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Title:
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Date:
2021-12-01

Citation:
Niu, X., Motro, M., Will, L. A., Cornelis, M. A. & Cattaneo, P. M. (2021). Does rapid maxillary expansion enlarge the nasal cavity and pharyngeal airway? A three-dimensional assessment based on validated analyses. Orthodontics and Craniofacial Research, 24 (S2), pp.124-133. https://doi.org/10.1111/ocr.12526.

Does rapid maxillary expansion enlarge the nasal cavity and pharyngeal airway? – A three-dimensional assessment based on validated analyses

Running Title: 3D evaluation of upper airway after RME

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/OCR.12526

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Author contribution statement

Xiaowen Niu contributed to design the protocol, collected the data at Aarhus University, measured, analyzed, interpreted all the data, and drafted the manuscript.

Melih Motro collected and interpreted the data at Boston University, and revised the manuscript for important intellectual content, and approved the version to be published.

Leslie A Will interpreted the data and revised the manuscript for important intellectual content, and approved the version to be published.

Marie A Cornelis designed the protocol and revised the manuscript for important intellectual content, and approved the version to be published.

Paolo M. Cattaneo designed the protocol, trained the examiner for the measurements, helped in interpreting the data, revised the manuscript for important intellectual content, and approved the version to be published.

Declaration of interest

Declarations of interest: none

Data availability of statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Acknowledgements

We thank Alona Isenshtat and Shadi Gera, postgraduate students at the Section of Orthodontics, Department of Dentistry and Oral health, Aarhus University, for helping with data collection; and the State Scholarship Fund from China Scholar Council (201609110098).

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Article type : Research Article

Does rapid maxillary expansion enlarge the nasal cavity and pharyngeal airway? – A three-dimensional assessment based on validated analyses

Abstract

Objectives: To evaluate the three-dimensional changes following rapid maxillary expansion (RME) of the nasal cavity (NC) and pharyngeal airway (PA) in growing patients, using innovative and validated evaluation methods. To investigate whether a correlation between skeletal expansion and increase in airway volume exists.

Settings and sample population: Records of patients who had cone-beam computed tomography taken before and after orthodontic treatment with or without RME, were retrospectively collected and divided into two groups: 1) RME, 39 patients (mean age 10.40 ± 1.74 years); and 2) control, 29 patients, matched for age (mean age 11.07 ± 1.45 years) and follow-up period.

Material and methods: Total and partial volumes of the NC and the PA were calculated. The PA centerline was determined to assess the minimal cross-sectional area and hydraulic diameter. Paired and unpaired t-test were applied to compare the difference between time points and between groups. One-way ANOVA and post hoc Tukey's tests were used to compare subgroups with respect to changes in palatal width and lacrimal ducts distance.

Results: All of the NC, PA, and skeletal parameters were significantly enlarged after RME. The NC volume and inter-molar distance in the RME were significantly larger compared to the control group. The initially

lower mean values of minimal cross-sectional area and hydraulic diameter in the RME group when compared to the control group, normalized after RME treatment.

Conclusions: Based on validated analyses, the nasal cavity volume increase was evident after RME in the long term after controlling for growth.

Introduction

Maxillary deficiency may be considered an aetiology of sleep-disordered breathing (SDB), particularly obstructive sleep apnoea in children.[1] On the other hand, the opposite may also be true as obstruction of the nasal and pharyngeal airway (PA) may shift nasal breathing to mouth breathing, subsequently causing developmental deficiencies in craniofacial structures.[2, 3] In a questionnaire-based screening study, Huynh et al. found that SDB was primarily associated with a long and narrow face with a narrow palate, dolichofacial pattern, high mandibular plane angle and severe maxillary and mandibular crowding.[4] The European Respiratory Society Task Force has recommended rapid maxillary expansion (RME) as a treatment option for children with SDB and maxillary constriction.[5]

RME has been proven to be an effective technique to increase the transverse skeletal dimension of the maxilla by opening the midpalatal suture, regardless of the type of palatal expander used.[6] During expansion, the force created by the expander is transmitted to the craniofacial complex, which results in disarticulation of the maxillary halves along the maxillary circumferential and midpalatal sutures,[7] indicating that this treatment modality may have some implications for the nasal cavity (NC) size, airway dimensions, and airway resistance.[8] Camacho et al. performed a systematic review with meta-analysis on sleep studies in children who had been treated for obstructive sleep apnoea by RME, with the results suggesting that RME also improves apnea-hypopnea index and lowest oxygen saturation in children.[9] A recent meta-analysis suggested that RME enlarges the NC, but also that the enlargement should be considered with caution; first, because of limited methodological quality; second, because these changes are seemingly not maintained in the long term.[10]

To our knowledge, there are two randomised controlled clinical trials, which have evaluated airway changes following RME treatment.[11, 12] However, none of these studies included inactive control groups. Thus, the real influence of RME on nasal airway dimensions and functions, considering the influence of growth, has not been fully elucidated.

