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# Three-dimensional volumetric changes in the airway of growing unilateral complete cleft lip and palate patients after bone-anchored maxillary protraction

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**Introduction:** This prospective controlled study evaluates volumetric, length, and average cross-sectional area (aCSA) airway changes in growing patients with unilateral complete cleft lip and palate after 1.5 years of bone-anchored maxillary protraction therapy. **Methods:** Thirty-five growing unilateral complete cleft lip and palate patients with maxillary deficiency were included (aged 11.3 ± 0.5 years). Cone-beam computed tomography scans were obtained before bone-anchored maxillary protraction (BAMP) therapy and after 1.5 years. A growing group without cleft (n = 18) patients served as a control group at 1.5 years posttreatment (aged 13.1 ± 1.2 years). Volumetric, length, and aCSA changes of the total airway, nasopharynx (NP), middle pharynx, and inferior pharynx airway were evaluated. **Results:** After 1.5 years of BAMP therapy, a significant increase was observed in the total airway volume and the NP ($P<0.01$). The middle and inferior pharynx showed an insignificant tendency of volumetric increase. Compared with the control group, a significantly larger airway volume could be observed in the total airway and NP ($P<0.05$). The aCSA of the NP increased significantly compared with pretreatment. **Conclusions:** The total airway and NP volumes significantly increased in growing subjects with cleft lip and palate after 1.5 years of BAMP therapy to a level comparable to a control group without cleft. Volumetric increase in the NP in the BAMP group is mainly attributed to the increase in its cross-sectional area. BAMP can therefore be recommended as an effective therapy for patients with cleft lip and palate with positive effects on airway development. (Am J Orthod Dentofacial Orthop 2022;■:■-■)

Bone-anchored maxillary protraction (BAMP) has been reported to treat Class III malocclusions with a hypoplastic maxilla in growing subjects with or without cleft. Treatment outcomes generally showed favorable results in skeletal, dental, and facial profile changes with significant orthopedic effect and esthetic improvement.[1-3] BAMP is recognized for its positive effect in the zygomaxillary region; however, studies in the literature remain scarce on the effect of this intervention outside the jaw regions such as the airway.

The airway in children with cleft can be significantly obstructed at several locations and levels in the airway because of skeletal deformities, scar formation from previous surgeries like the repair of the palate, and the intrinsic underdevelopment of the maxilla in subjects with cleft.[1-5] Incidence of obstructive sleep apnea (OSA) and sleep breathing disorder (SDB) in children with cleft varies from 22.0% to 37.5%,[4,6,7] much higher than the 2%-3% incidence of OSA or SDB in children without cleft.[8,9] All these findings were based on clinical diagnostics, such as questionnaires or polysomnography. Quantitative studies, including the airway

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All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and none were reported.
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Submitted, November 2020; revised and accepted, July 2021.
0889-5406/$36.00

https://doi.org/10.1016/j.ajodo.2021.07.021

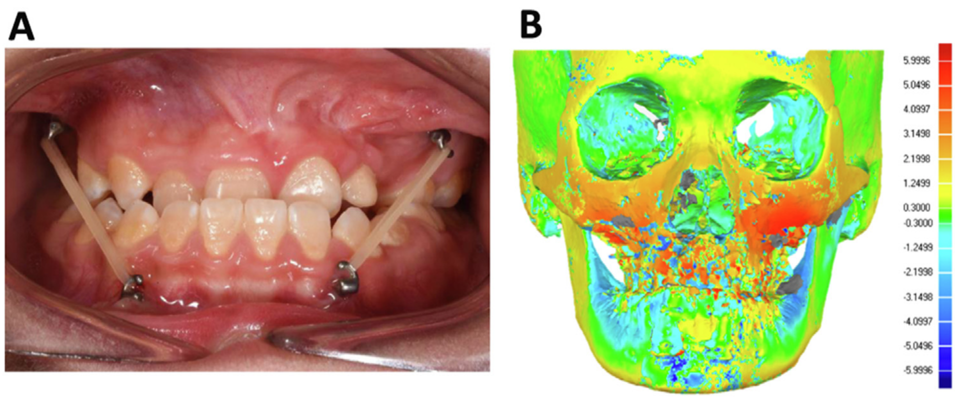


**Fig 1.** Clinical treatment of BAMP and expected skeletal effect: **A,** A clinical picture of maxillary protraction with elastics on bone anchors; **B,** A color mapping of CBCT models illustrating the skeletal effect of BAMP treatment on a patient. *Green*, no changes; *yellow* and *red*, outward movement; *blue*, inward movement.[2]

volumetric and cross-sectional area measurements that are important to understand the growth of the airway, are lacking.[10]

Since the introduction of cone-beam computed tomography (CBCT), several studies have been published on the 3-dimensional (3D) evaluation of airway changes after dentofacial orthopedic or orthognathic interventions. In growing subjects with maxillary deficiency treated with a facemask protraction, results are contradictory regarding the effect on the airway.[11-13] In adult patients with a maxillary deficiency treated with only LeFort 1 maxillary advancement, no observable changes were found in the nasopharynx (NP) or the oropharynx (OP)[14]; when a double jaw surgery was performed with mandibular setback and maxillary advancement, the upper airway volume increased, whereas the lower airway volume decreased, resulting in the total airway volume unchanged.[15,16]

Only 1 study reported airway changes after BAMP treatment for 1.2 years in a group of 28 subjects without cleft. The results showed a significant volumetric increase of the OP airway to the same level as the control subjects without a cleft at the same age, indicating that BAMP treatment could negatively affect the airway volume.[17] However, this study did not investigate the NP region, which, when its cross-sectional area decreased, could be an important reason for the development of OSA in patients with maxillary deficiency.[4] To date, no report has been published on volumetric airway changes in subjects with cleft treated with BAMP.

