NONINVASIVE DETERMINATION OF PERFUSED BLOOD VESSEL DIMENSIONS USING A PRESSURE-DIAMETER RELATIONSHIP

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ABSTRACT- Based on the decisive effects of the hemodynamic and mechanical environments on the development and remodeling of arteries in vivo, several groups have cultured tissue-engineered vessels and excised vessels in various mechanically active perfusion systems. Accurate estimates of vessel dimensions are required to obtain accurate estimates of the applied forces and resulting stresses needed for such studies. The measured pressure drop along the length of the vessel could be used to calculate the inner diameter, but practical considerations, including the modest accuracy of many pressure transducers, limit this approach. Here we show that when real-time measurements of the pressure drop and the outer diameter during a vasoactive event are fit to a theoretical model, offset errors in the pressure measurement can be compensated for and estimates of vessel wall area with an average error of 4.1% are achieved.

***Keywords*-Vascular biology, biomechanics, vessel geometry, noninvasive measurement**

INTRODUCTION

Several groups have cultured tissue-engineered vessels in mechanically active perfusion systems, leading to the consensus that mechanically active environments benefit engineered vessels (Ziegler and Nerem, 1994; Niklason et al., 1999; Seliktar et al., 2000). Accurate estimates of applied forces and resulting stresses and strains could facilitate the design and interpretation of such studies and characterization of engineered vessels.

Several sets of equations are available to calculate stresses and strains in the vessel wall from transmural pressures and vessel dimensions. A primary limitation in applying these equations to rapidly-growing/remodeling tissue-engineered vessels is the accuracy of (preferably noninvasive) measurements of vessel dimensions. Precise measurements of the outer diameter, D_o, can be acquired noninvasively in real-time with laser scanning systems. By assuming that cross-sectional area of the artery wall (A_x) was constant, Brant et al. (1988) calculated the inner diameter w.r.t., $D_i(t)$, from $D_o(t)$.

The assumption of constant A_x likely will not hold over the long-term culture of excised arteries or engineered vessels. Therefore, independent measurement of $A_x(t)$, $D_i(t)$ or wall thickness, h(t), is required, but an inexpensive, completely noninvasive, off-the-shelf system does not exist. Here we develop and evaluate a technique that uses the pressure drop from a point upstream to a point downstream of a perfused vessel and $D_o(t)$ to calculate A_x, thereby providing $D_i(t)$, and h(t).

MATERIALS AND METHODS

The perfusion system has been described in detail (Clerin et al., 2002) and consists of a peristaltic pump that pushes perfusion medium through the blood vessel at a constant rate. Extracorporeal pressure probes located upstream and downstream of the vessel are attached to the corresponding Triton Cardiovascular Measurement Module. A laser scanning system measures $D_o(t)$ of the vessel. Data are digitized and recorded on a PC using LabView software.

The pressure drop, ΔP, due to fully-developed laminar flow of a Newtonian fluid through a straight, constant inner diameter, circular tube, is given by the Hagen-Poiseuille law. To ensure fully-developed flow, a length of constant-diameter tubing is typically inserted between each pressure probe and the artery. Therefore, the total pressure drop between the pressure transducers, $\Delta P_T(t)$, is the sum of the pressure drop along the vessel and other pressure drops. For a given constant flow system, the sum of these other pressure drops is fixed, ΔP_f, or

$$\Delta P_T(t) = \Delta P_f + \frac{128Q\mu L}{\pi} \cdot \frac{1}{D_i^4(t)} \qquad (1),$$

where Q is volumetric flow rate, μ is viscosity, L is length of the tube, and D_i is inner diameter. The inaccuracy of typical in-line pressure probes over time (with up to 2 mmHg drift/day) limits the usefulness of (1) for calculating D_i. Since A_x need not be constant over long times, eliminating D_i from (1) and solving for A_x yields

$$A_x(t) = \frac{\pi}{4}\left(D_o^2(t) - \sqrt{\frac{128Q\mu L}{\pi(\Delta P_T(t) - \Delta P_f)}}\right) \qquad (2).$$

Equation (2) could be used to calculate A_x using real-time data for $\Delta P_T(t)$ and $D_o(t)$ and readily-measured constants (Q, μ, L, and ΔP_f), but the accuracy of the calculated A_x still suffers from measurement error associated with $\Delta P_T(t)$. Assuming the primary source of error is an offset error, ε_p, at a given time the measured pressure, $\Delta P_M(t)$, is related to $\Delta P_T(t)$ by $\Delta P_M(t) = \Delta P_T(t) + \varepsilon_P$. Substituting this equation into (2) yields,

$$A_x(t) = \frac{\pi}{4}\left(D_o^2(t) \;\; - \sqrt{\frac{128Q\mu L}{\pi(\Delta P_M(t) - \varepsilon_P - \Delta P_f)}}\right) \qquad (3).$$

Over short times, the vessel wall is nearly incompressible so $A_x(t)$ should be constant. Therefore, ε_P can be estimated using (3) by minimizing Std.$[A_x(t)]$/Avg.$[A_x(t)]$ over a short time during which $\Delta P_M(t)$ and $D_o(t)$ are changing (e.g., a vasoactive event). From the average A_x, (1) is used to calculate $D_i(t)$, from which the wall thickness, h(t), is calculated; $h(t) = [D_o(t)-D_i(t)]/2$.

