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Craniofacial shape in children with and without a positive otitis media history

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Abstract

Objectives—Past studies using traditional morphometric approaches have reported a handful of differences in craniofacial dimensions between individuals with and without otitis media (OM). In this study, a geometric morphometry (GM) approach was used to determine if craniofacial shape is different among children with no history of OM and a history of recurrent acute OM (RAOM) at two different ages.

Methods—Nineteen standard landmarks were identified on lateral cephalometric radiographs from 79 children (41 Control, 38 RAOM) at 4 years and 52 children (27 Control, 25 RAOM) at 6 years of age. Following Procrustes superimposition of the landmark coordinate data, comparisons of group differences in overall size and shape were performed. Discriminant function analysis and principal component analysis were used to determine which, if any, aspects of shape variation distinguished RAOM from Control groups.

Results—At 4 years of age, craniofacial size and shape were significantly different between RAOM and Control groups ($p < 0.05$). Shape differences were evident in the relative positions of the mandible, cranial base, external acoustic meatus, sphenoid and palate. Those shape differences were not found in the 6-year old group.

Conclusions—At 4 years of age, the RAOM and Control groups have distinct craniofacial morphologies, but by 6 years of age these differences have largely disappeared. This is consistent with the clinical observation that excess RAOM risk resolves around 6 years of age and the hypothesis that this resolution is partially a result of age-related craniofacial changes.

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Keywords

Craniofacial shape; Geometric morphometrics; Otitis media; Children

1. Introduction

Otitis media (OM), an inflammation of the middle ear (ME) mucosa, is most prevalent in the pediatric population but also occurs in adolescents and adults [1]. Usually, OM onset is closely associated with the signs and symptoms of a viral upper respiratory infection [2]. Localized symptoms and signs of ME mucosal infection may signal extant OM, called acute OM (AOM), or may not, called OM with effusion (OME). While most OM episodes are self-limited, the mucosal inflammation can persist from months to years in a subset of affected children, a form of the disease called chronic OME (COME). In addition, some children experience frequent AOM recurrences (RAOM). COME and RAOM are difficult to manage conditions accompanied by complications such as hearing losses and balance disturbances that contribute to childhood morbidity [1].

There is an extensive literature describing the characteristic traits, behaviors, environments and conditions that may increase a child's risk for RAOM or COME. For example, past studies reported a high heritability for both COME and RAOM [3,4], and the risks for those expressions are increased by behaviors and environments that promote upper-respiratory virus infections [5], comorbidities such as nasal allergy, frequent colds, and gastro-esophageal reflux disease [2,6–9], and craniofacial dysmorphologies such as cleft palate [10,11]. Regarding the latter category of risk modifiers, more subtle craniofacial variants reflected in “head shape” [12–16], cranial base width, length and flexion angle [16–20], facial proportions [15–18], maxillary-mandibular interactions [21–26], and nasopharyngeal volume [27–31] have been reported to characterize children and adults with RAOM or COME.

Common to all of these morphological OM risk modifiers is their potential to disturb the functional anatomy and geometry of the Eustachian tube (ET) system resulting in ET dysfunction (ETD) [19,32,33]. The ET, a usually closed biological tube extending along the cranial base between the middle ear and nasopharynx, actively opens during swallowing and yawning to equalize middle ear and ambient pressures [34]. Clinical studies and animal experiments convincingly show that an inefficient ET opening mechanism, i.e. ETD, plays a causal role in the pathogenesis of OM, its persistence as COME and its recurrence as RAOM [35–39].

At present, a causal relationship between craniofacial morphology and excess OM risk remains hypothetical. Most past studies examining that relationship were designed as general surveys of a large number of constructed linear and angular craniofacial measures with “risk factors” that discriminate between control and disease groups identified using pairwise tests. The drawbacks of this methodology are the inability to separate size from shape and its susceptibility to false identifications of significant measures due to the multiple comparisons problem. In addition, the panel of craniofacial dimensions examined is not consistent across studies and only a few studies provided sufficient information to

characterize the OM phenotypes (no OM, COME, RAOM, chronic suppurative OM) being compared, though the risk modifiers are expected to be phenotype specific. Consequently, the identified panel of (candidate) morphological risk modifiers is extremely broad with few replicated members across studies. Often, as for example with cranial shape, identified associations with OM are not reproduced across studies even when the specific morphology is well characterized (e.g. the cephalic index) [13].

