Article

Change in the Constricted Airway in Patients After Clear Aligner Treatment: Retrospective Study

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Abstract: This retrospective study evaluated changes in the pharyngeal portion of the upper airway in patients with constricted and normal airway treated with clear aligners (Invisalign, Align). Additionally, the paper has assessed the change of tongue position in the oral cavity from lateral view. Evaluation was performed with specialized software (Invivo 6.0, Anatomage) on pretreatment and posttreatment pairs of cone beam computed tomography imaging (CBCT) data. The level of airway constriction, volume, cross-section minimal area, and tongue profile were evaluated. Patients with malocclusion, with pair or initial and finishing CBCT and without significant weight change between the scans, treated with Invisalign clear aligners were distributed in two groups. Group A consisted of fifty-five patients with orthodontic malocclusion and constricted upper airway. Control group B consisted of thirty-one patients with orthodontic malocclusions without any airway constriction. In the group with airway constriction, there was a statistically significant increase in volume during therapy ($p<0.001$). The surface of the most constricted cross-section of airway did not change significantly after treatment in any of the groups. The airway constriction was most frequently localized at the level of 2nd cervical vertebra. The final tongue position was different from initial in 62.2% of all clear aligner treatments.

Keywords: orthodontics; airway; clear aligners; 3D diagnostics; sleep apnea; CBCT

1. Introduction

As imaging techniques become increasingly advanced, the radiologic assessment of various head and neck disorders is also soaring to new heights. Recent advances in Cone beam Computed Tomography (CBCT) imaging have enabled precise diagnosis of head and neck morphology including airway, what increases the potential of prediction for the orthodontic treatment response.

Use of CBCT to evaluate the morphometric properties in maxilla-facial regions is a common scientific practice [1,2], albeit for soft tissue morphology is frequently employed magnetic resonance imaging [3]. In orthodontic therapy planning problems with teeth position, articulation, temporomandibular joint and intermaxillary relationships are diagnosed and addressed.

CBCT is used in orthodontics to acquire three-dimensional (3D) images of patients as an important step in diagnostics, also providing information about upper airway morphology with possible constrictions. It is known that obstruction of upper airway can lead to significant impact on quality of sleep, especially the crucial REM phase linked with various brain disorders [4,5] as the upper airway is stiffer and less compliant during REM sleep than during NREM sleep [6]. The loss of tone in upper airway muscles contributes to disorders of breathing especially during crucial REM sleep [7].

Not every upper airway constriction leads to sleep apnea, however even mild forms can damage the quality of sleep. The constriction of upper airway is often a multifactorial problem that results from possible hypertrophied adenoids, retrognathic mandible,

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atrophy of suprahyoid muscles especially lateral pterygoid muscle and genioglossus muscle [8], obesity, and many other factors. A multidisciplinary approach is necessary; however, it needs a reliable diagnostic as the importance of undisturbed breathing pattern and REM sleep is now better understood [9,10].

The malocclusion is evaluated as divergences on the x-y-z planes of space which are coronal, sagittal, and axial [11],[12],[13],[14] .The legacy 2D lateral cephalographic x-ray, posterior-anterior cephalograms and panoramic radiographs enlightened the pathway to 3D imaging, overcoming low resolution, imaging errors and superimposition of structures allowing calculation of the cross-sectional areas of the airway [15],[16],[17]. Such parameters elevate the precision of treatment of patients with orthodontic malocclusions and assist specialists to perform with highest details in their treatment plan [18]. Studies conducting a tridimensional evaluation of the upper airway have been proven reliable [12],[19] and point out that breathing through upper airways is of great importance for normal craniofacial development [20],[21]. During facial growth alterations in upper airway breathing, could affect the stomatognathic system and the development of the structures as well as their functions [22],[23].

Obstructive sleep apnea (OSA) is the most common sleep disorder represented by repetitive nocturnal upper airway collapse accompanied by intermittent hypoxia, fragmented sleep, fluctuations in blood pressure and highly active sympathetic nervous system activity [24],[25]. Significant is also the role of sleep questionnaires for the diagnosis of OSA [26]. Usually, the number of apnea/hypopnea incidents per night determines the level of severity of OSA, measured in apnea/hypopnea index (AHI) [27],[28]. This index is the primary outcome of Polysomnography (PSG).

PSG is an important tool for identifying OSA, but it is a costly and time-consuming procedure. In 2019 an Italian team consisting of Finamore et al used an innovative, non-invasive technique to provide clinically relevant information about OSA called breath analysis finding out that the Fractional exhaled Nitric Oxide, which is a vasodilator, is higher in OSA patients. This new promising method could potentially assist in identification, treatment, and monitoring of the patients under mechanical ventilation [29]. OSA affects more than 50% of the adult population, in non-communicable disease patients the 27,9% males and the 23,8% females [30]. In patients with cardiovascular disease the prevalence of the OSA is between 50% to 80% and in half of the subjects with heart failure the mortality and the prognosis are worse [31]. OSA is prevalent in the medical field confirmed by Greek research held by Alexandropoulou et al. in Greek secondary and tertiary hospitals that the 27,7% of the staff experienced daytime sleepiness out of the 444 Greek nursing staff population [32].

The signs of OSA include snoring while sleeping, unrested sleep, narcolepsy, cognitive impairment, mood elevations, personality changes and daytime sleepiness. Increased daytime sleepiness is the link between obstructive sleep apnea and depressive symptoms investigated by a Turkish team led by Celik Y. et al. [33].

In population of children with snoring that was investigated by HsiehHui-Shan et al., the screening that consisted of home sleep pulse oximetry, combined with adenoidal-nasopharyngeal ratio (ANR) showed higher effectiveness than ANR and tonsil size [34],[35]. Furthermore, based on the data that were acquired in the study held by Celikhisar H. There is positive correlation between the accident statuses of drivers with OSAS severity so awareness should be raised also in professional heavy equipment operators during their certification period [36].

Standard treatment method for OSA is considered positive airway pressure (CPAP) therapy, oral devices advancing mandible forward and suppressing the function of the tongue or even orthodontic treatment focusing on correcting and expanding the dental arches, creating a wider hard palate, affecting hard and soft tissues, changing the position of the tongue creating more space on the upper airway. Surgical intervention including unilateral or bilateral sagittal split osteotomy (BSSO) in combination to repositioning of maxilla or even nasal and/or palatal surgery, skeletal modification of the muscular

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support of the floor of the mouth including genioglossus advancement and hyoid suspension are among the prevalent choices.

Surgery that focuses on adjustments of soft tissues such as tonsils, adenoids, frenula and tongue can be also effective such as nerve stimulation [37],[38] and more specifically hypoglossal nerve stimulator during the breathing process could stimulate change of the tongue position and avoid obstructive incidence from happening but of course candidates for this kind of treatment should cover special criteria such as moderate to severe OSA, body mass index (BMI) over 32, assessed location of the collapse confirmed by drug-induced sleep endoscopy [39].

