Published in final edited form as:

Cleft Palate Craniofac J. 2010 November ; 47(6): 600–610. doi:10.1597/09-131.

Finite Element Analysis of Eustachian Tube Function in Cleft Palate Infants Based on Histological Reconstructions

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Abstract

Introduction—The prevalence of otitis media with effusion approaches 100% in infants with cleft palate (CP), and disease pathogenesis is believed to be caused by eustachian tube (ET) dysfunction.

Objectives—Quantify the functional consequences of ET anatomy in infant CP specimens, and identify the relative importance of various tissue biomechanical properties on ET function in infants with CP.

Methods—Finite element models of ET anatomy and physiology were developed by using image analysis and three-dimensional (3D) reconstruction techniques. Models were developed using histological images of ET structures obtained from five infant CP specimens. The models were parameterized, and the effects of varying model parameters, which included tensor veli palatini and levator veli palatini force, ET cartilage, periluminal mucosal compliance, and hamular position on resistance to airflow through the tubal lumen, were determined.

Results—Of the evaluated parameters, only applied tensor veli palatini muscle force and compliance of the periluminal mucosa and cartilage tissues were significant predictors of resistance to airflow through the ET during muscle-assisted opening.

Conclusions—Finite element models of ET function in the CP infant identified tensor veli palatini muscle force as a direct predictor and mucosal/cartilage compliance as an indirect predictor of ET opening during muscle-assisted lumen dilations. Hamular position and levator veli palatini force were not found to have an effect on ET function in CP infants.

Keywords

cleft palate infants; eustachian tube function; finite element models

Otitis media with effusion (OME) is a disease condition characterized by middle ear (ME) mucosal inflammation and the presence of effusion (fluid) within the normally air-filled ME cavity (van Cauwenberge, 1988). This effusion impairs the normal transducer function of the ME, which causes a conductive hearing loss and mild to moderate deafness in affected

persons (Grant et al., 1988). The prevalence of OME approaches 100% in the population of infants born with cleft palate (CP) (Paradise et al., 1969; Grant et al., 1988). Moreover, the disease and its complications do not usually resolve after surgical reconstruction of the palate (Robinson et al., 1992; Spauwen et al., 1992; Nunn et al., 1995; Guneren et al., 2000), and prevalence remains high throughout childhood and into adolescence in individuals with surgically repaired and unrepaired palatal clefts (Lokman et al., 1992; Sheahan et al., 2003; Timmermans et al., 2006). The evolution of palatoplasty reconstruction techniques has focused on reducing the number of follow-up surgical procedures and on achieving normal voice quality (Marsh et al., 1989; Noorchashm et al., 2006). Surgical innovations (e.g., Furlow double-opposing z-plasty, radical intravelar veloplasty) and refinements (e.g., greenstick fracture of the hamulus, releasing lateral incisions) were developed to further these goals. To date, prevention or reduction in the amount of OME has been an ancillary concern, except for any secondary benefit derived from the palatoplasty itself.

Most past studies support a causal role for poor eustachian tube (ET) function in the pathogenesis of OME (Bluestone and Doyle, 1988). The ET is a collapsible upper respiratory airway that extends from the ME to the posterior nasopharynx (NP). Although the ET is normally closed to prevent NP pathogens from entering the ME, the ET must be opened periodically to equilibrate ME pressures to ambient conditions and drain effusion fluid that develops in the ME during infectious OME. Anatomically, the ET consists of a posterior, osseous tube with a continuously patent lumen that is an anterior extension of the ME airspace. This portion of the ET is coupled to an anteriorly more complex membranocartilaginous tube that links the bony portion to the NP. The membranocartilaginous tube is firmly attached to the cranial base and is composed of a slitlike lumen surrounded by mucosal tissue that is bounded medially by a hook-shaped cartilage and laterally and inferiorly by a membranous wall. Two muscles are intimately associated with the membranocartilaginous portion of the ET: the tensor veli palatini muscle (mTVP) and the levator veli palatini muscle (mLVP). The mTVP takes its origin from the cranial base and lateral wall of the cartilaginous portion of the ET, proceeds inferolaterally to round the hamulus as a tendon, and inserts into the palatal aponeurosis. The mLVP runs unattached inferior to the ET lumen, takes its origin from the inferior aspect of the bony portion of the ET, and merges with its opposite in the midline of the soft palate (Rood and Doyle, 1978; Huang et al., 1997; Kuehn and Moon, 2005).