This prospective controlled trial aimed to evaluate volumetric airway changes at different anatomic levels of the airway derived from 3D CBCT in growing patients with cleft and maxillary deficiency after 1.5 years of treatment with BAMP (T1), compared with subjects at the same age without cleft or BAMP treatment.

Although a previous article reported results on skeletal 3D changes after BAMP using a small sample size (n = 18) (Fig 1, *B*), this paper is based on a prospective clinical trial and reports results on airway changes after BAMP (Fig 1, *B*).[2] This prospective clinical study was conducted in agreement with the rules established by the Ethics Committee at the University Medical Centre Groningen (Clinical Study Register no. 201700423; ethical approval no. METc 2017/318, The Netherlands National Trial Registration no. NTR6559 was registered on April 07, 2017). Informed consent was obtained from the parents or legal guardians of all the study subjects.

For the treatment group, a minimal number of 21 patients was required after a power analysis, with a medium effect size of 0.5 and a power of 0.80. All patients were treated by one orthodontist (Y.R.) at the Department of Orthodontics of the University Medical Center Groningen in the Netherlands. Various interdisciplinary treatments within the same medical center were performed. The treatment protocol has been published previously.[2] Briefly, it consisted of BAMP and mild dental alignment with fixed appliances or a removable biteplate. Four Bollard bone plates were placed by an experienced oral surgeon (J.J.) under local or general anesthesia, depending on the patient. Protraction was implemented with intermaxillary elastics with 150 g of initial force on each side, starting 3 weeks after placing the 4 bollard bone plates (Fig 1, *A*). The force was increased after 2-3 months up to 200-250 g of force. Elastics were deemed worn 24 h/d and must be changed at least once daily, transferring a forward and downward directed force on the maxilla.[2,18] In some patients, a removable biteplate in the maxilla or mandible was used, only for a short time. The inclusion criteria for the subjects were (1) previously secondary bone transplantation by the same surgeon (J.J.), (2) a skeletal Class III relationship with an ANB angle <0° or a negative Wits value in millimeters, (3) a sagittal overjet ranging from 2 mm and −5 mm, (4) both lower permanent canines have erupted, and (5) no presence of anterior forced bite or a vertical occlusal overclosure. All CBCT scans were indicated for clinical diagnostic reasons. Scans were made between May 2012 and December 2019.

A control group without cleft, with a full skull CBCT scan available at an age comparable with the subjects with cleft at T1, was included to compare the airway volumes of the treatment group after 1.5 years of BAMP. The CBCT scans of the control group were derived from the database of the orthodontic department at the University Medical Centre Groningen between 2015 and 2019. The same CBCT acquisition protocol was applied to the control group.

The inclusion criteria for the control subjects were (1) no cleft lip and palate or any other craniofacial anomaly, (2) a skeletal Class I or mild Class II relationship with an ANB angle ranging from 0° to 6°, and (3) no previous orthodontic treatment or only mild alignment with partially fixed appliance. For the control subjects, CBCT scans were made for diagnostic reasons (eg, impactions, dental development, agenesis, or supernumerary teeth).

All the CBCT scans are made by the same experienced x-ray technician (A.D.). A KaVo 3D eXam CBCT unit (KaVo Dental GmbH, Bismarckring, Germany) for scans before April 2016, and the Planmeca ProMax 3D Mid (Planmeca Oy, Helsinki, Finland) for scans after April 2016. The KaVo 3D used a 170 × 230-mm field of view, set at 120 kVp, and 42.5 mA with an isotropic voxel size of 0.3 mm. All the scans with the Planmeca ProMax 3D Mid (Planmeca Oy, Helsinki, Finland) had a field of view of 170 × 200 mm, 90 kVp, and 20.25 mA, and an isotopic voxel size of 0.3 mm. Patients were placed in a sitting position in the CBCT scanner with the Frankfort Horizontal (FH) plane parallel to the ground. To prevent a roll in the CBCT acquisition, the patients were placed with both pupils horizontal to the floor. Patients were asked not to move, swallow, or breathe normally. The dentition was in a maximal occlusion for all patients.

Based on 5 soft and hard tissue anatomic landmarks, 5 cross-sectional planes were defined to assess the airway.[18] In Table I, the definition and description of the borders and reference planes are provided. These 5 planes consisted of 2 frontal planes and 3 axial planes.