Invisalign was introduced by Align Technology (Santa Clara, in California) in 1999 as the pioneer of clear aligner system for comprehensive orthodontic treatment. Continuous updates improve the quality of aligner materials, attachments on teeth, tooth movement staging, introduction of interproximal reduction and intermaxillary elastics allow a wider spectrum of malocclusions to be addressed.

The proper diagnostics methods during the patient examination and treatment planning are essential for the orthodontist to build a correct and effective treatment plan. An orthodontist, with understanding of the malocclusion in contextual comprehension of the intermaxillary relationship, tongue posture, airway, and bone morphology, can build a customized treatment plan for his patient. Effective treatment is important to preserve patient compliance, albeit in aligner therapy this might not be enough. Frequently patients are coached during aligner therapy with a smart mobile app as their treatment compliance is essential to its success and such a smart solution can be utilized not only to improve aligner and elastic wear but also for reporting of possible sleep disruptions or other patient feedback providing valuable research data [40].

An imprint of the dental arches either by old-fashioned alginate dental impressions and then by secondary scanning from a technician or with the direct digital intraoral scanning from the orthodontist is important to obtain and allow the study of the dental arches in digital form. Software such as OrthoCAD (Cadent, Inc., Carlstadt, New Jersey, United States) allow the analysis of the digital casts and provide information about measurements of discrepancy, proportionally and available dental spaces. The 3D controls provided by the software of Invisalign - ClinCheck (Align Technology, San Jose, California, United States) enable the clinician to adjust the treatment plan and add precise movements in the teeth such as rotation, inclination, tipping, torque, intrusion, extrusion, angulation both root and crown 3D control tools.

Very often the AP discrepancy is an outcome of an underlying skeletal discrepancy best dealt in growing patients with growth modification. In growing patients, the growth modification could be achieved traditionally with functional appliance, fixed Class II correctors or with headgear and once the skeletal pattern has been corrected to Class I the clear aligners can be used as second phase of treatment. In clear aligner technology the mandibular advancement feature can be used to address Class II skeletal discrepancies in growing patients with mandibular retrognathia. In Class III patterns that are characterized by maxillary retrusion, growth modification with protraction face mask can be first attempted and after Class I has been established the treatment can be followed by clear aligners.

In cases that the AP discrepancy is mild, dental camouflage can be accepted in combination with elastics wear or/and premolar extraction. In severe cases that the dental camouflage is not possible, orthognathic surgery will be required for correction of the underlying skeletal problem and it can involve sagittal split mandibular osteotomy or maxillary osteotomy or even combination of both arches. From modern approaches to correct dental Class II a 3D printed distalizer can be utilized [41].

Comprehension of the biomechanics of clear aligner technique, capability of digital treatment planning and predictable treatment protocols are the keys to have any treatment with clear aligners successful.

An important tool in orthodontic diagnostics is the lateral cephalometry which has played an important role in upper airway analysis in previous decades. However, the

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morphology of the airway is not evaluated precisely using the lateral cephalometry since the three-dimensional airway can't be properly visualized in two-dimensional analysis as shown in the lateral cephalometry [42]. A meta-analysis performed by Armalaite J. Et al. concluded that the reduced upper posterior pharyngeal space (SPAS) could be a prognostic parameter for suspecting OSA, while the mandibular plane to the hyoid bone (MP-H) could be used as a predictor when differentiating normal subjects and patients with OSA [43].

Cone beam computed tomography is widely used in the field of dentistry and in orthodontics to obtain three-dimensional (3D) images of patients. 3D cephalometric analysis is taught nearly fifteen years on medical faculties already [44]. The malocclusion is evaluated as divergences on the x-y-z planes of space which are coronal, sagittal, and axial [45]. The legacy 2D lateral cephalographic x-ray, posterior-anterior cephalograms and panoramic radiographs opened their way to 3D imaging overcoming low resolution, imaging errors and superimposition of structures allowing calculation of the cross-sectional areas of the airway axial [46]. Parameters like that elevate the precision of treatment of patients with orthodontic malocclusions and assist specialists to perform with highest details in their treatment plan [47].

Research published by Tsolakis in 2016 about the comparison of the CBCT and acoustic reflection for upper airway analysis found out that the correlation between the two methods was high while there weren't found any differences when measuring anterior nasal volume or minimal cross-sectional area, concluding that the CBCT is an accurate method for measuring anterior nasal volume, pharyngeal volume, and pharyngeal minimal cross-sectional area [48].

The diagnosis and treatment of sleep-disordered breathing require reliable and accurate upper airway analysis. Studies conducting a tridimensional evaluation of the upper airway have been proven reliable and point out that breathing through upper airways is of great importance for normal craniofacial development [47],[49]. During facial growth alterations in upper airway breathing, could affect the stomatognathic system and the development of the structures as well as their functions.

The aim of this study is to present a concept and method of 3D evaluation of upper airway morphology and tongue position from initial and final CBCT accompanying the orthodontic treatment with clear aligners. This paper compares the clinical effect of aligner therapy on upper airway morphology in patients with constriction prior to the treatment and patients without constriction. The negative effect of upper airway constriction on sleep quality and human cognitive functions is well known. This study sheds some light on the link between orthodontic correction of malocclusion and airway morphology that is poorly scientifically explored so far.

2. Materials and Methods

2.1 Concept, Hypothesis and PICO

Pre-treatment and post-treatment airway can be 3D evaluated on CBCT diagnostic records made during orthodontic aligner treatment. Segmentation and evaluation of airway morphology from CBCT is done with specialized software, tongue position from CBCT is evaluated with orthodontist.

The clinical effect of corrected occlusion and/or intermaxillary relationship can influence the upper airway morphology in the oropharyngeal portion of the pharynx (**Figure 1**).

Working hypothesis of this paper was a presumption that if the pre-treatment constriction of airway is an outcome of disturbed occlusion and/or incorrect intermaxillary relationship, an orthodontic correction shall result in characteristic improvement of this constricted airway morphology. Especially in comparison to an un-constricted control group treated with the same methods.

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Null hypothesis presumes that if orthodontic aligner treatment has no effect on the upper airway morphology and tongue position, there shall be no significant difference on upper airway morphology between pre-and post-treatment of non-growing patients.

PICO framework if this paper is the following:

- Patients were **55** adults with malocclusion with initial and final CBCT, without significant BMI change between the CBCT scans and with observed airway constriction on the pre-treatment CBCT.
- Treatment with clear aligners (Invisalign).
- The control group or **31** patients with malocclusion without any airway constriction were treated with the same approach.
- The outcome of the treatment was a hypothetical difference in airway and tongue position that was evaluated.