Furthermore, according to White, the principal problem in patients with obstructive apnea is the collapse of the PA.[13] In order to identify the most constricted part of the PA, a study of the PA morphology seems more indicated than volume assessment. In particular, minimal cross-sectional area (CS) and minimal hydraulic diameter (D_H) are important parameters to describe the PA morphology.[14, 15] The hydraulic diameter, D_H, is a

commonly used parameter when assessing flow in non-circular tubes and channels. D_H is defined as four times the cross-sectional area of flow divided by the wetted perimeter. Thus, in case of a circular tube, the D_H is simply the diameter of the tube, while for non-circular ducts, similar to a collapsed PA, the D_H depends on the ratio between the area and the perimeter. This fact suggests that the D_H might be a critical measure, more so than the CS, for characterizing the PA morphology. The changes of minimal CS and minimal D_H and their locations along the PA following RME treatment have not been reported previously.

Therefore, the aim of this retrospective study was to evaluate the three-dimensional (3D) changes that occur after RME treatment in the NC and the PA of growing patients, using an innovative and validated evaluation method, and to investigate whether a correlation exists between changes in skeletal width and airway volume. The null hypothesis was that NC and PA volumes do not increase after orthodontic treatment with RME, and that no relationship exists between changes in skeletal width and the airway.

Materials and methods

This was a retrospective study using radiological records prescribed for orthodontic treatment needs. The protocol of the study and the use of the data was reported in Denmark (Datatilsynets journalnummer

2015-57-0002 og Aarhus Universitets journalnummer 2016-051- 000001, løbenummer 1393) and received approval in Boston (Boston University #H-32515).

Patients of this multicentre study were obtained from the patient database of the Postgraduate Clinic of the Section of Orthodontics, Department of Dentistry and Oral Health, Aarhus University and the CBCT repository of the Department of Orthodontics and Dentofacial Orthopedics, Henry M. Goldman School of Dental Medicine, Boston University. Inclusion criteria for the RME group were: 1) patients aged 6-13 years; 2) patients treated with RME as an initial part of their comprehensive orthodontic treatment; 3) cervical vertebral maturation < 4;[16] 4) pre- and post-treatment large-field-of-view CBCTs (i.e., including all the craniofacial structures required for cephalometric analysis); 5) an interval between two CBCTs shorter than 36 months. Exclusion criteria were: 1) previous orthodontic treatment; 2) systemic diseases; 3) craniofacial anomalies; 4) temporomandibular joint disorders; 5) pharyngeal pathology and/or nasal obstruction, including adenoidectomy and tonsillectomy; 6) any CBCTs in which the airway was not clear, not fully contained in the volume, or with significant artifacts; 7) major variation in the head and craniocervical orientation (>5 degrees) between T0 and T1 CBCTs.[17] The RME group consisted of patients with maxillary constriction treated with Hyrax-type maxillary expanders attached to the maxillary first molars and extended forward to the first premolars or primary first molars. The expansion protocol was one or two quarter turn screw activation per day until a slight amount of overcorrection was achieved. Then the screw was locked and the expander remained on the teeth as a passive retainer for a 4-6 month period.

An age-matched group with class I malocclusion was selected from the same database (control group); subjects from this control group received CBCTs for oral surgery indications (i.e., impacted teeth). Patients had received comprehensive orthodontic treatment (excluding functional appliance therapy or maxillary protraction) and had pre- and post-treatment CBCTs with the characteristics described for the RME group. From the selected records, 39 subjects were included in the RME group, whereas 29 subjects were included in the control group.

Based on an alpha significance level of 0.05 and changes in the volume of the nasopharynx with and without RME treatment (i.e., 1720±1511 mm^3 and 813±1007 mm^3, respectively),[18] the calculated power of this study was 0.83.

Both the CBCTs for the RME and control groups were taken with two scanners: a NewTom 5G (QR, Verona, Italy) (110 kVp, 5 mA, 0.3 mm isotropic voxel dimension, 18 seconds of scanning time with 3.6 seconds of exposure time, a field of view (FOV) of 18 cm × 16 cm), and an i-CAT Classic scanner (Imaging Sciences International, Hatfield, Pa) (120 kVp, 5 mA, 0.3 mm isotropic voxel dimension, 17 seconds of scanning time with 7 seconds of exposure time, a FOV of 23 cm × 17 cm). In the RME group, 15 out of the 39 patients were taken with the NewTom scanner, while the remaining 24 patients were taken with the i-CAT scanner. In the control group, 12 of 29 patients were taken with the NewTom scanner and the remaining 17 patients were taken with the i-CAT scanner. All the patients had the before- and after-treatment scan taken with the same CBCT machine. Scanning protocols for acquisition with both scanners ensured that the subjects were in centric occlusion with their lips and tongue in a resting position; during scanning, the patients were also instructed to stay still to prevent motion artefacts. Raw data obtained from the CBCTs were exported into DICOM format and imported into a specific software (Mimics 21, Materialise, Leuven, Belgium).

