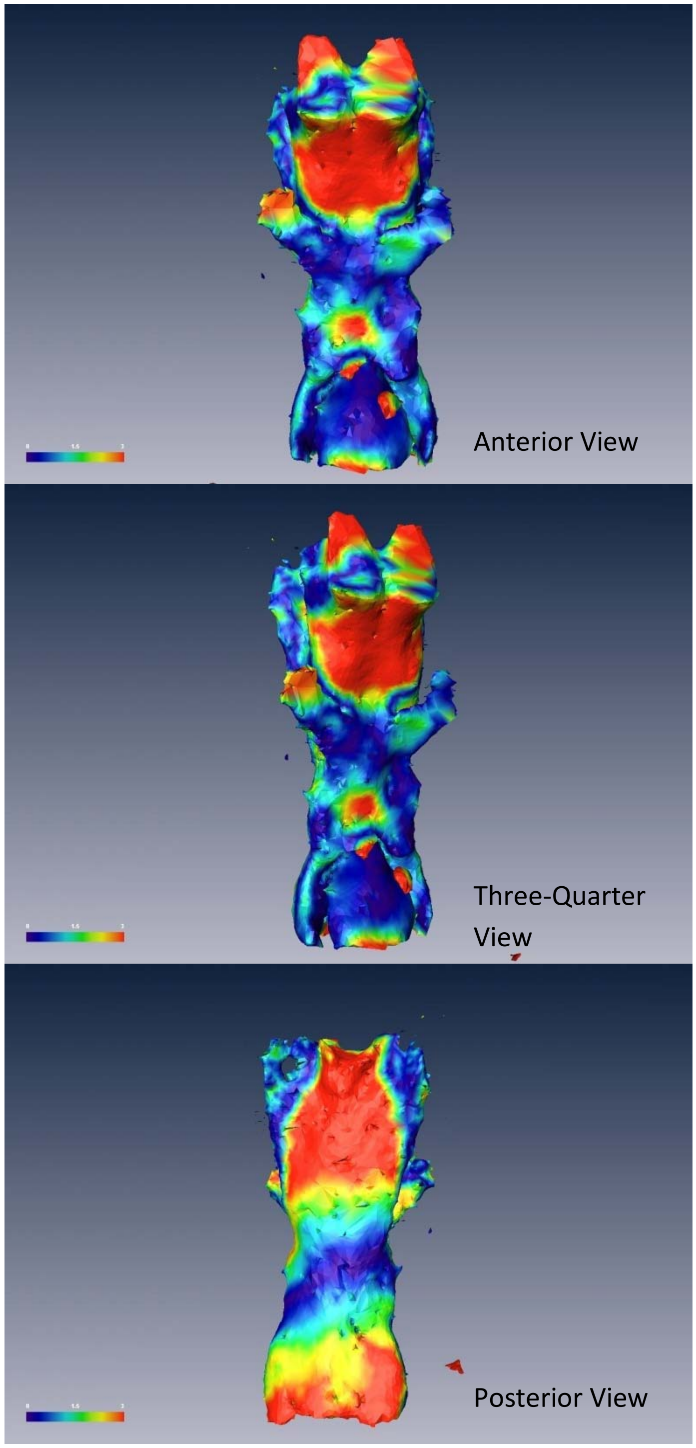
Three-Quarter View



Posterior View

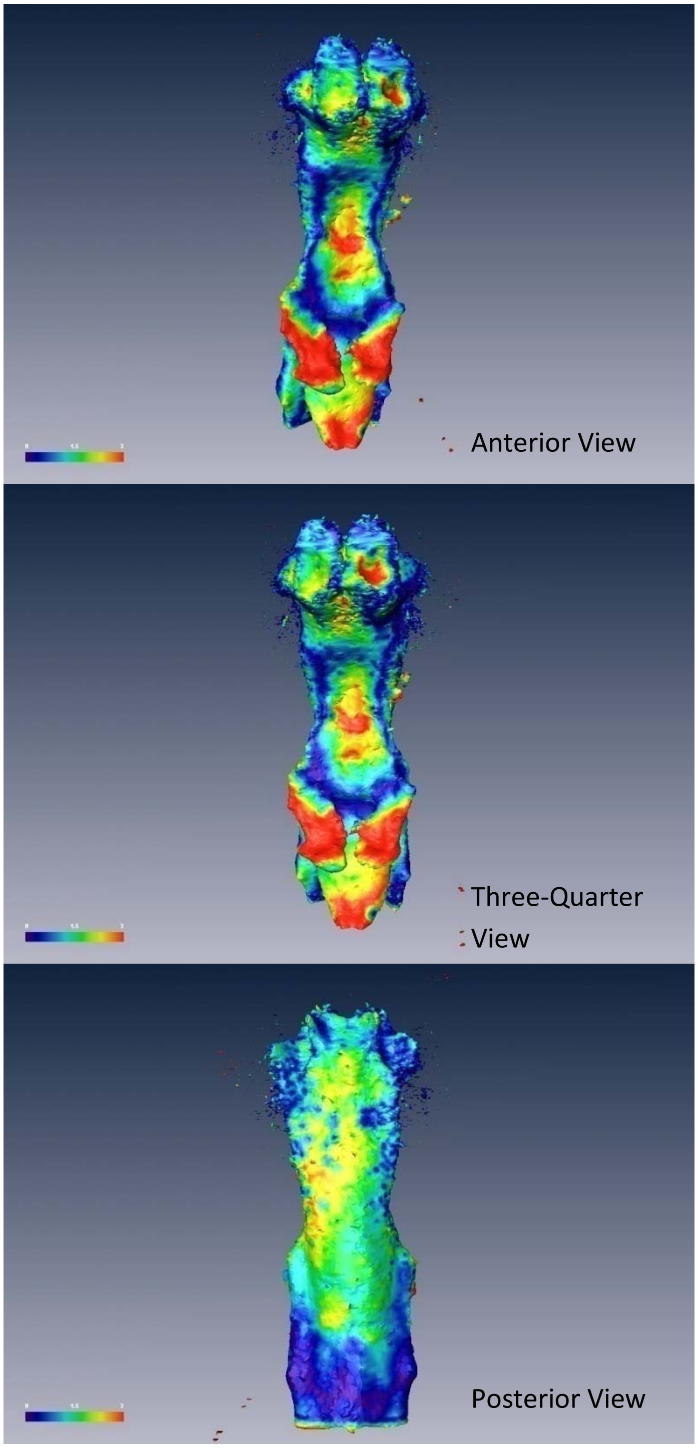
4mm maxillary advancement	t2-t0 (%)
Whole Airway	-26.1
Nasophyarnx	41.11
Oropharynx	-42.5
Hypophyarnx	-21.05

Subject 6



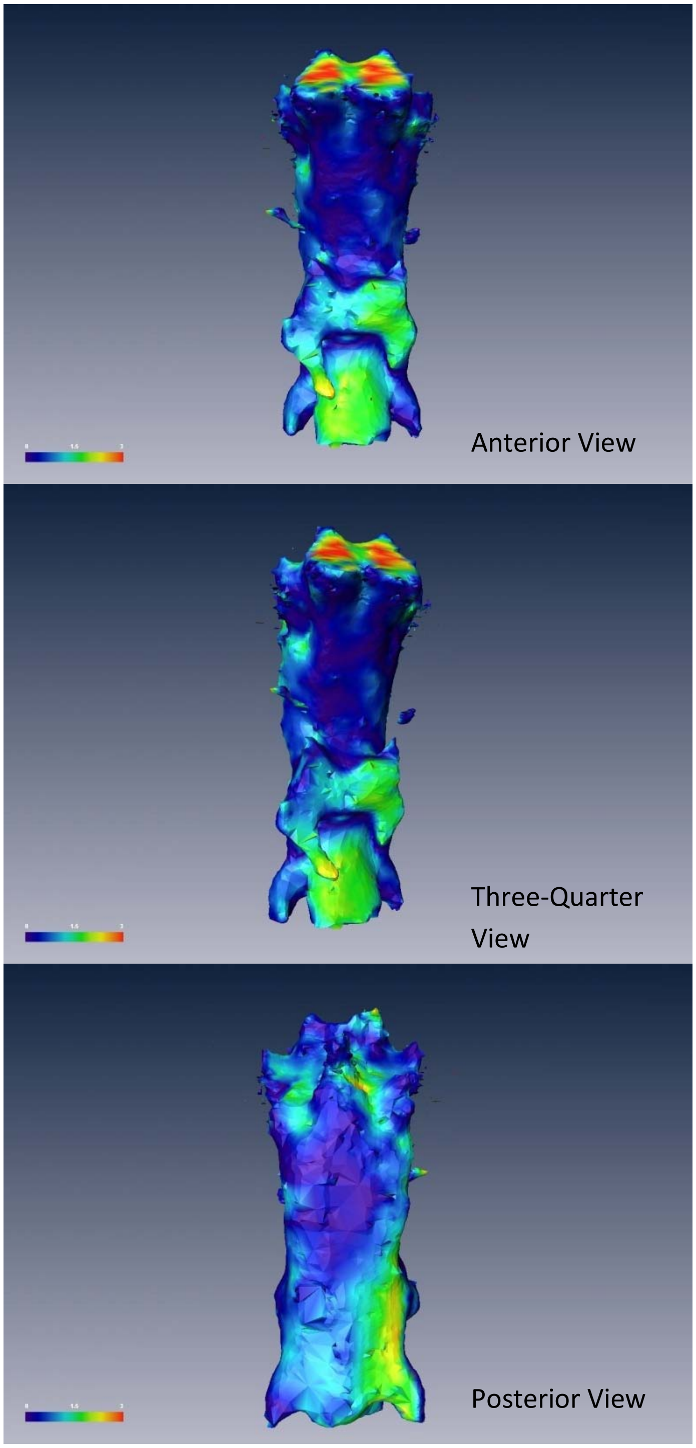
5mm maxillary advancement	t1-t0 (%)
Whole Airway	12.23
Nasophyarnx	205.29
Oropharynx	8.44
Hypophyarnx	-33.31

Subject 7



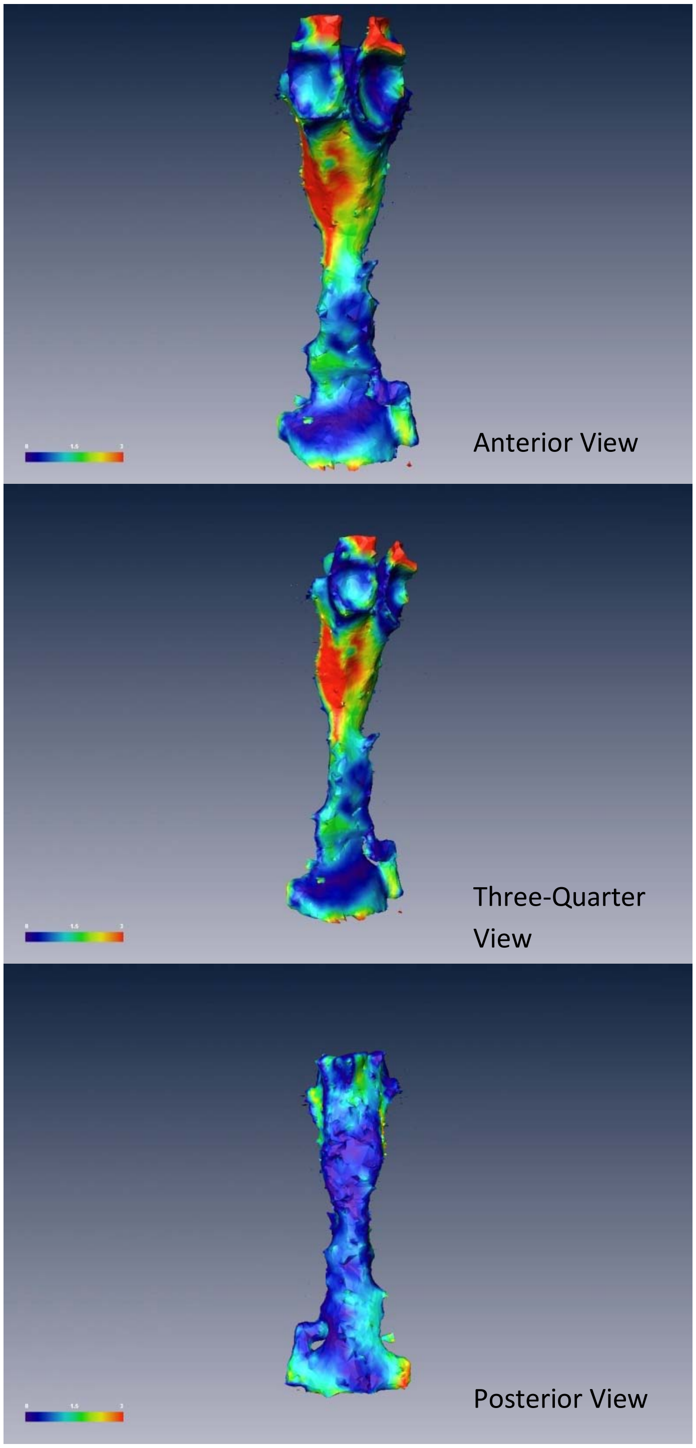
5mm maxillary advancement	t2-t0 (%)
Whole Airway	-9.54
Nasophyarnx	32.13
Oropharynx	-9.48
Hypophyarnx	-36.77

Subject 8



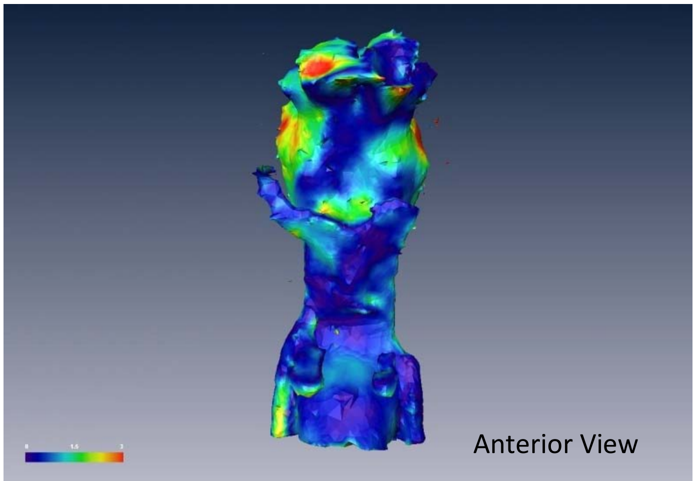
5mm maxillary advancement	t2-t0 (%)
Whole Airway	19.08
Nasophyarnx	140.3
Oropharynx	11.4
Hypophyarnx	12.33

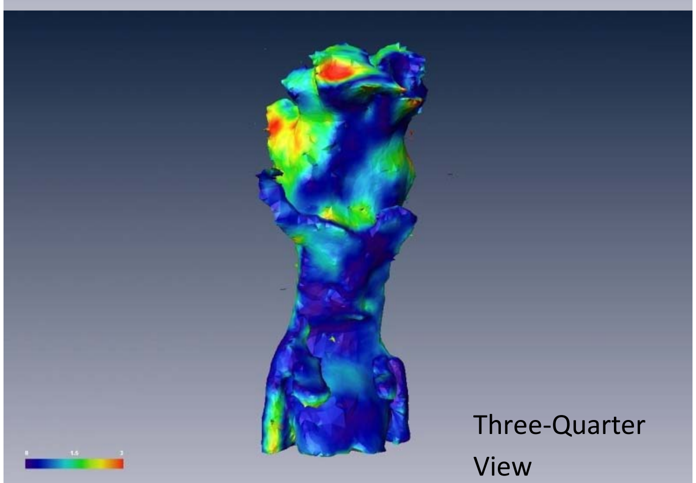
Subject 9

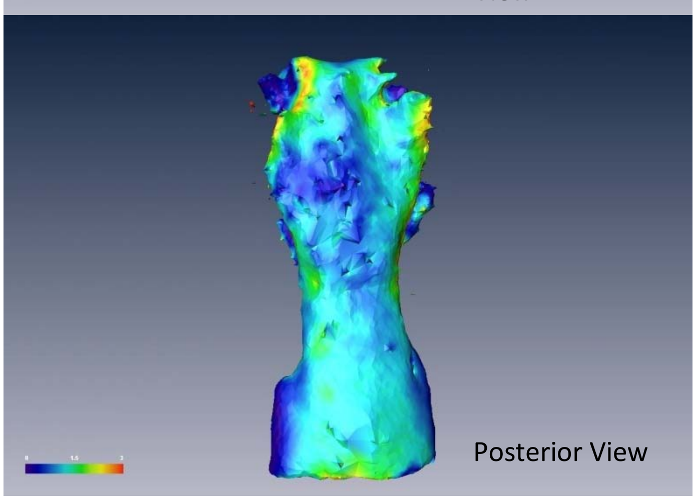


5mm maxillary advancement	t2-t0 (%)
Whole Airway	33.37
Nasophyarnx	82.66
Oropharynx	15.81
Hypophyarnx	23.88