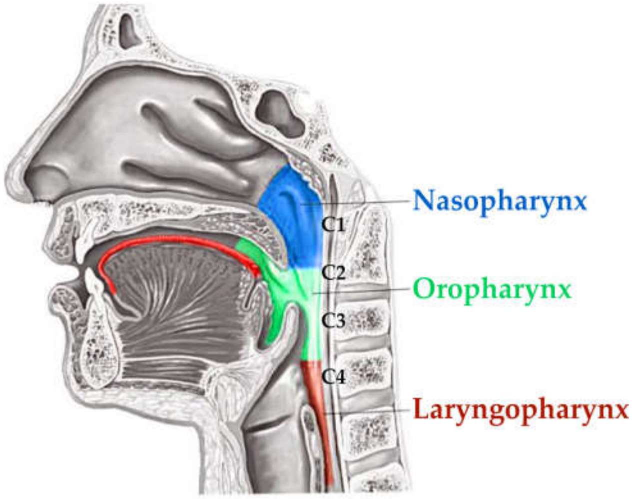

Figure 1. Schematic drawing of tongue position in the oral cavity and oropharynx portion of pharynx where the airway changes after aligner therapy were evaluated.

2.2. Borders of the Airway

The upper border of airway was defined by the diagonal line connecting the anatomical point of Sella Turcica and the posterior nasal spine (PNS). Sella turcica of pituitary (hypophyseal) fossa is a midline, dense structure in the sphenoid bone, which houses the pituitary gland. The posterior nasal spine represents the most posterior point of the maxillary line and nasal floor seen on the lateral projection of the CBCT of the patient (**Figure 2**).

The lower border was defined as the base of the epiglottis, the soft tissue that leads air further in lungs dividing the upper respiratory system to the lower as well as the respiratory with the digestive. The borders were defined by the study of dos Santos et al. in 2020 during their trial to correlate airway volume and maximum constriction area location in different dentofacial deformities [42].

The level of constriction has been determined by the level of the cervical vertebrae (CV) again using the CBCT of the patient in the section of airway in the software Invivo Anatomage. The cervical vertebrae can be divided into three parts, the upper border, the middle, and the lower border. Each of the cervical vertebrae can be divided into these three levels and the constriction of the airway can be defined accordingly. The most common borders that airway constriction was found are the middle border of CV2, the upper border of CV3 the Middle of CV3 as well as the lower border of CV3.

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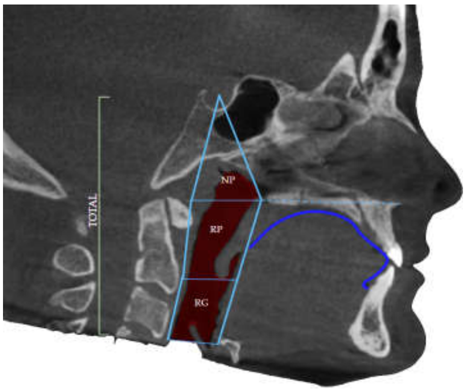


Figure 2. Defined borders of the airway volume consist of the nasopharyngeal (NP) portion, as well as oropharyngeal regions: retropalatal (RP) and retroglossal (RG) and dorsum linguae identification.

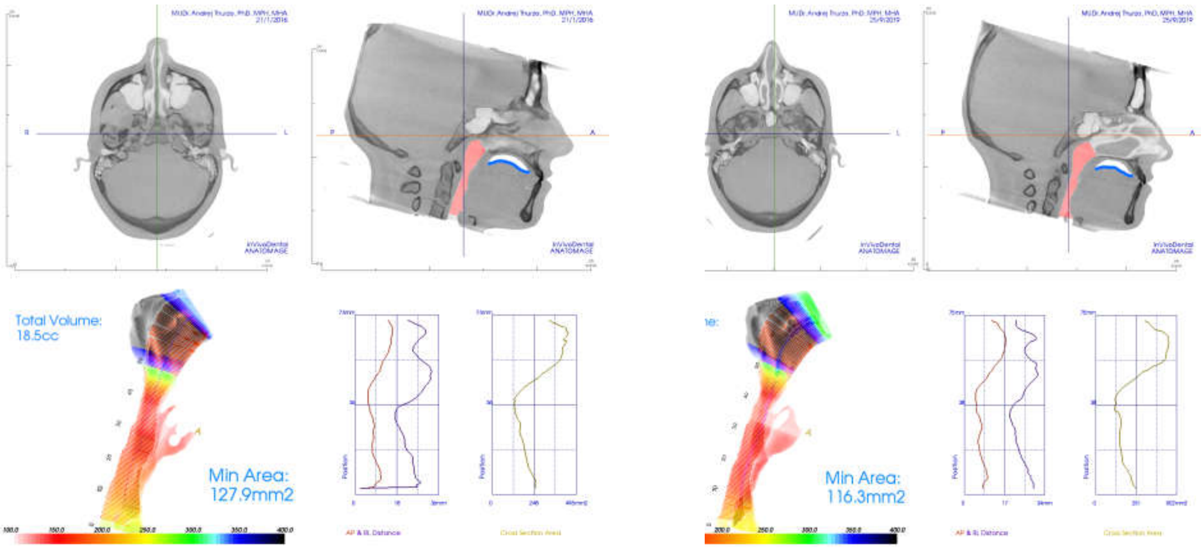
When the software analyzes the input data and evaluates the airway, different colors of the color spectrum visualize the constriction of the airway. The severe airway obstructions are represented by black, dark red, red followed by orange, yellow and green. The green color categorizes the airway into adequate passage of air followed by blue and white representing the widest airway dimension.

2.3 Group selection and clinical evaluation

Only adult non-growing patients were selected without any significant BMI change between an average two-year span between CBCT scans. The first group consisted of patients with constricted airway identified at the CBCT 3D analysis, while the second group included patients with adequate airways without significant difficulties or abnormalities in their breathing pattern during day or during sleep. In total the first group number of patients was **55** with constriction of their airway while the second group was the control group consisting of **31** patients.

An important criterion was the CBCT scan of the skull showing all the skeletal craniofacial structures of the head and neck necessary for the analysis. The initial as well as the final CBCT after treatment were necessary for the research. All CBCT scans were indicated by an orthodontist within the complex orthodontic treatment planning or as pre-finish evaluation due to relevant clinical reasons.

Example of the software 3D evaluation of the airway from the CBCT shows pre-treatment airway constriction (**Figure 3a**) and post-treatment evaluation after orthodontic therapy (**Figure 3b**). This example shows rather insignificant improvement of the airway constriction as well no significant change of tongue posture (blue).



(**a**) (**b**)

Figure 3. Examples of CBCT 3D analysis of airway with evaluation of constriction in the software Invivo 6, from Anatomage (Santa Lara, CA, USA). (**a**) Pre-treatment CBCT with constriction; (**b**) Post-treatment CBCT analysis with insignificantly improved airway constriction and unchanged tongue position.

The evaluation of the tongue position was added to methodology in effort to objectivize the airway changes as these might be affected by tongue different position between initial and final CBCT scan. The tongue can affect the airway clearance.

Research from 2016 published by Pliska et al. in American Journal of Orthodontics and Dentofacial Orthopedics was focused on the effect of orthodontic treatment on the upper airway volume in adults. In this retrospective study authors have examined the effects of orthodontic treatment with and without extractions on the airway clearance. The Wilcoxon signed rank test was used to compare volumetric and minimal cross-sectional area changes from pretreatment to posttreatment. Conclusions of this research were that "dental extractions in conjunction with orthodontic treatment have a negligible effect on the upper airway in adults" [50].

