World Journal of Otorhinolaryngology-Head and Neck Surgery (2021) 7, 133–138

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.keaipublishing.com/WJOHNS; www.wjent.org

Research Paper

Changes in pneumatization of the maxillary air sinuses in Korean adults following biomimetic oral appliance therapy

G. Dave Singh [a,*], Hee Nam Kim [b]

[a] Institute of Craniofacial Sleep Medicine, Vivos Therapeutics, Inc., 9135 S Ridgeline Blvd Suite #100, Highlands Ranch, CO 80129, United States
[b] Star White Dental Clinic, South Korea

Received 10 October 2019; received in revised form 8 July 2020; accepted 19 July 2020
Available online 19 October 2020

KEYWORDS
Pneumatization;
Maxillary air sinus;
Biomimetic;
Oral appliance therapy;
Palatal expansion

Abstract *Objective:* For the treatment of obstructive sleep apnea in adults, mandibular advancement devices (MADs) are often used. Since adults with a prognathic mandibular phenotype are at risk of developing an unfavorable facial profile, midfacial development using biomimetic oral appliance therapy might provide a suitable alternative. However, the effect of this procedure on the maxillary air sinuses is unknown; therefore, changes in sinus pneumatization were investigated in this study.
Methods: After obtaining informed consent, 16 consecutive Korean adults with midfacial hypoplasia had 3D cone-beam (CB) CT scans taken, and biomimetic upper appliances (DNA appliance®, Vivos Therapeutics, Inc., USA) were constructed.
All subjects were instructed to wear the device 12–16 h/day. Each month, examination for the progress of midfacial development was recorded. Post-treatment, a follow-up 3D CBCT scan was undertaken with no device in the patient's mouth. Pre- and post-treatment linear and volumetric measurements were obtained using appropriate software, and compared statistically using *t*-tests.
Results: The mean age of the sample was 25.0 yrs $\pm$ 8.7. The mean treatment time was 15.5 mths $\pm$ 5.2. Post-treatment, the transpalatal bone width increased from 35.3 mm $\pm$ 3.0 to 38.5 mm $\pm$ 2.0 ($P < 0.001$); the maxillary air sinus volume on the left side increased from 18.8 $cm^3 \pm 6.5$ to 20.0 $cm^3 \pm 6.0$ ($P < 0.05$), and from 18.5 $cm^3 \pm 5.7$ to 19.7 $cm^3 \pm 5.8$ ($P < 0.05$) on the right side.

* Corresponding author. Fax: +1 866 201 3869.
E-mail addresses: drsingh@drdavesingh.com, drsingh@vivoslife.com (G.D. Singh).
Peer review under responsibility of Chinese Medical Association.

Production and Hosting by Elsevier on behalf of KeAi

https://doi.org/10.1016/j.wjorl.2020.07.007

Conclusions: Biomimetic oral appliance therapy may be able to increase the maxillary air sinus volume in adults. In view of these preliminary findings, further studies on the effect of enhanced pneumatization on paranasal sinus function and sleep parameters are warranted.

Introduction

The maxillary air sinuses are often anatomically described as pyramidal-shaped cavities within the maxilla. Smith et al[1] investigated neonatal maxillary sinus development in primates histologically and immunohistochemically for the distribution of osteoclasts, osteoblasts and osteopontin. They noted that expansion of the sinus roof and floor appeared to correspond to vertical midfacial growth. However, expansion of the lateral walls was more variable, and influenced by adjacent structures, such as the deciduous molars. Their overall results were consistent with the structural-architectural hypothesis of sinus formation, in that most expansion occurred in regions unopposed by adjacent structures. Conversely, the appearance of these air-filled cavities within the spatial matrix of the craniofacial complex may simply be opportunistic. To address this notion, Smith et al[2] compared pneumatization in anthropoid primates that possess maxillary sinuses to squirrel monkeys, which do not. Using micro-CT scans and histomorphometric techniques, the spatial position of the paranasal sinuses and size of the adjacent dental structures was measured. In the primates, pneumatization extended alongside the deciduous premolars but in squirrel monkeys, the homologous spaces did not develop. It was concluded that differences in tooth size/position and larger orbits may account for the resulting dimorphism, likely by limiting the space available for posterior expansion of the sinus. In this way, paranasal sinuses appear to be associated with skeletal elements that border on several functional matrices, the spatial dynamics of which act as developmental constraints on pneumatic expansion. Therefore, pneumatization may simply be a secondary, opportunistic growth mechanism that replaces redundant bone with air cavities.