**Table I.** Definition and description of the borders and reference planes to define the airway

| *Borders* | *Description* |
|---|---|
| Most superior border | Sphenoid sinus (SS) plane: Axial plane parallel to FH, passing through the inferior part of the floor of the sphenoid sinus |
| Most inferior border | Epiglottis (E) plane: Axial plane parallel to FH, passing through the superior part of the epiglottis |
| Anterior border | Posterior nasal spine (PNS) frontal plane: frontal plane perpendicular to FH, passing through PNS |
| Posterior border | Second cervical vertebra-related pharyngeal airway (C2P) plane: Frontal plane perpendicular to FH, passing through the posterior part of the second cervical vertebra |
| Lateral border | Maxillary sinus (MS) plane: Sagittal plane perpendicular to FH, passing through the lateral surfaces of the maxillary sinus (left and right) |
| PNS plane | An axial plane parallel to FH, passing through PNS |
| U plane | An axial plane parallel to FH, passing through the inferior point of the uvula |
| PNS plane frontal | The frontal plane is perpendicular to FH, passing through PNS |

| | | *OP* | |
|---|---|---|---|
| *Borders* | *NP* | *MP* | *IP* |
| Superior | SS plane | PNS plane | U plane |
| Inferior | PNS plane | U plane | E plane |
| Anterior | PNS frontal plane | PNS frontal plane | PNS frontal plane |
| Posterior | C2P plane | C2P plane | C2P plane |
| Lateral | MS plane | MS plane | MS plane |

Note. All horizontal borders were based on a sagittal view. The superior border of the MP and inferior border of the IP were used for the OP.

The total airway is divided into 3 segments: NP, middle pharynx (MP), and inferior pharynx (IP). The MP and IP combined to form the OP. In Figure 2, the reference planes and the divided airway segments were provided 2-dimensional (2D) and 3D at a sagittal view.

All volumetric measurements of the airway were performed in Romexis (version 4.6.0.4; Planmeca). To standardize the 3D images, they were reoriented using the FH (FH) as the reference plane. The FH was constructed from the upper point of both porions of the external auditory meatus and the lower border of the orbital rim on the noncleft side. Because of CBCT acquisition, a roll or yaw in the surface model was present; the head orientation was adjusted.

The method used in the present study on volumetric measurements of the airway was adapted

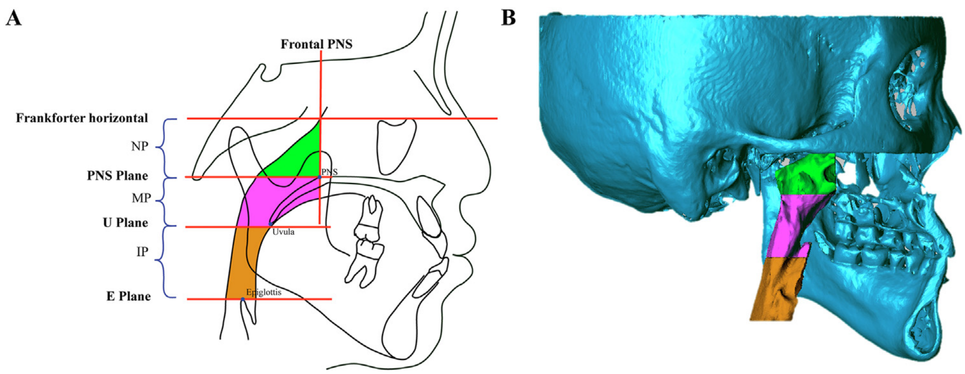


**Fig 2.** Airway segments and reference planes at a sagittal view: **A,** A 2-dimensional lateral view of the airway with the subdivided airway; **B,** A 3D reconstructed airway with the 3 segments with colors corresponding with the description in **A**. *Green*, NP; *purple*, MP; *orange*, IP. PNS, U, and E planes are parallel to the FH; the frontal PNS plane is perpendicular to the FH.

