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Surface Area-Volume Relationships for the Mastoid Air Cell System and Tympanum in Adult Humans: Implications for Mastoid Function

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Abstract

Conclusions—The middle ear (ME) surface area/volume ratio (SA/V) is greater than that of the tympanum. The rate of ME pressure decrease between Eustachian tube openings is proportional to the ME SA/V. This analysis showed that the MACS will not function as a ME gas reserve under the assumed conditions, but could, if the blood perfusion/surface area is much greater for the tympanum than the MACS and is lesser for greater MACS volumes.

Objective—Measure the surface and volumes for the MACS and tympanum and evaluate if the MACS could function as a ME gas reserve.

Methods—Twenty adult subjects with a wide range of MACS volumes had a CT scan of their MEs. Using Image J software, the left and right surface areas and volumes of the tympanum and MACS were reconstructed. These data were entered into a simple perfusion-limited model of transmucosal gas exchange between ME and mucosal blood. The model predicted that the MACS would function as a ME gas reserve if the SA/V for the ME is less than that for the tympanum, or equivalently, if the tympanum SA/V divided by the ME SA/V is less than a critical value of 1.

Results—Both MACS and tympanum surface areas were linearly related to their volumes. MACS surface area and volume and the ME SA/V were significantly greater than those for the tympanum. Solving the model equation using the measured values yielded a critical value of 1.4 which was significantly greater than 1.

Keywords

Adults; Mastoid; Volume; Surface Area

INTRODUCTION

During periods between openings of the Eustachian tube (ET), the normal middle ear (ME) is a closed, relatively non-collapsible (with the exception of tympanic membrane displacements), gas-filled, bony cavity located within the petrous portion of the temporal bone. The ME can be anatomically and functionally subdivided into two communicating airspaces, the tympanum and the mastoid air-cell system (MACS). The tympanum is essentially a single, large air-cell that contains the ME ossicles which couple movements of the tympanic membrane to those of the oval window and, thus, functions as the peripheral transducer organ for hearing. In contrast,

the MACS is a multiply partitioned, cellular, air-space that increases ME volume, but does not participate directly in sound transduction. Both the MACS and the tympanum are lined by a mucosa that embeds a network of blood vessels that that can serve as the source/sink for gas exchange between the ME and local mucosal blood. While the function of the MACS is debated [1], numerous studies show that MACS volume is indirectly related to the predisposition of the ME to certain pathological conditions including cholesteatoma and otitis media [2–6]. One hypothesis advanced to explain this relationship is that the MACS functions as a ME gas reserve such that MEs with larger MACS require less frequent ET openings to maintain near-ambient total pressure [1].

For normal tympanum function, total ME gas pressure needs to be maintained at near-ambient levels. However, both the tympanum and MACS passively exchange gases with the local blood across their respective mucosa [7–9]. While the O₂, CO₂ and H₂O partial-pressures in the ME and blood are in approximate equilibrium, at ambient ME pressure, the ME to blood N₂ partial-pressure gradient approximates 5.8 kPa [10]. This gradient drives the progressive loss of N₂ from the ME which results in decreasing ME pressure. At an ambient-ME pressure difference of approximately 2.5 kPa, the ME mucosal capillaries become permeable to fluids and an effusion develops in the normally air-filled ME, a pathological condition not different from the clinical presentation of otitis media with effusion [11]. For MEs with good ET function, this is prevented by the transient, muscle assisted openings of the ET which resupply gas to the ME and, thus, re-establishes near-ambient ME pressure.

The MACS will function as a gas reserve for the ME by slowing the rate of physiological ME pressure decrease if the rate of change in the ME partial-pressure of N₂ is less for MEs with a developed MACS and if that effect is accentuated by larger MACS volumes [1]. If valid, the slower rate of ME pressure decrease for larger MACS volumes will decrease the required number and/or efficiency of ET openings to preserve near ambient ME pressures and prevent ME pathology in ears with constitutionally marginal or even poor ET function.