The current study was designed to explore the validity of the structure-function hypothesis using methods that avoid many of the methodological criticisms listed above. Specifically, the formal mathematical techniques of geometric morphometry [40,41] (GM) were used to reconstruct and mathematically describe complex representations of craniofacial shape based on a set of standard landmarks identified on lateral cephalometric X-rays. The landmarks chosen capture previously identified regions that discriminate between affected and unaffected children. Our basic hypotheses are: (1) craniofacial shape is different in children with a well-documented history of RAOM when compared with unaffected Controls, and (2) these shape differences involve components of the cranial base and palate. The comparison was performed at two age points (4 and 6 years) in order to test the additional hypothesis that these shape differences will decrease with advancing age so as to correspond with the clinically observed reduction in RAOM risk around 6 years of age [42].

2. Methods

The materials analyzed in this report derive from an ongoing, NIH-funded, longitudinal study designed to characterize the changes in craniofacial anatomy, ET function (ETF) and OM prevalence in young children enrolled at 3 years of age and followed through 8 years of age. Study participants were recruited from the general Pittsburgh area by targeted advertisement. As part of this study, data on craniofacial morphology (via anthropometry, dental casts, cephalometric X-rays and MRI scans) are collected at standardized time intervals. Further, detailed data are routinely collected on ETF, middle ear status (otomicroscopy, tympanometry) and episodes of OM, RAOM and COME. Upon entry to the study, the enrolled children are assigned to 1 of 3 groups (Control, COME or RAOM) based on a history provided by the parent and review of personal physician and, when available, hospital records. The criteria for Control included no significant history of OM (no COME or RAOM episodes) and no history of receiving tympanostomy tubes. Children were classified as RAOM if they had 3 or more episodes of AOM in one year or 5 or more episodes of ME effusion, at least 2 AOM, by study entry or tympanostomy tubes inserted for RAOM during the year prior to study enrollment with or without intervening episodes of OME. Children were classified as COME if they did not have RAOM, but had 3 or more consecutive months of middle ear effusion bilaterally, 6 consecutive months of effusion if unilateral or 3 or more episodes of OME lasting for at least 2 months with at least one episode of OME or tympanostomy tubes insertion in the year prior to entry [13]. Children were excluded from study participation if presenting with cleft palate, other craniofacial anomalies, syndromes predisposing to OM, or orthodontic treatment, cholesteatoma or ear surgery other than tympanostomy tube insertion. The study was approved by the University of Pittsburgh Institutional Review Board (IRB).

The present study compared the Control and RAOM groups; the COME group and other subgroup sample sizes were too small to be included in the comparison. At 4 years of age, data for a total of 41 Control and 38 RAOM children were available. At 6 years, the currently available sample is 27 Control and 25 RAOM children. The sample demographics are presented in Table 1. There were no significant differences between the Control and RAOM group in terms of the age, sex or racial distribution ($p > 0.05$). Lateral cephalometric images were recorded using standard clinical procedures from the enrolled children in the two groups at ages 4 and 6 years. Using the tpsDig2 program [43], 19 standard cephalometric landmarks (Table 2), were identified on each image (Fig. 1) by the first author and those identifications were repeated after at least 2-weeks. The first author was blinded to the child's group assignment during both landmarking sessions. There were no significant differences in landmark coordinates between the two sessions (intra-class correlation coefficient > 0.99 for each landmark). The X and Y coordinates for two measures of each landmark on all images were averaged and imported into the program MorphoJ v1.05f for GM analysis [40,44,45].