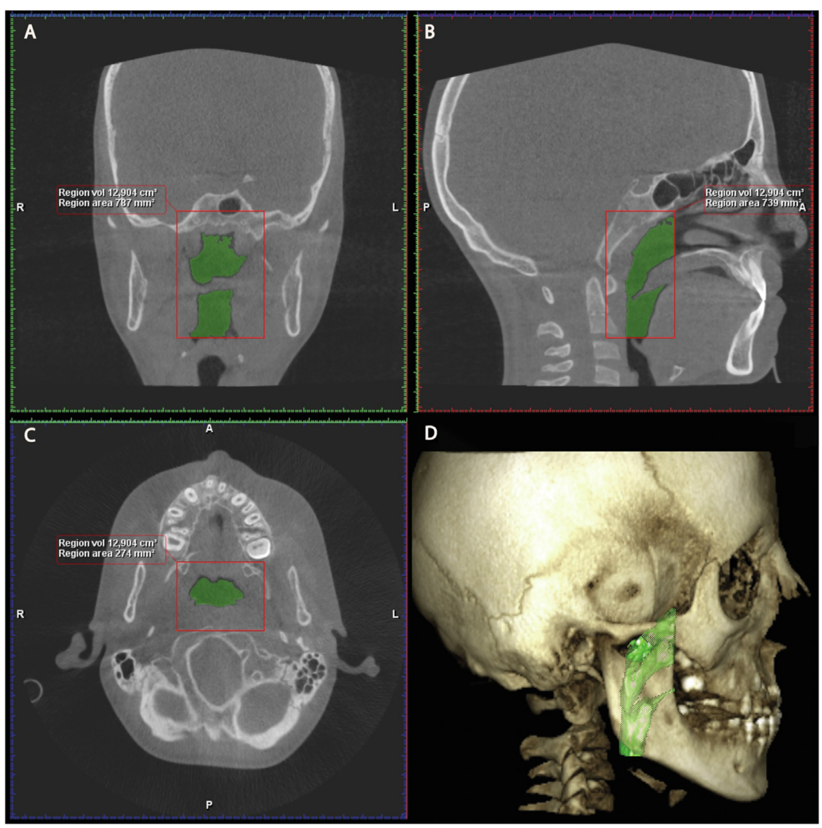


**Fig 3.** An example of airway measurements using the cube measure tool in Romexis: **A,** Coronal view; **B,** Sagittal view; **C,** Axial view; **D,** A 3D surface model. To standardize all the 3D images, they were firstly reoriented according to the FH. All images were of the same magnification.

from a previously reported method,[19] with the advantage that the created borders and planes are always parallel to the reference plane (the FH). This minimizes errors in creating a consistent anatomic border. Airway volumes were calculated using the "cube measure" tool (see an example in Fig 3). First, the upper border of the airway parallel to the FH was determined, then the lower border and both the anterior and posterior borders (Fig 3, *A*). All axial (Fig 3, *B*) and coronal (Fig 3, *C*) slices were reviewed to confirm that the anatomic airway space was always included in the cube. After setting the borders, the airway volume was calculated. By calculating the volume, the length of each airway component is also measured, defined as the line perpendicular to the FH between the respective upper and lower borders.[20] The volume is calculated on the basis of the gray scale values of the voxels, ranging from 1 to 1000 gray values. The preset parameter for the air cavity was used to calculate the selected airway segment. The built-in software calculated the volume and length on the basis of these preset parameters, which can be adjusted when necessary. After calculating a specific segment of the airway, the borders were removed, and the next volumetric calculation was performed. The volume-length ratio was determined by dividing the volume by the length of the respective airway segment to indicate the average cross-sectional area (aCSA) of the airway. Therefore, choke points were determined as the smallest cross-sectional area in a selected airway segment.[19] As an exception, the choke point in the NP airway was set at the PNS plane, which is anatomically reproducible and clinically relevant. This is related to the NP airway being in an irregular triangle shape, with the narrowest point almost always at the top of the NP.

All volumetric, length, and choke point calculations were performed by 2 investigators (R.S. and A.S.) twice with at least 1 week in between with a maximum of 15 assessments per day to avoid any potential effect of fatigue. For 20 treated patients, all measurements were done twice by both investigators for an interobserver and intraobserver correlation.

### Statistical analysis

All the statistical analyses were performed with SPSS (version 23.0; IBM Corp, Armonk, NY) by one author (R.S.). First, all data for the volumes, lengths, and surface areas at pretreatment (T0) were tested for normal distribution with a Kolmogorov-Smirnov test for all the BAMP groups; the same applies to the control group at T1. For the changes in the treatment group between T0 and T1, a paired sample *t* test was used, with a Bonferroni correction of the *P* value. To compare the treatment groups with the control group, a 1-way analysis of variance test was used with a post-hoc Bonferroni correction. The level of significance of all tests was set for an uncorrected *P* value of $<0.05$. For the intraclass correlation, a Cronbach $\alpha$ test was used ($>0.81$), indicating an almost perfect agreement.

**Table II.** Characteristics of the treatment group (T0 and T1) and control group (T1)

| *Charactersistics* | *BAMP T0* | *BAMP T1* | *Control group T1* |
|---|---|---|---|
| Total (n) | 35 | 35 | 18 |
| Mean age (y) | 11.3 ± 0.5 | 12.8 ± 0.6 | 13.1 ± 1.2 |
| Male:female (n:n) | 23:13 | 23:13 | 9:9 |
| SNA angle (°) | 76.6 ± 5.5 | 77.2 ± 4.4 | 82.1 ± 4.0*,# |
| SNB angle (°) | 76.6 ± 5.0 | 77.2 ± 4.4 | 77.7 ± 3.7 |
| ANB angle (°) | −0.1 ± 4.6 | 0.2 ± 3.6 | 4.0 ± 1.6*,# |
| Wits (mm) | −2.0 ± 4.1 | −0.8 ± 4.0 | 1.8 ± 1.5*,# |
| ANS-PNS/GoGn (°) | 23.5 ± 6.5 | 24.2 ± 5.6 | 24.9 ± 4.7 |
| Sn/GoGn (°) | 35.8 ± 6.0 | 35.6 ± 5.2 | 30.4 ± 6.8*,# |
| U1 to ANS/PNS (°) | 107.1 ± 11.6 | 110.9 ± 7.6 | 105.5 ± 8.5 |
| L1 to GoGn (°) | 89.9 ± 7.7 | 88.6 ± 6.1 | 97.0 ± 6.5*,# |
| Interincisal angle (°) | 136.9 ± 11.8 | 135.4 ± 8.6 | 131.2 ± 10.9 |
| Overjet (mm) | −1.8 ± 3.0 | 0.1 ± 3.0* | 3.4 ± 1.2*,# |
| Overbite (mm) | 1.1 ± 2.2 | 1.1 ± 1.9 | 2.7 ± 2.1*,# |

*Significant difference compared with BAMP T1 group; #Significant difference compared with the control group.