Clinically, Lawson et al[3] reported that maxillary sinus hypoplasia can occur unilaterally or bilaterally, but CT scans revealed that it appears to retain its pyramidal configuration. In addition, the sinuses were rarely found to be excessively pneumatized, while a reduction in size/volume was more frequent. They concluded that while a range of developmental and pathologic conditions influence maxillary sinus morphology, its biologic response is somewhat limited. Therefore, the physiologic mechanism of sinus pneumatization is a natural phenomenon that has been known and studied for centuries,[4,5] but has rarely been deployed therapeutically. In this regard, Wehrbein and Diedrich[6] quantified progressive pneumatization of the maxillary sinus after tooth extraction and orthodontic space closure, noting that the pneumatization tendency was higher after extractions in the molar region. More recently, Re et al[7] reported that tooth movement through the maxillary sinus can be used as part of a therapeutic protocol, if appropriate forces are used. They reported orthodontic movement of an upper premolar through the maxillary sinus, using an implant inserted into the retromolar pad as anchorage. They also noted that the premolar that was moved through the sinus maintained its periodontium and alveolar bone. In addition, the implant used for anchorage remained osseo-integrated; however, the origins and functions of pneumatization remain elusive. Therefore, the aim of this study is to evaluate changes in maxillary air sinus volume in adult patients diagnosed with clinical midfacial hypoplasia, following biomimetic oral appliance therapy (BOAT).

Materials and methods

Setting and sample population

After obtaining informed consent, 16 consecutive patients were recruited for this study. The rights of the subjects were protected by following the Declaration of Helsinki. Inclusion criteria were: adults aged >18 yrs diagnosed with clinical midfacial hypoplasia (such as a narrow hard palate); good compliance; no history of hospitalization for craniofacial trauma or surgery; no congenital craniofacial anomalies, and a dentate upper arch. The exclusion criteria included: age <18 yrs; lack of compliance; active periodontal disease; poor oral hygiene, and systemic bisphosphonate therapy.

Materials and methods

After careful history-taking and craniofacial examination, we undertook 3D scans using a CBCT machine (HDXwill, Dentri-s, Seoul, South Korea). Strict positioning protocols were used, and a 20 s scan was performed using a wide (13 cm) field of view with a voxel size of 0.25 mm. A neuromuscular bite registration was obtained in the upright-sitting position with corrected jaw posture in the vertical axis for each subject. Upper and lower polyvinylsiloxane impressions were also obtained. The upper model was then mounted using the hamular notch-incisive papilla (HIP) plane method on a Stratos articulator (Ivoclar-Vivadent, Amherst, USA), and the lower model was mounted relative to the upper model, using the bite registration captured in the physiologic rest position. Following a diagnosis of midfacial hypoplasia, a biomimetic upper appliance (DNA appliance®, Vivos Therapeutics, Inc., USA) was prescribed for each subject. Biomimetic oral appliance therapy (BOAT) aims to mimic natural growth and development of the facial complex, and the system is designed to correct craniofacial and upper airway issues in both children and adults.[8–11] The design used in this study had: 6 (patented) anterior 3D axial springs™, midline anterior and/or posterior jackscrews, occlusal pads, retentive clasps and a labial bow (Fig. 1). All subjects were instructed to wear the device during the late afternoon, early evening and at nighttime (for approx. 12–16 h in total), but not during the daytime and not while eating, partly in line with the circadian rhythm of tooth eruption,[12] although this only occurs in children. The appliance was adjusted approx. every 4 weeks when all subjects reported for review. At each monthly follow-up, examination for the progress of midfacial development was recorded. Adjustments to the devices were performed to optimize their efficacy. Only gentle pressures were transmitted to the teeth, and the functionality of the device was checked with the subject activating a mild force on biting. Treatment was deemed to be completed when the clinical transpalatal bone width was approx. 38 mm.

After midfacial segmentation was completed, the minimum transpalatal bone width at the cervical margin of the mesio-palatal cusp of the first molar (Fig. 2) was measured prior to midfacial development. For volumetric reconstruction of the maxillary sinuses (Figs. 3 and 4), appropriate software was implemented (Morpheus3D, Morpheus Co. Ltd., Seoul, South Korea). Next, the 3D volume of the right and left maxillary sinuses, excluding the nasolacrimal duct, was computed in all cases (Fig. 5). The measurement protocol was repeated three times to determine the percentage measurement error. Post-treatment, these data measurements were repeated, and the findings were subjected to statistical analysis, using *t*-tests.