On the contrary another research of Wang 2012 in Angle orthodontist researching changes of pharyngeal airway size and hyoid bone position following orthodontic treatment of Class I bimaxillary protrusion concludes a significant correlation between the retraction distance of lower incisor and the airway behind the soft palate, uvula, and tongue. Wang et al. as well summarize that "the pharyngeal airway size became narrower after the treatment. Extraction of four premolars with retraction of incisors did affect velopharyngeal, glossopharyngeal, hypopharyngeal, and hyoid position in bimaxillary protrusive adult patients" [51].

In this study two independent clinicians evaluated change of tongue on the CBCT lateral view in relationship to surrounding oral cavity. Evaluation of the change of the tongue position in the oral cavity was binary (Yes/No). The upper contour of the dorsum linguae was identified (**Figure 4**) and compared between initial and final scans. Only significant changes of the contour of dorsum linguae were evaluated as "different posture". The clinicians were unable to recognize if the recorded position from the final CBCT was the true relaxed position of the patients` tongue or just temporary situation during final CBCT scanning. Various clinical situations were evaluated. In situations where the contour of the dorsum linguae could not be differentiated from surrounding soft tissues it was considered in continuous contact. If such continuous contact was on initial and as well final CBCT scan, tongue position in oral cavity was evaluated as unchanged, albeit treatment could have changed teeth positions in alveoli and thus oral cavity shape and physical borders for tongue changed (**Figure 4 top**). **Figure 4** shows three distinct examples of clinical situations where not necessarily worsened position of tongue posture results in worsening of airway constriction (**Figure 4 below**) or post-treatment change of tongue position in the oral cavity (**Figure 4 middle**) improving even previously unconstructed airway.

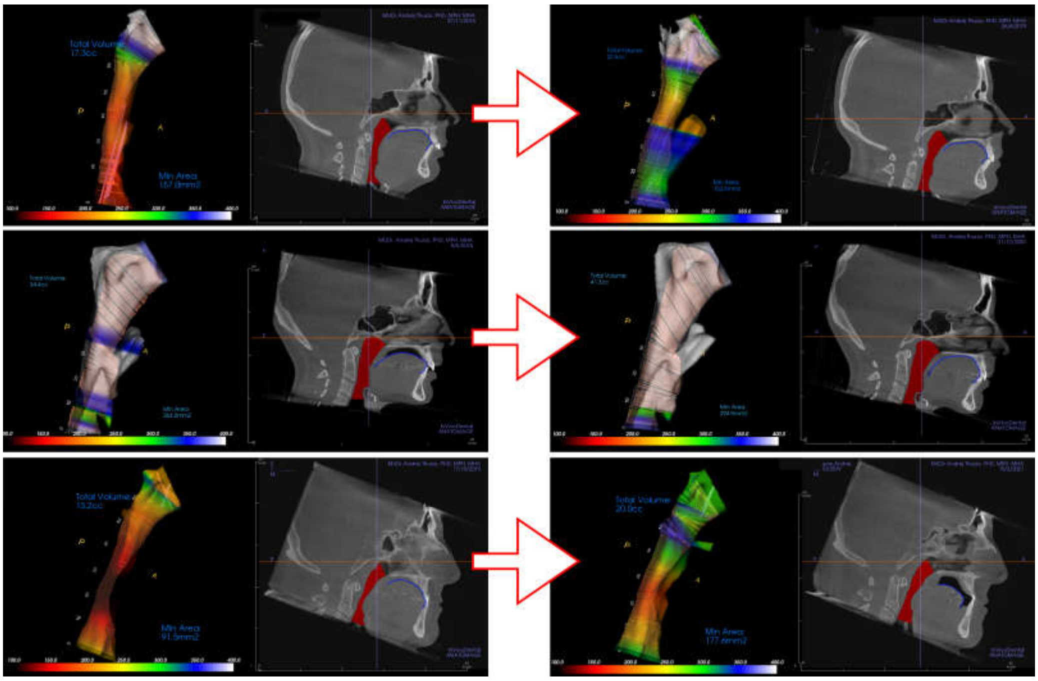


Figure 4. Various clinical situations in airway and tongue position in oral cavity show from the top: (1) initially constricted airway ending in un-constricted setup with tongue in connection with upper palate and incisors with obvious change of lower incisors position; (2) in the middle is shown situation of patient from control group with permanently un-constricted airway with changed tongue position; (3) example on the bottom shows improvement in the airway clearance despite tongue position in the oral cavity is posterior in comparison to initial CBCT.

2.4 CBCT and Instructions to the patients

All the CT studies were performed by radiologists/ assistants in a private clinic in Bratislava using the same CBCT (CT i-CAT Imaging Sciences International, Hatfield, USA); the scanning protocol was 120 kV, 36.9 mA, 13 × 23 cm field of view, 0.3-mm voxel.

Before scanning, the patients were instructed not to move their head, nor to swallow. Furthermore, they were asked to have maximum occlusion/ intercuspidation to avoid discrepancy and reduce the variation [52].

2.5 Software analysis- Invivo 6.0 Anatomage

Two observers evaluated all the CBCT scans of all patients before and after the treatment independently and analyzed them using the software Invivo Anatomage (version 6.0 Imaging, Santa Lara, CA, USA). The initial and final Dicom (Digital Imaging and Communications in Medicine) images were imported into the software, observed, and evaluated. Each analysis was stored in separate file as native *.inv format.

While using the software the position of the head of each patient's head position was corrected using the 3D orientation widget and parameters such as Frankfurt horizontal line, superimposition of the skeletal base of the skull in the level of Sella Turcica and bony maxilla.

The observers performed the analysis by selecting and defining anatomical points and skull characteristics using Invivo in the section of 3D analysis.

When the selection was completed, the software automatically calculated the results which were numerical values and angles. The data of the analysis before and after the

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treatment were gathered in **Table that is provided as a supplementary material to this paper**.

The table included pseudonymous identification of the patient, the airway data analysis as well as the skeletal- hard and soft tissue analysis. The personal data of each patient consisted of the name, the surname, the gender, the starting age, starting year and the year that the patient finished their treatment. All personal information was removed after data collection was completed and graphical data was anonymized. In the final table the portion of airway analysis calculated the volume of the airway within defined boundaries, the minimum area of the most constricted section, and the level of the maximum constriction before and after the treatment. The level of the airway constriction has been determined by skeletal cervical vertebrae.

2.6 Aditional parameters collected and evaluated

The data collected from both groups, the one with constricted airways and the control group, were all gathered in one complete Microsoft Excel file (Microsoft Corporation, Redmond, Washington, USA). The file consisted of columns representing the skeletal information obtained from the CBCT analysis as well as information about the treatment with clear aligners and status of the airway before and after the completion of the treatment. The patient answers from clinical examination were recorded in the patient journal and transferred to the final table in a format suitable for the statistical software processing.