Shape comparisons were done separately for each age group (4 and 6 year). The first step in the analysis was a Procrustes superimposition of the raw landmark coordinates to center, rotate and scale the landmark configurations [46]. This iterative process allows multiple homologous shapes (e.g. from different individuals) to be aligned within a standardized coordinate system, resulting in a new set of transformed coordinates representing only shape (also known as Procrustes shape coordinates). Because group differences in size (allometry) can also affect shape, it is usually beneficial to remove the portion of the variance in shape accounted for by size prior to group comparisons of shape. Regression of Procrustes shape coordinates on centroid size, a measure of size independent of shape and defined as the square root of the sum of squared distances of a set of landmarks from their centroid, was used to accomplish this. Centroid size was compared between RAOM and Control groups using ANOVA. The regression residuals (allometry-free shape coordinates) were tested for differences in mean shape between groups [47] by computing the Procrustes distance (the square root of the sum of squared differences between corresponding landmarks in two superimposed configurations) and then calculating a permutation-based p -value (1000 resampling runs) to determine statistical significance.

Two different multivariate data reduction methods summarized the relevant shape variation in the datasets. Discriminant function analysis (DFA) yields a weighted equation (a discriminant function) optimized to maximize separation between the a priori identified groups (Control and RAOM). The ability of the discriminant function to separate Control from RAOM group was evaluated using a Hotelling's T^2 test (p -value determined by permutation with 1000 resamples). The second analytical technique, principal component analysis (PCA), in contrast, does not assume any group structure. PCA is used routinely in GM analyses to define the major modes of shape variation in a dataset. Extracted principal components (PCs) are defined such that the first component describes that greatest amount of shape variation, with each subsequent component describing smaller amounts, until 100% of the shape variance is accounted for. Each subject received a score for each extracted PC and these scores were used in the further analyses. To identify PCs capable of separating the Control from RAOM group, we compared the mean score for the two groups on each PC

using an ANOVA (for PCs covering 90% of the shape variation). Because the geometric information encoded in the landmarks is retained during all stages of the analysis, intuitive and meaningful visualizations can be used to show the shape variation associated with a particular discriminant function or principal component. Here we use simple wireframe deformations to show relevant aspects of shape variation.

3. Results

3.1. Four year old cases and controls

Centroid size, a measure of overall size, for RAOM cases was significantly larger than for Controls ($F(1,79) = 25.73, p < 0.001$). As expected, regression analysis showed that centroid size and shape were not significantly related ($p = 0.388$), with centroid size explaining only 1.29% of the shape variation. In terms of overall shape, there was a statistically significant difference in the Procrustes distance between the RAOM and Control groups ($p = 0.026$), indicating distinct mean shapes for the two groups.

The discriminant function was statistically significant ($T^2 = 99.75; p = 0.035$), indicating that it was capable of separating the groups based on shape. The shape variation associated with the discriminant function is shown using wireframe models in Fig. 2. Compared with Controls, the RAOM group exhibited an inferiorly displaced palate and pterygoid region, clockwise rotation of the mandible, posterior displacement of the cranial base, and increased anterior and posterior facial heights.

The PCA yielded 34 components, of which PC1 to PC17 explained 90.38% of the shape variation. After correcting for multiple comparisons ($0.05/17 = 0.003$), there was a statistically significant difference in mean score between the RAOM and Control group for PC4 (7.51% of the variation) ($F(1,79) = 9.33, p = 0.003$); mean scores on the remaining PCs failed to show any significant differences. The shape variation associated with PC4 was similar to that seen in the DFA wireframe in the cranial base and palate, but the mandible body was rotated superiorly resulting in a more acute gonial angle (Fig. 3).

3.2. Six year old cases and controls

There was no significant difference in centroid size between RAOM cases and controls ($F(1,48) = 1.45, p = 0.234$). Regression analysis revealed that the relationship between centroid size and shape was not significant ($p = 0.054$) with centroid size explaining only 3.75% of the shape variation. The Procrustes distance between the RAOM and control groups was not significantly different ($p = 0.088$), indicating equivalence between the groups in terms of craniofacial shape. Furthermore, the discriminant function was not able to distinguish between the two groups on shape ($T^2 = 131.28; p = 0.327$). In the PCA, the first 14 PCs explained 90.00% of the variation and none separated the study groups.