Results

The mean age of the final sample was 25.0 yrs ± 8.7 (7 females; 7 males). The mean treatment time was 15.5 mths ± 5.2. The 3D measurement error was found to be <1% and further measurements were warranted. Pre-treatment, the mean minimum transpalatal bone width at cervical margin

Fig. 1 The biomimetic device design (fabricated by STAA Dental Laboratory, South Korea) used in this study with 6 (patented) anterior 3D axial springs™, midline anterior and/or posterior jackscrews, occlusal pads, retentive clasps and a labial bow.

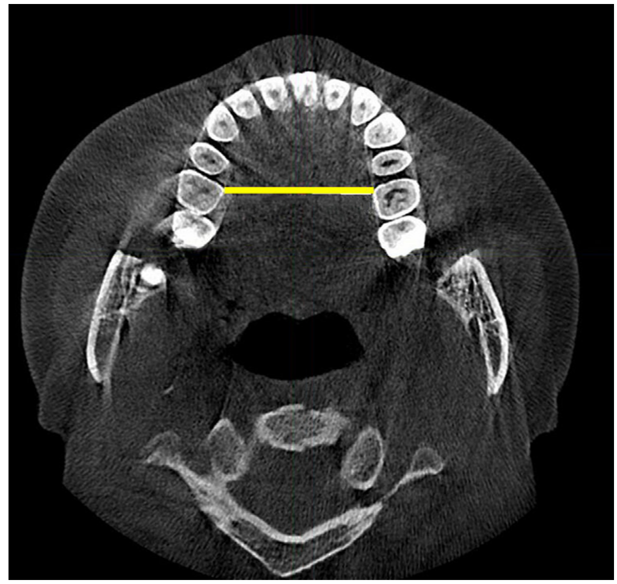

Fig. 2 The minimum transpalatal bone width at the cervical margin of the mesio-palatal cusp of the first molar was measured prior to midfacial development and post-treatment. The yellow line indicates a width of approx. 35.2 mm in this case.

of the mesio-palatal cusps of first molars was found to be 35.3 mm ± 3.0 and it increased to 38.5 mm ± 2.1 ($p < 0.001$) post-treatment. In addition, the mean maxillary air sinus volume on the left side was 18.8 cm^3 ± 6.5 pre-treatment and increased to 20.0 cm^3 ± 6.0 ($p < 0.05$) post-treatment, while the mean maxillary sinus volume on the right increased from 18.5 cm^3 ± 5.7 pre-treatment to 19.7 cm^3 ± 5.8 ($p < 0.05$) post-treatment. Table 1 summarizes these findings.

Discussion

This present study examined the effects of a biomimetic approach to palatal expansion on the maxillary sinuses in adults with midfacial hypoplasia. To ensure precision, a sub-millimeter voxel size of 0.25 mm was deployed in the imaging protocols utilized for the 3D CBCT scans, which is intermediate in the typical range of 0.10–0.30 mm in the specifications for craniofacial CBCT imaging. In addition, the CBCT scans were measured in triplicate using software of validated accuracy but subjective bias can never be excluded completely. Despite these limitations, none of the subjects complained of discomfort when wearing the device after a period of habituation, which typically last 24–72 h, and none of the subjects reported any adverse reactions to BOAT. In the present study, we report some changes in the pneumatization of the maxillary air sinuses in non-growing adults with midfacial hypoplasia following BOAT.

The origins of craniofacial pnuematicity remain obscure. Márquez[13] reviews the temporo-spatial complexities and diversity of paranasal sinus growth and development in an attempt to provide an improved understanding and deeper