Subject 10

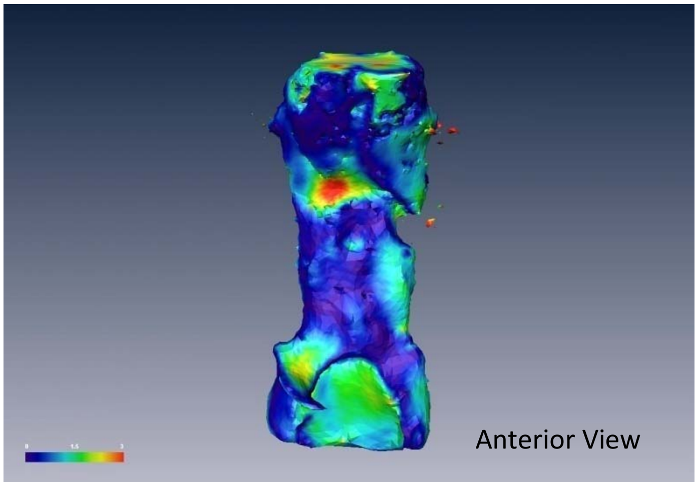


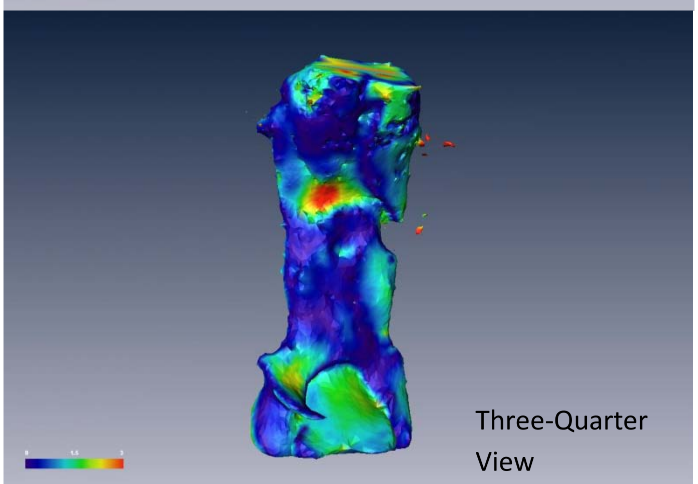


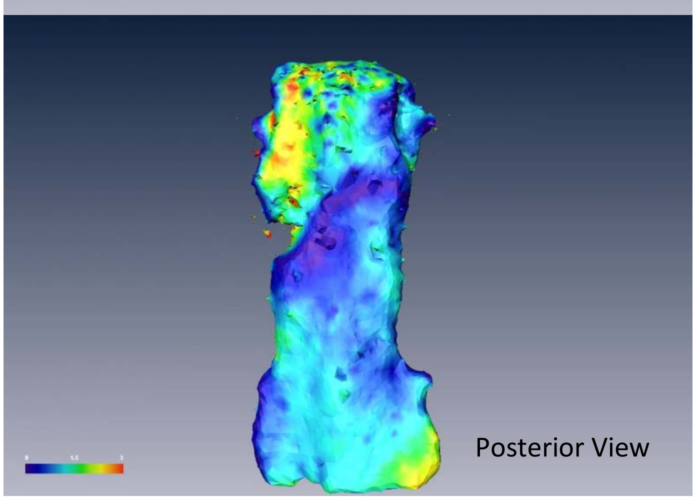


5mm maxillary advancement	t2-t0 (%)
Whole Airway	31.31
Nasophyarnx	51.98
Oropharynx	23.71
Hypophyarnx	33.88

Subject 11

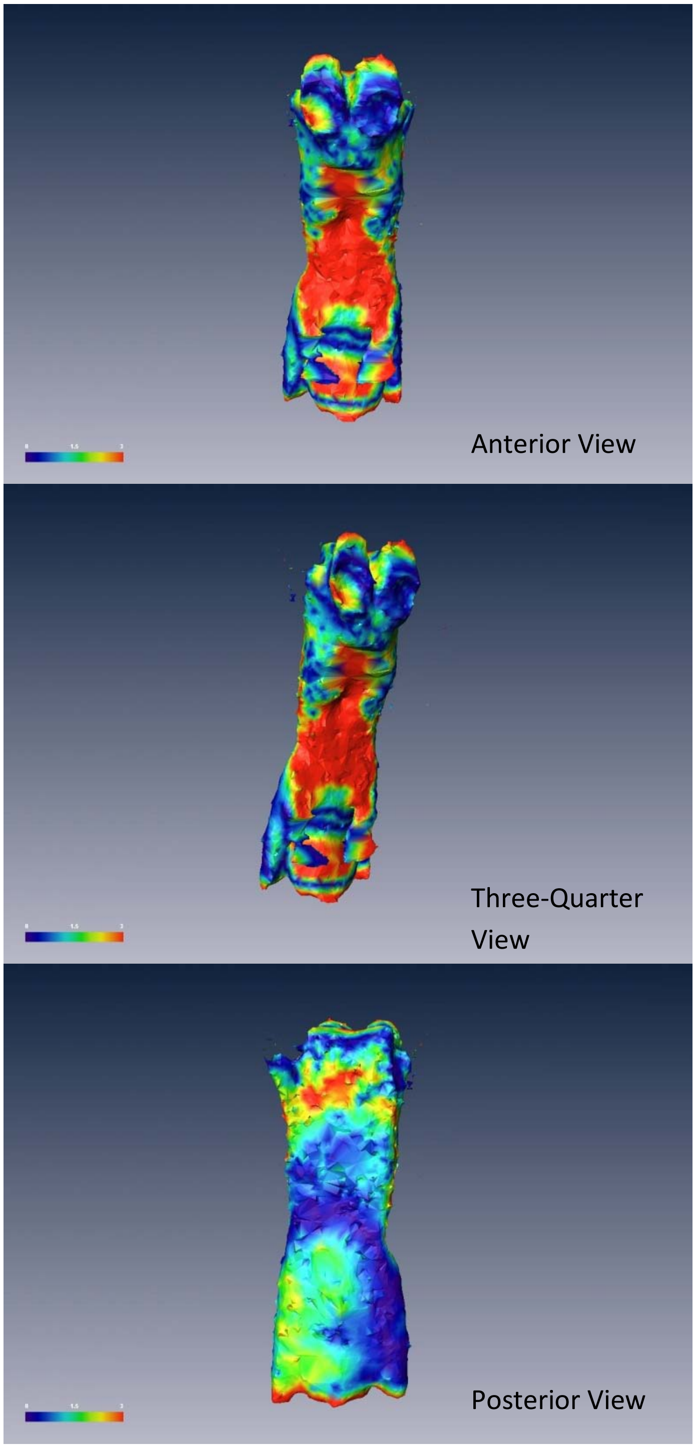






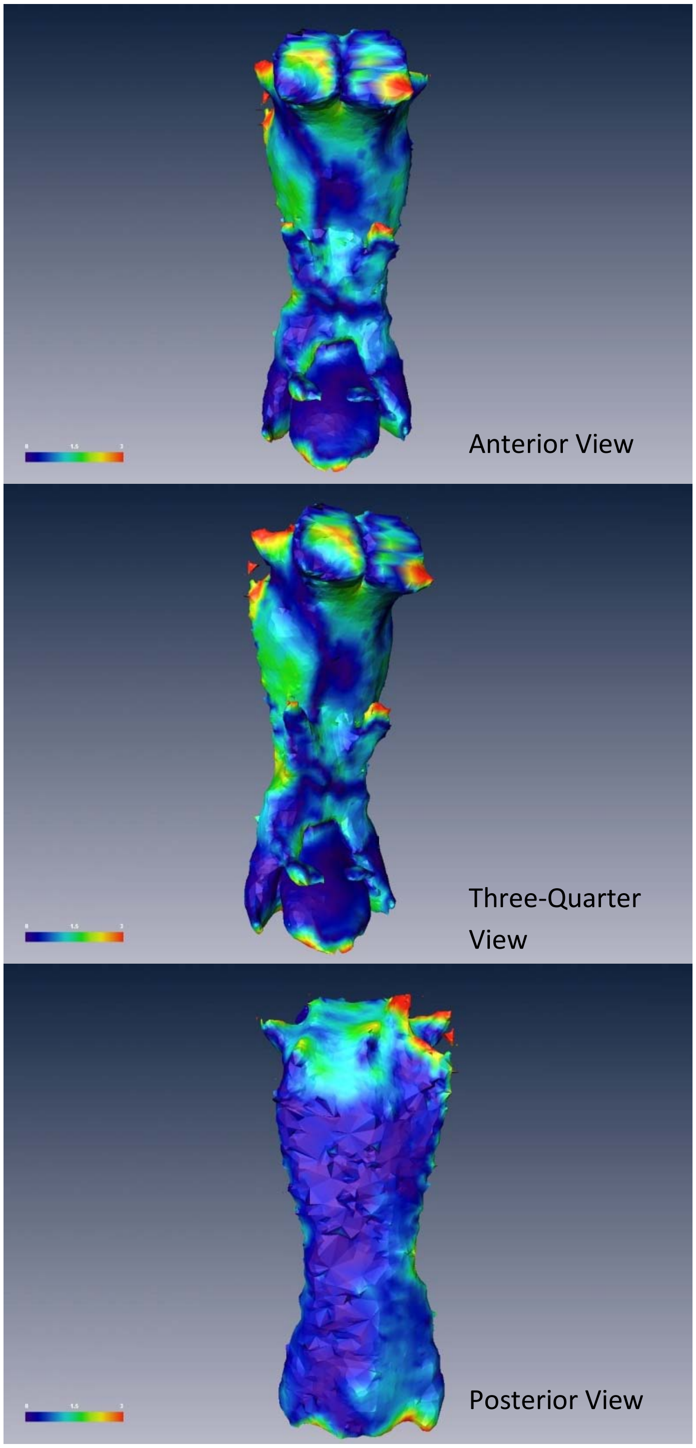
5mm maxillary advancement	t2-t0 (%)
Whole Airway	18
Nasophyarnx	64.07
Oropharynx	-10.62
Hypophyarnx	11.03

Subject 12



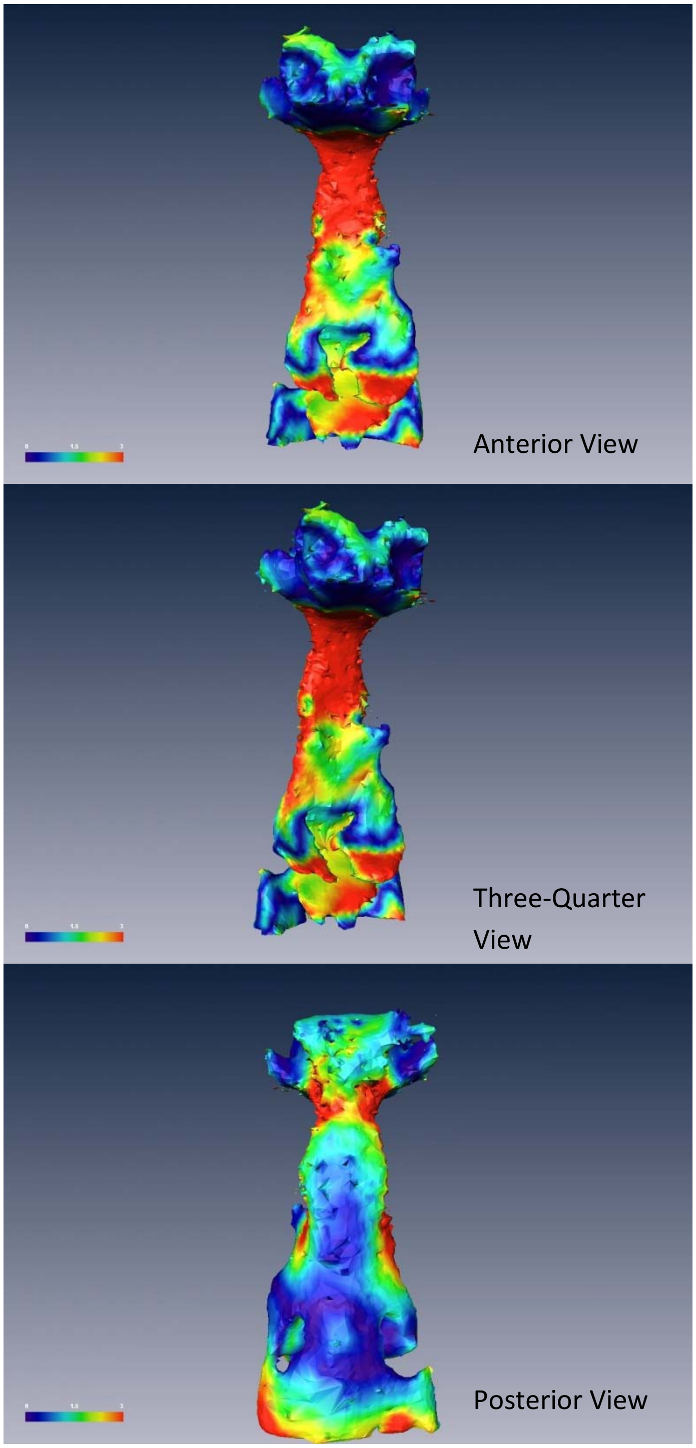
6mm maxillary advancement	t2-t0 (%)
Whole Airway	36.16
Nasophyarnx	62.44
Oropharynx	35.85
Hypophyarnx	17.64

Subject 13



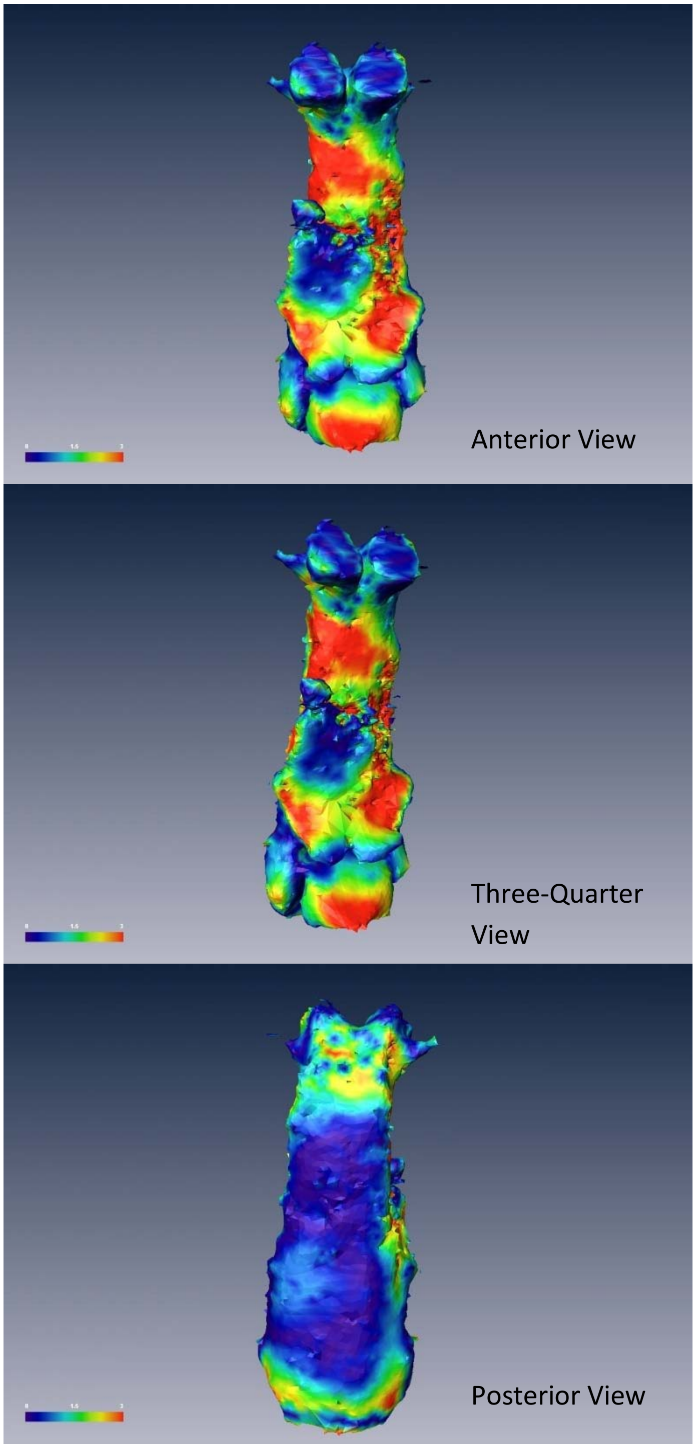
6mm maxillary advancement	t2-t0 (%)
Whole Airway	-4.3
Nasophyarnx	29.75
Oropharynx	-8.11
Hypophyarnx	-13.55