4. Discussion

The results for most, but not all, relevant studies suggest that subtle variations in “head shape” [12–16], cranial base width, length and flexion angle [16–20], facial proportions [15–18], maxillary-mandibular interactions [21–26], and nasopharyngeal volume [27–31] can

affect an individual's risk for the different OM expressions. Usually, this hypothesized morphology–pathology relationship is attributed to variant-associated changes in the functional anatomy and geometry of the ET system that either cause or increase the risk for developing ETD. Support for this hypothesis includes results of functional-anatomic studies in infants and children with cleft palate, a severe craniofacial dysmorphology [48,49] and the observed synchronous changes in the functional anatomy of the ET system (more favorable), ET opening efficiency (increased) and prevalence of OM, COME and RAOM (decreased) during growth and development of children from birth to about 8 years [1,32,50,51]. However, past studies of the morphology–pathology relationship rarely assess the same set of morphological characteristics, frequently use methods susceptible to false positive associations, often failed to characterize the OM phenotype under study, and reported inconsistent results [13].

Validation of the morphology–pathology hypothesis would have clinical utility with respect to assigning a child's relative risk for the different OM expressions based on simple morphometric assessments. It could also identify the specific abnormal morphology to target for therapy in each affected child to prevent and/or resolve the OM expression. A review of published studies showed that clinical application of the morphology–pathology relationship is ongoing in some orthodontic practices. Specifically, a number of published studies report that mechanical orthodontic expansion of the palate improves ETF and hearing and resolves COME and RAOM in older children who were not preselected based on palatal architecture [24,52–55]. However, those studies have a number of methodological deficiencies that preclude accepting the clinical efficacy of palatal expansion, even in children with initially small palatal widths/heights. The paucity of replicated results makes application of these interventions premature.

This study was designed as a formal test of the morphology–pathology hypothesis in children with a well-characterized history of RAOM and demographically matched Controls with no prior history of OM. The morphologies explored as potential predictors of disease risk were the geometric shape of craniofacial regions that contain features previously identified to affect OM risk. The formal statistical methodology of GM analysis [40,56] was used to abstract, reconstruct, mathematically describe, and compare the complex representations of craniofacial shape derived from a set of standard landmarks identified on lateral cephalometric X-rays. While not used in past studies of OM risk, this focus on shape has a number of advantages over the traditional linear and angular descriptors employed. First, the single construct of morphological shape captures information on the positional inter-relationships of all included landmark, i.e. it is an inclusive descriptor. Second, multivariate statistical procedures operating on landmark coordinates can extract a limited set of descriptors that capture a predetermined percentage of the total variance in and among contained landmarks, i.e. identify morphological shape descriptors. Third, comparative multivariate statistical methods operating on the set of extracted shape descriptors can assign statistical significance to between-group differences in those descriptors as well as estimate the accuracy of a descriptor or set of descriptors with respect to assigning group membership for individual cases. Fourth, constructed wire-frame depictions of the characteristic shape for each comparator group and of the variability in the characteristic shape for any group allow for intuitive study of shape differences. Finally, because the definition of

morphological shape controls for all operations allowable in maintaining shape identity, significant between-group differences detected in any shape descriptor is geometrically meaningful.

The results support the tested hypothesis that craniofacial shape is significantly different between 4 year old, but not 6 year old, RAOM and Control children. This finding is consistent with the clinical observation that excess RAOM risk often resolves around 6 years of age and the hypothesis that this resolution is due, in part, to age-related craniofacial changes. Some of the observed differences correspond roughly to those reported in earlier, more traditional craniofacial studies of OM populations. Differences in the spatial relationships between the mandible, cranial base, external acoustic meatus, sphenoid and palate in the 4 year old RAOM group when compared to the Control group. The ET-ME system is essential in maintaining ME pressure and preventing disease. Functional adequacy of the system depends on the musculoskeletal system of swallowing and palate elevation, which involves muscles that originate and insert on the cranial base, palate, and mandible. This study identified differences in skeletal spatial morphology between the RAOM and Control groups that can affect the associated musculature and thus change the muscle efficiency for ET opening. Specifically, in the RAOM (i.e., disease) group, the palate and pterygomaxillary fissure are inferiorly displaced, the middle cranial base and external acoustic meatus are posteriorly displaced, and the posterior cranial base is shortened in comparison to the Control group (Figs. 2 and 3).