Considering that the grey value scale in different CBCTs is not constant,[19] the threshold levels used to segment and visualise the NC and PA were determined for each CBCT. A mask was created using the appropriate threshold, which was used to generate the corresponding 3D model of the UA. The 3D model of the craniofacial structures was also built to help perform the 3D analysis.[14, 20] The NC was visualized and segmented using a semi-automatic segmentation approach.[21] A PA centreline was calculated using the "Fit Centerline" tool in the "Analyze" menu (Figure 1F).[21]

Landmarks and measurements

Landmark definitions for the dental, skeletal, and airway parameters as well as plane definitions are presented in Table 1a. Four linear measurements were assessed to evaluate the transverse skeletal changes after expansion (Figure 1, A). Two reference planes were defined: Frankfort Horizontal, used as the horizontal plane; and Sagittal SN plane, used as the sagittal plane. The total PA was divided into three parts according to the location of the PNS-So, PNS-Ba, and occlusal and E planes; and their volumes were

assessed (Table 1b and Figure 1, D and E). Based on the midline of the total PA, CS and D_H were assessed, both perpendicular to the centreline (Figure 1, F). The distance between the two centroid points of the lacrimal foramen (inter-LF distance) and the distance between the two most inferior points of the lacrimal ducts (inter-LD distance) were evaluated (Figure 1, B and C). One examiner (X.N.), who was blinded to the intervention group, conducted all measurements.

Statistical analysis

Ten randomly selected records were re-evaluated by the same operator (X.N.), repeating the full measurements' sequence, one month after the preliminary data collection, to assess the intra-operator reliability. The measurement error was analysed using the Dahlberg formula.[22] Reliability was ranked according to the intra-class correlation (ICC) value, and paired t-test was performed for double measurements. The data were checked for normal distribution with Q-Q plots. Independent sample t-tests were used to validate the consistency of both groups at T0 in terms of age, and to compare the outcome variables at T1. Paired sample t-tests were used to compare changes from T0 to T1. The Friedman analysis of variance (ANOVA) for repeated measures followed by post hoc Tukey tests were used to compare subgroups with respect to transversal change (assessed by the change in palatal width and inter-LD distance) compared with the control group. Scatter diagrams and Pearson's correlation coefficients were prepared to check the association between the changes in palatal width and inter-LD distance with the NC and PA measurements. All analyses were performed using Stata 15 CI (StataCorp, College Station, Texas, USA). A 2-tailed p-value of 0.05 was considered significant.

Results

The mean age of the patients was 10.4 ± 1.7 years in the RME group and 11.1 ± 1.5 years in the control group (Supplementary Table S1). The follow-up period for the RME and the control group was 22.6 ± 10.3 months and 22.9 ± 4.3 months, respectively. The demographic data for both groups were not statistically different ($p > 0.05$), which confirmed that both groups were matched for both age and follow-up duration.

The calculation of the error of the method revealed that the errors were small for all the measurements, that the coefficient of reliability was good for all measurements, and that there was no systematic error in measuring (Supplementary Table S2).

Regarding the width measurements, the inter-molar distance was significantly lower in the RME group than in the control group at T0 ($p = 0.006$). After treatment, all width measurements were significantly increased in the RME group. At the same time, the inter-molar distance and the inter-LD distance were also significantly larger than in the control group (Table 2, Figure 2).

For NC volume, a significant difference was seen between groups at T0 ($p = 0.031$), but no difference was seen at T1 (Table 2). After treatment, in the RME group, the NC volume displayed a statistically significant increase (1673 mm^3, $p = 0.000$), whereas the increase was non-significant in the control group. A statistically significant net change was observed in the RME group compared with the control group ($p = 0.029$) (Table 2, Supplementary Figure S1). In order to evaluate whether changes were associated with the amount of palatal expansion, the treatment group was divided twice into two subgroups: first, according to change in palatal width after treatment: RME 1 (Palatal width change ≤ 2 mm) and RME 2 (Palatal width change ≥ 2 mm); second, according to inter-LD distance change after treatment: RME 3 (inter-LD distance change ≤ 0.8 mm); RME 4 (inter-LD distance change ≥ 0.8 mm). ANOVA revealed that among all the outcomes measured, only the NC volume showed significant differences between the subgroups and the control group. Post hoc analysis for NC revealed that only RME 2 and RME 4 showed statistically significant differences compared with the control group ($p = 0.038$ and $p = 0.036$, respectively) (Tables 3a and 3b).

Regarding PA measurements, no significant differences were found between groups at T0 and T1. After treatment, all volumes in the PA showed a significant increase in the RME group; this was also the case for the control group, except for the oropharynx. However, no significant difference was observed when these changes were compared between groups (Table 2, Supplementary Figure S1).

Significant differences were observed for both minimal CS and minimal D_H in the RME group after treatment. Even so, no statistically significant difference was observed compared with the control group (Table 2, Supplementary Figure S1). Figure 3 shows the mean values and 95% confidence interval (CI) at each control point for both the RME and the control group. The minimal values for the two groups are at point 30-35 before and after treatment.

Supplementary Figure S2 shows the correlations between transverse dimensions and nasal airway measurements. From these data, it is clear that positive correlations exist for all measurements in the RME group. However, no statistically significant correlation was present.

Discussion

The main purpose of this study was to precisely evaluate changes in NC and PA morphology following RME treatment at long-term follow-up using an innovative and validated evaluation method.[21] Many studies have reported that RME seems to enlarge the nasal airway, including the NC and nasopharynx.[18, 23, 24]. However, a recent systematic review and meta-analysis showed that long-term stable results could not be demonstrated.[10] This is also reflected in the conclusion from the consensus paper recently published by the American Association of Orthodontists, suggesting that RME should not be used as a preventive intervention to limit the insurgence of OSA in growing subjects, as the definite diagnosis should be done by a physician.[25]

The present study had a follow-up period of 22.62 months. The results were compared with an age-matched control group to account for the effects of growth.