Photographic documentation or the intraoral scanning of the dental arches of the patient provided information about the initial dental status and dental relationship including the Angle class categorized in 3 classifications, Class I, II and III. Initial Class and final Class were taken into consideration.

Another data assessed in the table was the total airway volume defined in cc, minimal constriction area in mm^2 and the level of the constriction of the airway according to level of cervical vertebrae. The Invivo 6 software provides visualization of airway as well as calculate the volume of the air. Selected points across the airway provide the volumetric result adjusting both the upper and the lower border of the airway.

Into further consideration were taken the following parameters used during the treatment like operation, either it involves the use of intermaxillary (between upper and lower arch) elastics, or the special feature of the design of aligners called wings that are assisting the forward step movement of the mandible.

Parameters such as SNA and SNB were giving information about the position of the maxilla and the mandible regarding the stable skeletal parameters of Sella and point N (Nasion).

ANB indicates the angular relationship between the position of the maxilla and the mandible before and after the treatment. Value U1 to SN indicates the angular change of the inclination of upper incisors regarding the base of the skull.

L1 to NB parameter shows the bodily protrusion of the lower incisors. overjet (OJ) represents the horizontal (anterior posterior) overlap of the maxillary central incisors over the mandibular central incisors as well as the difference between the final overjet to the initial overjet.

PP-MP value or else NL-ML (nasal line to palatal plane) represented the inclination of the mandible in relation to maxilla which was a vertical relationship. MP-SN Ang 2D also represented a vertical relationship, regarding the inclination of the mandible (lower arch) in the base of the skull or else wise the rotation of the mandible in the base of the skull.

The final skeletal parameter was the gonial angle representing the angle of the mandible.

The position of the tongue was observed in both initial and final CBCT analysis and in the case of difference in posture the change was noted.

Using Invivo 6.0 Anatomage, the orthodontist can analyze, segment, and export the airway in special format named Standard Tessellation Language (STL) file and using 3D printing could expand the possibilities in additional analysis.

2.7 Data collection and Statistical analysis

Group A was defined as the patients treated with clear aligner therapy (Invisalign) with upper airway constriction prior to the treatment.

Control group B represented a set of patients treated from the initial stage without identified airway constriction, based upon CBCT 3D analysis.

Patients were adults without significant weight change (± 4%) between the initial and final scan.

All 3D comparative analyses of the CBCTs before and after treatment were performed in the years 2021-2022, work on this study started in 2017. Data was evaluated by professional statistician acknowledged at the end of this paper. Obtained data were statistically analyzed using SPSS 23.0 software (Chicago, IL, USA) and GraphPad Prism 6.01 (La Jolla, CA, USA). The threshold of statistical significance was set to $p < 0.05$.

2.8 Aditional analysis

Additional helpful diagnostic tools were exported from the 3D software Invivo such as panoramic and cephalometric x-ray, temporo-mandibular joint (TMJ) visualization, inferior alveolar nerve tracking, differential map of hard and soft tissues asymmetries pre-treatment and post-treatment by creating a half mirror image according to patient's one side of the face. Information like these was introducing the Golden ratio soft tissues and made the orthodontic treatment more soft tissues driven. Also, 3D dental casts and 3D extra-oral face-scan were imported in the software and were adjusted to the skeletal and soft tissues of the patient and allowed further analysis.

3. Results

3.1. Clinical structure of the selected dataset

Of 120 consecutive patients 86 were fitting the selection criteria. Most frequent reason for exclusion was significant change of their BMIs` during/after pandemics. From the selected, 64% were identified with some form of upper airway constriction on the initial CBCT. 36% had adequate airway, defined as control group. Of all included treatments this total the 72.1% were female and the 27.9% male with average treatment time of 2.1 years.

Intermaxillary elastics were used in 61.8% in group A and 74.2% in group B(control). Wings were used in 5.5% of group A and 6.5% (control).

Also, 5.5% of group A and 3.2% of group B (control) underwent orthognathic intervention.

Initial malocclusions were divided into Classes according to Angle defined by the position of canines and molars. The distribution was:

20.9% Class I,
66.3% Class II*,
12.8% Class III*.

While at the end of the treatment with clear aligners the percentages were:
65.1% Class I,
32.6% Class II*,
2.3% Class III*.

* As Class II and Class III were considered even unilateral or extraction cases upon position of first molars.

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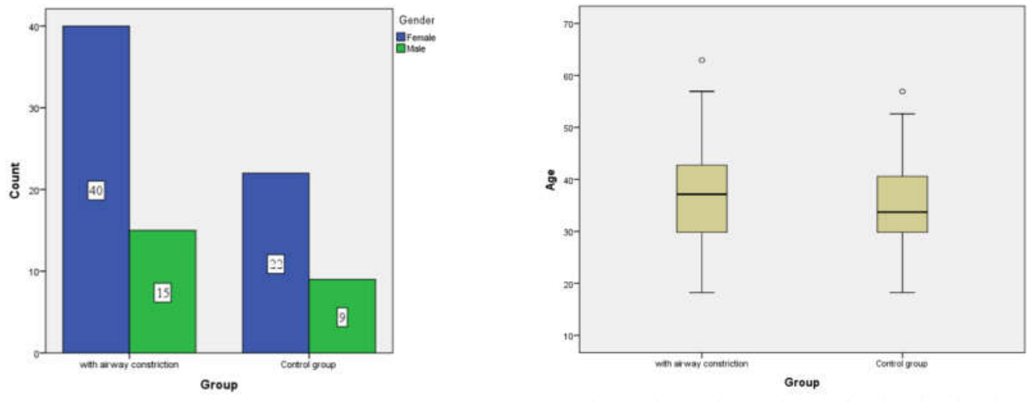
Group A and Control group do not differ statistically significantly in the proportion of women and men (**Figure 5a**). Age distribution in the groups do not differ statistically significantly (**Figure 5b**).

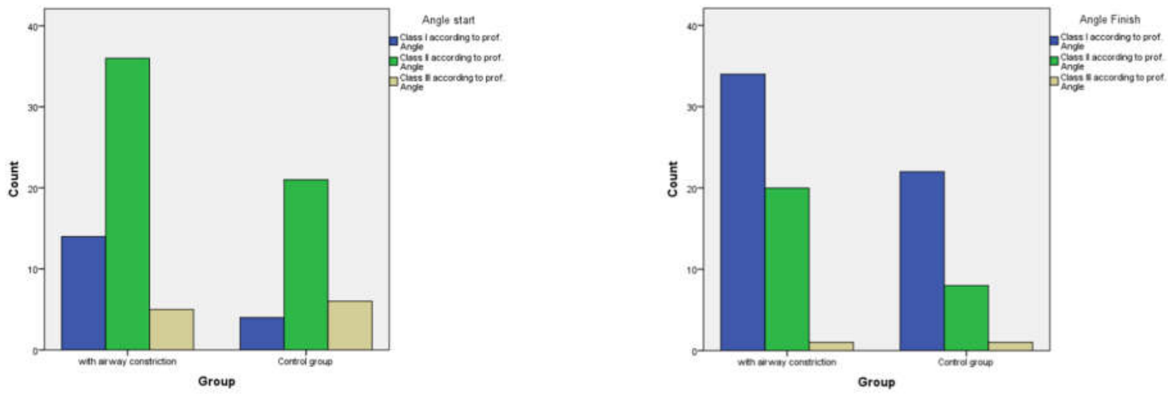


(**a**) (**b**)

Figure 5. Sex and age distribution between groups; **(a)**The groups do not differ statistically significantly in the proportion of women and men. **(b).** The groups do not differ statistically significantly in the proportion of women and men.