Subject 14



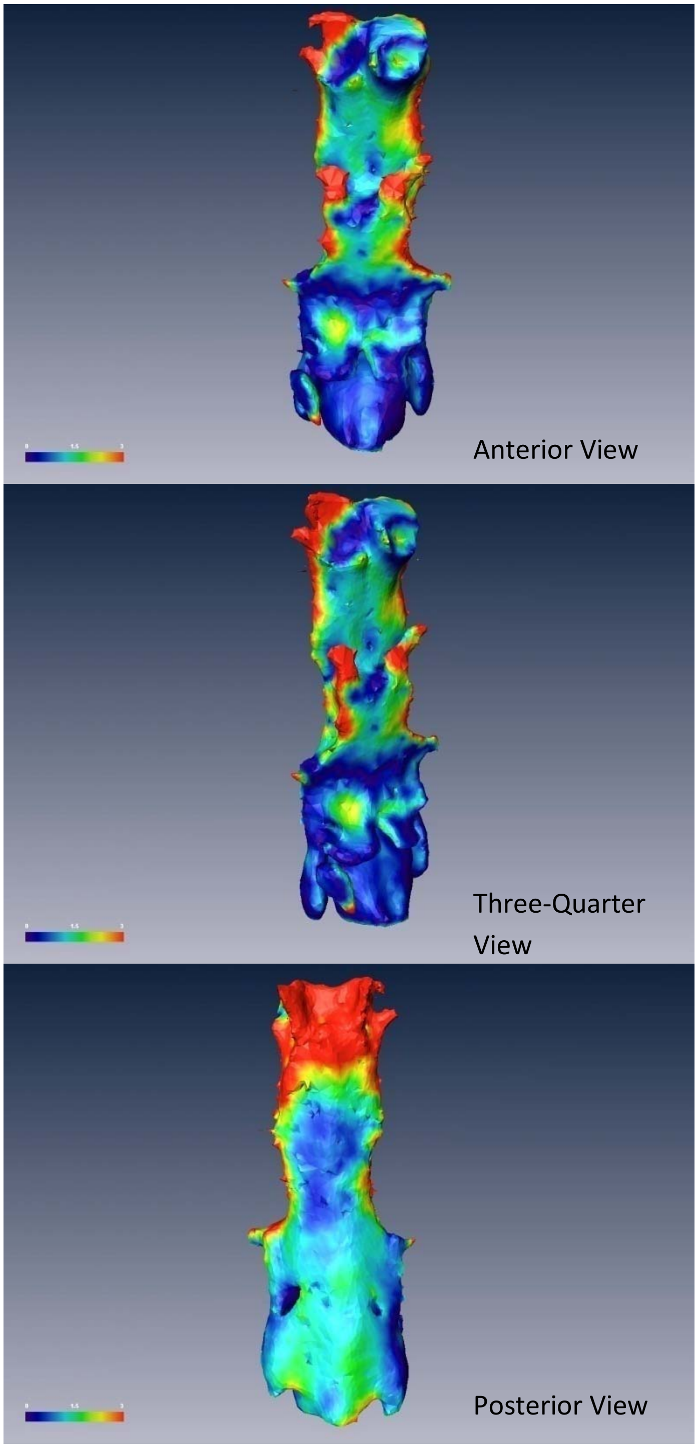
6mm maxillary advancement	t1-t0 (%)
Whole Airway	77.28
Nasophyarnx	-42.78
Oropharynx	190.41
Hypophyarnx	26.24

Subject 15



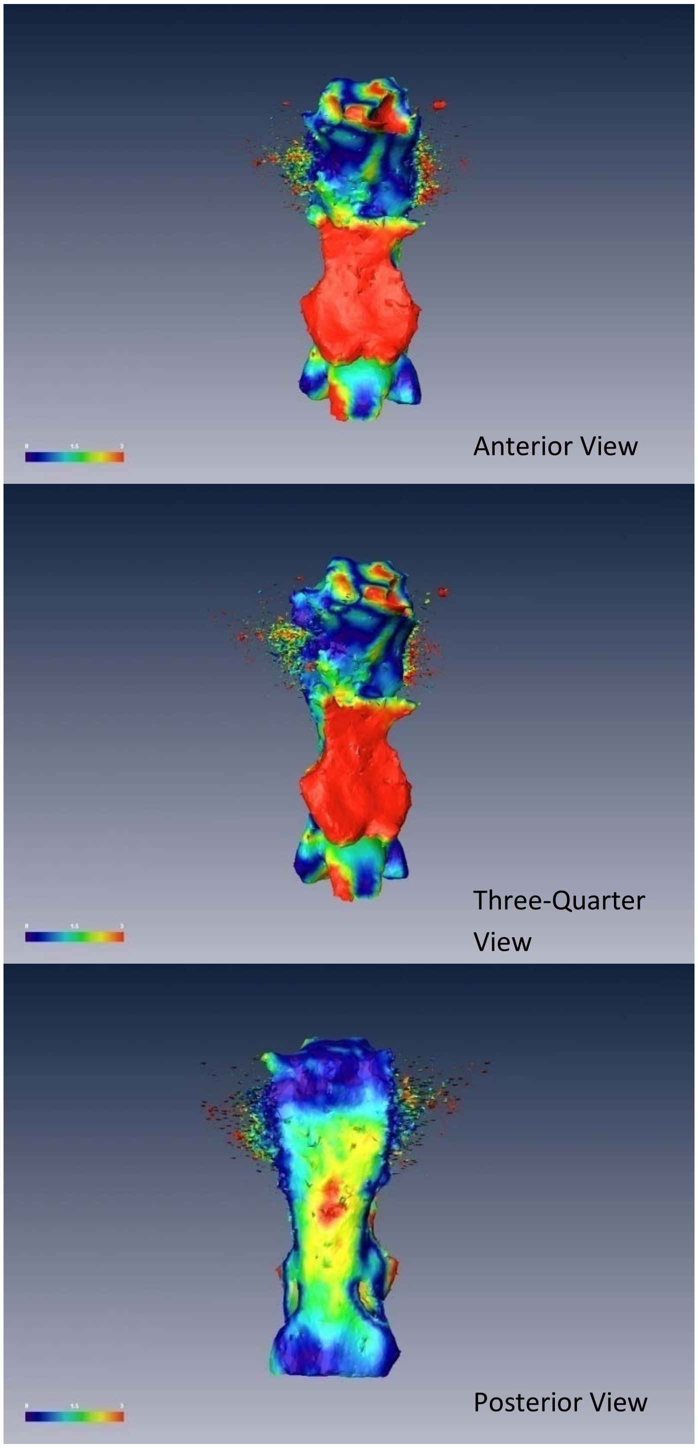
7mm maxillary advancement	t2-t0 (%)
Whole Airway	44.38
Nasophyarnx	154.37
Oropharynx	64.05
Hypophyarnx	3.93

Subject 16



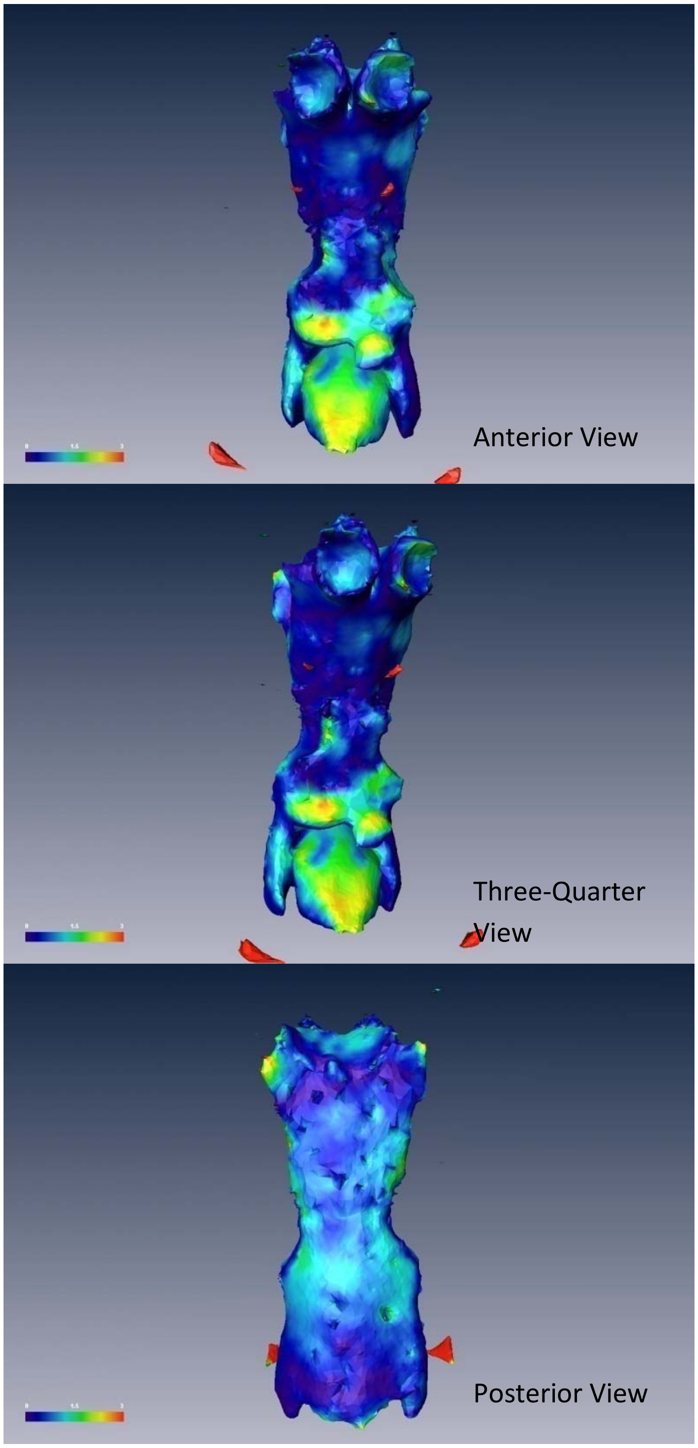
8mm maxillary advancement	t2-t0 (%)
Whole Airway	-26.97
Nasophyarnx	-85.73
Oropharynx	-33.58
Hypophyarnx	-5.46

Subject 17



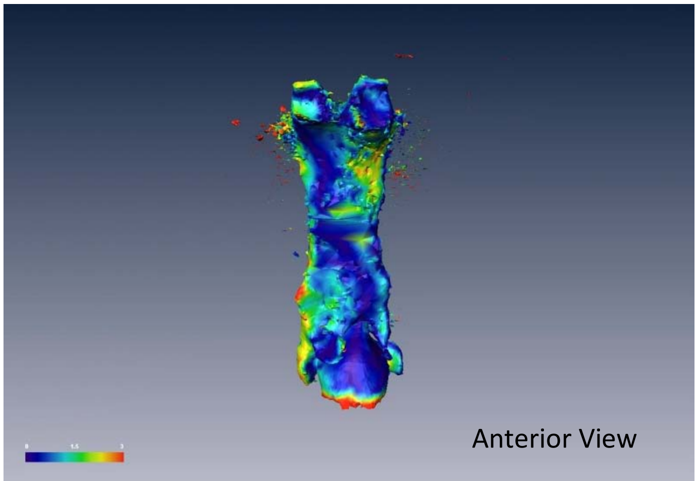
8mm maxillary advancement	t2-t0 (%)
Whole Airway	-9.45
Nasophyarnx	-37.99
Oropharynx	15.68
Hypophyarnx	-21

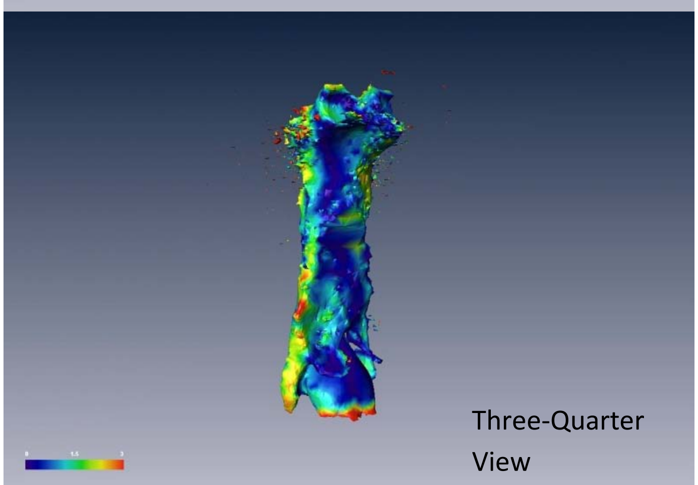
Subject 18

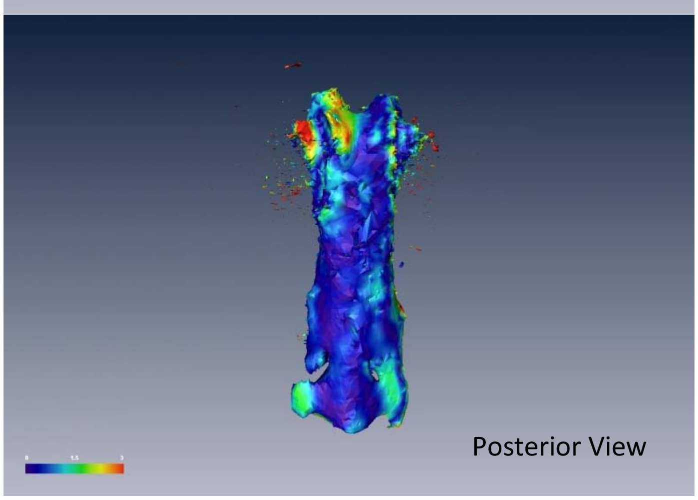


4mm mandibular setback	t2-t0 (%)
Whole Airway	4.51
Nasophyarnx	16.94
Oropharynx	8.53
Hypophyarnx	-12.25