Under conditions of normal function, the lumen of the membranocartilaginous portion of the ET is usually closed because of tissue pressures in the surrounding mucosa, but it can be opened periodically by contraction of the mTVP, which imposes an inferolateral vector force on the lateral wall of the ET. Although mLVP contraction is observed to displace the tubal cartilage, medially and superiorly dilating the nasopharyngeal orifice of the ET, this luminal opening is regionally localized and does not extend to the more distal parts of the ET lumen (Rood and Doyle, 1982). Periodic openings of the ET allow for gas transfers between ME and NP and the consequent equalization of ME and ambient pressures (Bluestone and Doyle, 1988). In animals, physical obstruction of the ET lumen or debilitating mTVP function but not mLVP function results in the progressive development of ME underpressures (ref. ambient) and OME (Ryan et al., 1989; Ghadiali et al., 2003).

Past studies of ET function in CP patients both before and after palate repair document an inability to open the ET during activities typically associated with mTVP contraction (e.g., swallowing), as well as other functional abnormalities (Bluestone, 1971; Bluestone et al., 1975; Doyle et al., 1980; Doyle et al., 1986; Tasaka et al., 1990; Takahashi et al., 1994). Because the two muscles intimately associated with the ET—the mTVP and the mLVP—have insertions within the palate, OME in CP patients has been attributed to ET dysfunction caused by abnormal interactions between those muscles and the ET (Huang et al., 1997). A

number of studies have focused on the anatomy of the ET and paratubal muscles in histologically processed specimens recovered from CP individuals (Matsune et al., 1991a, 1991b; Takasaki et al., 2000). Although differences in the morphology of the ET cartilage, mTVP, and mLVP between CP and “control” specimens have been noted, their effects on tubal function could only be inferred and remain speculative. In addition to anatomical variations, experimental studies in animals indicate that changes in tissue biomechanical properties may influence ET function (Ghadiali et al., 2002a; Ghadiali et al., 2003). To investigate potential interactions between tissue anatomy and tissue biomechanics, we previously developed two-dimensional (2D) computational models of ET function in a group of healthy adult subjects with “normal” anatomical relationships (Ghadiali et al., 2004). However, these models assumed a simplified 2D anatomy and did not account for the abnormal tissue anatomy that exists in CP patients. As a result, it is not known how the pathological 3D tissue anatomy present in CP subjects influences structure-function relationships in the ET.

The present report describes methods for constructing 3D computational models of ET function in CP infants. These models use biophysical principles to directly simulate both tissue deformation and airflow through the ET lumen during swallowing. A sensitivity analysis with these functional-anatomical models was used to predict the functional consequences of the underlying anatomy and to identify the relative importance of various tissue biomechanical properties for ET function in CP infants.

Methods

Specimen Acquisition and Processing

Extended temporal bone specimens that included ME, cranial base, ET, and associated musculature were recovered at autopsy from five infant CP cases (#506-W, F, 1 mo; #578-W, F, 1 mo; #598-W, M, 3 yr; #847-W, M, 2 mo; #849-W, F, 3 mo) and were processed for histological study through the use of previously described methods (Sando et al., 1986). For each specimen, 30-micron sections were cut perpendicular to the long axis of the ET from the nasopharyngeal orifice to the bony portion of the ET, and every 20th section was stained with hematoxylin and eosin. Stained sections were analyzed with the use of MetaMorph image analysis software (Molecular Devices, Sunnyvale, CA) to obtain outlines of the different tissue elements: cartilage, periluminal mucosa, ET lumen, mTVP, mLVP, and cranial base (Fig. 1). During this procedure, outlines representing the attachment of the cartilage to the cranial base (section 1, Fig. 1a) and the location of muscle action on various tissue elements (sections 2 through 5, Fig. 1a) were noted to allow for efficient specification of boundary conditions (see later for details). In the processed specimens, the ET lumen is artificially opened as the result of tissue dehydration, but the models were constructed with a closed lumen to better simulate *in vivo* conditions. Therefore, the lumen was always drawn tangential to the medial edge of the open lumen.