Although this study represents an advance in the characterization of craniofacial morphology in relation to RAOM risk, it is not without limitations. The sample sizes are still relatively small, thus the results should be interpreted with appropriate caution until they can be independently replicated or assessed in the larger sample. Because other forms of OM, including COME, were not included in the present analysis, uncertainty remains with respect to whether the results are generalizable. Other limitations result from the imaging modality and choice of landmarks. Cephalometry is inherently limited in its ability to capture complex three-dimensional anatomy and creates spatial distortions that could mask important aspects of morphology. Moreover, only lateral radiographs were available, precluding us from assessing craniofacial changes in the coronal plane, though medio-lateral shifts involving the palate and cranial base may be highly relevant. Finally, no direct measures of the associated musculature were available, meaning that the functional implications of our findings must be inferred from the skeletal changes. Three-dimensional CT and MRI based studies may obviate some of these limitations and could focus more directly on anatomical regions specific to the ET system.

5. Conclusion

This analysis identified differences in craniofacial size and shape among 4 year old children with different OM histories (RAOM and controls), which were not observed at 6 years of age. The clinical utility of the morphology–pathology paradigm lies in the potential to assign OM risk levels to a given child based on morphological assessment, to identify the specific cause of the increased risk and to suggest treatment options based on that cause. Those applications require not only that a morphology is significantly different between affected

and non-affected groups, but also that the morphology accurately assigns an individual's membership to one group or the other, i.e. is sensitive and specific. Future studies should attempt to capture 3-dimensional shape changes, and focus on landmarks specifically chosen to characterize the shape of the ME-ET system.

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Abbreviations

AOM	acute otitis media
COME	chronic otitis media with effusion
DFA	discriminant function analysis
ET	Eustachian tube
ETD	Eustachian tube dysfunction
ETF	Eustachian tube function
GM	geometric morphometry
ME	middle ear
OM	otitis media
OME	otitis media with effusion
PC	principal component
PCA	principal components analysis
RAOM	recurrent acute otitis media

References

1. Bluestone, CD.; Klein, JO. Otitis Media in Infant and Children. 5. B. C. Decker, Inc; Ontario: 2007.
2. Mandel EM, Doyle WJ, Winther B, Alper CM. The incidence, prevalence and burden of OM in unselected children aged 1–8 years followed by weekly otoscopy through the “common cold” season. *Int J Pediatr Otorhinolaryngol.* 2008; 72(4):491–499. [PubMed: 18272237]
3. Casselbrant ML, Mandel EM, Fall PA, et al. The heritability of otitis media: a twin and triplet study. *JAMA.* 1999; 282(22):2125–2130. [PubMed: 10591333]
4. Rovers M, Haggard M, Gannon M, Koeppen-Schomerus G, Plomin R. Heritability of symptom domains in otitis media: a longitudinal study of 1,373 twin pairs. *Am J Epidemiol.* 2002; 155(10): 958–964. [PubMed: 11994236]
5. Doyle WJ, Alper CM, Buchman CA, Moody SA, Skoner DP, Cohen S. Illness and otological changes during upper respiratory virus infection. *Laryngoscope.* 1999; 109(2 Pt 1):324–328. [PubMed: 10890787]
6. Rovers MM, Hofstad EA, Franken-van den Brand KI, et al. Prognostic factors for otitis media with effusion in infants. *Clin Otolaryngol Allied Sci.* 1998; 23(6):543–546. [PubMed: 9884810]