In analysis of the application of elastics, wings, or surgery interventions there was no statistically significant difference between groups.

Neither initial nor final distribution of patients` Angle Classifications was statistically significant between the groups. As **Figure 6a** shows, the dominant group in patients with constricted airways were patients in Class II. However, Class II patients were also dominant in the un-constricted (Control group). In the finishing CBCT, the majority in both groups are patients in the first Angle Class, albeit Class II persists due to the strict evaluation upon molar position. This includes extraction cases, unilateral Class II or non-surgical camouflage treatments in adults (**Figure 6b**).



(**a**) (**b**)

Figure 6. Distribution in Angle classification **(a)** Initial scan shows Class II as the dominant group in patients with constricted airways as well as in the un-constricted (Control group). **(b)** In the finishing stage, the majority in both groups are patients in the first Angle Class, albeit Class II persists due to the strict evaluation upon molar relationship, including extraction cases, unilateral Class II or non-surgical camouflage treatments in adults.

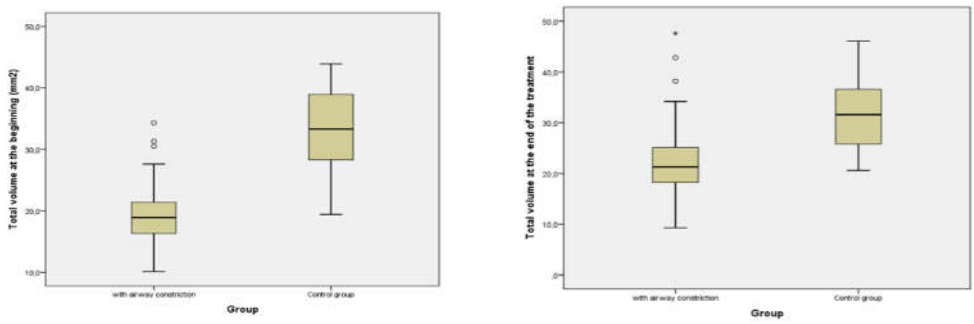
3.2 Evaluation of the changes in the airway

- Volume (mm^3),
- Minimal Area(mm^2),

- Level of constriction.

3.2.1. Volumetric changes in the airway

The volume of the airway before the treatment at group A had a value of 19.37 cm^3 with standard deviation of 5.15 and after the treatment 22.29 cm^3, while the control group had 33.18 cm^3 initially and after treatment the value was 32.25 cm^3. As **Figure 7a** (pretreatment) and **Figure 7b** (posttreatment) show, the aligner treatment has improved the volume in Group A (with pretreatment airway constriction), albeit resulted in slight insignificant decrease of airway in the control group. In the group with airway constriction, there was a statistically significant increase in volume during therapy ($p<0.001$).



(**a**) (**b**)

Figure 7. Comparison of volumetric changes of the airway before and in the finish of aligner treatment; (**a**) Pre-treatment; (**b**) Post-treatment increase of airway volume in Group A and decrease in control group.

3.2.2. Surface of the airway cross-section at the level of highest constriction

There has been a significant increase of 16.69 mm^2 at the mean value of the cross-sectional minimal area of the airway at the group with the already constricted airway after the treatment with clear aligners. In the control group, there has been a reduction of 13,4 mm^2. At the beginning, the minimum area in the control group was statistically significantly larger ($p < 0.001$). Also, at the finish of the aligner therapy, the minimum area in the control group remained statistically significantly larger ($p < 0.001$) compared to the group with constriction.

Before treatment the mean value of the minimal cross-section airway was 130.28 mm^2 versus 146.97 mm^2 after treatment as shown in **Figure 8**.

The Wilcoxon Signed Ranks test showed **36** positive ranks and 19 negatives out of the **55** patients meaning that the minimal area at the end of the treatment was larger in 36 cases. The mean value at the beginning for the Control group was 246.68 mm^2 versus 233.2v8 mm^2 after the end of the orthodontic treatment.

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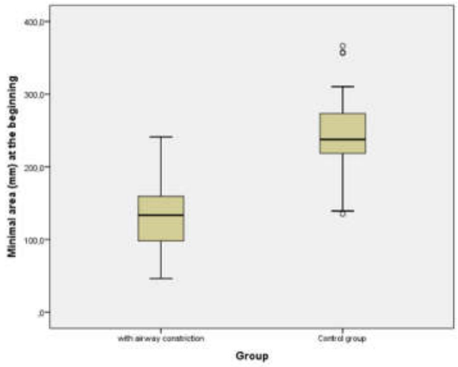
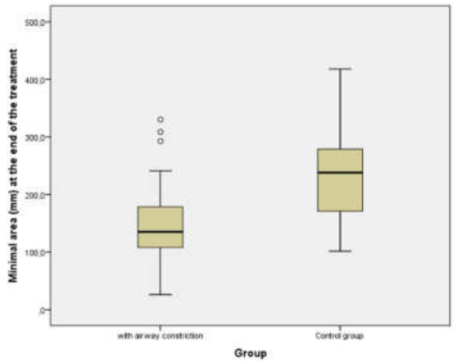


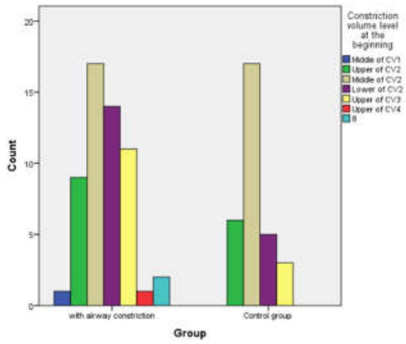


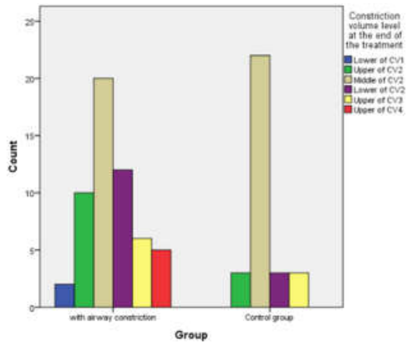
(**a**) (**b**)

Figure 8. Comparison of changes of the surface of the airway cross-section at the level of highest constriction; (**a**) At the beginning of aligner treatment; (**b**) Post-treatment - the surface of the most constricted cross-section of airway did not change significantly after treatment in any of the groups.