**Table III.** Volumes of the treatment group (T0 and T1) and control group (T1)

| *Variables* | *BAMP T0* | *BAMP T1** | *Control T1#* |
|---|---|---|---|
| Total airway (mm³) | 13036 ± 4102* | 14499 ± 4032# | 11701 ± 2807 |
| OP (mm³) | 9140 ± 3225 | 10072 ± 3021 | 9030 ± 2592 |
| NP (mm³) | 3911 ± 1515* | 4538 ± 1850# | 3000 ± 1365 |
| MP (mm³) | 4899 ± 1654 | 5449 ± 1559 | 5604 ± 2094 |
| IP (mm³) | 4078 ± 1782 | 4369 ± 1718 | 3692 ± 1223 |

*Significant difference compared with BAMP T1 group; #Significant difference compared with the control group.

## RESULTS

Thirty-eight patients were recruited for the study. During the data analysis phase, 3 patients were excluded; 2 patients because of uncorrectable software error during CBCT acquisition (insufficient volume stitching) and 1 patient because of bone plate removal after infection. A total of 35 (23 males, 12 females) participants were finally included, with a mean age of 11.3 ± 0.5 years at T0 and 12.8 ± 0.6 years at T1. The total control group consisted of 18 patients (9 males, 9 females; mean age, 13.1 ±1.2 years). Sample and cephalometric characteristics of the treatment and control subjects are presented in Table II. No significant difference was detected between the 2 groups in age. As expected, the control group showed typical cephalometric features of skeletal Class I or mild Class II relationship.

All volumes and lengths at T0 were normally distributed. The same applies to the airway length, which was also normally distributed.

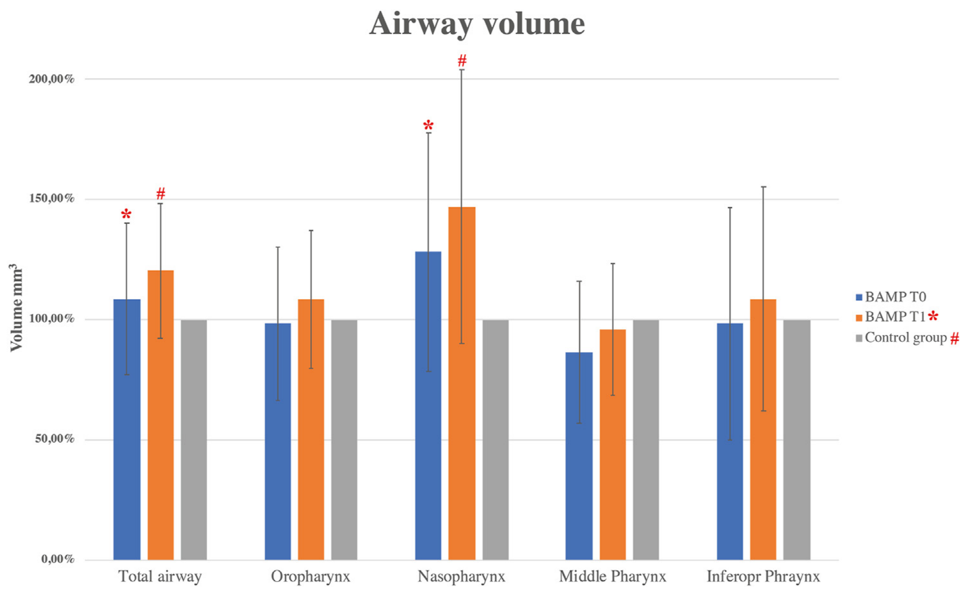


**Fig 4.** Bar graph of the volumes of different airway subdivisions. *Indicates a significant difference compared with the BAMP T1 group; #Indicates a significant difference compared with the control group. The average volumetric measurements of the control group were set as 100% for each airway subdivision. Volumetric measurements of the individual subjects in the BAMP group were calculated as the percentage ratio in relation to the control average.

The volumes of all groups are presented in Table III. Figure 4 presents a bar graph of the percentage ratio between the groups for visualization. Large individual variations were observed in the volumetric measurements of the airway. During the observation period, total airway and NP volumes changed significantly after 1.5 years of BAMP ($P$ = 0.007 and $P$ = 0.001). On average, the total airway volume increased by 1463 $\pm$ 3020 mm$^3$ (ie, approximately 11%). The NP airway increased by 626 $\pm$ 1020 mm$^3$, responsible for approximately half of the total airway volume increase. The MP and IP volumes showed a nonsignificant increase.

Compared with the control group, the BAMP treatment group showed significantly larger total airway and NP volumes at T1 ($P$ = 0.042 and $P$ = 0.005).