RME is frequently used to correct transverse skeletal and dental problems. RME was first described by Angell in 1860,[26] and many types of palatal expanders and their effects on skeletal and dental structures have been studied since then.[27-29] The present study compared the changes following tooth-borne Hyrax expander treatment. After treatment, all dental and skeletal measurements in the RME group showed a significant increase, indicating a transversal widening. The distance between the inferior points of the lacrimal ducts (i.e. inter-LD distance) and palatal width changes were significantly larger in the RME group than in the control group. Debate continues about how the mid-palatal suture opens following RME in the horizontal plane, i.e., whether it occurs in a parallel or triangular manner. A study by Ballanti showed that the maxillary opening occurs in an almost parallel manner,[27] whereas other studies have shown that the suture opening adheres to a triangular pattern.[30, 31] Our results indicated that the anterior maxilla was significantly enlarged after accounting for the growth factor. Paredes assessed the skeletal and dental tipping after maxillary expansion by calculating the fulcrum locations and applying an angular measurement.[32] They superimposed 3D models of the zygomaticomaxillary complex of an RME patient and indicated the rotational pattern of the zygomaticomaxillary complex. In our study, the distance between the inferior points of the lacrimal ducts (i.e. inter-LD distance) was enlarged more than the distance between the superior points of the lacrimal ducts (i.e. inter-LF distance) (1.15 mm, and 0.42 mm, respectively), which confirmed that expansion does not follow a parallel pattern on the coronal view.[31]

Skeletal expansion during RME is not limited to the palate. As the palate constitutes the lower border of the NC, and as the lateral walls of the NC are moved away when opening the palatal suture, an enlarged NC would be an expected effect of RME.[33] Because of the complex architecture of the NC, previous studies using CBCT have focused mainly on the changes of the posterior upper airway.[1, 34] In the present study, both the NC and the PA were investigated. Regarding segmentation of the NC, a novel approach was used in which masks were sketched manually every ten slices, and then the "smart expand" tool was used to dilate the masks until they reached the sketched border. This approach has been tested previously and its reliability was confirmed.[21] A recent systematic review and meta-analysis reviewed the studies analysing the volumetric changes of NC after RME,[10] showing that an average increase of 1500 mm^3 of the NC volume may be expected after 3 months of retention. The result of the present study showed an increase in NC volume of 1673 mm^3 22 months after RME, with a statistically significant net increase of about 1100 mm^3 when compared with the control group. To our knowledge, the number of studies evaluating the relationship between the expansion achieved using RME and the increase in airway volume is limited.[10] Our results indicated no strong correlations between transversal widening and volume increase. However, the results from the subgroup analysis showed that increasing skeletal expansion is associated with NC volume

increases, both anteriorly and posteriorly. This was more evident for the NC than for the nasopharynx: After treatment, the nasopharynx volume increase was about 150 mm^3 larger in the RME than in the control group, but this difference was not statistically significant. This is probably because the tooth-borne hyrax expanded the palate in a V-shaped pattern, with a wider expansion at the anterior nasal spine than at the posterior nasal spine.[35] Although significant after-treatment changes were observed in the PA parameters for the RME group in the present study, the intergroup comparison revealed no significant differences. Contrary to the present study, Iwasaki et al. reported significant positive differences for total PA and retropalatal volume compared with a matched control group when assessing volumetric PA changes.[36] El et al. evaluated the oropharyngeal airway and nasal passage volume changes that occur 2 years after RME using CBCT; comparing RME with a group matched for age and follow-up, they concluded that RME creates a significant increase in nasal passage volume, which is in agreement with our results.[18]

The minimal CS and minimal D_H are important parameters in identifying the most constricted part of the PA. Chang et al. investigated changes in the CS of the PA in 14 patients after RME.[1] They found that the minimal CS was located in the retropalatal airway in 11 patients and in the retroglossal airway in three patients; and that the minimal CS covered a 4.2 mm^2 area. However, they did not specify the approach used to identify the minimal CS. El et al. indicated that the area of the most constricted region is at the level of the base of the tongue.[18] In our study, the midline of the PA was extracted according to the shape of the PA, and around 50 control points were defined for each centreline, which equals one control point per millimetre. The CSs were measured at each control point perpendicular to the centreline. Figure 3A shows that the minimal CS was located in the oropharynx region at the base of the tongue, thus corroborating the results of El et al.[18] The same figure also shows that before treatment, the mean values of minimal CS and minimal D_H of the control group were larger than those of the RME group at almost every point, yet after treatment most of the values in the RME group overlapped or exceeded those of the control group. Table 2 showed no statistically significant increase in area after treatment compared with the controls. However, the minimal CS increase of 26.3 mm^2 in the RME group was greater than that of the control group (14.49 mm^2).