3.2.3. Position of the highest constriction

The locality of constriction on all **86** cases has been assessed. **Figure 9** shows the localizations before and after the treatment. The most common constriction was identified at the level of the 2nd cervical vertebrae (CV2) in the oropharyngeal portion of the pharynx. After the treatment with Clear Aligners, the most persisting constriction level the Middle of CV2 got even higher values but the rest appeared to have reduction. There was no statistically significant difference between both groups.





(**a**) (**b**)

Figure 9. Representation of the level of airway constriction according to the level of the cervical vertebrae as shown at the cephalometric lateral x-ray exported from the CBCT, (**a**) Pre-treatment levels of constriction; (**b**) Post-treatment levels of highest constriction (smallest clearance).

3.3. Change of tongue position in the oral cavity from lateral view

The dorsum of the tongue (dorsum linguæ) was evaluated as the profile contour of tongue position on the CBCT. The final contour was compared to contour from initial CBCT. Observed difference as is shown a different position of the tongue on **Figure 3** and **Figure 4**. Aligner treatment in patients with constriction on the initial CBCT resulted in changed position of the tongue in 61.1% cases and similarly 63.3% in the control group (**Figure 10**).

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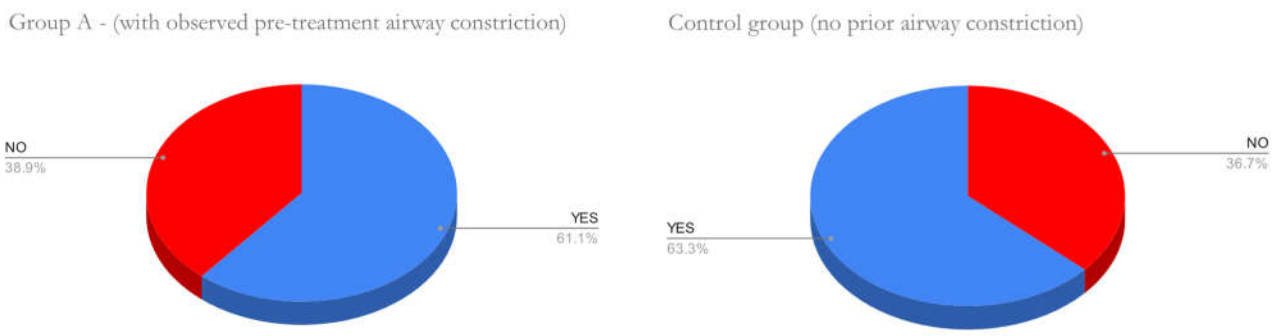
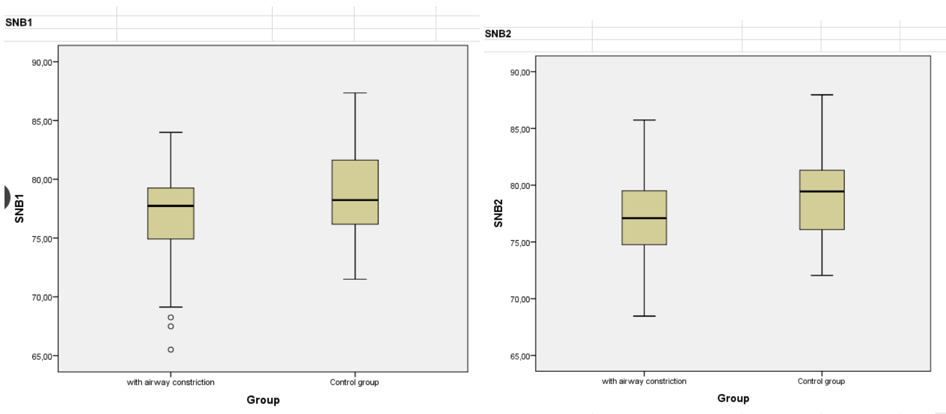


(a) (b)

Figure 10. No significant difference between groups was observed. Difference of tongue contour towards palate and incisors between pre-treatment and post-treatment CBCT was assessed. (**a**) In Group A with significant pre-treatment airway constriction a change of tongue position was observed in 61.1% of cases; (**b**) similarly 63.3% cases of the control group had change in the tongue position after treatment.

3.4. Results of skeletal analysis

The skeletal analysis evaluating skeletal (hard tissue) parameters in Group A in SNA and SNB found no significant statistical difference. SNA and SNB are angles formed by Sella Turcica which is a bony depression in the sphenoid bone in the skull, hard tissue nasion which is the most anterior point of frontonasal suture and point A and point B at maximum convexities of maxilla and mandible respectively. At group B there was found statistical difference SNB2 (p=0.031) and SNB2 (p= 0.059) presented at **Figure 11**.



(a) (b)

Figure 11. Values of SNB angle in both groups A and B. The angle SNB formed by the points 1) Sella Turcica, 2) hard tissue Nasion 3) point B, (**a**) Pre-treatment SNB angle in group A (left) and group B (right); (**b**) Post-treatment SNB angle in group A (left) and group B (right).

Another parameter that was taken into consideration was ANB, an angle formed by the skeletal points A and B and the point Nasion, but with no statistical difference found. Dental parameter that was also examined was U1SN representing the inclination of the upper central incisors to the SN (Sella-Nasion) line with a mean value of 99.40° before and 97.81° after treatment in group A and 105.74° and 100.12° respectively at control group B.

A comparison of the values of the lower central incisors' inclination in reference to the cephalographic lines NB is presented at the following **Table 1** in both groups.

Table 1. Inclination of the lower central incisors, Test of Normality.

	Statistic	df	Significance Correction
L1NB1 Group A L1NB1 Group B (Kolmogorov- Smirnova)	,101 ,130	55 31	,200 ,199
L1NB2 Group A L1NB2 Group B (Kolmogorov- Smirnova)	,090 ,092	55 31	,200 ,200
L1NB1 Group A L1NB1 Group B (Shapiro- Wilk)	,943 ,964	55 31	,012 ,380
L1NB2 Group A L1NB2 Group B (Sapiro- Wilk)	,969 ,961	55 31	,165 ,313

The overjet represents the horizontal distance between the upper and the lower dental arch and their comparison before and after the treatment in group A with clear aligners.

OJ1 represents the initial overjet while OJ2 is the after-treatment overjet as shown at **Table 2**. Similar results are shown at Group B (control) when the mean value OJ1 is 4,08mm versus 3,33mm. The following parameters concerning the gonial angle and the relationship of the skeletal bite were not significant.

Table 2. Comparison between Initial and Final Overjet of the Group A.

	Overjet 1	Overjet 2
N Valid Missing	 55 0	 55 0
Mean	4.0113	3.5545
Minimum	-3.18	1.89
Maximum	11.29	6.65

4. Discussion

Results of this study confirmed its working hypothesis that improvement of the occlusion and/or intermaxillary relationship results in improvement of the airway clearance especially in the cases where prior constriction was present. In simplified approximation, the upper airway constriction was present in proportion AI : AII : AIII as 3 : 7 : 1. AII was also dominant in the group without airway constriction.