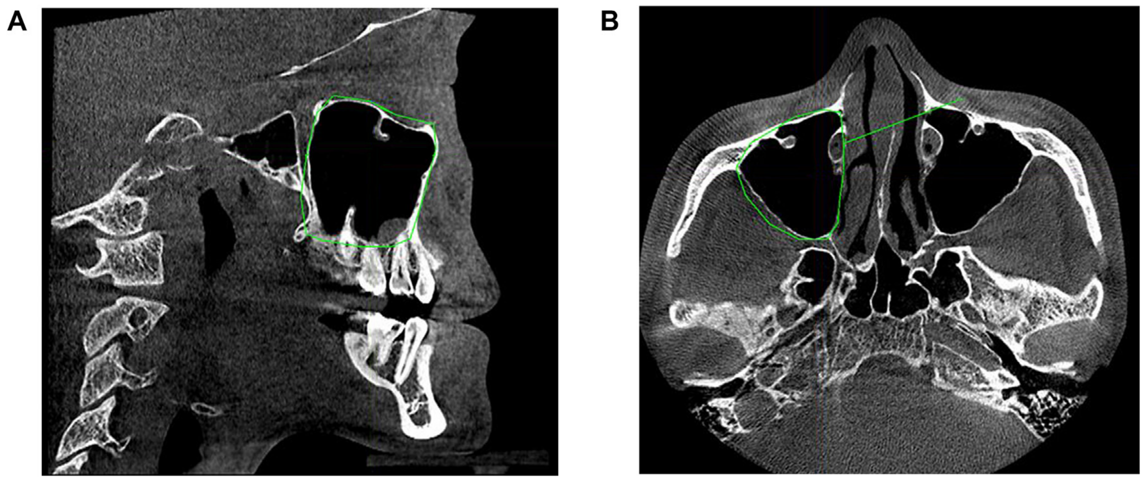

Fig. 3 Volumetric reconstruction of the maxillary sinuses, using appropriate software (Morpheus3D, South Korea). The green outlines indicate the regions of interest, excluding the nasolacrimal duct, which is indicated by the straight green line.

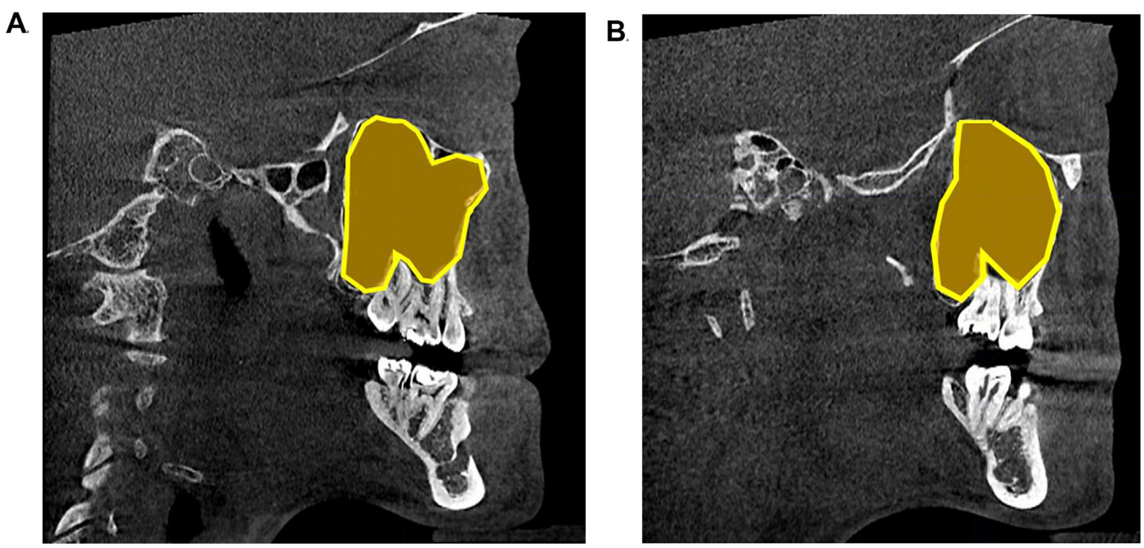

Fig. 4 After midfacial segmentation was completed, the 3D volumes of the right and left maxillary sinuses were computed, as indicated by the yellow outlines and enclosed shaded areas.

appreciation of these specialized craniofacial functional spaces. Briefly, the earliest known postcranial skeletal pneumatization in some dinosaurs is similar to the cervical air sacs of birds.[14] Extant birds have a unique pulmonary system that consists of a dorsally-anchored lung with several bellow-like air sacs to direct inspired air through the lung. Sereno et al[15] consider that the evolution of avian air sacs may have been driven by lung ventilation *inter alia*. Indeed, Butler et al[16] support the contention that post-cranial skeletal pneumatization and, therefore, avian air-sacs were likely present in a common ancestor and, consequently in the evolution of the respiratory systems in bird-like dinosaurs. In some respects, therefore, the paranasal air sinuses, specifically the maxillary air sinus, might be viewed as vestigial organs of the upper airway that were once necessary for respiration.