Model Construction

For each specimen, the outlines for sequential sections were incorporated into a 3D solid model that included the cartilage and the mucosal tissue by using the Pro/Engineer CAD program (PTC Software, Needham, MA). A cubic spline algorithm was used to generate smooth lofted surfaces linking the sequential sections of each specimen and to create a solid model of the cartilage and mucosal tissues. The solid model was then loaded into the finite element analysis (FEA) program, ADINA (ADINA R and D, Watertown, MA). FEA was used to solve the differential equations that govern tissue deformation in the solid domain and fluid flow in the fluid domain over a series of finite elements. For this purpose, the global geometry was resolved as a series of points or nodes that were connected with

individual elements to create a mesh that represents the original structure. For these models, rotational degrees of freedom were not allowed, and the model utilized linear finite elements.

Model Parameterization

To complete the functional model, material properties were assigned to each element so that the mesh accurately represented both the original geometry and the type of tissue to be simulated. Boundary conditions were defined, and forces acting on the eustachian tube associated with mTVP and mLVP muscle contractions were then applied.

In the models, both the cartilage and the mucosal tissue were treated as Neo-hookean or two-parameter Mooney-Rivlin hyperelastic materials. Cartilage and mucosal tissue were assumed to be almost incompressible with a Poisson's ratio of $\nu = 0.49$. The modulus of elasticity, E , and Poisson's ratio were used to calculate the material properties that define a Mooney-Rivlin material, as in equations (1) and (2):

$$\kappa = \frac{E}{3(1 - 2\nu)} \quad (1)$$

$$C_1 = \frac{E}{4(1 + \nu)} \quad (2)$$

where κ is the bulk modulus and C_1 is a material constant. Typical values reported in the literature for cartilage elastic modulus and vocal fold mucosa elastic modulus are $E_{\text{cart}} \sim 300$ kPa and $E_{\text{mucosa}} \sim 50$ kPa (Chan and Tize, 2003; Hung et al., 2004). However, *in vivo* studies reported that ET compliance in infants and young children may be twofold greater than that in adults (Takahashi et al., 1994). Therefore, baseline elastic moduli assigned for the cartilage and mucosal tissue for modeling the infant CP ET were $E_{\text{cart}} = 150$ kPa and $E_{\text{mucosa}} = 25$ kPa. We note that the Neo-hookean model is an extension of Hooke's law for the case of large deformations, and similar hyperelastic models have been used to simulate the deformation of glandular/ fatty tissue (Yin et al., 2004) and cartilage in the ear canal (Qi et al., 2006). Although the Mooney-Rivlin material model partially accounts for large tensile deformations, it assumes a linear dependence of shear stress on shear deformation and therefore may not be valid for large shearing deformations.

The next step in model development requires the specification of appropriate boundary conditions based on anatomical relationships. The first boundary condition represents attachment between the ET cartilage and the cranial base, which was modeled as zero displacement in all directions because of the firm attachment of the two structures (black surfaces, Fig. 2b). The other boundary condition represents the attachment of the cartilaginous ET to the bony portion of the ET, which allows for in-plane displacements only. Therefore, a boundary condition of zero displacement in the z-direction was specified at the proximal and distal ends of the model (gray surfaces, Fig. 2b).

Simulation of ET opening during swallowing was accomplished by applying mTVP and mLVP muscle forces to appropriate tissue surfaces. During contractions, the mTVP exerts an anteroinferolateral force on the lateral aspect of the tubal cartilage and membranous wall that is directed toward the pterygoid hamulus (Rood and Doyle, 1978), and the mLVP exerts a superomedially directed force onto the inferior surfaces of the membranous wall and cartilage (Finkelstein et al., 1990). Recently, correlations between experimental