Results also identified the most frequent location of upper airway constriction in the level of the second cervical vertebrae. An unconfirmed hypothesis is that this constriction could be most prevalent at this level due to the hypertrophy of the adenoids/tonsils.

In average, every second patient had a different posture of the tongue at the final CBCT. There was no significant difference in this finding between both groups. It is impossible to prove the causal nexus of tongue posture, treatment, and airway constriction, by this research paper. Nevertheless, it would be valuable scientific contribution to identify an established link between the most probable cause and its resulting effects. Not in every case an upper arch expansion and mandibular advancement led to less constricted airway. Better understanding of the link between tongue position and airway clearance is necessary. Tongue position shall be evaluated also in transversal direction.

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Recent study by Lin et al. 2022, demonstrates that hypertensive patients tend to have larger upper airway length, smaller total airway volume and smaller width of upper airway, predisposing them to the risk of developing Obstructive Sleep Apnea (OSA). As the prevalence of OSA is increasing, dental practitioners should be equipped with basic knowledge about OSA [53].

The null hypothesis of this paper has been rejected as results proved that most of the treatments resulted in positive volumetric change of the airway, albeit no significant change of the area in the point of most prominent constriction.

CBCT imaging is a precious tool that assists in localization of constriction of the upper airway but is restricted during the time of exposure that is why it creates limitation of precise evaluation of the airway. The amount of increase and decrease of the volume of the airway during the inspirium and exspirium cannot be precisely captured during the exposure of the CT. The total volume of the airway, the minimal area and maximum constriction could have different values during the process of breathing. Antosz et al. 2015, comments on “the flaw of using CBCT to measure airway changes in subjects with sleep apnea due to the fact that the CBCT is static and could vary within the same patient from one day to the next and from one moment to the next“ [54].

CBCT does not function as the sole tool for diagnostics for obstructive sleep apnea, but special sleep studies, oximetry and other measurements are necessary to diagnose OSA. CBCT of the maxillofacial region frequently reveals a high percentage of clinically relevant additional findings [55]. In general, there is a lack of evidence related to the 3D pharyngeal airway space changes after orthodontic treatment. The largest effect in adults with characteristic characterized by mandibular retrognathism is orthognathic treatment with mandibular advancement surgery achieved by means of bilateral sagittal split osteotomy (BSSO) advancement surgery. This intervention leads to a significant, immediate increase in the total airway volume, and minimum constriction area. All these changes remained stable at a one-year follow-up [56]. Recently various digital methods were introduced for quantification of airway changes suitable for retrospective studies [57].

This paper does not present any special quality of aligner orthodontic treatment in comparison to other orthodontic techniques, but rather clarifying a uniform technique in the treatment. Either way there is a plethora of different treatment modalities in every orthodontic technique that makes the clinical approach difficult to compare. Neither are clinical conditions and extend of patient malocclusion or compliance scientifically comparable. The effect of the clear aligners includes expansion of the hard palate in the form of crown tipping and body teeth movement buccally. In some cases, skeletal anchorage or elastics were involved. The evidence that confirms that pure dental expansion could cause remodeling of the upper airway remains unknown.

A recent retrospective study published by Diwakar et al. 2021, focused on the effect of craniofacial morphology on pharyngeal airway volume that was calculated using CBCT. Important finding of this study is that pharyngeal airway space differs significantly between males and females [58].

Studies have been made to assess dimensional changes in the upper airway after appliance or surgical therapy in patients with OSA and to find correlation of CBCT findings with treatment outcome. The evidence of CBCT measured anatomic airway changes with surgery and dental appliance treatment [38] but there is insufficient literature pertaining to the use of CBCT to assess treatment outcomes to reach a conclusion [47].

Furthermore, study about reliable volumetric assessment of the nasal airway published by Mupparapu et al. 2021, concluded that there is lack of a gold standard, but it is possible to quantify the nasal airway volume and its reduction [49].

While Zhang C. at al reported the reproducibility and accuracy of an algorithm, airway segmetor (AS), designed for nasal airway space analysis using a 3D printed anthropomorphic nasal airway model. The 3D printing technique was found to be clinically reliable and accurate tool for the segmentation and reconstruction of the nasal space [59].

Limitations of this study are various aspects including the limitation of patient selection due to the body mass index change that seemed more frequent in patients with CBCT prior to 2020 and after pandemics. As well as finishing CBCT scan is particularly justified when it brings a clear benefit to the patient` treatment when compared with conventional imaging techniques. CBCT should be considered for clinical orthodontics for selected patients [60].

Another limitation of this study is the fact, that pharyngeal airway space differs significantly between males and females and that head posture in relation to the neck when standing in the CBCT can deform the airway despite the head position is repositioned, airway deformation remains. Similarly, a logical limitation is unnatural tongue spasm during CBCT in unrelaxed patients, which is difficult to identify. Final limitation is necessity to evaluate tongue position also in lateral directions.

5. Conclusions

Patients undertaking clear aligner therapy experienced changes in the upper airway volumes. In the group with airway constriction, there was a statistically significant increase in volume during therapy ($p<0.001$). Volumetric change in the control group with no pre-treatment constrictions was insignificant.

The surface of the most constricted cross-section of airway did not change significantly after treatment in any of the groups.

The position of the smallest clearance of the airway in the pharynx was similar for both groups. The most prominent constriction was localized at the level of 2nd cervical vertebra.

In average 62.2% of all before-after CBCT evaluations of aligner treatments noted a change in the tongue position and its relationship to incisors and palate.

Supplementary Materials: There are no supplementary materials except for an anonymized data table supporting the results, referenced in the Data Availability Statement.

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, G.F. and A.T.; methodology, G.F.; software, G.F.; validation, G.F. and A.T.; formal analysis, G.F. and A.T.; investigation, G.F.; resources, A.T.; data curation, G.F.; writing—original draft preparation, G.F. and A.T.; writing—review and editing, G.F. and A.T.; visualization, G.F.; supervision, G.F. and A.T.; project administration, G.F. and A.T.; funding acquisition, G.F. All authors have read and agreed to the published version of the manuscript."

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Institutional Review Board Statement: Ethical review and approval were waived for this study due to the reason that no special diagnostics were performed in the typical clinical workflows of the patients and research was performed retrospectively on existing CBCT and other clinical data.

Informed Consent Statement: Written informed consent was obtained from all subjects involved in the study prior undertaking the orthodontic aligner therapy, albeit the written informed consent for publication must be obtained only from participating patients who can be identified (including by the patients themselves).

Data Availability Statement: Anonymized Data supporting the reported results are freely availabl e at: https://docs.google.com/spreadsheets/d/1Niq3Yt5SYumA4EQh-ZMq9F19AssL6CvhRBqfcDgI8iY/edit?usp=sharing accessed on 24th of July 2022. Authors ensured that data shared is in accordan ce with consent provided by participants on the use of confidential data.

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