Subject 19

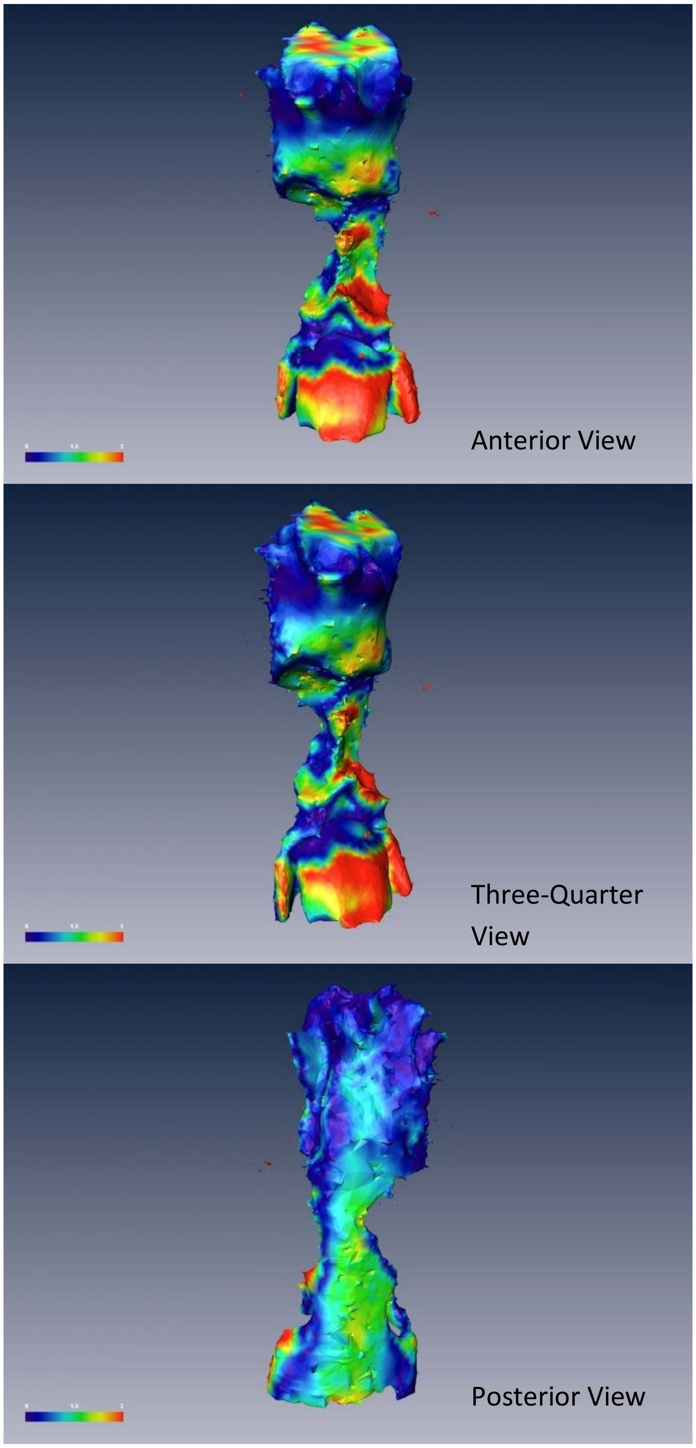






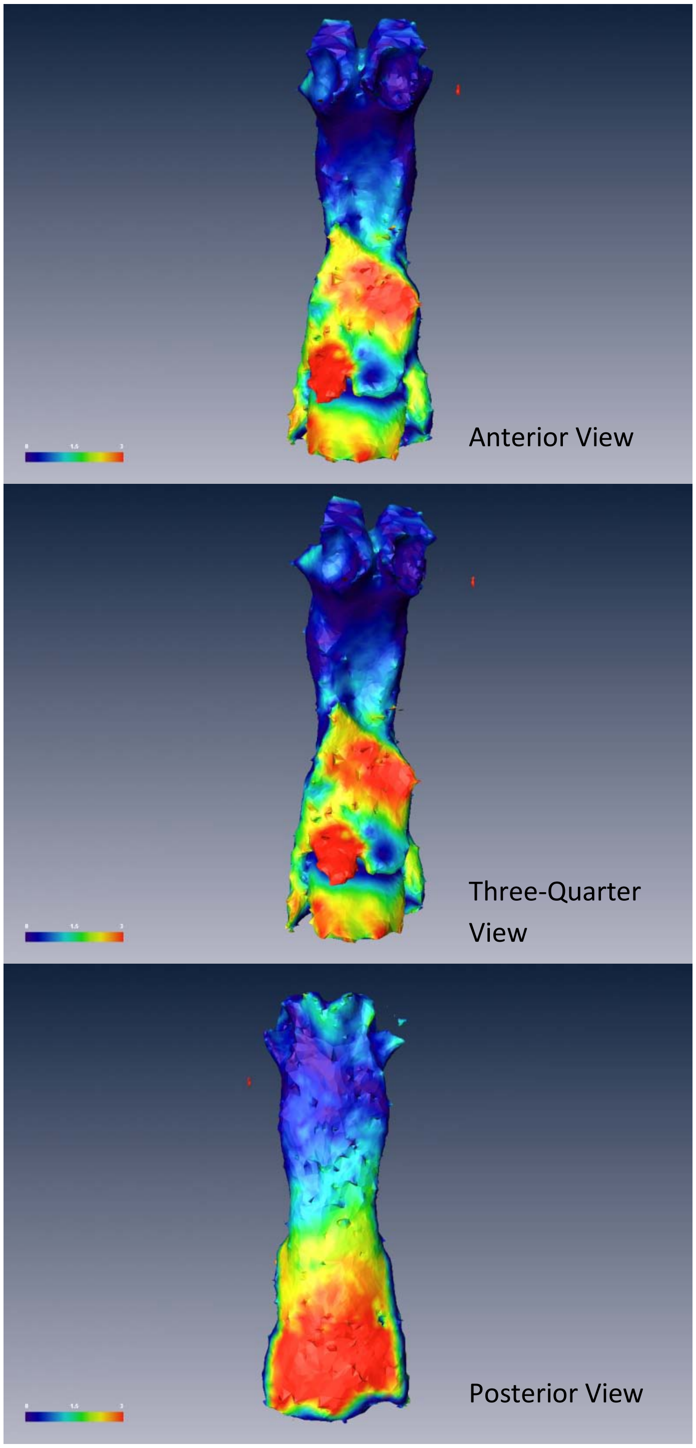
4mm mandibular setback	t2-t0 (%)
Whole Airway	-7.93
Nasophyarnx	-25.94
Oropharynx	12.13
Hypophyarnx	-7.16

Subject 20



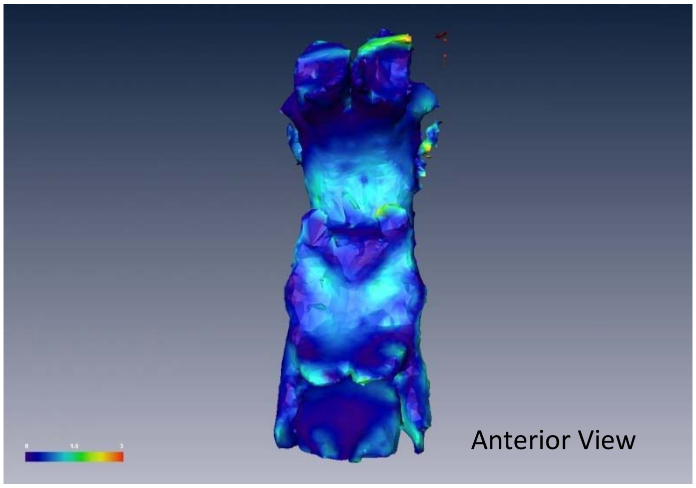
4mm mandibular setback	t2-t0 (%)
Whole Airway	3.31
Nasophyarnx	11.4
Oropharynx	7.66
Hypophyarnx	-10.68

Subject 21

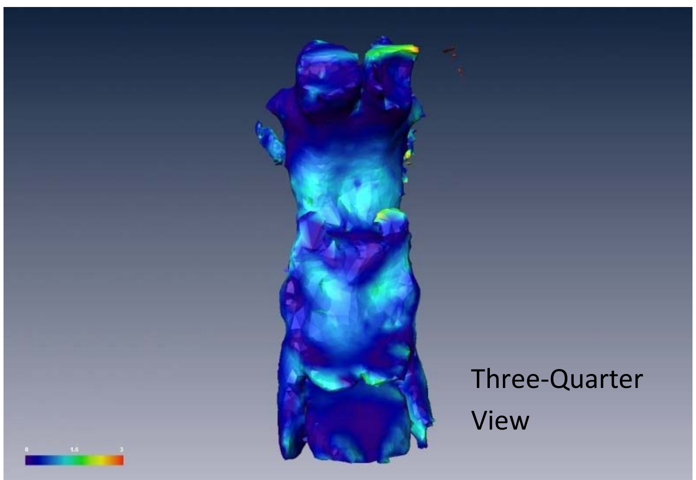


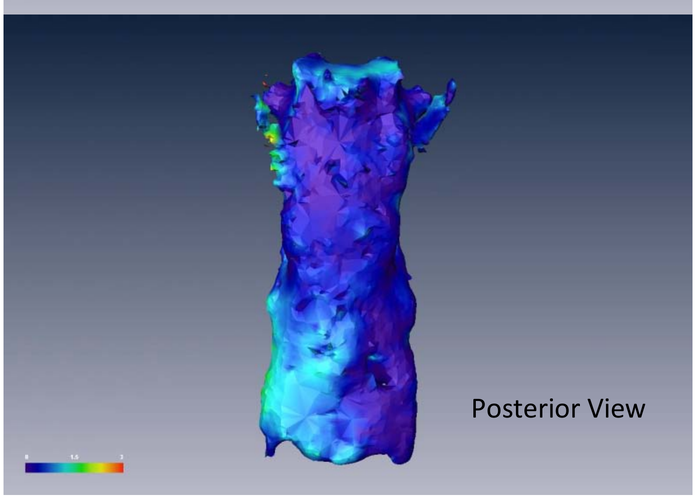
4mm mandibular setback	t2-t0 (%)
Whole Airway	6.26
Nasophyarnx	1.05
Oropharynx	-3.47
Hypophyarnx	19.86

Subject 22

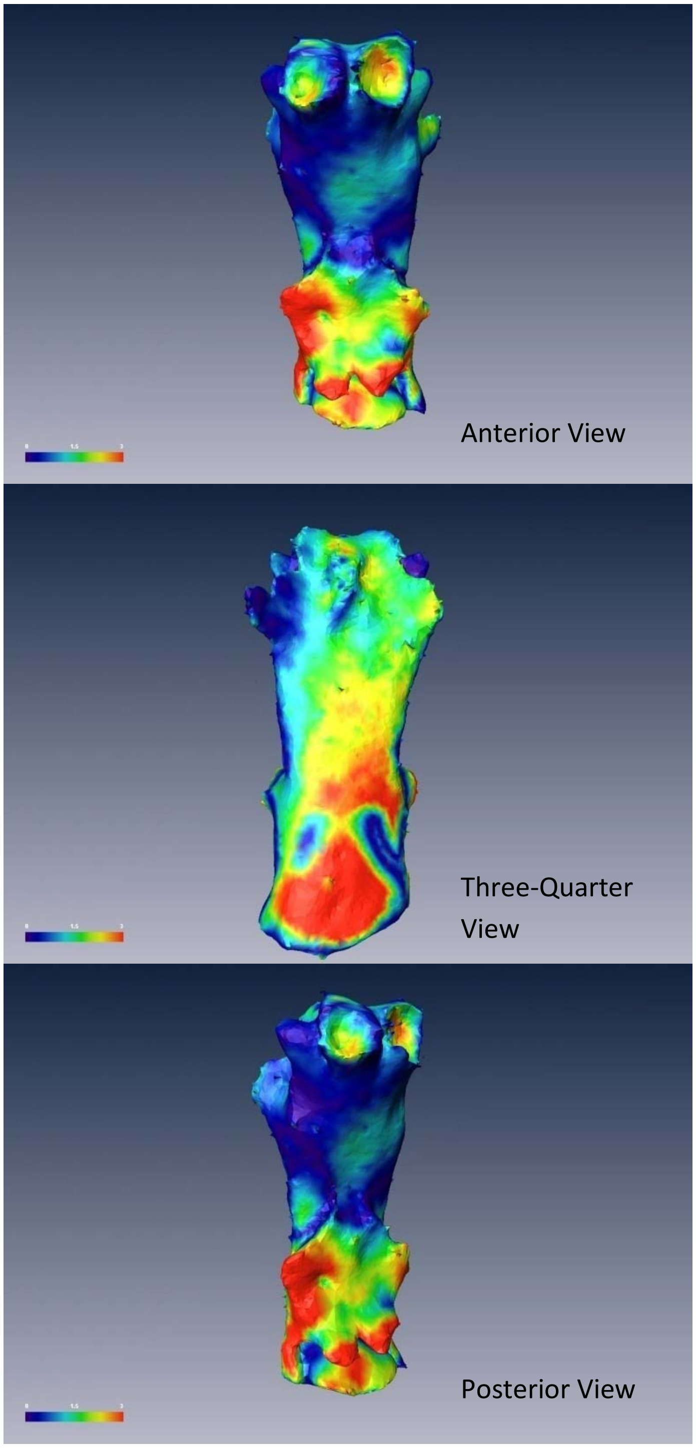


5mm mandibular advancement	t2-t0 (%)
Whole Airway	7.76
Nasophyarnx	23.25
Oropharynx	-0.43
Hypophyarnx	-2.67



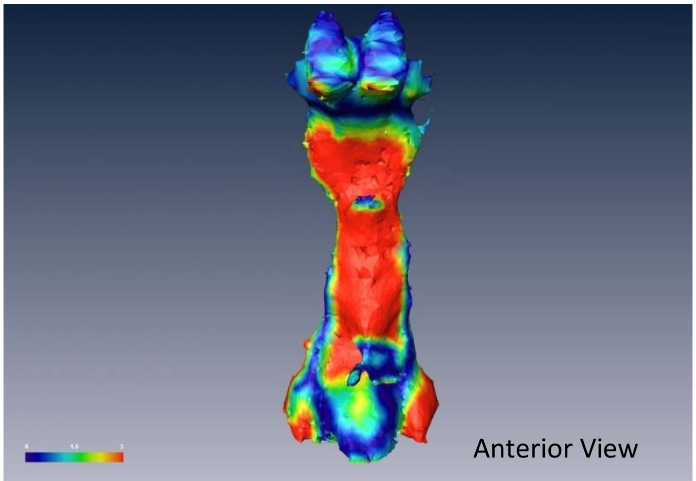


Subject 23

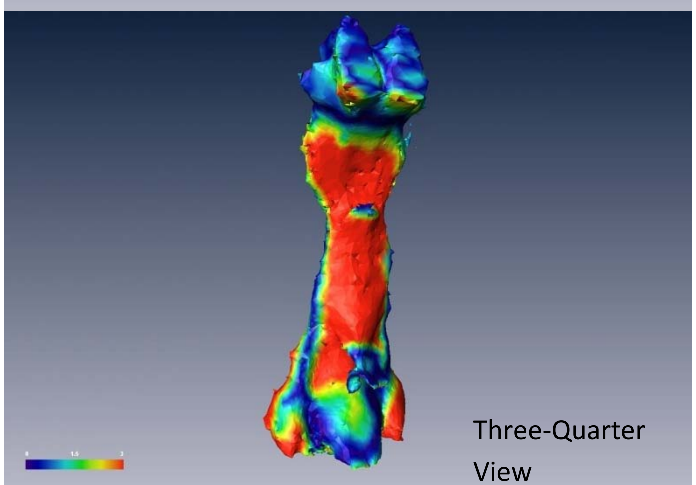


6mm mandibular advancement	t2-t0 (%)
Whole Airway	22.8
Nasophyarnx	54.15
Oropharynx	16.61
Hypophyarnx	31.63