measurements of jaw movement and finite element simulations have been used to estimate craniofacial muscle force magnitudes of ~50 to 70 N in adults (Rohrle and Pullan, 2007). These data are consistent with our previous models of adult ET (Ghadiali et al., 2004), which used 50 N as a baseline value for mTVP force and 5 N for mLVP force. The mLVP force is lower because of this muscle's out-of-plane contraction with respect to the ET cross-section. However, infants with CP would be expected to have a lower muscle force than adults. To account for this reduction in force, the MetaMorph image analysis package (Molecular Devices, Sunnyvale, CA) was used to calculate the average cross-sectional area of the mTVP and mLVP muscles for both CP specimens used in this study, as well as for the adult specimens used in our previous study (Ghadiali et al., 2004). These data showed that the ratio of adult to CP infant cross-sectional areas for the mTVP was 1:0.2 and for the mLVP was 1:0.5. Because the amount of force applied by a muscle is proportional to its cross-sectional area (Raadsheer et al., 1999), we estimated baseline forces in infants with cleft palate of 10 N and 2.5 N for the mTVP and mLVP, respectively. We note that in this study, the mTVP and mLVP magnitudes were systematically varied about the baseline conditions, and as a result, we consider the range of mTVP and mLVP forces used in this study to encompass the likely range that would exist in CP infants.

mTVP and mLVP forces are indicated in Figure 2a, where it should be noted that the force vectors of the mTVP are all directed to the same physical point in space—the pterygoid hamulus. The mTVP force is a follower load such that as the solid model deforms, the vectors change direction to always point to the hamulus. The mLVP force was modeled as a pressure normal to the surface being acted upon and is also displacement dependent.

Model Deformation and Calculation of Fluid Flow

To simulate model deformation and ET opening under applied muscle forces, a nonlinear, large displacement finite element routine (Bathe, 1996) was used as specified by the following equations:

$$\frac{\partial \sigma_{ij}^s}{\partial x_j} = 0, \quad \sigma_{ij}^s = \frac{1}{2} \left(\frac{\partial W}{\partial \epsilon_{ij}} + \frac{\partial W}{\partial \epsilon_{ji}} \right), \quad \epsilon_{ij} = \frac{1}{2} \left(\frac{\partial d_i}{\partial x_j} + \frac{\partial d_j}{\partial x_i} \right) \quad (3)$$

where σ^s is the Cauchy stress tensor, W is the strain energy density, ϵ is the strain, and d_i is the displacement of each mesh node. All equations are written in indicial notation, where i, j represents an “xyz” Cartesian coordinate system. As is shown in Figure 3a, solution of these equations resulted in tissue deformation and an opened lumen, which then was extracted from the model using a series of scripts written in MatLab (Mathworks, Natick, MA), TecPlot (Tecplot, Inc., Bellevue, WA), and the Rhinoceros 3D CAD package (McNeel North America, Seattle, WA). The extracted lumen geometry under conditions of applied muscle forces was then meshed with the ADINA FEA program for further analysis.

3D computational fluid dynamics (CFD) was used to quantify airflow in the deformed lumen. CFD takes into account the complex geometry of the deformed lumen and does not require assumptions regarding fully developed flow, although steady-state conditions were assumed for this study. For the extracted open lumen, flow is governed by the incompressible continuity and Navier-Stokes equations:

$$\rho \frac{\partial v_i}{\partial x_i} = 0 \quad \text{and} \quad \rho \frac{\partial v_i}{\partial t} + \rho v_j \frac{\partial v_i}{\partial x_j} = - \frac{\partial p}{\partial x_i} + \mu \frac{\partial^2 v_i}{\partial x_i \partial x_j} \quad (4)$$

where ρ is the density of air (1.229 kg/m^3), μ is the viscosity of air ($1.8 \times 10^{-5} \text{ Pa}\cdot\text{s}$), and v is the velocity vector. To quantify ET function, no slip boundary conditions were applied to the walls of the lumen, an initial normal pressure of 1961 Pa (200 mm H₂O) was applied to the ME side of the lumen, and a zero pressure condition was applied to the nasopharyngeal side of the lumen. As is shown by the velocity magnitude contours in Figure 3b, solution of equation (4) resulted in a complex velocity profile that varied along the length of the ET. For these conditions, the typical velocity scale of air flowing throughout the lumen is on the order of 25 m/s. This corresponded to a maximum Reynolds number (ratio of inertial to viscous forces) of ~25 to 30, which is consistent with laminar flow through the deformed lumen. The flow rate during muscle-assisted deformation of the lumen was determined by integrating the velocity profile in the cross-section located in the middle of the lumen. Once the flow rate in the lumen was determined, the extent of lumen opening was quantified by calculating the flow resistance parameter:

