

PREDICTED EFFECT OF MORPHOMETRIC MEASUREMENT TECHNIQUE ON MATHEMATICAL DESCRIPTIONS OF MIDDLE EAR GAS EXCHANGE

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ABSTRACT

Development of a mathematical model of middle ear gas exchange could improve understanding of underlying physiology and possibly lead to improved treatments for Otitis Media. Previous models of gas exchange [1] used empirically determined gas exchange rates to predict transport and it has been suggested that these models can be improved by incorporating measured physiological and morphometric parameters, similar to work done by Weibel [2] in the lung. Measurement techniques for diffusional lengths (DL_{O_2} , DL_{CO_2} , DL_{N_2}) within the middle ear mucosa previously specified [3] may not account for the heterogeneous nature of capillary distribution throughout mucosal tissue. Here we test the hypothesis that alternative diffusional length measurement techniques improve the mathematically calculated gas exchange predictions.

Introduction

Otitis Media, or inflammation of the middle ear (ME), is the most commonly diagnosed childhood disease; yet the contribution to disease pathogenesis of the underlying ME gas exchange is not completely understood. The ME cleft is a bony non-collapsible body cavity which contains an air space compartment, and is internally lined with a mucosal layer that is perfused with blood. During OM conditions, loss of pressure regulation in the ME results in development of significant and painful underpressures due to gas exchange driven by a gradient between blood and ME concentrations of oxygen, carbon dioxide and nitrogen.

Previously, mathematical models were used in an attempt to better understand ME gas exchange [1]. These models were compartmental in nature, employing lumped transport parameters derived from measured exchange constants to predict gas exchange rates. Gas exchange in the lung was modeled extensively by Weibel [2] using a detailed analysis of morphometric parameters to determine pulmonary diffusing capacity. This approach was later applied by Ars and colleagues to modeling ME gas exchange [3], however their

definition of diffusional length was ad-hoc and may not properly represent diffusional resistance. The measurement was performed perpendicular to the long axis of the cross-section of the vessels, shown in Figure 1, accounting for gas exchange along a path from the vessel center of gravity to the ME air space. The “effective” diffusional length was an average of these distance measurements, and may not account for appropriate distribution of capillaries throughout the mucosa. There, inhomogeneities in capillary position and density could lead to significant differences in local mucosal gas exchange. An alternative approach that may better reflect gas diffusion patterns would involve analysis of a ME mucosa cross-section with an arbitrarily point selection along the ME/airspace interface to then determine the diffusional length as a direct line from the random point to the nearest capillary. This measurement can capture information on both capillary position and density by allowing areas of tissue with no capillary present to have (infinitely) high resistance to gas exchange. In this study we perform simulations of the diffusional fields in a model mucosa of the middle ear to evaluate which morphometric approach yields parameters that best reflect the diffusional resistance of the middle ear mucosa.

Methodology

Our model simulates gas exchange across cross sections of middle ear mucosal tissue by incorporating measured physiological material properties and utilizing a detailed model geometry (Figure 1). The steady-state diffusion equation as given in Eqn. 1,

$$\alpha D \nabla^2 P = M \quad (1)$$

was employed to calculate gas exchange throughout the two-dimensional system based on partial pressure gradients between local blood gas concentrations in the capillary and those in the ME air space. The model assumes no species flux at the bone interface and a uniform gas tension in the ME air space. The detailed model

simulations based on Eqn 1 are compared to predictions based on a simple one-dimensional diffusion model:

$$\alpha D \frac{\partial P}{\partial x} = M \quad (2)$$

The simple one-dimensional model is evaluated using two different measures of the average diffusion distance: DL(a), as defined and used by Ars et al and DL(b), the parameter we propose as more reflective of gas diffusional resistance.