Currently it is thought that the function of the paranasal sinuses may be to: decrease the weight of the skull (ostensibly for flight); increase the resonance of the voice; protect against craniofacial trauma; guard against nasal temperature fluctuations; humidify and warm inspired air, as well as initiating immunologic defenses[17] against microbial infections. In addition, since nitric oxide (NO) is present in high concentrations in the paranasal air sinuses, it is thought that the sinus' epithelial pneumocytes produce NO,[18] which guards against bacterial and viral infections. In contrast, only weak NO synthase activity is found in the epithelium of the nasal cavity. It is also thought that the NO produced during T2R38 gene activation regulates mucosal defenses against gram-negative bacteria, by increasing mucociliary clearance. Thus, the widespread role of T2R38 may prove to have therapeutic potential in cases of chronic

A

B

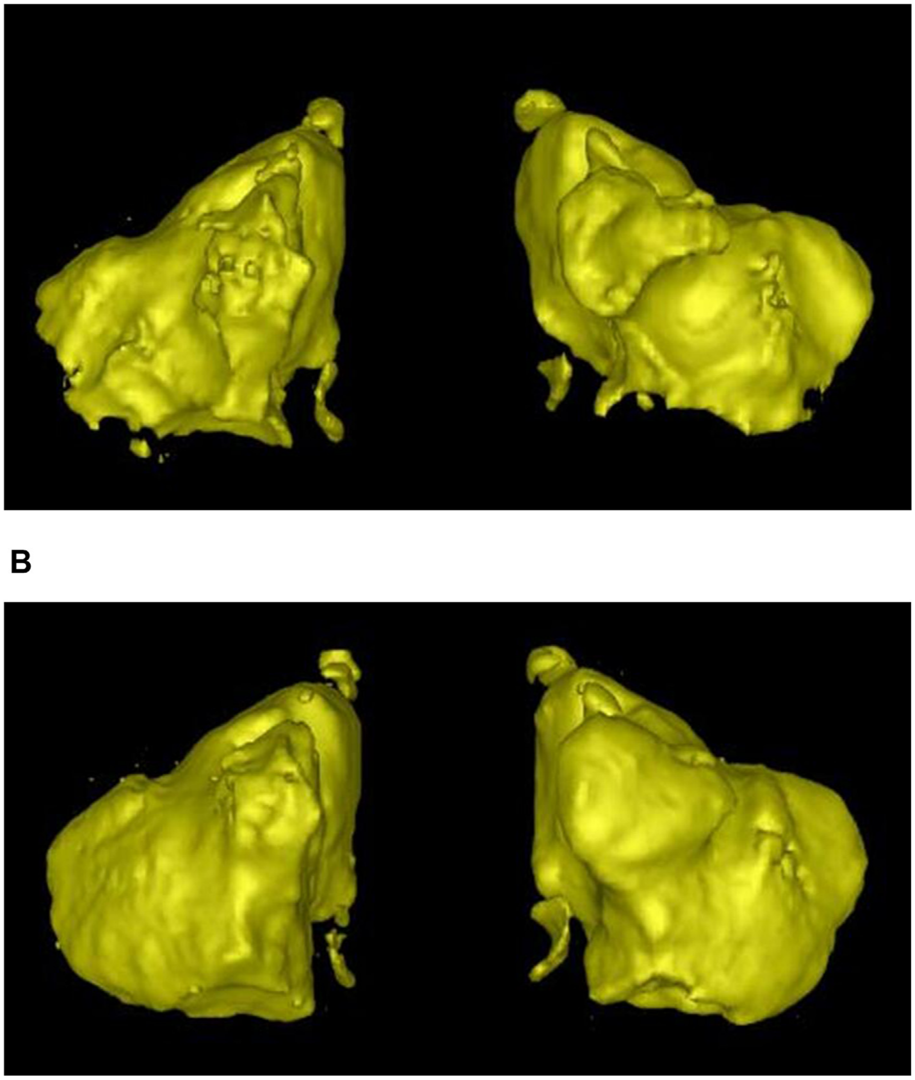

Fig. 5 After midfacial segmentation was completed, the 3D volumes of the right and left maxillary sinuses pre- and post-treatment were reconstructed and measured, as indicated by the yellow 3D objects.