7. Rovers MM, Zielhuis GA, Straatman H, Ingels K, van der Wilt GJ, van den Broek P. Prognostic factors for persistent otitis media with effusion in infants. *Arch Otolaryngol Head Neck Surg.* 1999; 125(11):1203–1207. [PubMed: 10555690]
8. Doyle WJ, Friedman R, Fireman P, Bluestone CD. Eustachian tube obstruction after provocative nasal antigen challenge. *Arch Otolaryngol.* 1984; 110(8):508–511. [PubMed: 6540079]
9. Doyle WJ, Ingraham AS, Fireman P. The effects of intranasal histamine challenge on Eustachian tube function. *J Allergy Clin Immunol.* 1985; 76(4):551–556. [PubMed: 4056243]
10. Stool SE, Randall P. Unexpected ear disease in infants with cleft palate. *Cleft Palate J.* 1967; 4:99–103. [PubMed: 5229150]
11. Marasovich WA, Mazaheri M, Stool SE. Otolaryngologic findings in whistling face syndrome. *Arch Otolaryngol Head Neck Surg.* 1989; 115(11):1373–1380. [PubMed: 2803721]
12. Mann W, Jonas I, Munker G. Growth influence on tubal function. *Acta Otolaryngol.* 1979; 87(5–6):451–457. [PubMed: 463517]
13. Casselbrant ML, Swarts JD, Mandel EM, Doyle WJ. The cephalic index is not different among groups of children aged 36–48 months with chronic otitis media with effusion, recurrent acute otitis media and controls. *Int J Pediatr Otorhinolaryngol.* 2013; 77(3):334–337. [PubMed: 23280277]
14. Stolovitzky JP, Todd NW. Head shape and abnormal appearance of tympanic membranes. *Otolaryngol Head Neck Surg.* 1990; 102(4):322–325. [PubMed: 2113257]
15. Di Francesco R, Paulucci B, Nery C, Bento RF. Craniofacial morphology and otitis media with effusion in children. *Int J Pediatr Otorhinolaryngol.* 2008; 72(8):1151–1158. [PubMed: 18514333]
16. Di Francesco RC, Sampaio PL, Bento RF. Correlation between otitis media and craniofacial morphology in adults. *Ear Nose Throat J.* 2007; 86(12):738–743. [PubMed: 18217377]
17. Kemaloglu YK, Goksu N, Ozbilen S, Akyildiz N. Otitis media with effusion and craniofacial analysis-II: “mastoid-middle ear – Eustachian tube system” in children with secretory otitis media. *Int J Pediatr Otorhinolaryngol.* 1995; 32(1):69–76. [PubMed: 7607822]
18. Kemaloglu YK, Kobayashi T, Nakajima T. Analysis of the craniofacial skeleton in cleft children with otitis media with effusion. *Int J Pediatr Otorhinolaryngol.* 1999; 47(1):57–69. [PubMed: 10206395]
19. Todd NW. Cranial anatomy and otitis media: a cadaver study. *Am J Otol.* 1998; 19(5):558–564. [PubMed: 9752960]
20. Todd NW, Martin WS. Relationship of Eustachian tube bony landmarks and temporal bone pneumatization. *Ann Otol Rhinol Laryngol.* 1988; 97(3 Pt 1):277–280. [PubMed: 3377395]
21. McDonnell JP, Needleman HL, Charchut S, et al. The relationship between dental overbite and Eustachian tube dysfunction. *Laryngoscope.* 2001; 111(2):310–316. [PubMed: 11210881]
22. Azadani PN, Jafarimehr E, Shokatbakhsh A, Pourhoseingholi MA, Ghougeghi A. The effect of dental overbite on Eustachian tube dysfunction in Iranian children. *Int J Pediatr Otorhinolaryngol.* 2007; 71(2):325–331. [PubMed: 17141333]
23. Hildmann H, Lammert F, Meertens A, Scheerer WD. Relations between the nasopharynx, Eustachian tube distance and maxillary shape. *Laryngol Rhinol Otol (Stuttg).* 1982; 61(10):573–576. [PubMed: 6890607]
24. Hsu BS. The nature of arch width difference and palatal depth of the anterior open bite. *Am J Orthod Dentofac Orthop.* 1998; 113(3):344–350.
25. Jonas I, Mann W, Munker G, Junker W, Schumann K. Relationship between tubal function, craniofacial morphology and disorder of deglutition. *Arch Otorhinolaryngol.* 1978; 218(3–4):151–162. [PubMed: 580174]
26. Mew JR, Meredith GW. Middle ear effusion: an orthodontic perspective. *J Laryngol Otol.* 1992; 106(1):7–13. [PubMed: 1541899]
27. Tadic L, Vaskovic Z, Stojanovic S, Krsmanovic J. Relation between size of the nasopharynx and occurrence of chronic otitis media. *Srp Arh Celok Lek.* 2002; 130(Suppl 1):12–15. [PubMed: 12395456]
28. de Nery GC, Buranello FS, Pereira C, Di Francesco RC. Is facial pattern a predisposing factor for otitis media with effusion in children? *Braz J Otorhinolaryngol.* 2011; 77(1):84–87. [PubMed: 21340194]