In experiments using primates, transmucosal N₂ exchange was shown to be perfusion-limited [12]. Consequently, the rate of N₂ exchange across the ME mucosa is proportional to mucosal blood flow/volume which, in turn, is a function of the surface area available for exchange/volume [1]. In this study, we measured the surface area and volume of the MACS and tympanum from CT scans of adults with a wide range of MACS volumes. Using a simple mathematical model of perfusion-limited transmucosal N₂ exchange and these data, we tested the hypothesis that the MACS could function as a ME gas reserve.

METHODS

Protocol

The goals of this study were to measure the MACS and tympanum surface areas and volumes for a wide range of MACS volumes and to use these measures to determine if the MACS could function as a gas reserve for the ME. To that end, 28 adult subjects with and without a history of OM in childhood were recruited by advertisement, informed of the risks and benefits of study participation, and signed an institutionally approved informed consent. These subjects were then screened for entry by bilateral pneumatic otoscopy and tympanometry to document disease-free MEs and by taking bilateral ME x-ray's in Schuller projection and measuring the total pneumatized area for each MACS. Using these areas as estimates of MACS volume, the first 20 subjects with pneumatized areas evenly distributed across the expected range of values were selected for CT scanning (left ear: average=7.8±4.1, range=1.8–16.4 cm²; right ear: average=8.3±4.0, range=2.7–18.0 cm²; r=0.90 for the left vs. right pneumatized areas, p<.01). Eight subjects had pneumatized areas similar or identical to previously enrolled subjects and

by protocol (which limited CT scanning to 20 subjects) were discontinued from study participation.

These 20 subjects then had a CT scan of the ME in the transverse plane at a resolution of .031 mm/pixel and a slice thickness of 0.63 mm using a GE LightSpeed VCT system (General Electric Health Care). From each CT scan, a set of transverse images through the bilateral MACS regions (superior to inferior) at 0.25 cm intervals were selected for study. For the tympanum, every image was used for the reconstruction (i.e. interval=.63 mm). Using Image J software (<http://rsbweb.nih.gov/ij/>), these sections were imported, and the left and right MACS and tympanums were identified, segmented out and analyzed. For each MACS and tympanum section, the perimeter and area of all air-cells were highlighted, measured and summed across images. These sums were multiplied by the section interval to yield MACS and tympanum surface area (cm²) and volume (ml). This procedure is essentially identical to that used previously to measure MACS surface area and volume in adult subjects with normal MACS volumes [13]. The protocol was approved by the Institutional Review Board at the University of Pittsburgh.

Model Description

The total ME pressure is defined by the ideal gas law or:

$$P^{ME} = RT^{ME}(N^M + N^T)/(V^M + V^T), \quad 1$$

where P^{ME} is total ME pressure, R is the gas constant, T^{ME} is ME temperature, a constant, N^M and N^T are the total gas moles in the MACS and tympanum, and V^M and V^T are the volumes of the MACS and tympanum (constants). Differentiating this equation on time results in:

$$\delta P^{ME} / \delta t = RT^{ME}(\delta N^M / \delta t + \delta N^T / \delta t) / (V^M + V^T), \quad 2$$

where δ indicates change and t is time. Recognizing that the rate of change in ME pressure is equal to the rate of transmucosal N₂ exchange [10,12], the equation can be rewritten as:

$$\delta P_{N_2}^{ME} / \delta t = RT^{ME}(\delta N_{N_2}^M / \delta t) / (V^M + V^T) + (\delta N_{N_2}^T / \delta t) / (V^M + V^T), \quad 3$$

where the subscript indicates N₂ partial-pressure and N₂ moles. Now, if the MACS is completely sclerotic (i.e. $V^M=0$), the equation reduces to:

$$\delta P_{N_2}^{ME} / \delta t = RT^{ME}(\delta N_{N_2}^T / \delta t) / V^T, \quad 4$$