rhinosinusitis,[19] while NO may act more generically. In fact, in a preliminary study using BOAT, Hwang et al[20] were able to resolve some cases of pediatric rhinosinusitis in young Korean children. In addition, Park et al[21] measured paranasal sinus volume in healthy Asian adults, using CBCT scans. They reported that the mean fully grown maxillary air sinus volume was approx. 15 cm^3. This value is similar to the pre-treatment values that we found of approx. 18.5 cm^3 (Table 1) in our present study. On the other hand, in a study to correlate symptoms of chronic rhinosinusitis with radiologic imaging, Deeb et al[22] analyzed CT scans. For healthy control subjects in that study, the volume of the maxillary sinus was approx. 24 cm^3. In our present study, the post-treatment findings were of a similar dimension, since the mean maxillary air sinus volume was approx. 20 cm^3 on both sides (Table 1). Therefore, although our study was performed on Asian patients, post-treatment it appears that their maxillary air volume was similar to that of Caucasian subjects.

Table 1 Mean values and standard deviations of parameters measured in this study (Mean $\pm$ SD).

Time	Transpalatal width (mm)	Sinus volume (Left, cm^3)	Sinus volume (Right, cm^3)
Pre-treatment	35.3 $\pm$ 3.0	18.8 $\pm$ 6.5	18.5 $\pm$ 5.7
Post-treatment	38.5 $\pm$ 2.1	20.0 $\pm$ 6.0	19.7 $\pm$ 5.8
p value	$<$0.001	0.026	0.038

Notes: The mean age of the sample was 25.0 yrs $\pm$ 8.7. The mean treatment time was 15.5 mths $\pm$ 5.2.

Interestingly, there are very few studies that have investigated the effect of maxillary expansion on maxillary sinus volume. In children, Almuzian et al[23] studied the effects of rapid maxillary expansion (RME) on the upper airway, using CBCT scans. They found a correlation between changes in the maxillary sinus volume and dentoalveolar expansion. In teenagers,[24] CBCT scans were taken before and after maxillary expansion therapy with a banded Hyrax appliance. It was reported that while the maxillary sinus volumes remained unchanged, the procedure resulted in a wider hard palate. In our study, we also found that the transpalatal bone width increased from approx. 35 mm to 38.5 mm post-treatment, but this was allied with increases in maxillary sinus volume (Table 1). Tikku et al[25] consider that nasal obstruction can lead to impaired pneumatization that can result in dimensional changes in the sinus. They calculated maxillary sinus volume from CBCT scans, and reported that the mean maxillary sinus volume of mouth breathers was significantly less than that of nasal breathers. In fact, a previous study[9] reported an increased nasal volume in adults treated using BOAT, and subsequent changes might induce size changes in adult maxillary sinuses, as noted in this study. In summary, it appears that, unlike traditional palatal expansion, BOAT may represent a novel field of endeavor based on the well-recognized but under-utilized physiologic mechanism of pneumatization. Further studies on the effect of these findings on paranasal sinus dysfunction, such as rhinosinusitis, infective conditions and sleep disorders associated with nasal obstruction, are now required.

Conclusions

Biomimetic oral appliance therapy may be able to non-surgically and non-pharmaceutically increase the maxillary air sinus volume in adults.

Further studies on the effect of enhanced pneumatization on rhinosinusitis, infective conditions and sleep-related breathing disorders are indicated.

Declaration of competing interest

Prof. G. Dave Singh has no conflict of interest except that he is Founder and Chief Medical Officer, Vivos Therapeutics, Inc.

Dr Hee Nam Kim Hwang has no conflict of interest.

Acknowledgments

We would like to thank STAA Orthodontic Laboratory, Seoul, South Korea for fabricating all devices used in this study. In addition, we are grateful to Morpheus Co. Ltd., Seoul, South Korea for providing the software used in this study.

