INTRODUCTION
Generation of a complete map of arterial wall mechanical properties can improve treatment of cardiovascular diseases via contributions to design of patient specific vascular substitutes used to alleviate atherosclerosis and stenoses, which are predominant in arterial pathways (i.e., abdominal aorta, carotids, or femoral arteries). Clinically useful estimation of arterial properties from patient data requires both efficient algorithms and models that are both complex enough to capture clinically important properties and simple enough to allow rapid computation. In this study, we used mechanical models accounting for both elastic and viscoelastic wall deformation to analyze how vessel properties and associated model parameters vary with artery type. It is known that for the aorta wall, deformation is dominated by nonlinear elastic dynamics, while for the smaller vessels (e.g. the carotid artery) deformation is dominated by viscoelastic responses. The latter is correlated with composition of the vessels; the aorta contains significantly less smooth muscle cells (~40%) than the carotid artery (~60%), and has significantly more elastin (see Fig 1).

To predict vessel properties we used a two-parameter elastic model, a four-parameter Kelvin viscoelastic model, and a seven-parameter extended viscoelastic model that relate blood pressure and vessel area. We validated these models using experimental data from in-vitro measurements of vessel diameter and arterial blood pressure. To understand how the elastic and viscoelastic properties (represented by the model parameters) vary across vessel sites we compared two approaches: an ordinary least squares (OLS) approach that used pressure as an input to predict mechanical properties minimizing the OLS error between computed and measured values of vessel area, and a total least squares (TLS) method that used an optimal control formulation minimizing the TLS error including both area and pressure. Finally, to analyze results we employed standard statistical techniques.

METHODS
Experimental Methods
Eleven healthy Merino sheep (2 years old), weighing 25-35 kg, were included in this study to evaluate the biomechanical properties of the wall at 7 locations along the large and medium sized arteries (Fig 1B). Vessel segments (6 cm, measured in-vitro) were obtained in-vitro, and mounted in the circulatory mock (Fig 1A), stretched to their in-vivo length. Wall-thickness and zero-pressure radius were measured. Once mounted, blood pressure and vessel area were measured under physiological conditions induced by a Jarvik Heart. Pressure and area data were sampled at 200 Hz and stored for off-line analysis. Details of the experimental protocol can be found in [1].
Fig 2. A: Circulatory mock including a pneumatic pump (PP), a perfusion line connected to the chamber holding the vessel segment, a resistance modulator (R) and a reservoir. The reservoir was filled with thermally controlled Tyrode’s solution (A). The pressure (P) was measured with a transducer, and the diameter (D) was measured with a pair of ultrasonic crystals and a sonomicrometer. B: Vessel segments include 4 aortic segments (S1-S5), brachiocephalic trunk (S6), carotid (S7), and femoral (S6) arteries.

Model & Governing Equations

Data were analyzed using an elastic model (a), a Kelvin viscoelastic model (b), and an extended model viscoelastic model derived from Fung’s quasilinear viscoelasticity (QLV) theory (c) [2,3,4]. The models relate vessel area $A$ and blood pressure $p$. In the equations below, $\varepsilon$ denotes strain, $E$ denotes an elastic modulus, $h$ denotes wall thickness, $A_0$ denotes the zero-pressure area of the stretched vessel, $A_1$, $A_2$, $B_1$ are amplitudes, and $\tau_1$, $\tau_2$, $b_1$, $b_2$ are the viscoelastic relaxation factors.

(a) $p = \frac{E h}{r_0} \varepsilon$

(b) $\tau_1 \frac{d \varepsilon}{dt} + \varepsilon = \frac{r_0}{E h} \left( p + \gamma \frac{dp}{dt} \right)$, where $\gamma = 1 - \frac{A_0}{A}$.

(c) $\varepsilon = \left( \varepsilon(0) - \frac{r_0}{E h} p(0) \right) \left( B e^{-\gamma h} + (1 - B) e^{-\tau_2 h} \right) + \frac{r_0}{E h} p(0) + \frac{r_0}{E h} \int \left[ 1 - A_0 e^{-(\gamma h) \gamma} - A e^{-(\gamma h) \gamma} \right] \frac{dp}{dy} dy.$

Model parameters were computed using a standard simplex nonlinear optimization method that used blood pressure as an input, minimizing the ordinary least squares (OLS) error between computed and measured values of vessel area. Results revealed a nonconstant variance; thus assumptions for the OLS prediction were violated. We also showed that a TLS approach estimating model parameters using an optimal control formulation allowed prediction of parameters avoiding the constant variance bias. The latter has the advantage that of allowing computation of the error using both pressure and area as well as weighing all points in the time series equally. Furthermore, we found (not shown) that model parameters varied with location. Nonlinear stiffening, dominant in the aorta, could not be predicted by the models analyzed. Therefore, we propose that improved models developed to predict patient specific properties should include both nonlinear elastic and viscoelastic dynamics.

RESULTS

Results from computations are shown in Fig 2. We observed that the Kelvin model predicts dynamics of the data significantly better than the elastic model. Furthermore, using statistical comparison of the two models, we showed that the extended QLV model predicted data better for the carotid artery, where the deformation response is dominated by viscoelasticity (Fig 1), while the QLV model did not improve prediction of deformation in the aorta, which displays more complex nonlinear responses. It should be noted that to visualize these results it is essential that deformation is depicted using a parametric pressure-area plot, rather than a time-series plot (not shown). Results also showed that zero-pressure radius and wall thickness (measured) decreases away from central arteries (e.g. the aorta) while wall stiffness increases towards the periphery (i.e., toward the carotid artery).

CONCLUSIONS

Incorporating viscoelasticity in the model significantly decreases the least squares error and describes hysteresis observed in the data. We have shown that model parameters can be estimated using an OLS formulation that used blood pressure as an input to predict area, but that assumptions (constant variance) needed to formulate the problem were violated. We also showed that a TLS approach estimating model parameters using an optimal control formulation allowed prediction of parameters avoiding the constant variance bias. The latter has the advantage that of allowing computation of the error using both pressure and area as well as weighing all points in the time series equally. Furthermore, we found (not shown) that model parameters varied with location. Nonlinear stiffening, dominant in the aorta, could not be predicted by the models analyzed. Therefore, we propose that improved models developed to predict patient specific properties should include both nonlinear elastic and viscoelastic dynamics.

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