Similar to volume, large individual variations were also observed in the measurements of the length of the airway and the aCSA. Table IV presents all lengths, volume-length ratio, and aCSA.

The length of the total airway increased significantly to 2.8 $\pm$ 3.7 mm, after 1.5 years of BAMP ($P$ <0.01). The length of the NP, MP, and IP showed a nonsignificant increase. Compared with the control group, a significant difference in the IP was observed at both T0 and T1 ($P$ <0.05 and $P$ = 0.001). In all the other subdivisions of the airway, no difference in length could be found in comparison with the controls.

The aCSA of the total airway increased slightly to 14.5 $\pm$ 45.6 mm$^2$. At T1 BAMP, only the aCSA of the NP increased significantly with 25.2 $\pm$ 47.7 mm$^2$ ($P$ <0.01). For all other airway subdivisions, the aCSA remained unchanged. The aCSA of the NP was significantly larger in the BAMP group at T1 compared with the control group ($P$ <0.01). All other subdivisions of the BAMP group at T1 were not significantly different. The same applied to the T0 measurement in all divisions.

Regarding the choke point measurements, no significant change could be detected during the observation period in either BAMP or control group or between the BAMP and the control groups.

## DISCUSSION

Although 3D evaluation of dental and skeletal effects of dentofacial orthopedic treatment modalities on the airway has been previously reported, to our knowledge, this study is the first investigation of the volumetric changes on the airway in subjects with cleft lip and palate after 1.5 years of BAMP therapy.

Only 1 previous study evaluated the airway changes after BAMP therapy in growing patients without cleft,[17] with similar treatment duration and study subjects (ie, on average, 6 months older than our study). Regarding the airway measurements, the upper border in the noncleft

**Table IV.** Length and cross-sectional areas of the airway between T0 and T1

| *Variables* | *T0* | *T1* | *T1-T0* | *Control* |
|---|---|---|---|---|
| Length, mm | | | | |
| NP | 18.7 ± 3.1 | 19.2 ± 3.6 | 0.5 ± 2.6 | 18.9 ± 3.4 |
| OP | | | | |
| MP | 21.8 ± 4.0# | 22.7 ± 4.7 | 1.0 ± 2.8 | 25.0 ± 4.6 |
| IP | 24.5 ± 5.1* | 25.6 ± 4.7# | 1.1 ± 3.9 | 20.6 ± 3.4 |
| Total airway | 64.0 ± 6.4** | 66.8 ± 6.4 | 2.8 ± 3.7 | 64.4 ± 7.8 |
| aCSA, mm$^2$ | | | | |
| NP | 211.1 ± 81.1* | 236.3 ± 86.6# | 163.1 ± 76.9 | 25.2 ± 47.7 |
| OP | | | | |
| MP | 227.9 ± 79.4 | 244.8 ± 76.3 | 220.8 ± 72.2 | 17.0 ± 62.2 |
| IP | 172.6 ± 69.1 | 181.7 ± 79.1 | 180.5 ± 57.5 | 9.1 ± 65.2 |
| Total airway | 203.1 ± 58.5 | 217.5 ± 58.0 | 183.2 ± 44.9 | 14.5 ± 45.6 |
| Choke point, mm$^2$ | | | | |
| NP | 371.9 ± 187.4 | 396.4 ± 212.6 | 24.6 ± 85.3 | 288.5 ± 89.6 |
| OP | | | | |
| MP | 172.2 ± 96.0 | 174.6 ± 121.1 | 2.4 ± 87.4 | 152.5 ± 61.6 |
| IP | 150.4 ± 77.5 | 161.4 ± 95.2 | 11.1 ± 80.5 | 153.4 ± 50.6 |
| Total airway | – | – | – | – |

*Significant difference compared with BAMP T1 group; #Significant difference compared with the control group.

study was set from the most posterior point of the bony PNS to basion, and the inferior border at the base of the epiglottis to the inferior edge of the C3, compared with the tip of the epiglottis that we used. These differences make direct comparison difficult. Nevertheless, with the known, intrinsically underdeveloped maxilla and higher incidence of airway obstruction in subjects with cleft,[4,5] it is not surprising to observe a smaller volumetric change of OP airway in patients with cleft than in the subjects without cleft after the same treatment and duration.

Other treatment modalities for maxillary deficiency (eg, rapid maxillary expansion) in combination with a protraction facemask showed an average volume increase of 3001 ± 4128 mm$^3$ of the airway in 18 growing subjects with cleft, in comparison with an increase of 1463 ± 3020 mm$^3$ in 35 subjects with cleft in this study. However, the patients treated with a protraction facemask were 1 year younger with a more severe skeletal anomaly, and the treatment duration showed a large variation from 8 to 26 months. Unfortunately, the most significant increase we observed in the NP was not evaluated in the study with facemask treatment.[11] Using the same anatomic borders to define the airway, another study in patients aged 10 years without cleft treated with facemask and rapid maxillary expansion reported a significant volume increase of the NP, MP, and IP after 7 months of treatment. Notably, the volume of the NP increased to an average of 4387 mm$^3$, comparable to the average volume of 4538 mm$^3$ in our group with cleft. The same conclusion was found in that study that a significant difference existed in the NP airway volumes between the treated and untreated groups, in favor of the treated group.[21]

Regarding the effect of the orthognathic intervention, Almuzian et al[14] observed an increase of the upper NP of 671 mm$^3$ after LeFort I maxillary advancement, comparable to an increase of 626 mm$^3$ in this study. Though previous reports demonstrated that BAMP therapy moves the maxilla in similar directions as LeFort I surgery does,[1-3] this is the first time a similar effect on the volume of the upper NP airway was demonstrated from these 2 treatment modalities, indicating a potential advantage of BAMP treatment at a young age over an orthognathic surgery in adulthood.