$$R_v = \frac{\Delta P}{Q} \quad (5)$$

where ΔP is the applied pressure drop from the ME to the NP, and Q is the flow rate. Note that larger values of R_v represent poorer muscle-assisted ET function, and smaller values of R_v represent better muscle-assisted ET function and larger openings. We used R_v as the output parameter to facilitate comparisons with the experimental data. To quantify how sensitive ET function is to variation in a specific parameter, R_v was calculated over a range of parameter values varying between $\frac{1}{4}$ and 4 times the baseline value of the parameter while the values of the other parameters were held constant at their baseline values. Sensitivity, Δ , to parameter variation was defined as the ratio of the resistance value for a 4 times change in the parameter value. For example, sensitivity to changes in mLVP forces was calculated as follows:

$$\Delta_{\text{LVP}} = \frac{R_v(F_{\text{LVP}}=1.0\text{N})}{R_v(F_{\text{LVP}}=0.25\text{N})} \quad (6)$$

In this study, sensitivity was calculated for variations in total mTVP and mLVP force applied to the ET, the cartilage's elastic modulus, mucosal tissue elastic modulus, and changes in the x, y, and z locations of the hamulus. A within-subject repeated measures analysis of variance was used to document statistically significant differences in sensitivity.

Results

The CP infant ETs were highly variable with respect to both size and geometry. This is illustrated by the series of solid models for the five CP specimens presented in Figure 4. As is described below, despite this variation in morphology, changes in tissue biomechanics had relatively consistent effects on ET function.

The effects of varying mTVP and mLVP muscle forces on airflow resistance in the five CP infant models while other model parameters were held constant are presented in Figure 5a and 5b. As would be expected, increasing the mTVP force from 4 to 40 N was generally associated with decreasing ET resistance (i.e., greater luminal opening and greater airflow at a specified pressure gradient). In contrast, varying the mLVP force from .24 N to 6.5 N had little effect on ET resistance over the range of applied forces.

The effects of varying the elastic modulus for the ET cartilage from 30 to 1500 kPa and of varying the elastic modulus for the ET mucosa from 10 to 250 kPa on ET resistance while the other model parameters were held constant for the five CP models are shown in Figure 5c and 5d. Results show that increasing the elastic modulus of the mucosa or the cartilage (which makes the respective tissues stiffer) results in a decrease in luminal dilation and thus an increase in luminal resistance to airflow during applied muscle forces. Note that larger changes in R_v for a given change in the elastic modulus occur with the mucosal tissue, and this effect is quantified in the sensitivity analysis described later.

The effects of varying the pterygoid hamulus position in the x (medial-lateral), y (superior-inferior), and z (distal-proximal) directions on luminal resistance to airflow are shown for the five CP models in Figure 6a, 6b, and 6c. Variation in hamulus location was accomplished by moving the hamulus from its original location up to 100% of the available lateral/superior/distal measurement. More specifically, if all the tissue that makes up the ET measured 5 mm in the lateral direction at its widest point, then the hamulus point was allowed to vary 5 mm in the specified direction. For all models, little effect of hamulus position on resistance to airflow was noted for the ET lumen dilated by applied muscle forces.

Figures 5 and 6 clearly demonstrate that changes in tissue mechanics can significantly influence ET function in infants with CP. However, equivalent changes in these tissue mechanical properties do not produce equivalent changes in ET opening or flow resistance. To identify the relative importance of the different tissue mechanical parameters, we calculated sensitivity ratios according to equation (6) for each specimen and report these values in Table 1. Note that sensitivity ratios for movement of the hamulus were calculated as a ratio of the resistance at 0% to the resistance at 20% displacement. Statistical analysis via repeated measures analysis of variance indicated that the sensitivity of ET function to mTVP forces is greater than the sensitivity to mLVP forces ($p < .01$) and that ET function is more sensitive to changes in cartilage and mucosal tissue elasticity than to changes in mLVP forces ($p < .03$). No statistically significant differences were noted between sensitivities to x, y, and z hamulus positions ($p > .05$) and between unity and sensitivity values for mLVP force, x hamulus position, y hamulus position, and z hamulus position ($p > .13$). In addition, the sensitivity of ET function to mTVP forces, cartilage elasticity, and mucosal tissue elasticity is statistically greater than the sensitivity to x, y, or z hamulus position ($p < .04$). These results suggest that in CP infants, only the mTVP force and the elastic moduli for the ET cartilage and mucosa have a significant impact on muscle-assisted ET opening as measured by resistance to airflow.