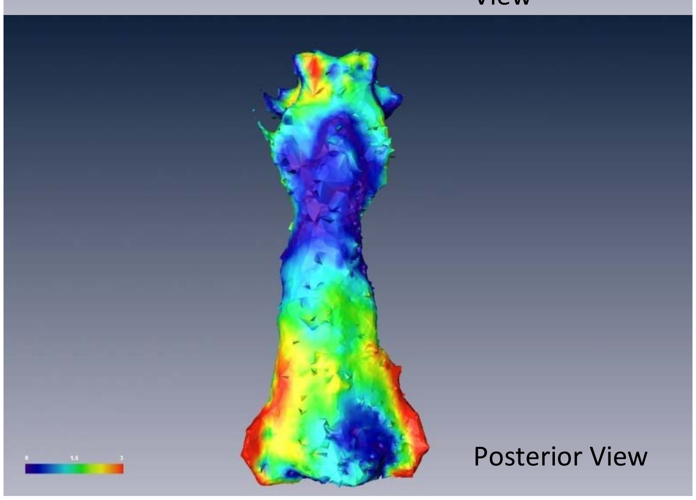
Subject 24



Anterior View



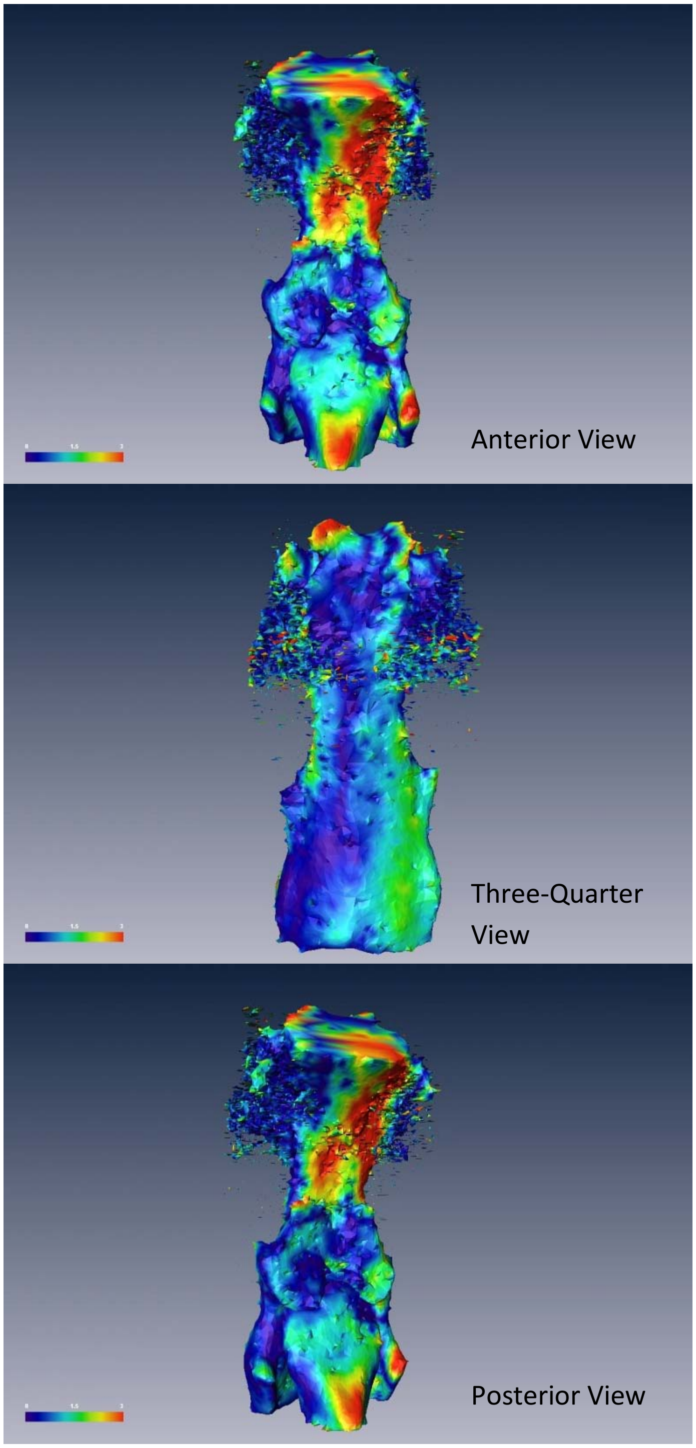
Three-Quarter View



Posterior View

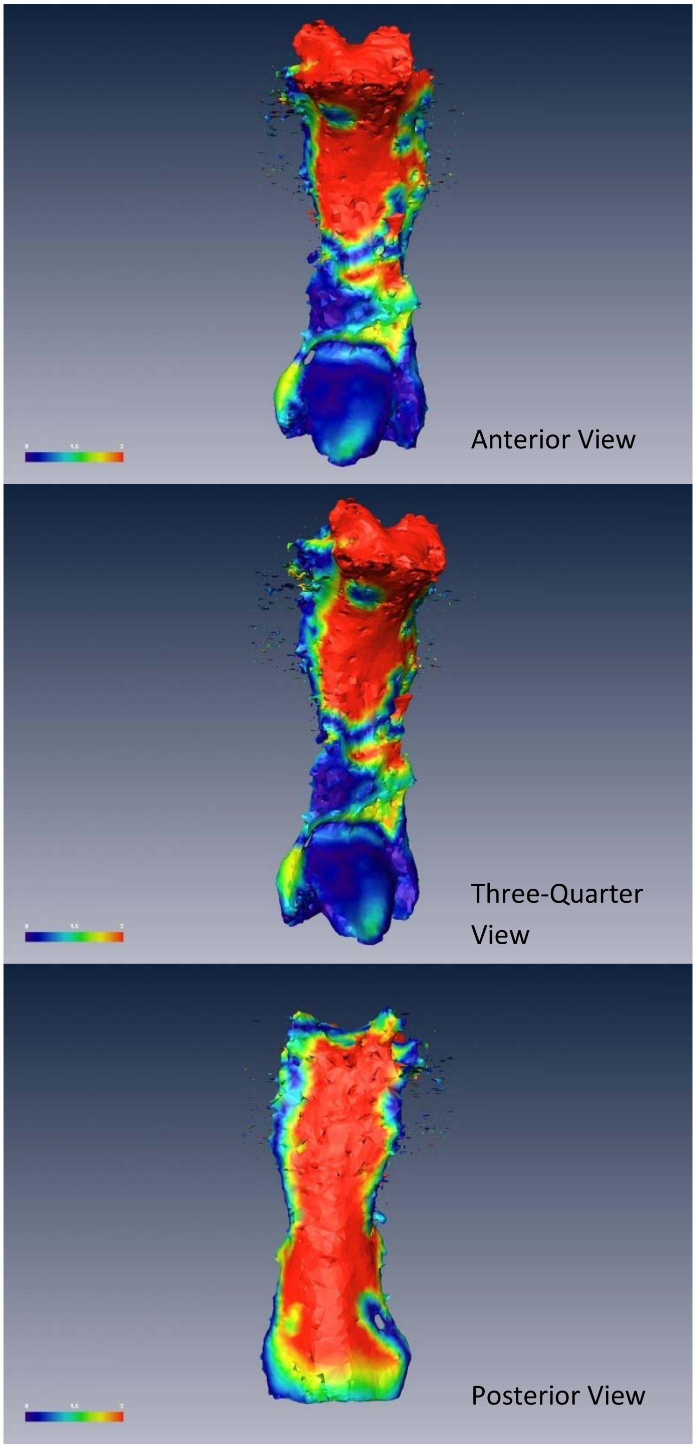
6mm mandibular advancement	t1-t0 (%)
Whole Airway	43.74
Nasophyarnx	42.78
Oropharynx	105.5
Hypophyarnx	-7.57

Subject 25



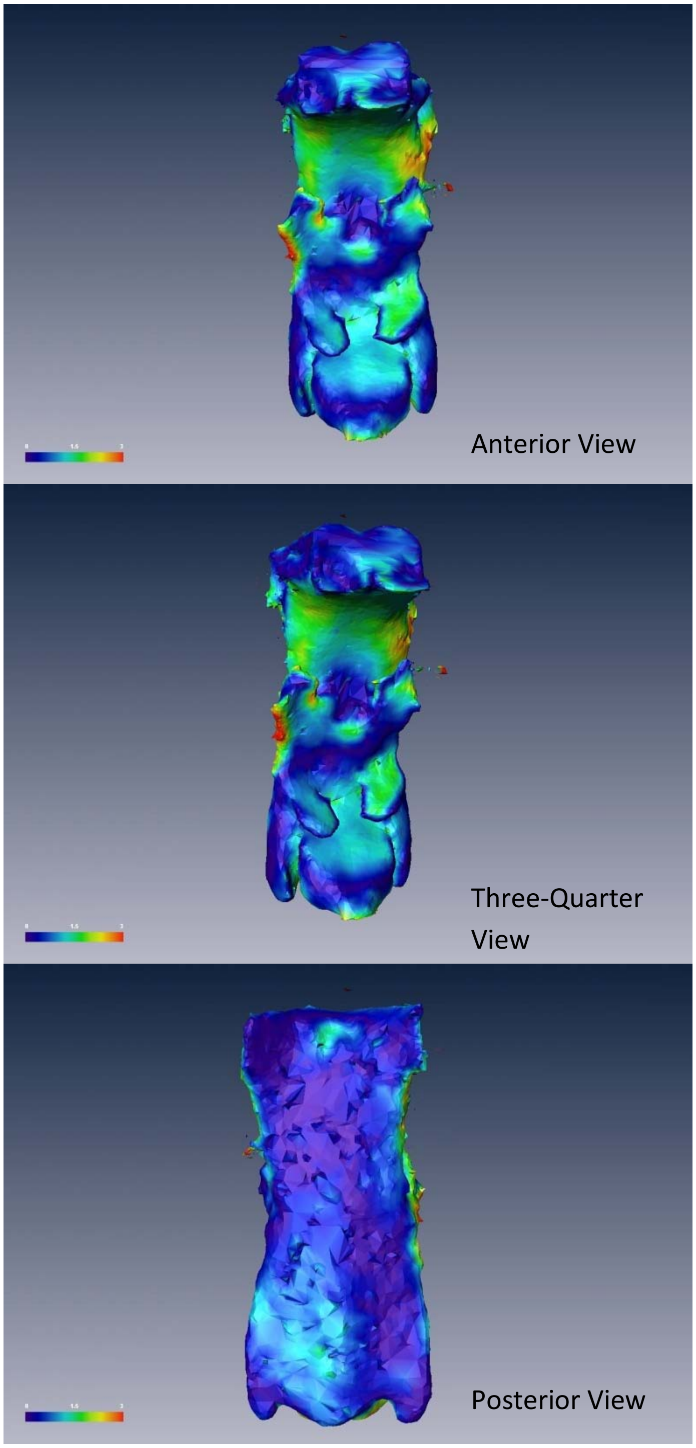
6mm mandibular advancement	t1-t0 (%)
Whole Airway	7.02
Nasophyarnx	17.23
Oropharynx	34.74
Hypophyarnx	-12.21

Subject 26



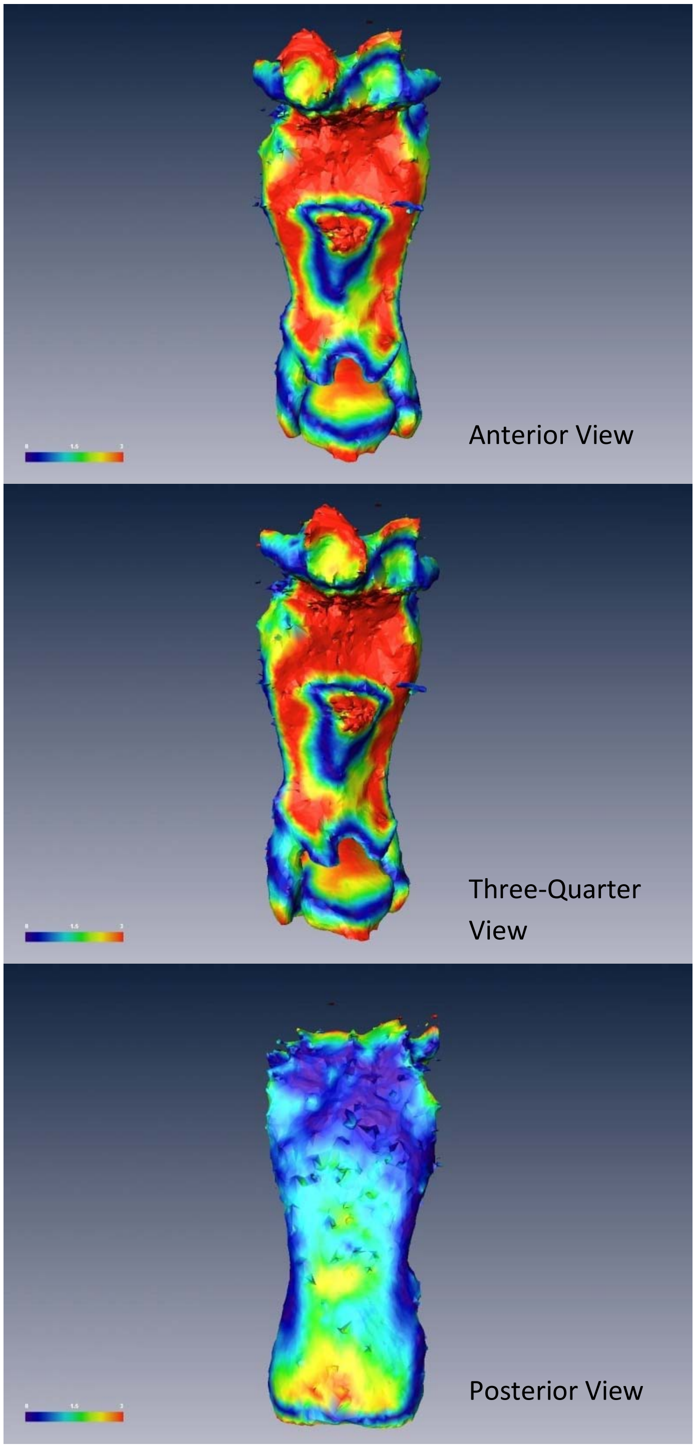
6mm mandibular advancement	t1-t0 (%)
Whole Airway	75.84
Nasophyarnx	133.6
Oropharynx	67.57
Hypophyarnx	66.5

Subject 27



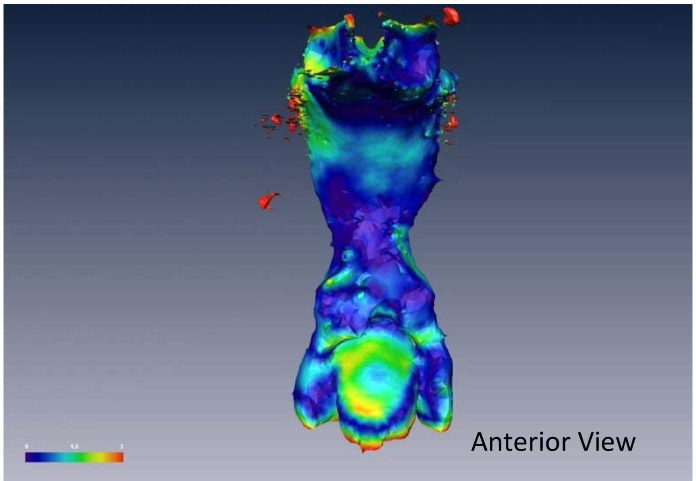
7mm mandibular advancement	t2-t0 (%)
Whole Airway	8.59
Nasophyarnx	-2.28
Oropharynx	12.45
Hypophyarnx	-0.94

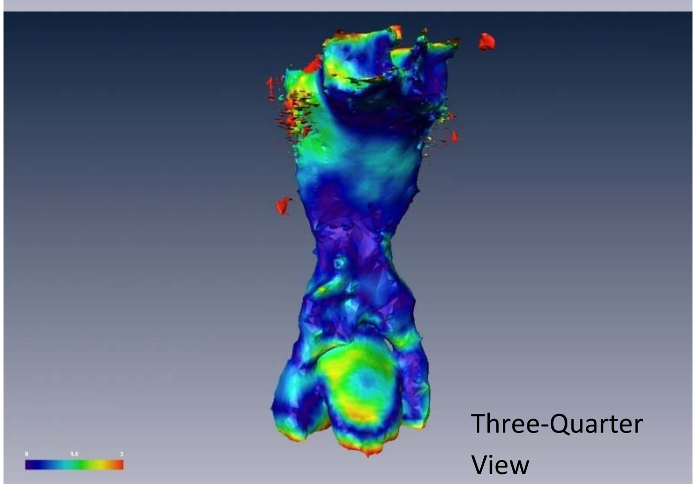
Subject 28

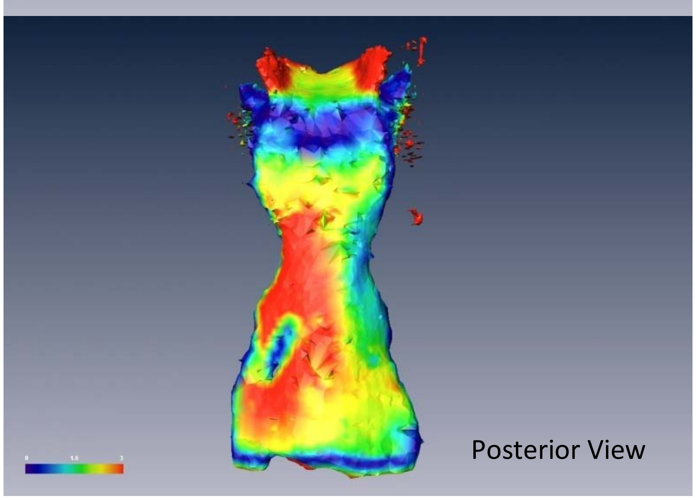


8mm mandibular advancement	t2-t0 (%)
Whole Airway	33.76
Nasophyarnx	-6.61
Oropharynx	45.4
Hypophyarnx	27.88