In most of the pharyngeal tract, the shape of the lumen is not circular and may assume irregular forms. As the shape of the duct greatly influences the resistance to flow, in fluid dynamics, D_H is often used to calculate the actual flow in non-circular ducts, especially in case of a turbulent flow. Therefore, D_H is also a crucial parameter when analysing the PA, especially in patients with obstructed breathing during sleep. The D_H could be measured along the centreline with the CS at the same control points. Figure 3C & D show that the minimal D_H in the two groups was positioned at similar locations as the minimum CS (i.e., from point 30 to point 35). Moreover, the figure shows a clear before-treatment trend with higher mean values on most of the parameters in the control group than in the RME group. Yet, after treatment, the values in the RME group are higher than those of the controls.

Due to the retrospective nature of the present study, some limitations were unavoidable. Only the effect of RME on the volumetric and skeletal changes was evaluated, while the transverse expansion at the suture has not been assessed. Furthermore, the CBCTs were taken with two different scanners, which may introduce a discrepancy. On the other hand, the same type of scanner was used for the before and after scans, which may compensate for the possible differences. Finally, the expansion protocol was not fully identical among all patients as some patients obviously still had deciduous molars. A well-designed prospective study would be recommended to take this aspect into consideration and to investigate whether the physical changes seen after RME are followed by significant improvements in respiration, physical activity and the children's quality of life.

Conclusions

This retrospective study comprehensively assessed the effect of the RME on the dental, skeletal, NC, and PA status, and compared the results with results obtained in a control group matched for age and follow-up period. RME produced a significant increase in NC volume, but no significant difference was observed in PA volume compared with the control group. When the palatal width expansion exceeded 2 mm, a statistically significant expansion of the NC volume was observed. The use of a new and validated evaluation method allowed to show that the initially lower mean values of minimal cross section and minimal hydraulic diameter in the RME group, when compared to the control group, normalized after RME treatment.

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Figure Legends

Figure 1. Landmarks and measurements. (A) Coronal CBCT image showing the left and right greater palatine foramen. (B) Sagittal CBCT image showing: 1. Centroid of the lacrimal foramen right (LF-R), 2. The most inferior point of the right lacrimal duct (LD-R). (C) 3D image showing the left and right lacrimal canal. 3. Centroid of the lacrimal foramen left (LF-L), 4. The most inferior point of the left lacrimal duct (LD-L). (D) Sagittal CBCT image showing, 5. The midpoint of the sella-basion line (So), 6. The most posteroinferior point on the clivus (Ba), 7. The most superior point of the epiglottis (E), 8. The most posterior point of the nasal spine (PNS), 9. The tip of the nasal bone (NTip), and 10. The most anterior point of the nasal spine (ANS). (E) 3D reconstruction of the nasal cavity (green), nasopharynx (yellow), velopharynx (pink) and oropharynx (purple), delimited by five anteroposterior planes. (F) The centreline for the total airway.

Figure 2. Box plots showing the differences of palatal width and Inter lacrimal duct distance (inter-LD distance) between T0 and T1 for two groups. *$p \leq 0.05$.

Figure 3. PA morphology analysis – location of the minimal CS and D_H of the PA with respect to control points for: Mean values ± SD are reported. *Indicated the minimal values of CS and D_H.

Supplementary Figure S1. Ladder plots showed the change in NC volume, PA volume, Minimal CS, and Minimal D_H over time for the RME and the control group. The red line indicates the change of the mean values.

Supplementary Figure S2. The correlations between transverse dimensions (palatal width and lacrimal duct) and nasal airway (nasal cavity and nasopharynx) measurements.

Table 1a: Landmarks selected for airway analysis

Points	Description
ANS	The most anterior point on the nasal spine
Ba	The most posteroinferior point on the clivus
E	Most superior point of the epiglottis
LD-L	The most inferior point of the left lacrimal duct
LD-R	The most inferior point of the right lacrimal duct
LF-L	Centroid of the Lacrimal foramen left
LF-R	Centroid of the Lacrimal foramen right
MoL	The distal-palatal tip of the first left molar in the upper jaw
MoR	The distal-palatal tip of the first right molar in the upper jaw
N	The intersection of the internasal and frontonasal sutures in the midsagittal plane
Ntip	The tip of the nasal bone
OrL	Orbital left, the most inferior anterior point on left orbit's margin
OrR	Orbital right, the most inferior anterior point on right orbit's margin
PNS	The most posterior point on the nasal spine
Pl	Centroid of the greater palatine foramen left
Pr	Centroid of the greater palatine foramen right
PoL	Porion Left: the most upper point on the left bony external auditory meatus
PoR	Porion Left: the most upper point on Right bony external auditory meatus
S	The midpoint of the sella turcica
So	The midpoint of the sella-basion line
ii	The point midway between the incisal edges of the maxillary central incisors
References planes	Description
Frankfurt plane	A plane passing through the inferior borders of the bony orbits, encompassed by OrR and OrL, and the upper margin of the auditory meatus encompassed by PoL.
Sagittal SN plane	Plane perpendicular to Frankfurt plane passing through S and N points
NTip-ANS plane	Plane through NTip and ANS points, perpendicular to Sagittal SN plane

PNS-So plane	Plane through PNS and So points, perpendicular to Sagittal SN plane
PNS-Ba plane	Plane through PNS and Ba points, perpendicular to Sagittal SN plane
Occlusion plane	Plane through MoL, MoR, and ii points
E plane	Plane through E point, parallel to Frankfurt plane