References

1. Smith TD, Rossie JB, Cooper GM, Mooney MP, Siegel MI. Secondary pneumatization of the maxillary sinus in callitrichid primates: insights from immunohistochemistry and bone cell distribution. *Anat Rec A Discov Mol Cell Evol Biol*. 2005;285:677—689.
2. Smith TD, Rossie JB, Cooper GM, et al. The maxillary sinus in three genera of new world monkeys: factors that constrain secondary pneumatization. *Anat Rec (Hoboken)*. 2010;293:91—107.
3. Lawson W, Patel ZM, Lin FY. The development and pathologic processes that influence maxillary sinus pneumatization. *Anat Rec (Hoboken)*. 2008;291:1554—1563.
4. Withalm A. Influence of nasal respiration in the development of the paranasal sinuses; a contribution to the problem of the inhibition of pneumatization in the sinuses. *Monatsschr Ohrenheilkd Laryngorhinol*. 1950;84:201—207.
5. Nowak R, Mehlis G. Studies on the state of pneumatization of the sinus maxillaris. *Anat Anz*. 1975;138:143—151.
6. Wehrbein H, Diedrich P. [Progressive pneumatization of the basal maxillary sinus after extraction and space closure]. *Fortschr Kieferorthop*. 1992;53:77—83.
7. Re S, Cardaropoli D, Corrente G, Abundo R. Bodily tooth movement through the maxillary sinus with implant anchorage for single tooth replacement. *Clin Orthod Res*. 2001;4: 177—181.
8. Heit T, Sebastian J, Singh GD. A novel combined protocol for the resolution of severe obstructive sleep apnea. *J Sleep Disord*. 2016;5:251—254.
9. Singh GD, Heit T, Preble D, Chandrashekhar R. Changes in 3D nasal cavity volume after biomimetic oral appliance therapy in adults. *Cranio*. 2016;34:6—12.
10. Singh GD, Griffin TM, Chandrashekhar R. Biomimetic oral appliance therapy in adults with mild to moderate obstructive sleep apnea. *J Sleep Dis*. 2014;1:5.
11. Singh GD, Heit T, Preble D. Changes in 3D midfacial parameters after biomimetic oral appliance therapy in adults. *J Ind Orthod Soc*. 2014;48:104—108.
12. Proffit WR, Frazier-Bowers SA. Mechanism and control of tooth eruption: overview and clinical implications. *Orthod Craniofac Res*. 2009;12:59—66.
13. Márquez S. The paranasal sinuses: the last frontier in craniofacial biology. *Anat Rec (Hoboken)*. 2008;291:1350—1361.
14. Wedel MJ. Origin of postcranial skeletal pneumaticity in dinosaurs. *Integr Zool*. 2006;1:80—85.
15. Sereno PC, Martinez RN, Wilson JA, Varricchio DJ, Alcober OA, Larsson HC. Evidence for avian intrathoracic air sacs in a new predatory dinosaur from Argentina. *PLoS One*. 2008;3, e3303.
16. Butler RJ, Barrett PM, Gower DJ. Postcranial skeletal pneumaticity and air-sacs in the earliest pterosaurs. *Biol Lett*. 2009; 5:557—560.
17. Cappello ZJ, Dublin AB. *Anatomy, Head and Neck, Nose, Paranasal Sinuses*. Florida: Treasure Island, Stat Pearls Publishing; 2018.
18. Keir J. Why do we have paranasal sinuses? *J Laryngol Otol*. 2009;123:4—8.
19. Yan CH, Hahn S, McMahon D, et al. Nitric oxide production is stimulated by bitter taste receptors ubiquitously expressed in the sinonasal cavity. *Am J Rhinol Allergy*. 2017;31:85—92.
20. Hwang H, Hwang C, West J, Singh GD. Changes in pediatric paranasal sinuses following biomimetic oral appliance therapy: 3 case reports. *Cranio*. 2019:1—6.
21. Park IH, Song JS, Choi H, et al. Volumetric study in the development of paranasal sinuses by CT imaging in Asian: a pilot study. *Int J Pediatr Otorhinolaryngol*. 2010;74:1347—1350.
22. Deeb R, Malani PN, Gill B, et al. Three-dimensional volumetric measurements and analysis of the maxillary sinus. *Am J Rhinol Allergy*. 2011;25:152—156.
23. Almuzian M, Ju X, Almukhtar A, Ayoub A, Al-Muzian L, McDonald JP. Does rapid maxillary expansion affect nasopharyngeal airway? A prospective Cone Beam Computerised Tomography (CBCT) based study. *Surgeon*. 2018;16:1—11.
24. Darsey DM, English JD, Kau CH, Ellis RK, Akyalcin S. Does hyrax expansion therapy affect maxillary sinus volume? A cone-beam computed tomography report. *Imaging Sci Dent*. 2012;42: 83—88.
25. Tikku T, Khanna R, Sachan K, Srivastava K, Munjal N. Dimensional changes in maxillary sinus of mouth breathers. *J Oral Biol Craniofac Res*. 2013;3:9—14.

Edited by Yu-Xin Fang