Subject 29

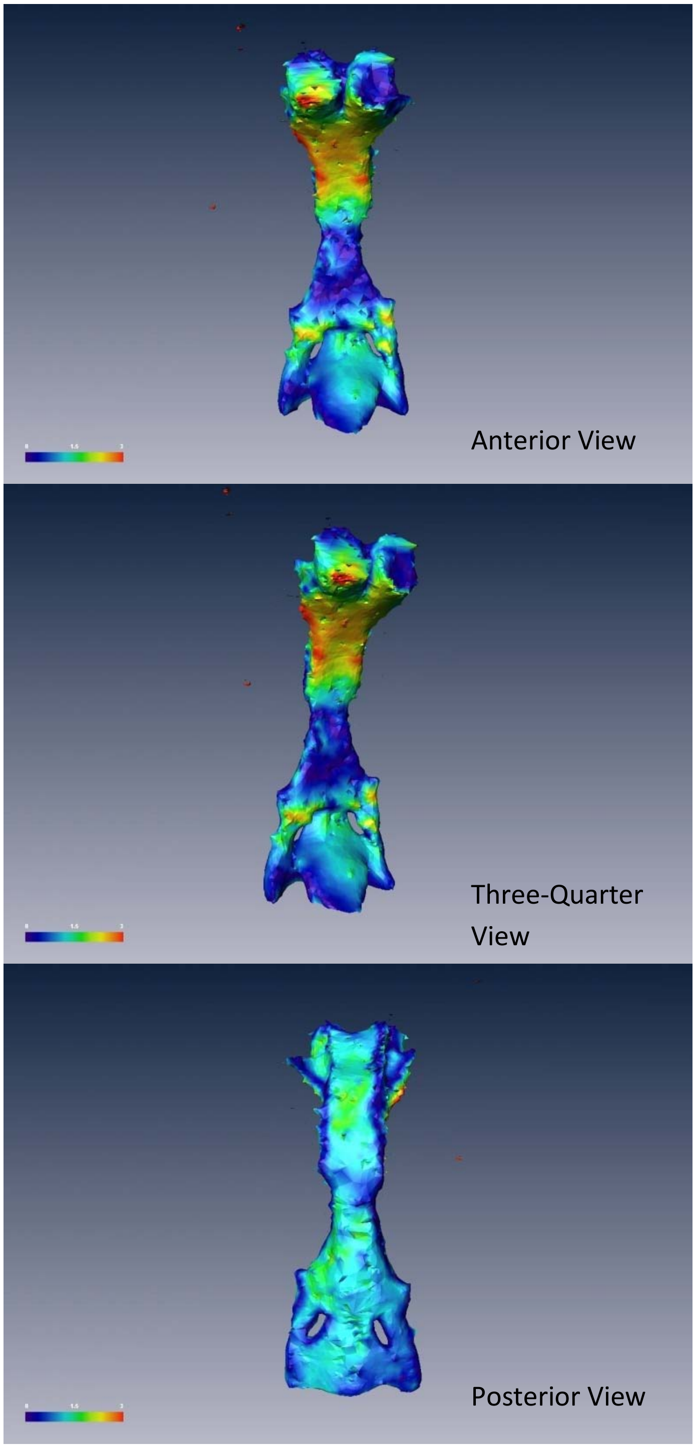

Anterior View


Three-Quarter View


Posterior View

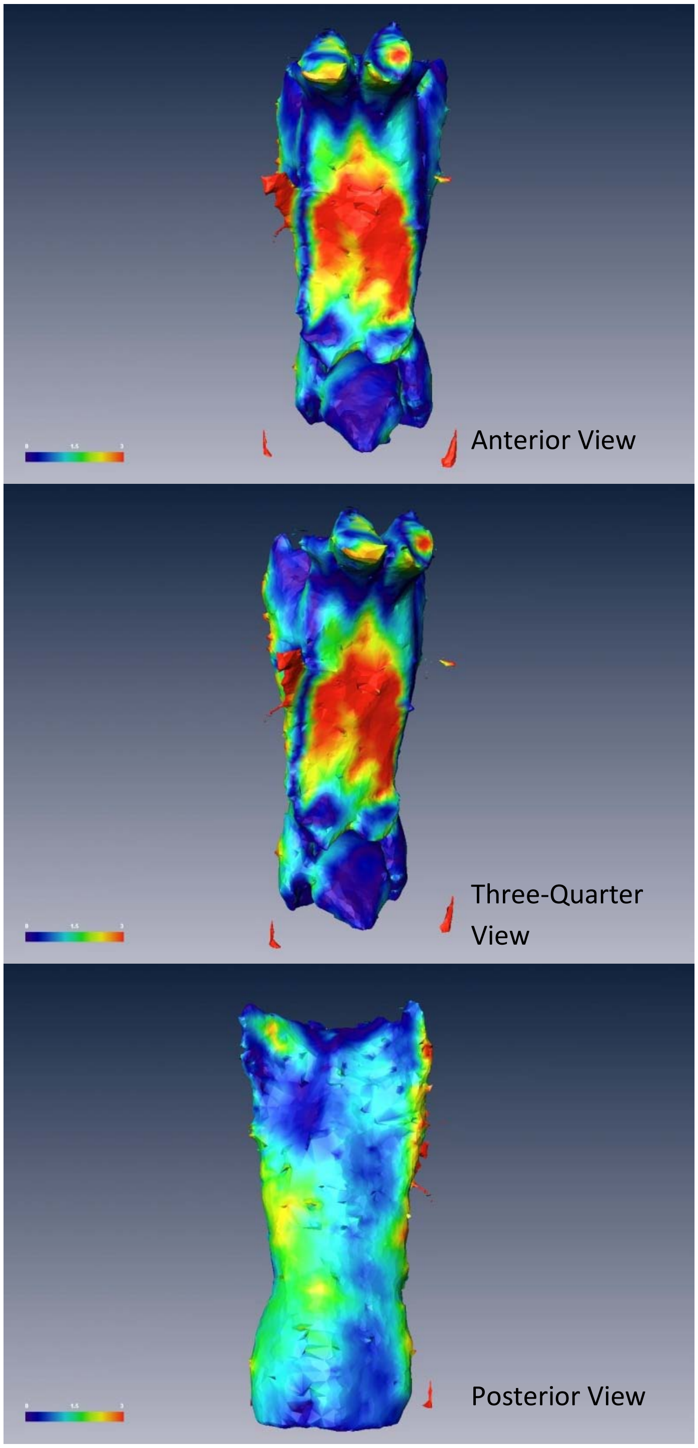
8mm mandibular advancement	t2-t0 (%)
Whole Airway	8.18
Nasophyarnx	-58.41
Oropharynx	36.97
Hypophyarnx	36.75

Subject 30



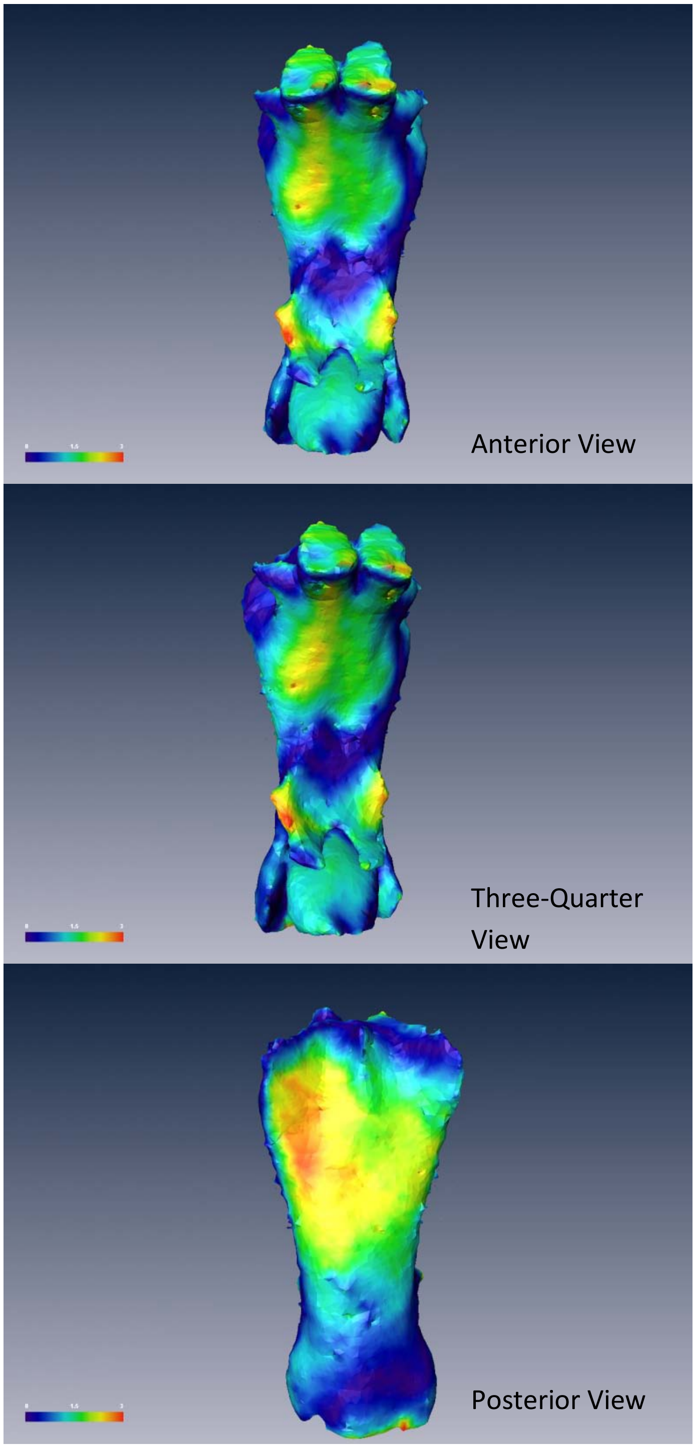
8mm mandibular advancement	t2-t0 (%)
Whole Airway	-3.37
Nasophyarnx	-17.72
Oropharynx	-3.99
Hypophyarnx	3.86

Subject 31



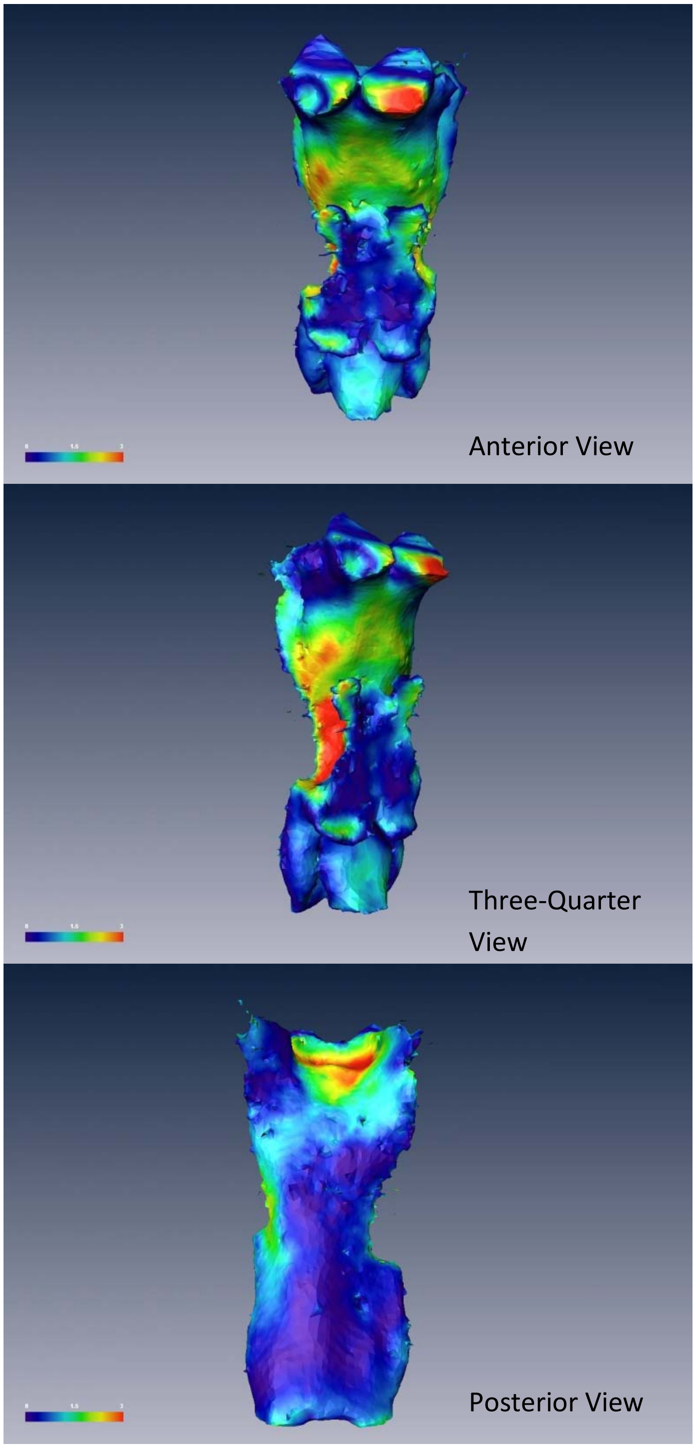
8mm mandibular advancement	t2-t0 (%)
Whole Airway	1.43
Nasophyarnx	0.81
Oropharynx	4.86
Hypophyarnx	-5.17

Subject 32



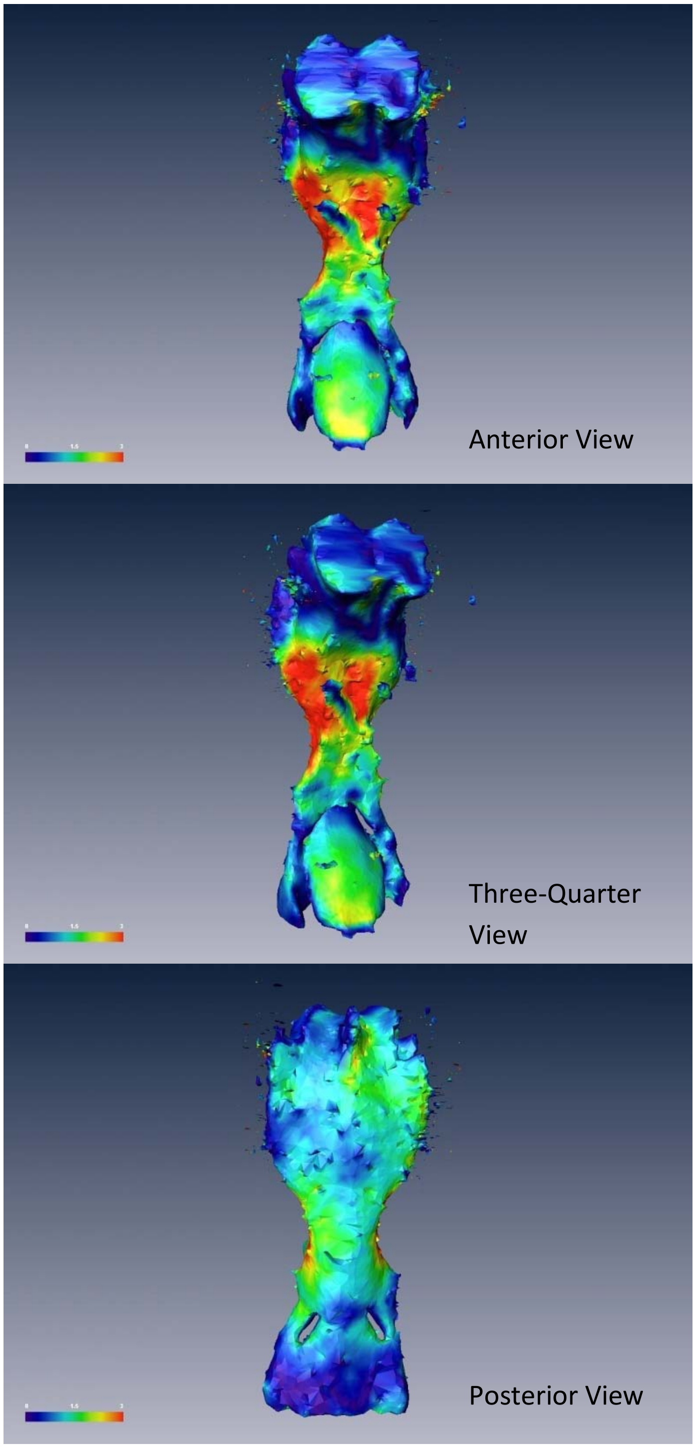
10mm mandibular advancement	t2-t0 (%)
Whole Airway	13.36
Nasophyarnx	-19.91
Oropharynx	37.78
Hypophyarnx	-12.73

Subject 33



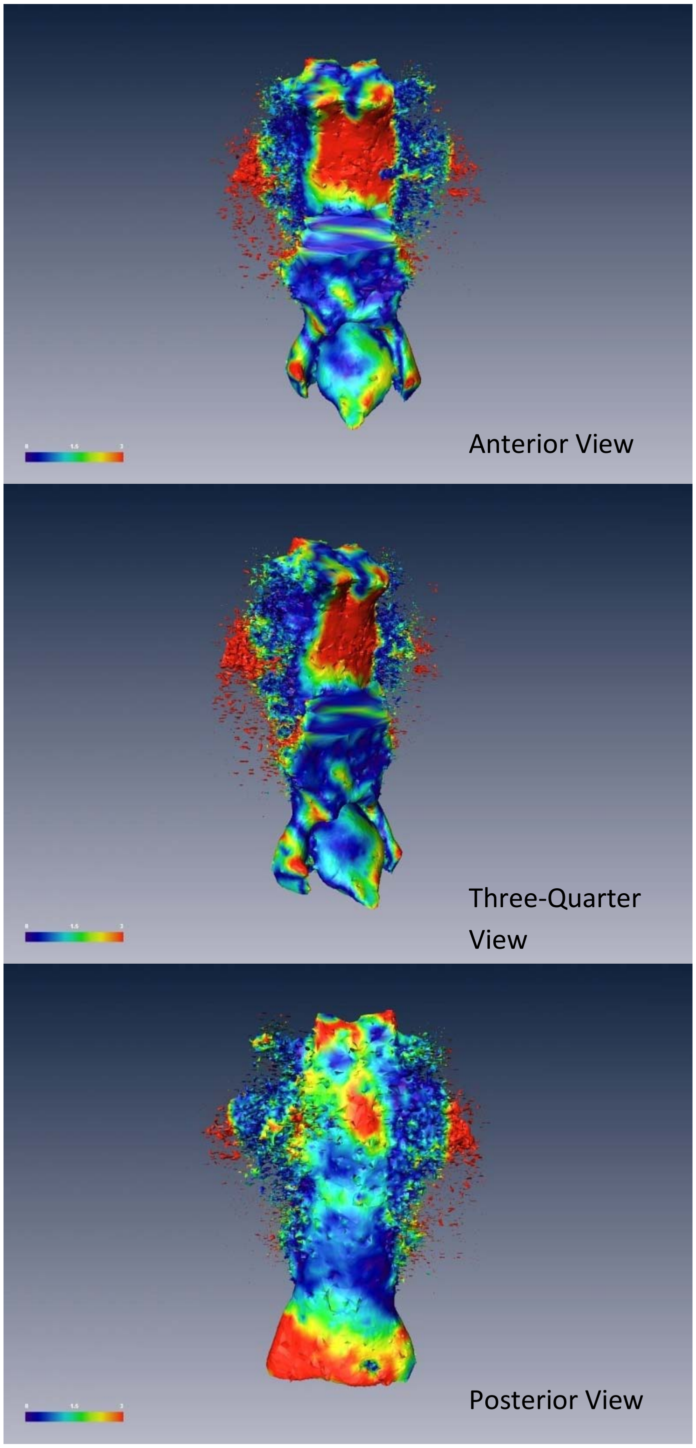
10mm mandibular advancement	t2-t0 (%)
Whole Airway	28.66
Nasophyarnx	-1.9
Oropharynx	43.16
Hypophyarnx	12.99