Contradictions exist in the current literature on the nomenclature of the airway, in which different anatomic landmarks were used for hard- and soft tissue planes to define various parts of the airway. In addition, the nomenclature used was inconsistent with different parts of the airway given the same name or the same parts of the airway given different names. Therefore, direct comparison without looking carefully at the definition of the airway components can be misleading. Importantly, the airway borders used in the present study were based on 5 easy-to-determine, reproducible anatomic landmarks in the midsagittal plane, an advantage over other studies which used many more anatomic landmarks or less reproducible ones.

Furthermore, in many studies, especially those on orthognathic patients, airway measurements were performed on patients in a supine position.[22] In CBCT head and body position of the subject have a significant effect on the volume and dimensions of the airway, as the airway consists of soft tissues surrounded by hard tissues.[23] A supine position alters the tongue and hyoid position, narrowing the airway space compared with when the subject is in an upright position. In addition, tongue movement and position could influence the airway volume to a certain extent. By placing the patient in the natural head position and by asking them to breathe normally, minimal effects of these factors could be expected in the present study.

Previous studies on airway changes after maxillary protraction were often conducted on 2D cephalometric radiographs, which have severe limitations in measuring the airway (ie, only changes at the sagittal and vertical dimensions could be observed). Therefore, not surprisingly, the outcomes of these studies were controversial. For example, Hiyama et al[24] and Kaygisiz et al[25] found a positive effect on the airway, whereas Baccetti et al[26] did not find any significant changes in the nasopharyngeal or oropharyngeal airway. Studies comparing 2D measurements direct from cephalometric and those reconstructed from CBCT demonstrated no correlation in the upper airway dimensions and insufficient correlation between anterioposterior distances and the corresponding cross-sectional areas in the same airway segment.[27,28] This is also supported by Abé-Nickler et al,[28] who showed that determination of the airway volume on a lateral cephalogram is inaccurate because of the great anatomic variability in the airway. This means comparing 2D reconstructions from our CBCT models with measurements from lateral cephalograms from historical archives is unreliable. We did not include an untreated control group using cephalograms from historical growth studies. In Figure 5, great variations of the airway in different subjects are illustrated from an axial or coronal view.

A highly clinically relevant part of the airway is the most constricted point, the so-called choke point, which determines the maximum airflow. The choke point in the BAMP group was mostly in the IP and increased during the observation period. The location of the choke point remained in the IP at T1. In addition, as all choke point measurements were made parallel to the FH, they did not necessarily represent the actual, most constricted point in the airway. Alternatively, choke points could be measured perpendicular to the airway axis, a disadvantage in that the airway axis changes during the observation period.

It has to be acknowledged that the positive effect observed in the nasopharyngeal airway should not be attributed solely to BAMP therapy in these growing patients. The human airway increases in length and volume between 8- and 18-years-old, which may continue to increase at various levels until 40-years-old.[29,30] As indicated by our results, there is a great individual variation, possibly related to the individual variations in the development at puberty.

A control group matched by age, gender, the severity of the skeletal and dental deformity, and CBCT scans available at both T0 and T1 would be ideal to evaluate the effect of BAMP therapy and normal growth. However, this is ethically impossible. In this study, the CBCT scans were obtained for diagnostic and treatment purposes only. The same ethical principles object to making CBCT scans in control subjects without cleft (see guidelines for the use of CBCT by Royal Dutch Dental Association). As an alternative, a control group matched by age at T1 was included. Previous studies have shown that including a control group matched at T1 is a reliable and clinically relevant alternative to indicate the magnitude of normal growth.[31-34] Nevertheless, considering large individual variations in the airway measurements, results from the control group need to be interpreted carefully. The volume of the NP is mostly compromised because of a hypoplastic maxilla, in which the OP is more affected by a hypoplastic mandible because of retrognathia.[35,36] Our results on the skeletal effect of BAMP treatment at T1 in children with cleft showed that the maxilla was displaced significantly forward and downward, and zygoma arch areas were displaced significantly forward and outward.[2] This indicates that although the maxilla in children with cleft remained hypoplastic compared with the control subjects, the more forward and outward position of the maxilla and zygoma complex may have contributed to the increased airway volume. In general, the positive effect of BAMP treatment in the zygomaticomaxillary complex in both sagittal and transversal dimensions corresponds to the significant increase of volume and aCSA in the NP airway; similarly, the minimal changes in airway length of the NP appear to be in line with the minimal downward movement of the zygomaticomaxillary complex after 1.5 years of BAMP treatment.