Table 1b: NC and PA volumes and cross-sections

	Description
NC measurment	
NC volume	Bounded anteriorly by NTip-ANS plane and posterior by PNS-So plane
PA measurments	
Nasopharynx volume	Bounded superiorly by PNS-So plane and inferiorly by PNS-Ba plane
Velopharynx volume	Bounded superiorly by PNS-Ba plane and inferiorly by occlusion plane
Oropharynx volume	Bounded superiorly by occlusion plane and inferiorly by E1-E2 plane
PA volume	Bounded superiorly by PNS-So plane and inferiorly by E1-E2 plane
Miminal CS	The minimal cross-sectional area in Total PA
Minimal D_H	The minimal hydraulic diameter in Total PA
Width	Description
Inter lacrimal duct distance (LD)	Distance between Ld-L and Ld-R
Inter lacrimal foramen distance (LF)	Distance between Lf-L and Lf-R
Inter-molar distance	Distance between MoL and MoR
Palatal width	Distance between Pl and Pr

Table 2. Statistical comparison of NC and PA

	Before Treatment (T0)					After Treatment (T1)					Treatment change (T1-T0)							
	RME		Control		Group differences	RME		Control		Group differences	RME			Control			Group differences	
	Mean	SD	Mean	SD	P	Mean	SD	Mean	SD	P	Mean	SE	P	Mean	SE	P	P	

NC volume	10795	2119	12047	2518	0.031*	12467	2401	12620	2239	0.798	1673	2013	0.000*	569	1876	0.113	0.029*
PA volume	8263	2441	8317	3180	0.939	10192	3241	10103	3452	0.914	1929	3035	0.000*	1786	3464	0.013*	0.860
Nasopharynx	1300	665	1665	937	0.068	1754	789	1975	840	0.283	454	604	0.000*	310	615	0.015*	0.348
Velopharynx	2685	1086	2710	1408	0.934	3318	1487	3396	1367	0.950	633	1129	0.001*	586	1124	0.011*	0.868
Oropharynx	4028	1670	3937	1838	0.832	5026	2255	4825	2503	0.727	998	2403	0.013*	888	2435	0.069	0.857
Minimal CS	84.78	36.94	102.14	56.64	0.136	111.07	56.24	116.63	59.22	0.770	26.30	49.17	0.002*	14.49	68.19	0.280	0.416
Minimal D_H	7.57	1.95	8.13	2.24	0.268	8.58	2.48	8.84	2.50	0.664	1.01	1.70	0.001*	0.71	2.33	0.125	0.550
Inter-molar distance	39.03	3.07	41.12	2.93	0.006*	42.36	3.35	41.68	3.58	0.425	3.33	2.98	0.000*	0.56	2.73	0.277	0.000*
Palatal width	26.17	1.49	26.89	1.74	0.070	27.64	1.71	27.95	1.79	0.491	1.47	1.22	0.000*	1.05	0.62	0.000*	0.090
Inter-LF distance	19.26	1.77	19.37	1.98	0.795	19.68	1.82	19.51	2.04	0.719	0.42	0.63	0.000*	0.14	0.94	0.446	0.135
Inter-LD distance	23.52	2.15	23.51	1.81	0.992	24.67	2.09	24.15	1.87	0.295	1.15	0.88	0.000*	0.64	0.77	0.000*	0.015*