Subject 34



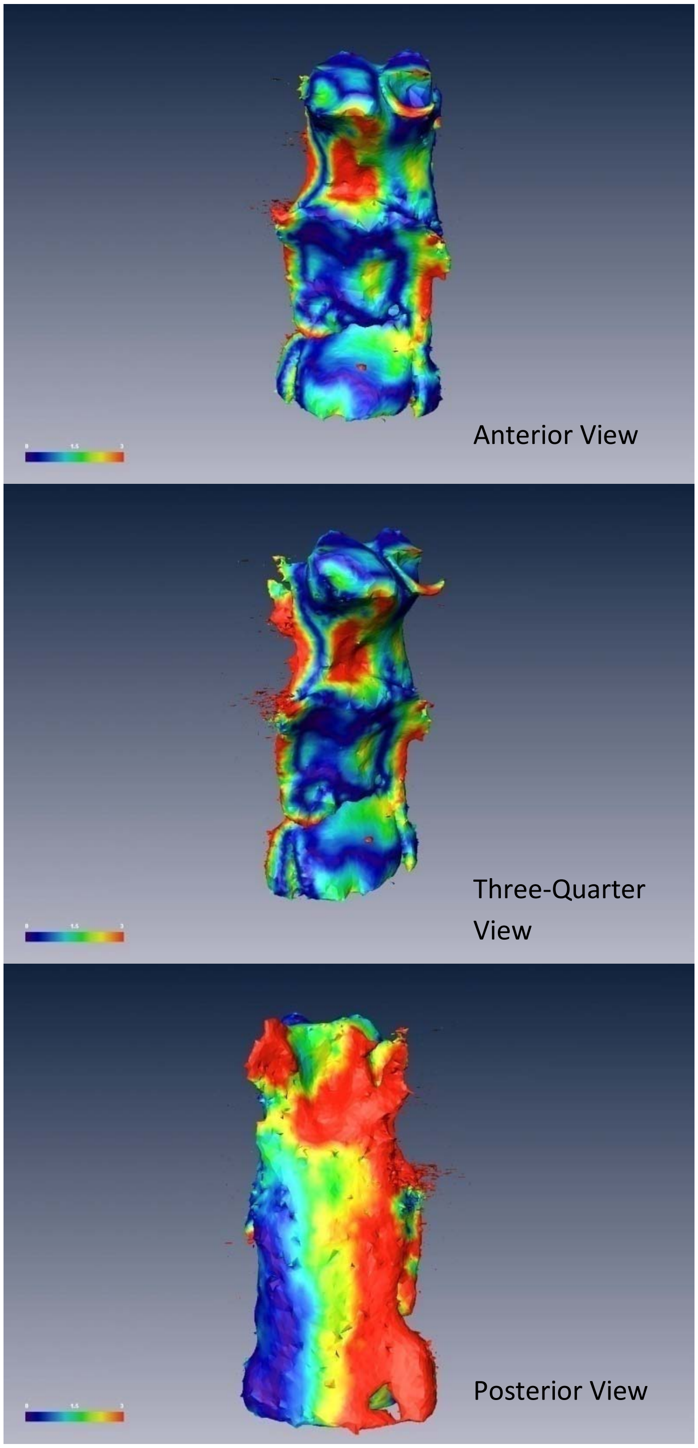
15mm mandibular advancement	t1-t0 (%)
Whole Airway	37.36
Nasophyarnx	-18.45
Oropharynx	61.22
Hypophyarnx	33.37

Subject 35



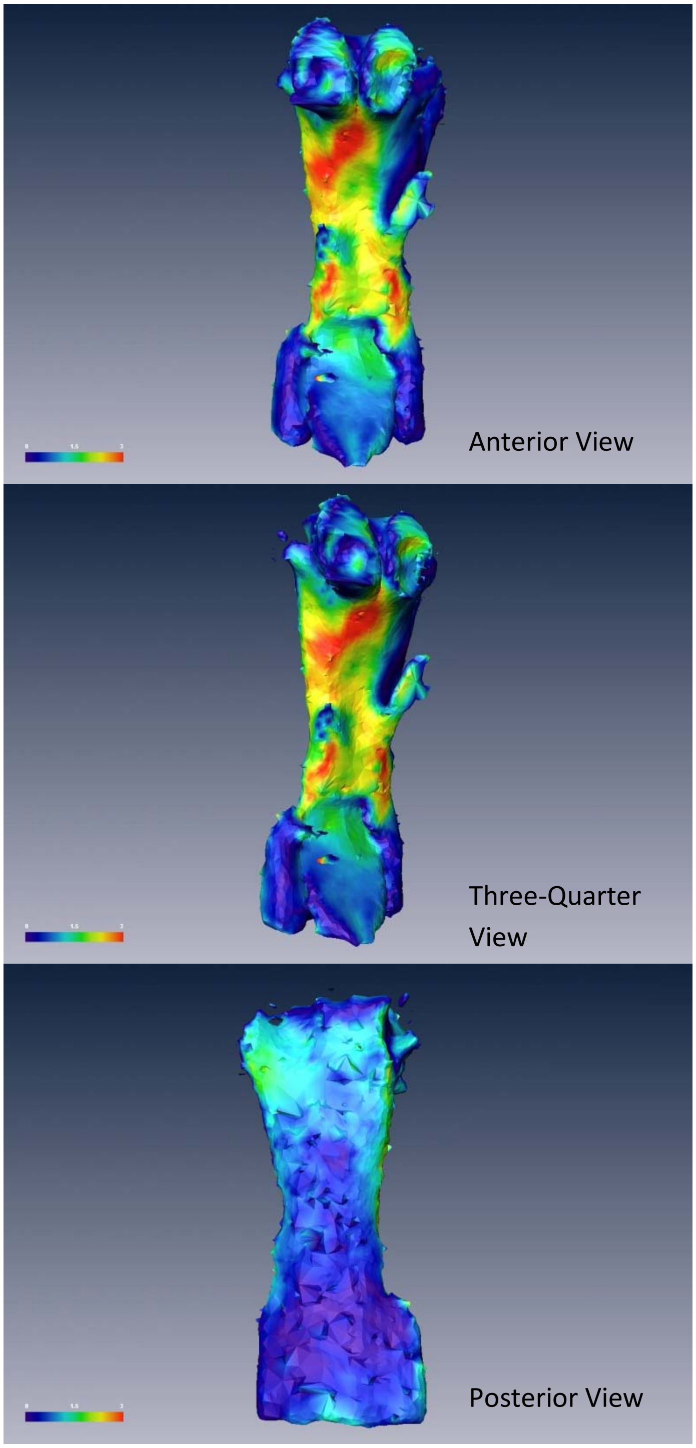
10mm maxillary advancement / 14mm mandibular setback	t2-t0 (%)
Whole Airway	-9.12
Nasophyarnx	5.98
Oropharynx	-9.26
Hypophyarnx	-13.78

Subject 36



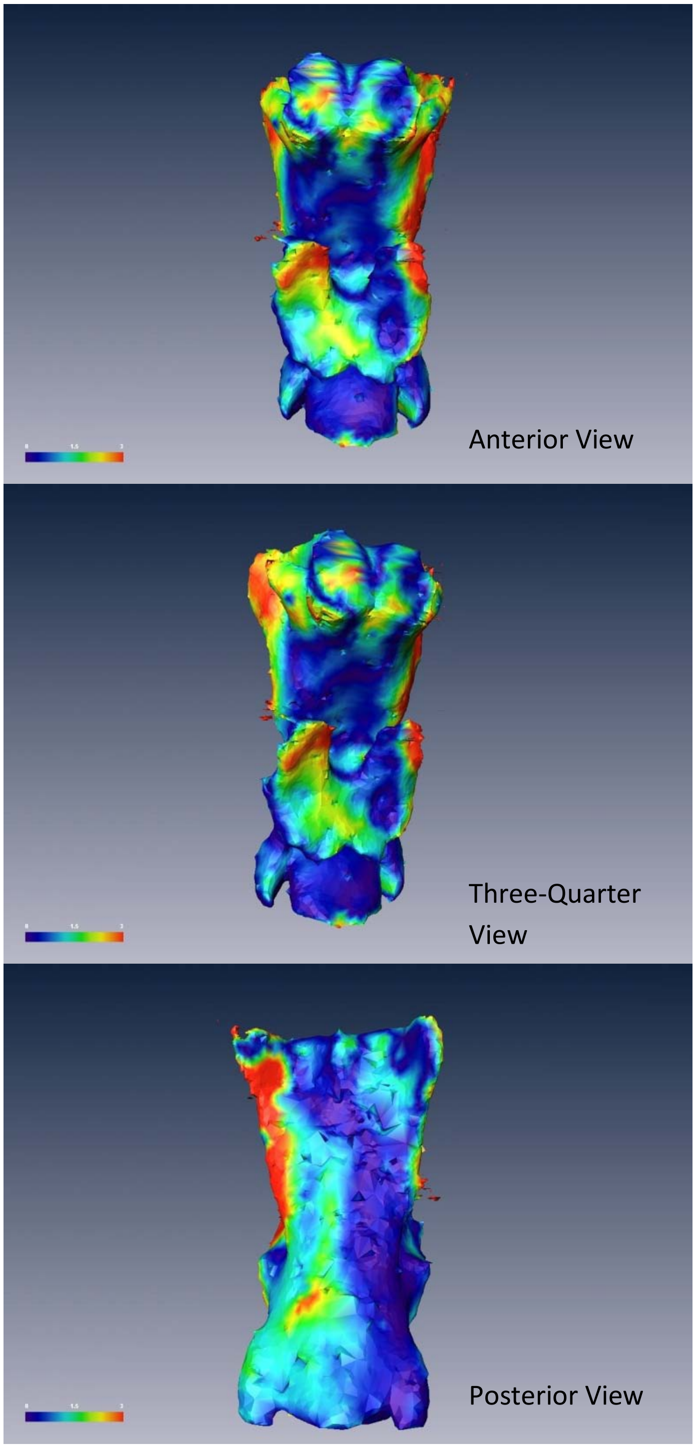
6mm maxillary advancement / 7mm mandibular setback	t2-t0 (%)
Whole Airway	-9.12
Nasophyarnx	5.98
Oropharynx	-9.26
Hypophyarnx	-13.78

Subject 37



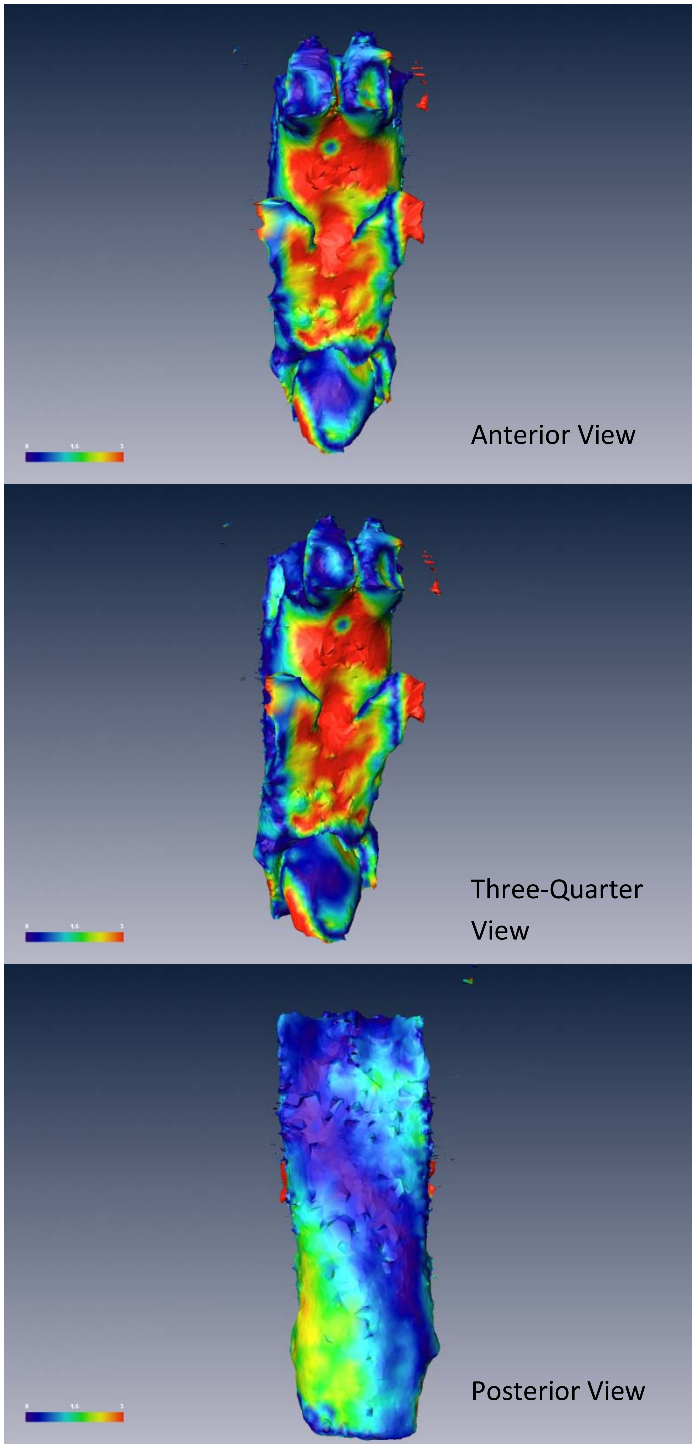
3mm maxillary advancement / 3mm mandibular setback	t1-t0 (%)
Whole Airway	26.78
Nasophyarnx	60.63
Oropharynx	25.23
Hypophyarnx	9.1

Subject 38



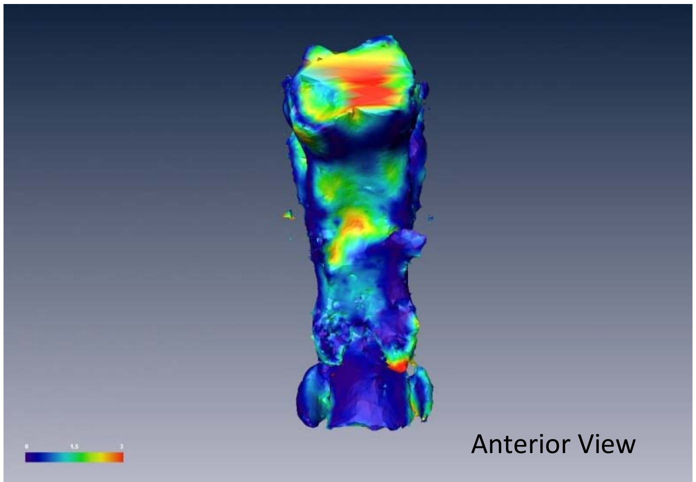
3mm maxillary advancement / 3mm mandibular setback	t1-t0 (%)
Whole Airway	-16.27
Nasophyarnx	-17.08
Oropharynx	-15.2
Hypophyarnx	-16.18

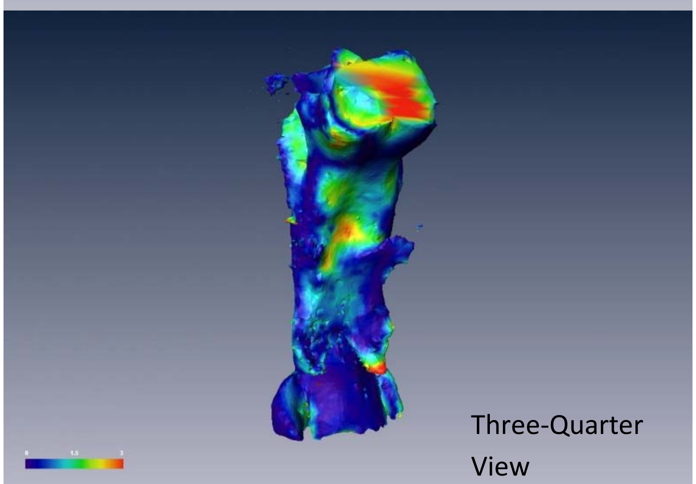
Subject 39

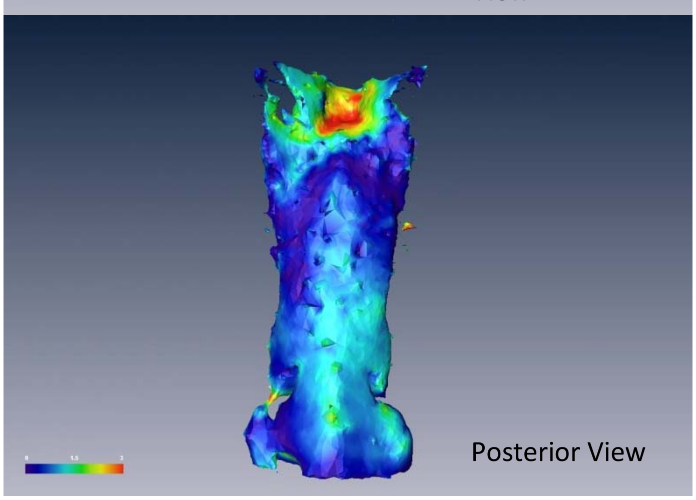


5mm maxillary advancement / 4mm mandibular setback	t2-t0 (%)
Whole Airway	16.56
Nasophyarnx	5.96
Oropharynx	19.49
Hypophyarnx	21.92