29. Niemela M, Uhari M, Lautala P, Huggare J. Association of recurrent acute otitis media with nasopharynx dimensions in children. *J Laryngol Otol.* 1994; 108(4):299–302. [PubMed: 8182313]
30. Renko M, Kristo A, Tapiainen T, et al. Nasopharyngeal dimensions in magnetic resonance imaging and the risk of acute otitis media. *J Laryngol Otol.* 2007; 121(9):853–856. [PubMed: 17224090]
31. Maw AR, Smith IM, Lance GN. Lateral cephalometric analysis of children with otitis media with effusion: a comparison with age and sex matched controls. *J Laryngol Otol.* 1991; 105(2):71–77. [PubMed: 2013733]
32. Doyle WJ, Swarts JD. Eustachian tube-tensor veli palatini muscle-cranial base relationships in children and adults: an osteological study. *Int J Pediatr Otorhinolaryngol.* 2010; 74(9):986–990. [PubMed: 20580443]
33. Suzuki C, Balaban C, Sando I, Sudo M, Ganbo T, Kitagawa M. Postnatal development of Eustachian tube: a computer-aided 3-D reconstruction and measurement study. *Acta Otolaryngol.* 1998; 118(6):837–843. [PubMed: 9870630]
34. Bluestone, CD. Eustachian Tube Structure, Function, Role in Otitis Media. BC Decker Inc; Hamilton, Ontario: 2005.
35. Bluestone CD, Doyle WJ. Anatomy and physiology of Eustachian tube and middle ear related to otitis media. *J Allergy Clin Immunol.* 1988; 81(5 Pt 2):997–1003. [PubMed: 3286738]
36. Doyle WJ. Functional Eustachian tube obstruction and otitis media in a primate model. A review. *Acta Otolaryngol Suppl.* 1984; 414:52–57. [PubMed: 6398609]
37. Casselbrant ML, Cantekin EI, Dirkmaat DC, Doyle WJ, Bluestone CD. Experimental paralysis of tensor veli palatini muscle. *Acta Otolaryngol.* 1988; 106(3–4):178–185. [PubMed: 3176963]
38. Casselbrant ML, Doyle WJ, Cantekin EI, Ingraham AS. Eustachian tube function in the rhesus monkey model of cleft palate. *Cleft Palate J.* 1985; 22(3):185–191. [PubMed: 3860312]
39. Bluestone CD. Studies in otitis media: Children's Hospital of Pittsburgh –University of Pittsburgh progress report – 2004. *Laryngoscope.* 2004; 114(11 Pt 3 Suppl 105):1–26. [PubMed: 15514559]
40. Zelditch, M.; Swiderski, D.; Sheets, H.; Fink, W. Geometric Morphometrics for Biologists: A Primer. Elsevier Academic Press; Amsterdam: 2004.
41. Adams D, Rohlf F, Slice D. Geometric morphometrics: ten years of progress following the 'revolution'. *Ital J Zool.* 2004; 71:5–16.
42. Kemal u YK, Göksu N, Özbilen S, Akyildiz N. Otitis media with effusion and craniofacial analysis-II: "mastoid-middle ear – Eustachian tube system" in children with secretory otitis media. *Int J Pediatr Otorhinolaryngol.* 1995; 32(1):69–76. [PubMed: 7607822]
43. Rohlf, F. tpsDig Version 2.10. Department of Ecology and Evolution, State University of New York; Stony Brook: 2006.
44. Klingenberg CP. Evolution and development of shape: integrating quantitative approaches. *Nat Rev Genet.* 2010; 11(9):623–635. [PubMed: 20697423]
45. Klingenberg CP. MorphoJ: an integrated software package for geometric morphometrics. *Mol Ecol Resour.* 2011; 11(2):353–357. [PubMed: 21429143]
46. Rohlf FJ. Shape statistics: Procrustes superimpositions and tangent spaces. *J Classif.* 1999; 16(2): 197–223.
47. Klingenberg CP, Monteiro LR. Distances and directions in multidimensional shape spaces: implications for morphometric applications. *Syst Biol.* 2005; 54(4):678–688. [PubMed: 16126663]
48. Doyle WJ, Reilly JS, Jardini L, Rovnak S. Effect of palatoplasty on the function of the Eustachian tube in children with cleft palate. *Cleft Palate J.* 1986; 23(1):63–68. [PubMed: 3484683]
49. Doyle WJ, Cantekin EI, Bluestone CD, Phillips DC, Kimes KK, Siegel MI. Nonhuman primate model of cleft palate and its implications for middle ear pathology. *Ann Otol Rhinol Laryngol Suppl.* 1980; 89(3 Pt 2):41–46. [PubMed: 6778347]
50. Bylander A, Tjernstrom O. Changes in Eustachian tube function with age in children with normal ears. A longitudinal study. *Acta Otolaryngol.* 1983; 96(5–6):467–477. [PubMed: 6637457]
51. Swarts JD, Casselbrant ML, Teixeira MS, et al. Eustachian tube function in young children without a history of otitis media evaluated using a pressure chamber protocol. *Acta Otolaryngol.* 2014; 134(6):579–587. [PubMed: 24828350]