SD, standard deviation; SE, standard error; *P≤0.05

Table 3a. Treatment group subgroup analysis

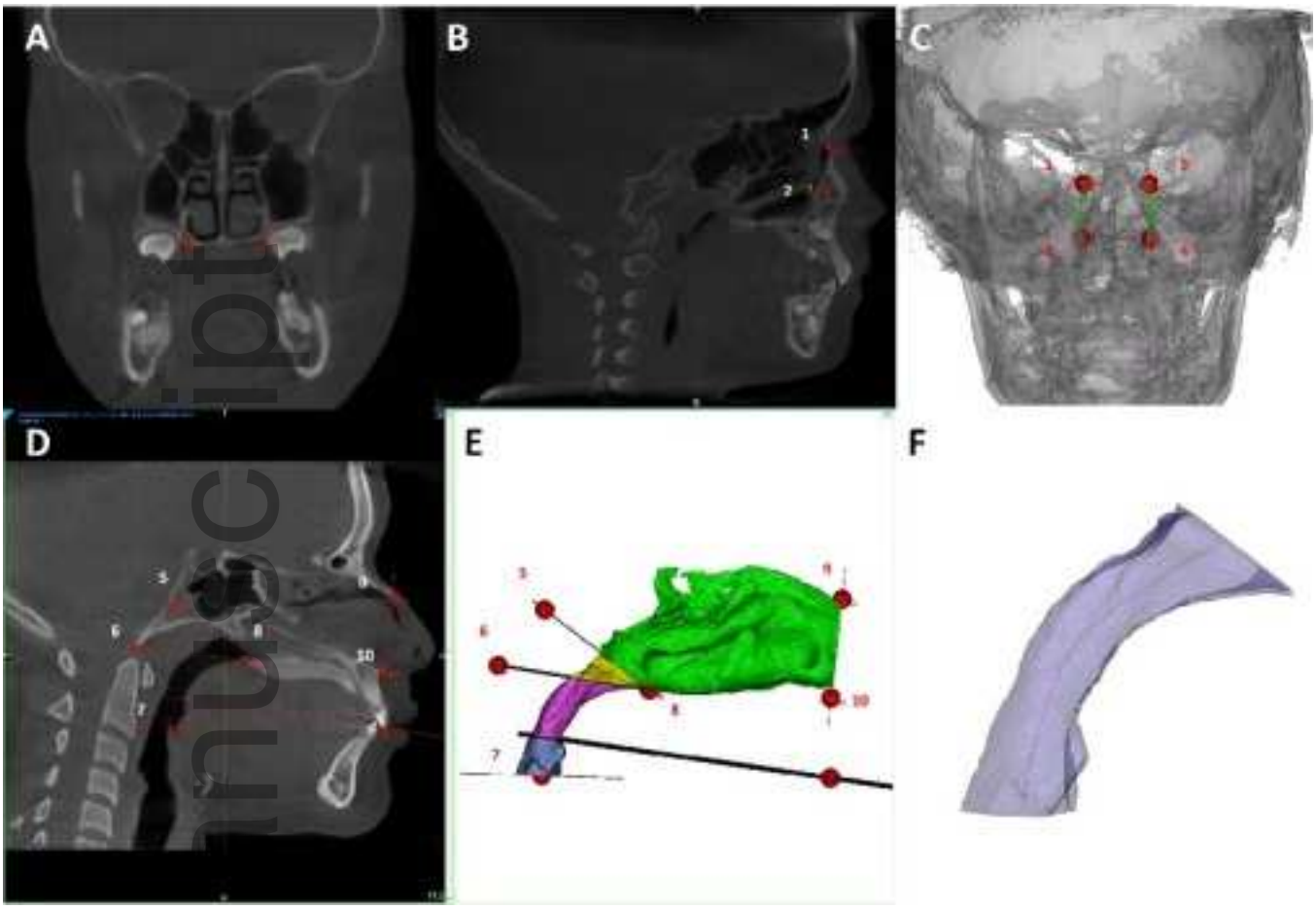
	RME 1 (Palatal width changed <2) (n=27)		RME 2 (Palatal width changed ≥2) (n=12)		Control group		RME 1 vs RME 2			RME 1 vs control			RME 2 vs control		
	Mean	SD	Mean	SD	Mean	SD	Mean Difference (RME1 - RME2)	SD	P	Mean Difference (RME1-Control)	SD	P	Mean Difference (RME2-control)	SE	P
NC volume	1391	1957	2306	2426	569	1876	-915	698	0.394	822	205	0.284	1736	317	0.038*

SD, standard deviation; SE, standard error; *P≤0.05

Table 3b. Treatment group subgroup analysis

	RME 3 (Inter-LD distance changed <0.8) (n=27)		RME 4 (Inter-LD distance changed ≥0.8) (n=12)		Control group		RME 3 vs RME 4			RME 3 vs Control			RME 4 vs Control		
	Mean	SD	Mean	SE	Mean	SE	Mean Difference (RME 3 - RME 4)	SE	P	Mean Difference (RME3 - Control)	SE	P	Mean Difference (RME 4 - Control)	SE	P
NC volume	1235	2003	2011	2197	569	1876	-776	651	0.462	666	587	0.529	1442	571	0.036*

SD, standard deviation; SE, standard error; *P≤0.05



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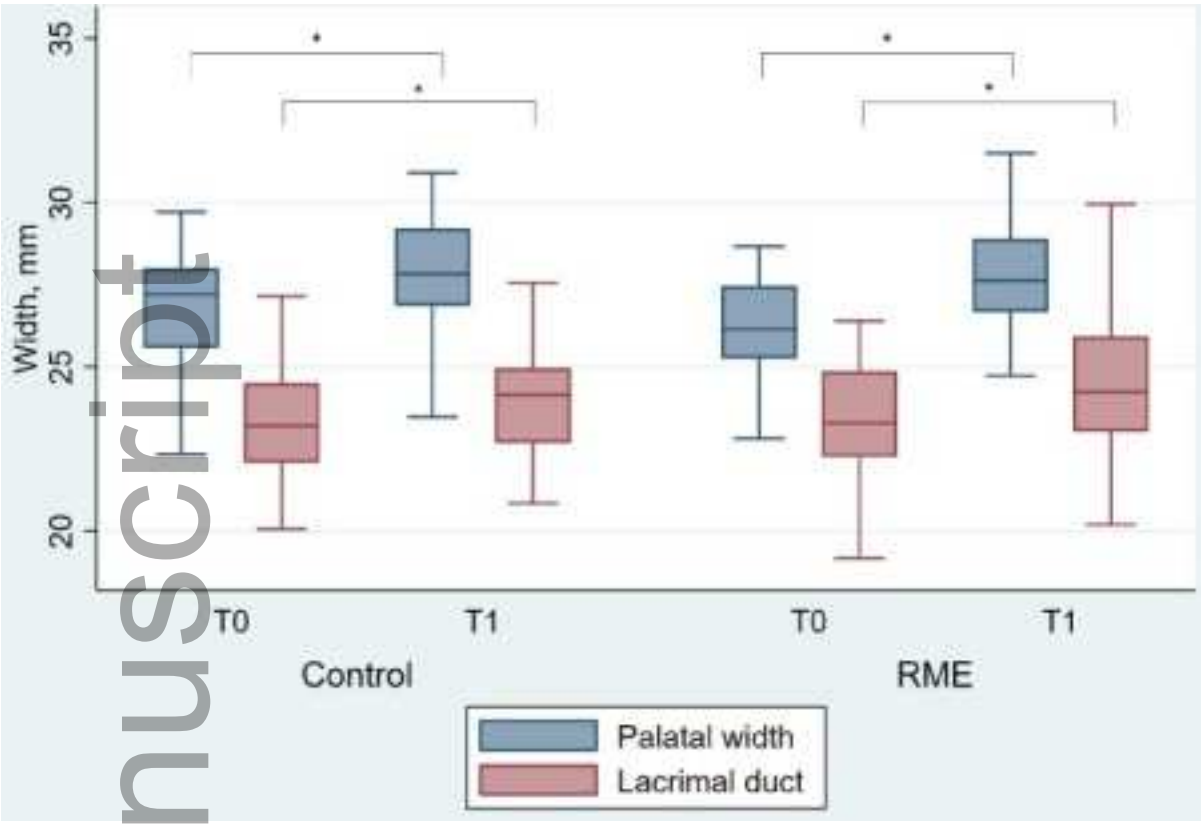