## CONCLUSIONS

This study demonstrated for the first time a significant volumetric increase of the total airway and NP airway volumes after 1.5 years of BAMP therapy in growing subjects with cleft to a level comparable to a control group without cleft with a skeletal Class I or mild Class II relationship. In the NP, the change in the airway volume in the BAMP group is mainly attributed to the increase in its cross-sectional area, which is of important clinical relevance. Considering the effect of normal growth in the airway, BAMP can be recommended as an effective orthopedic therapy for patients with cleft lip and palate with a positive impact on the airway volume. More research is needed on BAMP therapy on airway development in the long term and on validation of a unanimous definition of anatomic landmarks and boundaries of the airway.

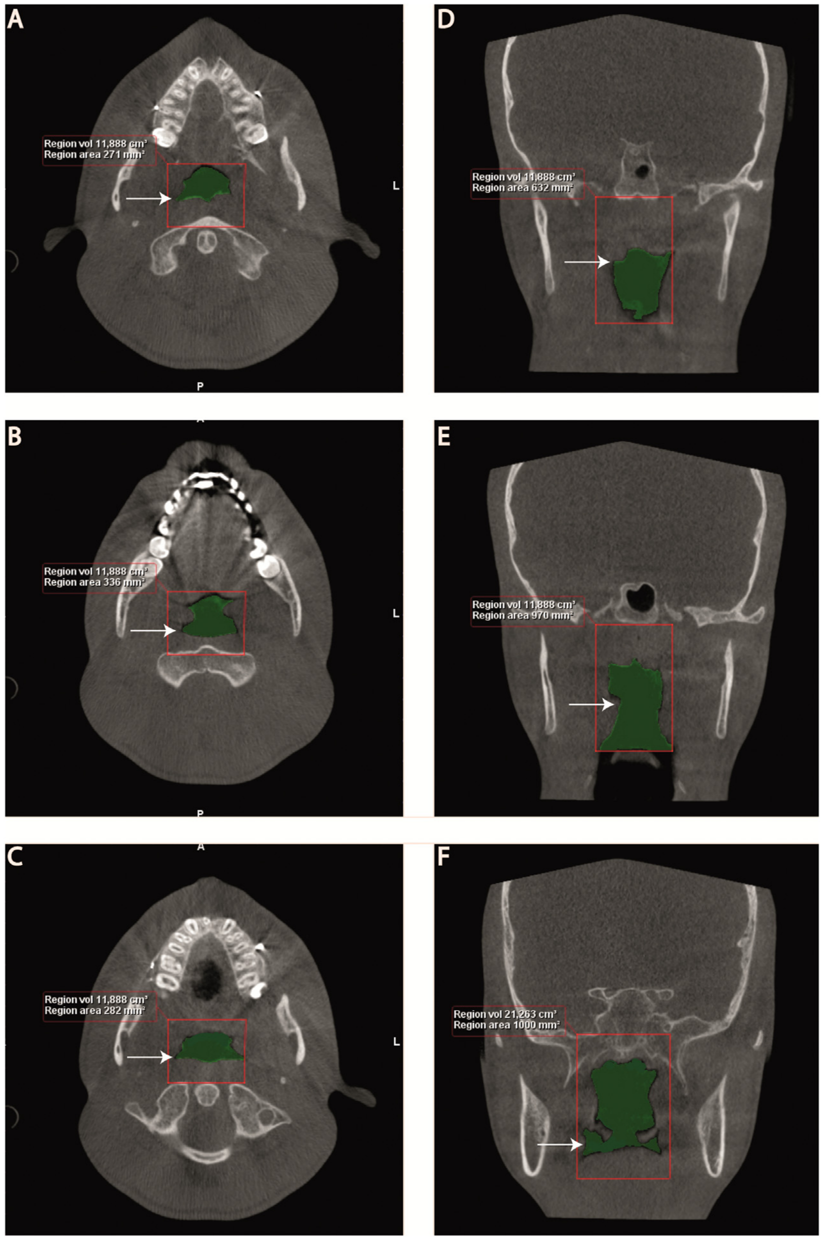


**Fig 5. A-C,** Axial slides of the airway. **D-F,** Coronal slides of the airway. The arrow indicates the great variety in transverse and sagittal dimensions.

## AUTHOR CREDIT STATEMENT

Ralph Steegman contributed to conceptualization, methodology, validation, formal analysis, investigation, data curation, original draft manuscript, visualization, and project administration; Adriaan Schoeman contributed to conceptualization, methodology, validation, investigation, data curation, and original draft manuscript; Arjan Dieters contributed to methodology, validation, investigation, manuscript review and editing, and visulization; Bert Jongsma contributed to formal analysis, resources, manuscript review and editing, and supervision; Johan Jansma contributed to investigation, resources, and manuscript review and editing; Joerd van der Meer contributed to conceptualization, methodology, validation, manuscript review and editing, and supervision; Yijin Ren contributed to conceptualization, methodology, formal analysis, investigation, data curation, original draft preparation, manuscript review and editing, and supervision.

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