and for the most-simple case of open N₂ exchange between the MACS and tympanum [14], the rate of change in ME N₂ partial-pressure will be slowed if the following inequality is satisfied:

$$RT^{ME}(\delta N^T / \delta t + \delta N^M / \delta t) / (V^T + V^M) < RT^{ME}(\delta N^T / \delta t) / V^T, \quad 5$$

or the rate of change in ME N₂ partial-pressure for an ear with a mastoid is less than that for the tympanum. Dividing both sides of the equation by the constants R and T^{ME} and substituting the terms of the Fick perfusion equation [15] for $\delta N_{N_2} / dt$ yields:

$$((S_{N_2}^B Q^M (P_{N_2}^M - P_{N_2}^B) + S_{N_2}^B Q^T (P_{N_2}^T - P_{N_2}^B)) / (V^T + V^M) < S_{N_2}^B Q^T (P_{N_2}^T - P_{N_2}^B) / (V^T)) \quad 6$$

where $S_{N_2}^B$ is the N₂ solubility in blood, a constant, $P_{N_2}^B$ is the N₂ blood partial-pressure, a constant, and Q^T and Q^M are the mucosal blood perfusion for tympanum and MACS, respectively. Under the assumption of open communication between the tympanum and MACS, $P_{N_2}^M = P_{N_2}^T = P_{N_2}^{ME}$ or the partial-pressure of N₂ in MACS and tympanum is equal to that of the ME. Therefore, $(P_{N_2}^M - P_{N_2}^B) = (P_{N_2}^T - P_{N_2}^B) = (P_{N_2}^{ME} - P_{N_2}^B)$. Substituting these results in equation 6 yields:

$$((S_{N_2}^B (P_{N_2}^{ME} - P_{N_2}^B) (Q^M + Q^T)) / (V^T + V^M) < S_{N_2}^B Q^T (P_{N_2}^{ME} - P_{N_2}^B) / (V^T)) \quad 7$$

and by dividing out the constants, equation 7 reduces to:

$$(Q^M + Q^T) / (V^T + V^M) < Q^T / V^T. \quad 8$$

The mucosal blood perfusions are proportional to the respective surface areas, or:

$$(bA^M + cA^T) / (V^T + V^M) < cA^T / V^T, \quad 9$$

where A^M and A^T are the surface areas and b and c are constants of proportionality defined by Q^M/A^M and Q^T/A^T for the MACS and tympanum, respectively. As a first approximation, b is assumed to equal to c , and the equation reduces to:

$$(A^M + A^T) / (V^T + V^M) < A^T / V^T // b = c. \quad 10$$

Multiplying both sides of equation by V^T and dividing by A^T yields:

$$(V^T / A^T) ((A^M + A^T) / (V^T + V^M)) < 1 // b = c, \quad 11$$

or the N₂ exchange rate for the MACS±tympanum multiplied by the inverse of that for the tympanum is a critical ratio for MACS functioning as a ME gas reserve. Now, recognizing that larger MACS volumes are associated with lesser ME disease [2–6], under the defined hypothesis, increasing MACS volumes should be associated with a decreasing critical ratio as defined in equation 11.

Note that the derivation of equation 9 is also applicable to diffusion-limited gas exchange where the relevant equation becomes:

$$(bA^M / H^M + cA^T / H^T) / (V^T + V^M) < (cA^T / H^T) / V^T, \quad 9a$$

where H^M and H^T are the thicknesses of the MACS and tympanum mucosa between the air-mucosa boundary and the mucosal blood.

Analysis

All data were entered into Microsoft Excel for analysis. Linear regression was used to determine the relationships between the values of selected variables. Between-group/ear comparisons were done using a paired or two-group Student's t test as applicable. Throughout, the format average $\pm$ standard deviation is used to summarize the data.