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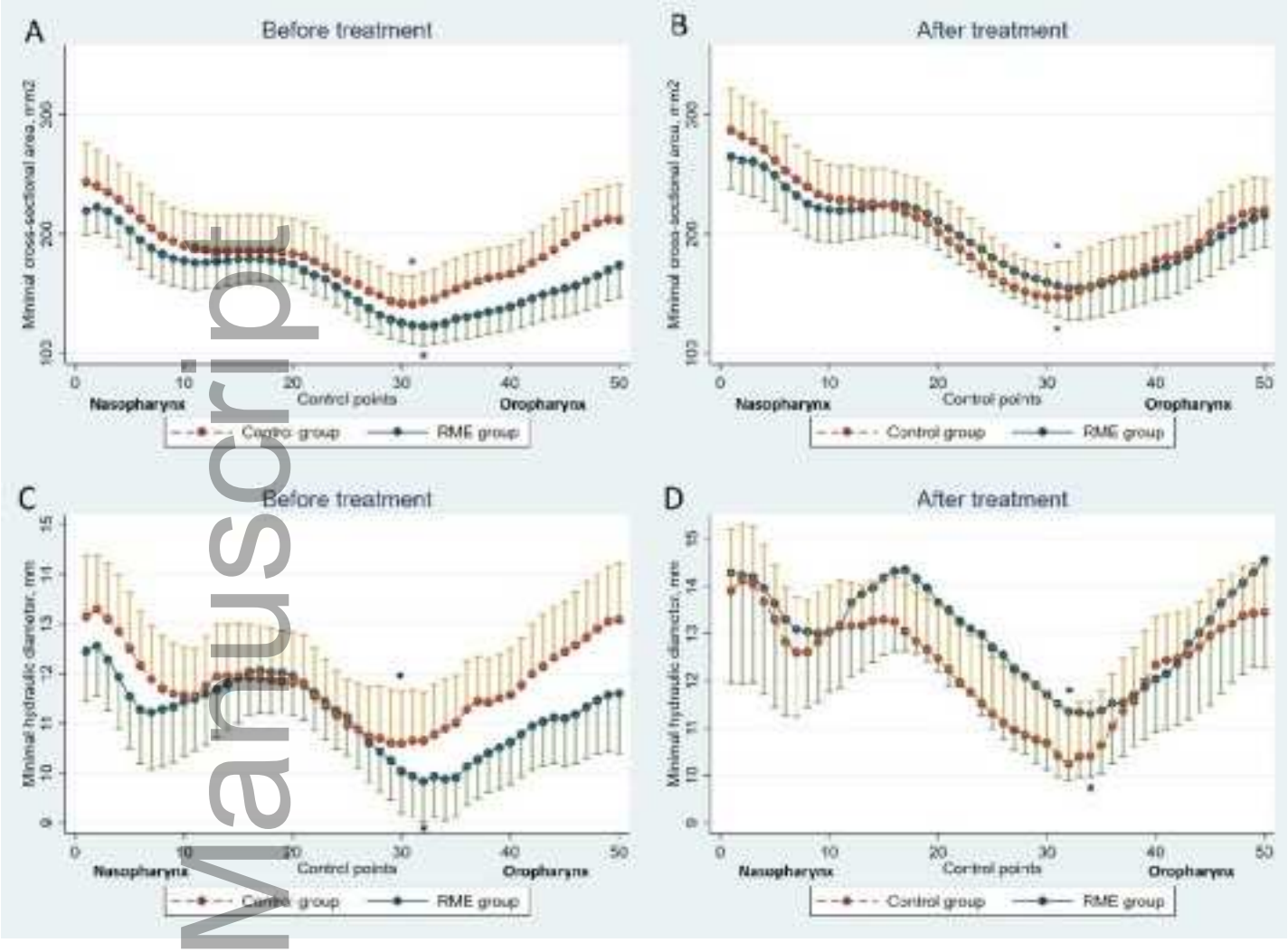

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