Subject 40

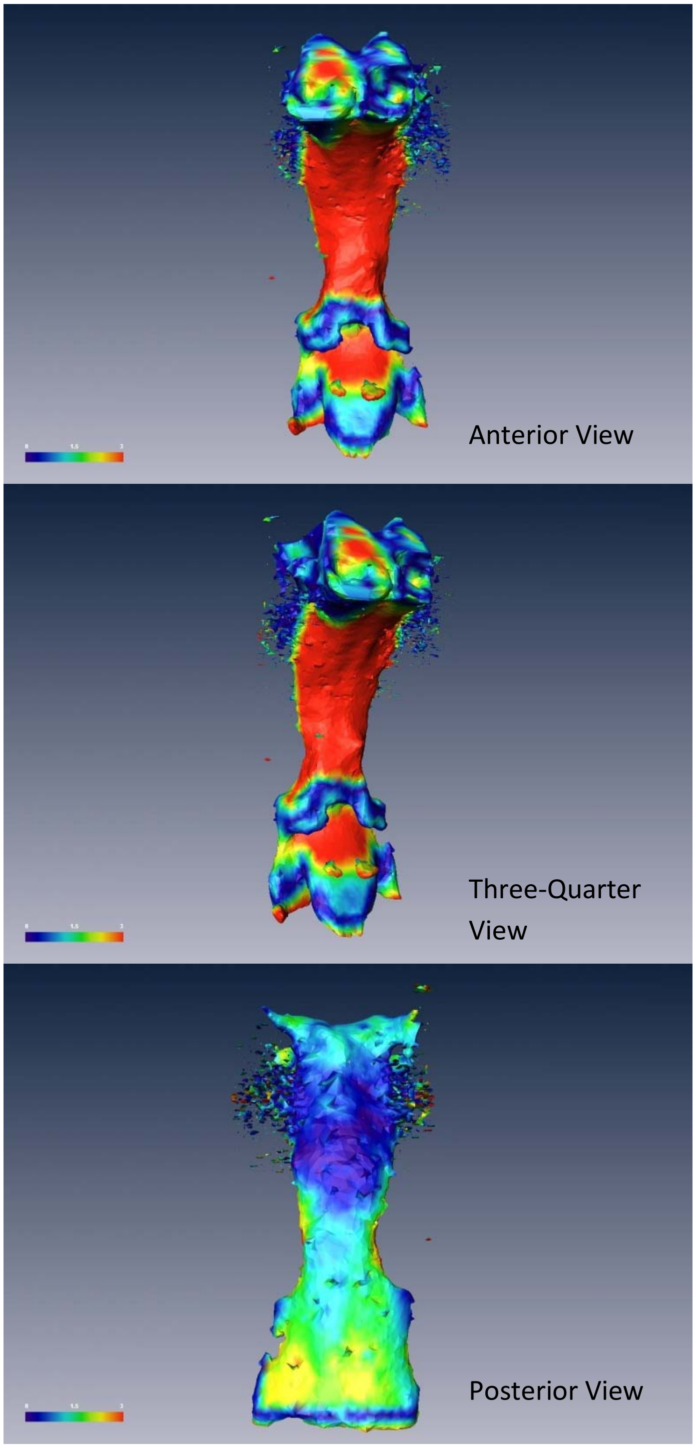






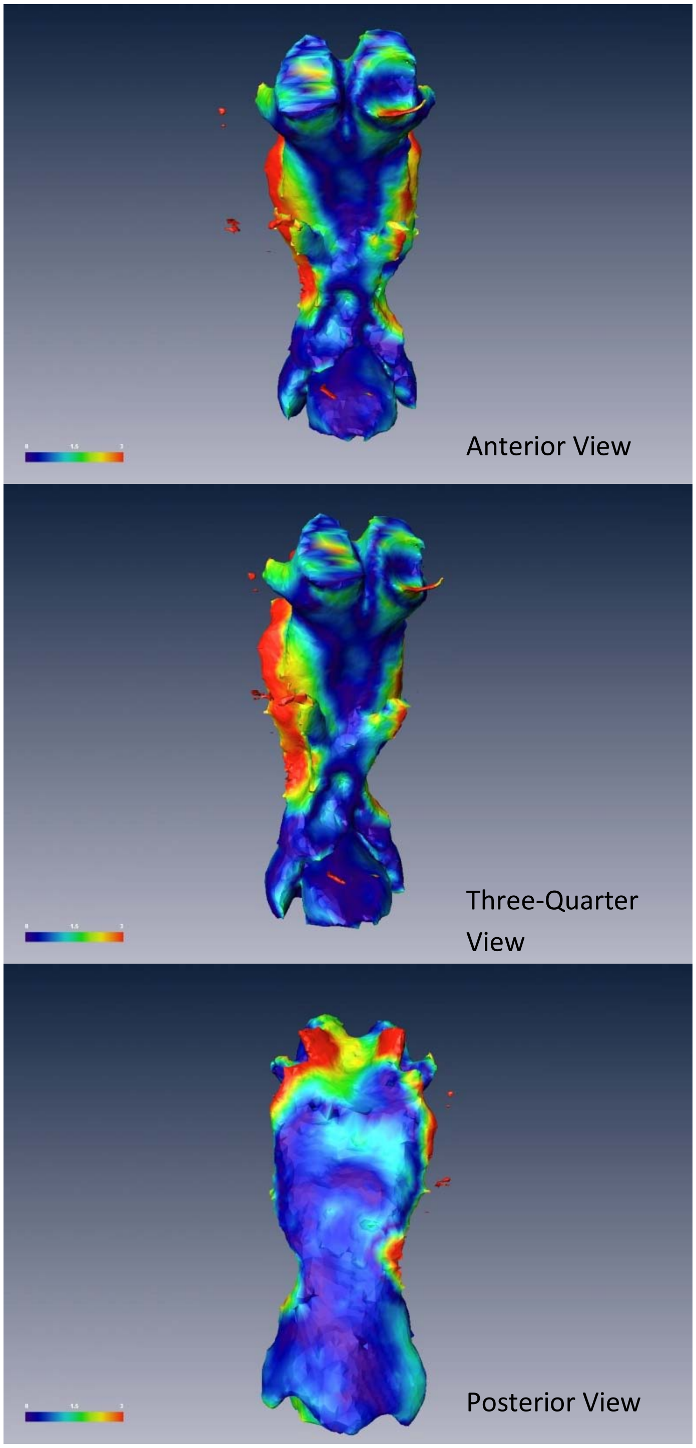
5mm maxillary advancement / 3mm mandibular setback	t1-t0 (%)
Whole Airway	17.16
Nasophyarnx	143.94
Oropharynx	15.21
Hypophyarnx	-5.17

Subject 41



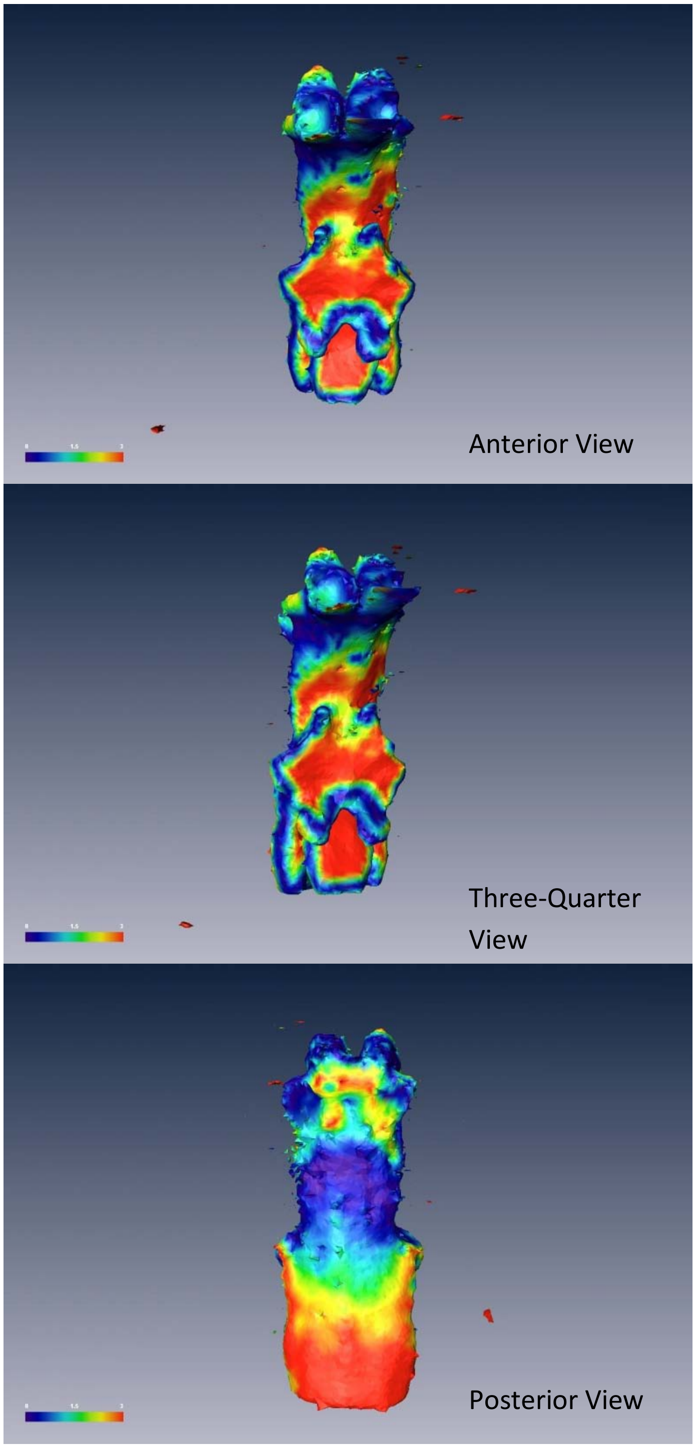
1mm maxillary advancement / 1mm mandibular advancement	t2-t0 (%)
Whole Airway	76.89
Nasophyarnx	-13.64
Oropharynx	134.93
Hypophyarnx	104.62

Subject 42



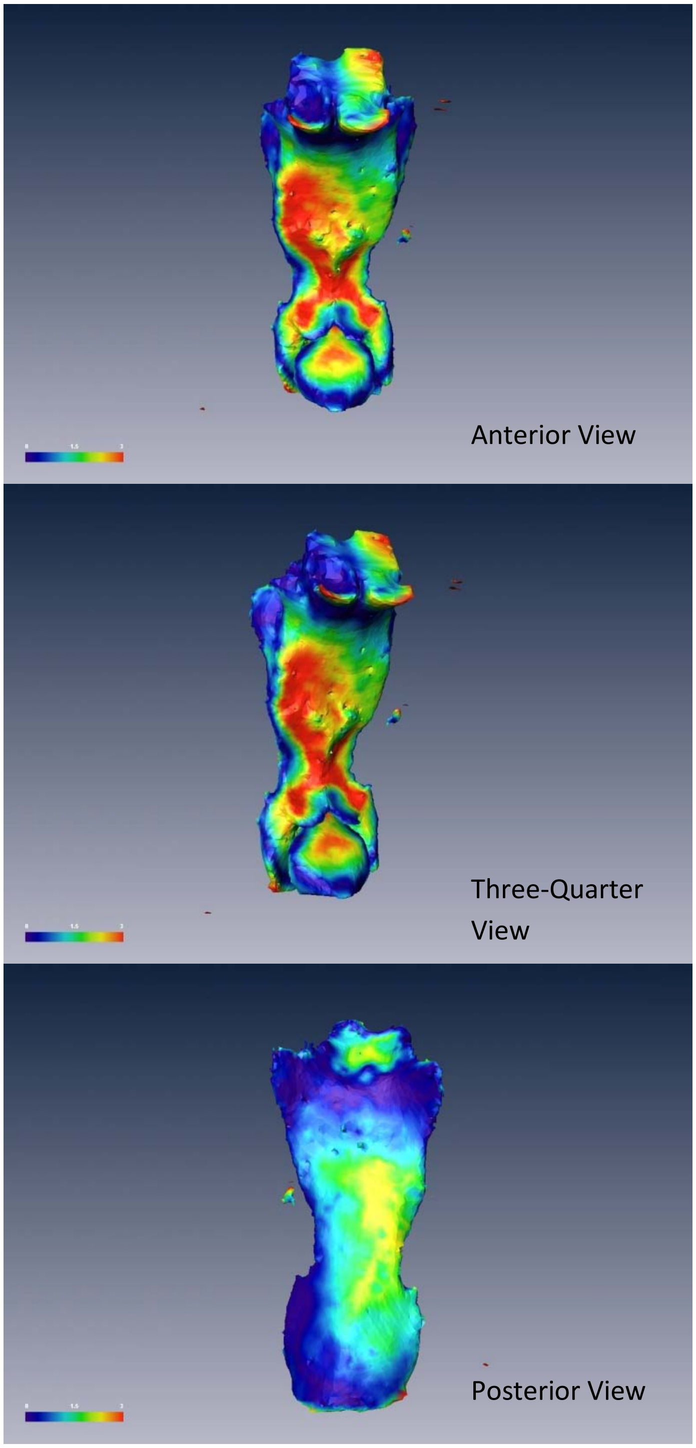
4mm maxillary advancement / 2mm mandibular advancement	t2-t0 (%)
Whole Airway	-14.2
Nasophyarnx	7.66
Oropharynx	-25.91
Hypophyarnx	-4.63

Subject 43



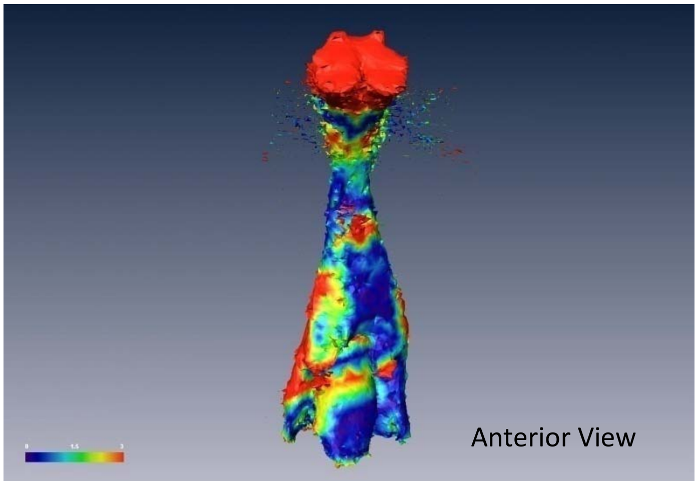
1mm maxillary advancement / 8mm mandibular advancement	t2-t0 (%)
Whole Airway	23.7
Nasophyarnx	23.78
Oropharynx	29.21
Hypophyarnx	8.95

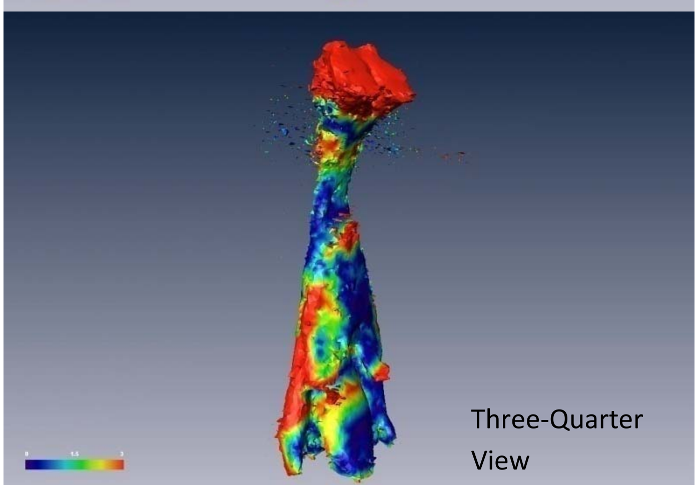
Subject 44

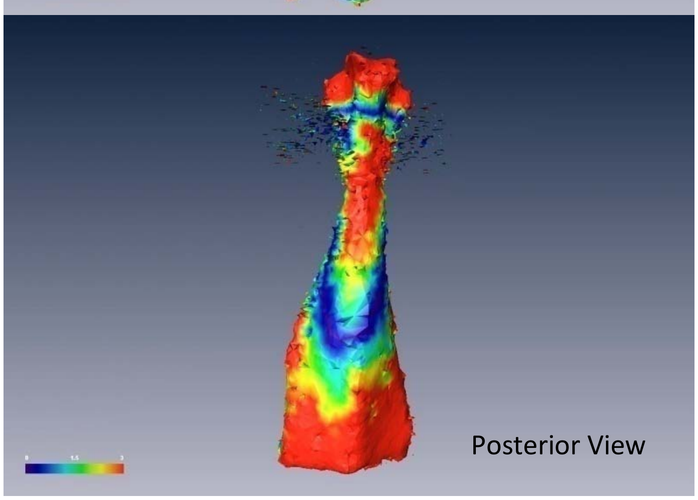


4mm maxillary advancement / 6mm mandibular advancement	t2-t0 (%)
Whole Airway	16.1
Nasophyarnx	50.58
Oropharynx	0.3
Hypophyarnx	21.28

Subject 45







10mm maxillary advancement / 10mm mandibular advancement	t1-t0 (%)
Whole Airway	-18.29
Nasophyarnx	-1.71
Oropharynx	21.35
Hypophyarnx	-60.9

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