Discussion

The present paper describes a method for translating anatomical data for infant CP specimens into their functional consequences using an FEA modeling platform. These FEA models account for the complex 3D anatomy/ morphology of various tissue elements in CP infants and, unlike previous observational studies (Matsune et al., 1991a, 1991b; Takasaki et al., 2000), can directly simulate the complex physical phenomena (i.e., tissue deformation and fluid/airflow) that govern ET function. Another advantage of these computational models is the ability to investigate how isolated changes in specific biomechanical properties influence ET function and to ascertain the relative importance of these parameters. The predicted functional results obtained with these models were robust given that the patterns of change in the chosen measure of ET function—luminal resistance to airflow—imposed by varying the different model parameters were consistent across specimens (i.e., the five developed models).

Moreover, many of the functional interpretations developed under the model are consistent with previous experimental findings and have important clinical implications for cleft palate repair. First, sensitivity analysis based on parameter variation data obtained from the model predicts that the magnitude of the mTVP force applied to the membranocartilaginous portion of the ET is the dominant muscular element responsible for ET opening. This prediction is supported by numerous past studies, which indicate that the TVP muscle is the only effective dilator of the ET lumen (Bluestone and Doyle, 1988). In addition, the sensitivity of ET function to changes in mTVP force documented by the model may have important implications for surgical procedures that directly or indirectly alter mTVP forces. For example, radical repositioning of the velar musculature, including division of the tensor tendon, during intravelar veloplasty has been shown to significantly improve velar function and reduce pharyngeal flap rates (Cutting et al., 1995; Sommerlad, 2003). However, in our computational model, division of the tensor tendon, which can be simulated as a reduction in mTVP force, is predicted to have negative effects on ET function. In the most extreme case, if the hamulus serves as a free pulley for the tendon (Dayan et al., 2005), dividing the tendon would be equivalent to reducing the mTVP force to zero. Because ET opening was found to be independent of mLVP forces, our computational model predicts that zero mTVP force would result in no ET opening and complete ET dysfunction. Alternatively, the tendon may have a direct insertion on the hamulus (Putz and Kroyer, 1999) or the maxillary tuberosity (Latham et al., 1980). In this case, dividing the tensor tendon would reduce the mTVP force but would not ablate it entirely. Figure 5a predicts that reduced mTVP forces result in higher flow resistance and less ET opening. Therefore, although dividing the tensor tendon has beneficial effects for palatal repair, our computational models predict that this procedure would have a negative impact on ET function. Other investigators have focused on developing surgical procedures that might improve ET function. Dayan et al. (2005) have proposed drawing the mTVP tendon tight and suturing it to the hamulus before dividing the tendon medial to the hamulus, and Butow et al. (1991) proposed using a tension sling to reestablish mTVP function. In our computational models, these procedures can be envisioned as increasing the mTVP muscle forces, which, as shown in Figure 5a, would lead to lower flow resistance and increased ET opening. Our models therefore predict that these tensor anchoring procedures would improve ET function.

It is interesting to note that our computational models also predicted that for CP infants, the amount of ET opening is insensitive to hamulus location (i.e., sensitivity ratios equal to one; Table 1). Although the mTVP vector is dependent on hamular position, past studies in animals and in humans indicate that redirecting that vector by hamular fracture during reconstructive surgery (Kane et al., 2000; Sheahan et al., 2004) or by transposing the mTVP tendon medial to the hamulus (Cantekin et al., 1980) had little effect on ET function or on the development or persistence of OME. Current computational models predict that the degree of ET opening is insensitive to lateral (x), superior (y), or distal (z) displacement of the hamulus and therefore is consistent with experimental findings regarding the limited importance of hamular position with respect to ET function. It is important to note that in our computational model, changing the hamulus position only changes the insertion angle of the mTVP vector with respect to mucosal and cartilaginous tissues. *In vivo*, movement of the hamulus might also change mTVP resting length, which could potentially decrease the force it can apply to the ET. As is shown in Figure 5a, our models predict that such a reduction in mTVP force would result in higher flow resistance and reduced ET function. Although hamular fracture might have simultaneous effects on both mTVP insertion vector and mTVP force, one advantage of our computational models is the ability to investigate how isolated changes in these parameters influence ET function. The data from our computational model clearly indicate that ET function is sensitive to mTVP force but is insensitive to mTVP insertion angle. Because hamular fracture or tendon translocation does not result in decreased ET function and/or adverse otological outcomes (Cantekin et al., 1980; Kane et al.,