52. Cozza P, Di Girolamo S, Ballanti F, Panfilio F. Orthodontist-otorhinolaryngologist: an interdisciplinary approach to solve otitis media. *Eur J Paediatr Dent.* 2007; 8(2):83–88. [PubMed: 17571932]
53. De Stefano A, Baffa C, Cerrone D, et al. Management of recurrent otitis media with rapid maxillary expansion: our experience. *B-ENT.* 2009; 5(1):13–17. [PubMed: 19455994]
54. Kilic N, Kiki A, Oktay H, Selimoglu E. Effects of rapid maxillary expansion on conductive hearing loss. *Angle Orthod.* 2008; 78(3):409–414. [PubMed: 18416625]
55. Kilic N, Oktay H, Selimoglu E, Erdem A. Effects of semirapid maxillary expansion on conductive hearing loss. *Am J Orthod Dentofac Orthop.* 2008; 133(6):846–851.
56. Adams DC, Rohlf FJ, Slice DE. Geometric morphometrics: ten years of progress following the ‘revolution’. *Ital J Zool.* 2004; 71(1):5–16.

Fig. 1. Right lateral radiograph showing the location of the 19 landmarks (numbers correspond to the landmarks listed in Table 2). Also shown is a tracing of the landmark linkages that outline the wireframe used in the GM shape visualizations.

Fig. 2. Wireframes showing shape variation associated with the DFA for the 4 year old children. The black wireframe represents the RAOM mean shape and the gray wireframe represents the Control mean shape. The scale factor was set at 5.

Fig. 3.

Wireframes showing shape variation associated with PC4 for the 4 year old children. The black wireframe represents the shape variation associated with PC4 in the RAOM group, while the gray wireframe represents the shape variation associated with PC4 in the Control group. The scale factor was set at 0.1.

Table 1

Demographic characteristics for the groups and subgroups.

Age group	OM group	N	Avg. age	Sex				Race		
				Male	Female	White	Black	Native American	Not reported	
4 years ^a	Control	41	4.2	22	19	29	6	1		5
	RAOM	38	4.1	19	19	25	7	1		5
6 years ^a	Control	27	6.3	13	14	18	5	0		4
	RAOM	25	6.2	14	11	14	5	1		5

^aNo significant differences in mean age or in the sex or race distribution between control and rAOM (all $p > 0.05$).

Table 2

List of the 19 standard landmark points, the abbreviation for each used to identify the points in Fig. 1.

#	Landmark	Abbrev.
1	Nasion	N
2	Frontonasal maxillary suture	FMN
3	Temporale	Te
4	Sphenoethmoidal point	SE
5	Pterygomaxillary fissure	Ptm
6	Pterygoid point	Pt
7	Sella	S
8	Porion	Po
9	Basion	Ba
10	Bolton's Point	Bo
11	Opisthion	Op
12	Hyoid	Hy
13	Orbitale	Or
14	Posterior nasal spine	PNS
15	Anterior Nasal Spine	ANS
16	Point A	A
17	Menton	Me
18	Gonion	Go
19	Articulare	Ar