Nine porcine arteries were perfused with a constant flow of 120 ml/min. A vasoactive event was induced in each artery (100 mM KCl; PBS). Mass of the vessel/(vessel length*density) (1.06 g/cm^3) yielded an invasive measure of the average A_x.

RESULTS

All vessels contracted in response to KCl addition as evidenced by increased $\Delta P_M(t)$ and decreased $D_o(t)$. A sample response is shown in Figure 1A from which A_x is calculated with or without incorporating the effects of ε_p (Figure 1B). Incorporating the effects of ε_p substantially improved the accuracy of the calculated A_x, reducing the average error from 10.2% to 4.1% (Figure 2).

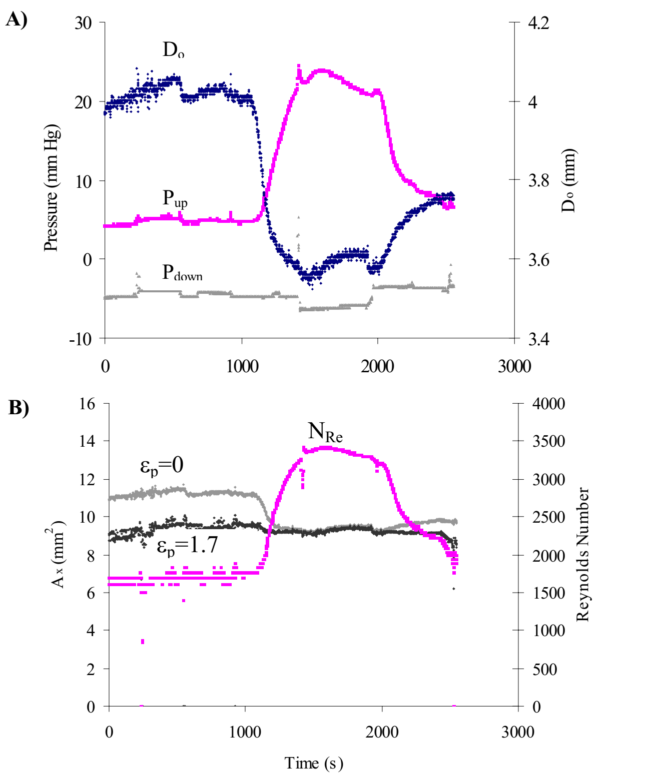

Figure 1. Panel A: Upstream pressure, downstream pressure, and outer diameter as a function of time for a carotid artery (100 kg pig). Panel B: Calculated A_x with no error correction of the measured pressure (ε_p=0) and with ε_p chosen to minimize the stdev/variation in the calculated A_x (ε_p=1.7 mmHg). N_{Re}>2300 for 1175 ≤t ≤2291 sec.

DISCUSSION

We have developed a method to estimate $D_i(t)$ from $D_o(t)$ and $\Delta P_T(t)$ by assuming steady, fully-developed, laminar flow of a Newtonian fluid through an artery with uniform circular cross section that varies only with time. Based on estimated $D_i(t)$, Reynolds numbers (N_{Re}) for all vessels exceeded the oft-cited threshold of 2,300 during at least a portion of the contraction (Figure 1B). The fact that A_x values calculated from data corresponding to N_{Re}<2,300 agreed well with those calculated for N_{Re} > 2,300 (e.g., Figure 1B) suggests that flow remains laminar. This belief is consistent with reports of laminar flows in perfused tubes for N_{Re} up to 11,000 and higher (Fung, 1997) and, at least transiently, up to 9,000 in arteries in vivo (Nerem, 1972).

Though the proposed model is very simple and does not take into account all of the complexities of a real system, it provides reasonably accurate estimates of vessel geometry from easily obtained, noninvasive measurements. This technique could be used to noninvasively monitor the growth of tissue-engineered vessels and the remodeling of excised vessels or in conjunction with existing models to calculate stresses in the vessel wall.

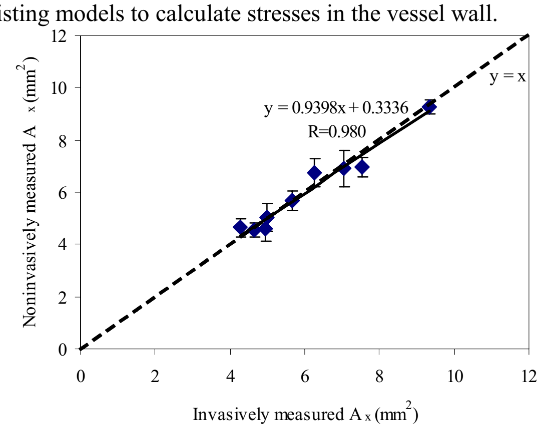

Figure 2. Noninvasively measured A_x versus invasively measured A_x. The dashed line (y=x) would represent a perfect agreement between the two measurements.

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