2000;Sheahan et al., 2004), we hypothesize that mTVP forces are not significantly altered during these procedures. Of course, validation of this computation-based hypothesis would require direct experimental measurements of the mTVP force during hamular fracture or tendon translocation.

The model also predicted that the degree of lumen opening is insensitive (i.e., sensitivity ratio equal to unity) to the amount of mLVP force applied to the ET, and this lack of importance for mLVP with respect to tubal opening is supported by past studies (Rood and Doyle, 1978; Finkelstein et al., 1990; Huang et al., 1997). We note that variations in mLVP force in the current computational models were not accompanied by any physical repositioning of the mLVP or changes in mLVP insertion that might occur during surgical reconstruction of the palate. For example, during intravelar veloplasty (IVV) and/or Furlow double-opposing z-plasty, repositioning of the mLVP is an operative variable that might affect both speech outcomes and ET function. Although this physical repositioning was not simulated in the current study, future studies could develop computational techniques that simulate tissue deformation during muscle repositioning, as well as associated changes in soft tissue structure (e.g., muscle insertions). Once muscle repositioning is simulated, parameter variation studies similar to the ones conducted in this manuscript could be used to investigate how repositioning of the mLVP influences ET function. These more advanced models may provide important information about how different repositioning procedures influence ET function and thus may help in the planning of appropriate surgical procedures for CP repair that also minimize the incidence of postsurgical OME.

Past *in vivo* studies in humans suggested that compliance of the ET cartilage is inversely related to ET functional efficiency (Takahashi et al., 1994). However, this hypothesis is contradicted by the results from current models, which suggest that ET cartilage (and mucosal) compliance is directly related to functional efficiency. We note that experimental measurements in CP subjects (Takahashi et al., 1994) used a summary measure of compliance, which recent studies indicate may not be as discriminating as measurements based on an engineering definition of compliance (Ghadiali et al., 2002b; Ghadiali et al., 2003). Therefore, resolution of this contradiction may require more extensive *in vivo* studies that better characterize ET compliance and its functional outcomes in CP subjects and/or more advanced computational models that account for other complex physical phenomena (i.e., mucosal adhesion and/or fluid-structure interactions).

Dayan et al. (2005) suggested that peritubal lymphoid hyperplasia due to nasal soiling with food may reduce ET function in CP subjects. In our computational model, peritubal lymphatic hyperplasia can be simulated as an increase in mucosal tissue stiffness (E_{muc}); as shown in Figure 5c, this would lead to very large flow resistances and a significant reduction in ET function. It is worth noting that our computational models predict that ET function is also sensitive to variations in cartilage tissue stiffness (Table 1). As a result, our models predict that any procedures or therapies that alter tissue stiffness, such as tissue ablation (Poe et al., 2007), could significantly alter ET function. Future refinement of the current computational models, which allow for direct simulation of surgical procedures (see earlier), may be useful in identifying and predicting how surgical alterations of various biomechanical parameters will affect ET function.

In addition to demonstrating consistency with most previous experimental data, the current computational models can be used to provide testable hypotheses. For example, model results suggest that ET function may be more sensitive to changes in mucosal tissue elasticity as compared with cartilage elasticity. Furthermore, the magnitude of the sensitivity parameters shown in Table 1 indicates that in CP infants, changes in mucosal elasticity may be more effective in altering/restoring ET function than changes in mTVP force magnitude.

Clearly, carefully designed experimental studies are required to test these computation-based hypotheses.