RESULTS

The study population consisted of 14 females and 6 males, aged 26.3 ± 6.4 (range=20.4 to 40.5) years. All subjects were Caucasian. Six (30%) subjects reported a history of otitis media during childhood. For the 20 subjects, the right and left MACS volume ($r=.81$), surface area ($r=.87$) and SA/V ($r=.75$) were highly correlated as were the right and left tympanum volume ($r=.87$), surface area, ($r=.66$) and SA/V ($r=.86$), all correlations were significant at $p<.001$. Thus, the values for the right and left ears of these variables are not independent and potentially represent redundant information. Consequently the reported comparisons were done for the right and left ears, separately.

Table I reports the average and standard deviations for the left and right MACS and tympanum volumes, surface areas and SA/Vs for all subjects. Also reported are the absolute values of a paired Students t test and probability levels for left-right comparisons and those for a 2-group Student's t test for the MACS-tympanum comparisons. None of the left-right comparisons were statistically significant, but all of the MACS-tympanum comparisons were significant, with the MACS having larger values than the tympanum.

For both tympanum and MACS, the left and right surface areas were a direct linear function of their respective volumes (MACS: slope= 7.20 ± 2.37 , $r=.59$, $p=.006$ for the left ear and slope= 17.91 ± 1.33 , $r=.95$, $p<.001$ for the right ear; Tympanum: slope= 8.40 ± 1.50 , $r=.80$, $p<.001$ for the left ear and slope= 8.42 ± 1.59 , $r=.99$, $p<.001$ for the right ear). These relationships are displayed in figure 1 for the MACS (a) and tympanum (b), respectively. Note that the value for the left MACS of one subject (#13, 40 year old, male without a history of otitis media), but not for the other MACS or either tympanum, was a significant outlier with respect to the linear relationship characteristic of all other MACS. That MACS was also an outlier for the otherwise linear relationships for the paired values of the other variables. Visual examination of the CT scans for that ear showed an abnormally high distribution of large air-cells throughout the MACS, a geometry that was atypical of all other MACS studied. Consequently, the data for that MACS were not included in the calculations of the derived variables described below.

The left-right values for ME SA/V ($r=.79$), tympanum SA/V ($r=.81$) and the critical value ($r=.71$) were directly related and all correlation coefficients were statistically significant ($P<.001$). The average values of the ME SA/Vs were 16.99 ± 2.87 and 15.76 ± 2.99 , of the SA/Vs for the tympanum were 11.57 ± 1.24 and 11.8 ± 1.52 , and of the critical values were $1.46\pm.29$ and $1.34\pm.23$ for the left and right ears, respectively. The left and right SA/Vs for the ME were significantly greater than the left and right SA/Vs for the tympanums, $t=7.72$, $p<.001$ and $t=5.29$, $p<.001$, respectively. As shown in figure 2, the right and left critical values were significantly greater than 1 ($t=6.78$, $p<.001$ and $t=6.50$, $p<.001$) and independent of their respective MACS volumes. Correlation coefficients between the left and right ear critical values and respective MACS volumes were: $r=.09$, $p=.701$ and $r=-.052$, $p=.825$, respectively.

DISCUSSION

In this study, the surface area and volume of the MACS and tympanum were measured from CT scans over a wide range of MACS volumes using methods previously described for the MACS [13]. Using a simple mathematical model of perfusion-limited transmucosal N2

exchange and these data, we tested the hypothesis that the MACS could function as a ME gas reserve. The developed model requires that N₂ is the only gas not in equilibrium between ME and mucosal blood [10]; transmucosal N₂ (and other inert gases) exchange between the ME and local mucosal blood is perfusion-limited [9,12] and the MACS and tympanum are in open communication in the air-phase [14]. All of these requirements are supported by experimental data. For the most-simple model used to test the gas reserve function of the MACS, it was assumed that the blood perfusion/surface area of mucosa is similar for all compartments of the ME, though this has not been validated by experiment.