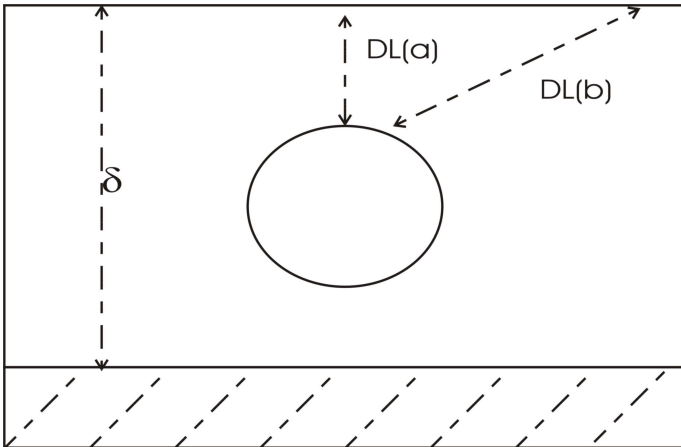


Figure 1. Model geometry shows cross section of ME tissue with capillary (in center). The representative section is bounded by bone along the bottom and the tissue/airspace interface along the top. A) Diffusional length measurement made by Ars et al, showing linear pathway between capillary and ME air space interface. B) Example of Diffusional length hypothesized to occur between random point along ME air space interface and capillary.

Results

A series of simulations were performed using random capillary placement within the mucosal geometry. Based on the defined model geometries investigated, the diffusional resistance predicted by the detailed simulations (Eqn 1) was better predicted by the simpler one-dimensional model (Eqn 2) using our alternative morphometric approach based on the diffusional distance parameter DL(b) compared to the approach proposed by Ars et al. An example of the diffusional fields within the mucosa predicted by the detailed simulations is shown in Figure 3.

Discussion

Understanding gas exchange in the middle ear in normal and pathological states (e.g. Otitis Media) can be improved by morphometric studies aimed at correlating changes in mucosa geometry with alterations in gas exchange. These morphometric approaches are most easily done by measuring effective diffusional distances and using these distances as a correlate of the overall diffusional properties of the middle ear mucosa. In this study we have used detailed simulations of gas exchange in a model of the mucosa to suggest a morphometric diffusion distance parameter which optimally

reflects diffusional gas exchange between the middle ear air space and the mucosa.

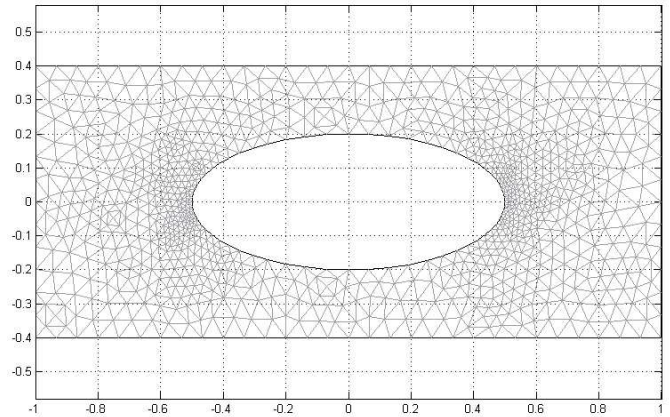


Figure 2. Finite Element Mesh Network Employed in Detailed Gas Flux Calculation.

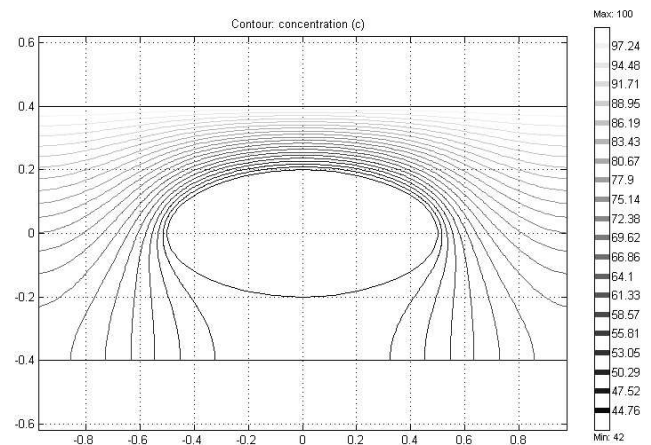


Figure 3. Contour Plot of Model Predicted Oxygen Diffusional Field Throughout Mucosa.

References

1. Doyle WJ. A mathematical model explaining the sources of error in certain estimates of gas exchange constants for the middle ear. *Ann Otol Rhinol Laryngol*, 2000,109:533-41.
2. Weibel D., *The Pathway for Oxygen*. Harvard Univ Pr., 1984.
3. Ars B., Wuyts F., Van De Heyning P., Miled I., Bogers J., and Van Marck E. Histomorphometric Study of the Normal Middle Ear Mucosa. *Acta Otolaryngol*. 117: 704-707, 1997.

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