As in all modeling studies, the current computational techniques have limitations with respect to the *in vivo* system. For example, the current models can only quantify the amount of static ET opening as a function of various biomechanical parameters, and they do not account for the complex time-dependent changes in lumen opening that occur *in vivo* during swallowing (Swarts and Bluestone, 2003). As a result, our sensitivity analysis can be used only to assess the relative importance of model parameters for ET opening and cannot be used to assess the importance of these parameters for other aspects of ET function (e.g., closure, transient transport of effusion fluid/air). Therefore, refinements to these models should focus on developing transient dynamic models that can investigate the complex time-dependent aspects of ET function. Another limitation of the models as developed is that they assumed “normal” palatal insertions for the mTVP and mLVP muscles—a condition that is not representative of infants with unrepaired palatal clefts. Therefore, these results should be interpreted under the restriction of a repaired palate wherein the “normal” insertions of these muscles are approximated. Nonetheless, the methods developed and evaluated in this paper offer the potential for predicting the effects of different surgical procedures for palatal reconstruction on ET function and, by implication, for resolving OME in that population.

Acknowledgments

Supported in part by NIH/NIDCD grants DC007230 and DC007667. We thank Ms. Julianne Banks for creating the digital scans of the specimens, and Dr. William J. Doyle for assisting in the editing and preparation of this manuscript.

This work was supported by NIH/NIDCD grants R01DC007230 and P50DC007667.

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FIGURE 1.

a, b, c: Distal, middle, and proximal histological sections of a CP specimen showing regional tracing/outlines of the cartilage, mucosal tissue, and ET lumen. Sections 1 through 5 represent the locations of loads/ boundary conditions as follows: 1, cranial base attachment; 2, mTVP attachment to the cartilage; 3, mTVP attachment to the mucosal tissue; 4, mLVP attachment to the mucosal tissue; and 5, mLVP attachment to the cartilage.

FIGURE 2.

Locations of loading and boundary conditions on finite element ET models. a: Location of mTVP and mLVP force vectors. b: Location of fixed boundary condition on medial cartilage surface (black surface) and of zero z-displacement on the proximal and distal ends of the ET (gray surfaces).

FIGURE 3.

a: Deformed finite element mesh of the ET with opened lumen caused by the action of muscle forces (gray = deformed cartilage, black = deformed mucosal tissue). b: Calculation of airflow velocity magnitude in the deformed lumen for an applied pressure drop of 200 mm H₂O. Integration of velocity field in the midsection was used to calculate flow rate.

FIGURE 4. Solid models of the ET cartilage (dark gray) and mucosal tissue (light gray) in the five CP specimens demonstrating wide variation in ET size and morphology.

FIGURE 5.

Effects of varying (a) mTVP force, (b) mLVP force, (c) mucosal tissue elastic modulus, and (d) cartilage elastic modulus on resistance to airflow through the dilated ET. Data represent independent parameter variations with all other model parameters held at baseline values.

FIGURE 6.

Effects of varying the pterygoid hamulus position in the (a) lateral or x direction, (b) superior or y direction, and (c) distal or z direction on resistance to airflow through the dilated ET. Data represent independent parameter variations with all other model parameters held at baseline values.

TABLE 1

Sensitivity Ratios for Each Subject for Variations in mTVP and mLVP Muscle Forces, Cartilage Elasticity, Mucosal Tissue Elasticity, and Changes in Hamulus x, y, and z Locations*

Subject #	Δ TVP	Δ LVP	Δ cart	Δ mucosa	Δ HamX	Δ HamY	Δ HamZ
P506	1.44	0.99	1.65	2.17	1.03	1.06	0.96
P578	2.23	1.00	1.63	3.17	1.05	1.02	1.05
P598	1.94	0.96	2.18	3.18	0.97	0.88	1.01
P847	1.37	0.95	2.99	4.74	1.23	1.40	1.11
P849	1.83	1.05	1.71	7.78	1.22	1.09	0.93
Average $\pm$ StDev	1.76 ± 0.36	0.99 ± 0.04	2.03 ± 0.58	4.21 ± 2.20	1.10 ± 0.12	1.09 ± 0.19	1.01 ± 0.07

* Δ TVP = sensitivity to mTVP forces; Δ LVP = sensitivity to mLVP forces; Δ cart = sensitivity to cartilage stiffness; Δ mucosa = sensitivity to mucosal stiffness; Δ HamX = sensitivity to hamulus x position; Δ HamY = sensitivity to hamulus y position; and Δ HamZ = sensitivity to hamulus z position; StDev = standard deviation.