That model showed that the MACS will function as a ME gas reserve if the transmucosal N₂ exchange rate/volume is greater for the tympanum than for the ME. As shown, this relationship can be expressed as the ratio of the SA/V for the tympanum to that of the ME. A critical value of that ratio was determined to be 1 with all ratios <1 supporting a ME gas reserve function for the MACS and all values greater than 1 indicating that the MACS acts as a gas sink (i.e. increases the rate of ME pressure decrease). The MACS function as a ME gas reserve was not supported by the data, as measurement of that ratio was approximately 1.4. A second requirement for that function is that the ratio decreases with increasing MACS volume which was also unsupported by the data. Consequently, for this simple model of perfusion-limited gas exchange and the relevant measures made in this study, we reject our hypothesis that the MACS could function as a ME gas reserve. It should be noted that this result is also consistent with a diffusion-limitation for transmucosal N₂ exchange (see equation 9b).

However, the results for one study of humans breathing gas mixtures containing high concentrations of the inert gas, N₂O, reported a curvilinear inverse relationship between the rate of ME pressure increase caused by blood to ME gas transfers and mastoid volume [8], a result predicted by mathematical modeling of the MACS as a ME gas reserve [1]. In contrast, an experimental study on monkeys showed that the rate of transmucosal inert gas exchange was not affected by physical blockage of the mastoid Antrum [16]. The reason for these contrasting results is unknown but a reconstruction of ME geometry for the monkey and other primates is ongoing.

A limitation of the developed model is that it ignored the contribution of regional blood perfusion/surface area between and within compartments (i.e. assumption that the proportionality constants b and c are equal). Consequently, the MACS could still function as a gas reserve if the blood perfusion/surface area is much greater for the tympanum than for the MACS and if that rate is an inverse function of MACS volume. To date, these measurements have not been made. A second limitation is that all persons studied were adults while otitis media is a disease of children. The growth and development of the MACS has not been studied with respect to its geometry and it is possible that younger children may have a different MACS geometry that is more favorable to its possible function as a ME gas reserve. This is currently being studied.

In summary, tympanum, MACS and total ME geometry are characterized by a SA/V that is independent of volume and that the SA/V for the ME is greater than that for the tympanum. This result suggests that the MACS acts as a gas sink with a developed MACS increasing the rate of change in ME pressure between ET openings, a result inconsistent with the MACS functioning as ME gas reserve. This result depends on the blood perfusion/surface area for the two compartments, parameters that are currently unknown. Also unknown are the changes in MACS geometry during growth and development and these areas are priority goals for future research in this area of study.

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Figure 1.

The MACS (a) and tympanum (b) surface areas as a linear function of their respective volumes for the left (open squares) and right (closed circles) ears. Note the outlier for the one left MACS at volume=21.4 and surface area=69.1.

Figure 2.
The left (open squares) and right (closed circles) critical values as a function of MAC volume.

TABLE

Average (Avg) and Standard Deviation (Std) for the MACS and Tympanum Volume, Surface Area and the SA/V, and the Paired Student's t (t) and Probability Level (P) for Left-Right Comparisons and the Students t and Probability Levels for the left and right MACS-Tympanum Comparisons

			Avg	Std	Left vs Right			MACS vs Tympanum		
					t	p	t	t	p	p
Volume	MACS	Left	5.45	4.92	0.02	0.98	4.35			<.001
		Right	5.46	3.58			5.98			<.001
	Tympanum	Left	0.66	0.11	0.53	0.60				
		Right	0.67	0.13						
Surface Area	MACS	Left	82.77	59.76	0.97	0.37	5.63			<.001
		Right	88.91	60.25			6.02			<.001
	Tympanum	Left	7.59	1.17	0.88	0.39				
		Right	7.80	1.37						
SA/V ratio	MACS	Left	17.37	4.78	0.94	0.36	5.26			<.001
		Right	16.70	3.71			5.47			<.001
	Tympanum	Left	11.57	1.24	1.33	0.20				
		Right	11.80	1.51						