Dynamic blood flow and wall shear stress in pulmonary hypertensive disease

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Rationale
Pulmonary hypertension (PH) is a debilitating condition with a range of contributing factors, making it difficult to assess and manage. Common to most types of PH is a remodelling of the medial and intimal layers of the vessel wall, which can progress to complete occlusion of the pulmonary arteries, fibrosis and lesions. Progression of remodelling is difficult to assess from clinical data (imaging and haemodynamic data) as it typically has an effect on small pulmonary arteries. Predicting the level of remodelling present in a patient from clinically obtainable data would allow stratification of patients to optimise treatment in PH. In this study we present a pulsatile model of blood flow in the pulmonary arteries of individuals which incorporates the key remodelling steps involved in PH and demonstrate how it can be used to assess disease progression.

Geometric Model
An anatomically based geometric model representing the lungs of an individual [1] was created by:
- Segmenting the lungs, lobes, and central airways, arteries and veins from CTPA images.
- Volume-filling airways, arteries and veins to the acinar (gas exchange unit) level.

Admittance of the pulmonary arteries

Terminal elements:
1. Characteristic admittance (γ) is calculated for each terminal element
   \[ Y = \frac{A}{\nu} \times \frac{1}{\nu^2} \]  
   where A is the cross sectional area of the vessel, ρ is blood density, c is the speed of sound in that vessel, and υ is a viscous factor, dependent on Reynolds’s number [2].
2. Boundary conditions are set terminal elements. By assuming that venous admittance is negligible, acinar admittance is calculated using a previously published description of the acinar ‘resistance’ vessels [3].
3. A reflection coefficient (R) is set at each terminal element, this is assumed to be R = 0.

Pressure and flow though the tree
Pulmonary artery pressure is defined as a Fourier decomposition of the pressure waveform in that artery and pressure (p) and flow (q) are then defined as:
   \[ p(t) = \sum_{n=-\infty}^{\infty} P_n \cos(n \omega t) \]
   \[ q(t) = \sum_{n=-\infty}^{\infty} Q_n \cos(n \omega t) \]

Stepping backward through the tree from terminals:
1. The characteristic admittance of each element is calculated using equation (1).
2. The effective admittance (γe) of an element is calculated from the admittance of its two daughters (γ1 and γ2), its characteristic admittance, vessel length l, and frequency of the input waveform as:
   \[ γ_e = \frac{1}{\sum_{n=-\infty}^{\infty} γ_n \cos(n \omega l)} \]
3. The reflection coefficient of an element is defined as:
   \[ R = \frac{Q_1 - Q_2}{Q_1 + Q_2} \]

Pulmonary Haemodynamics: Cardiac catheterisation is a common part of the clinical work-up in pulmonary hypertension. In chronic disease peripheral remodelling means that CT estimated occlusion is not sufficient to elevate model predicted pulmonary artery pressures to clinically measured values. By comparing predictions of pressure magnitudes at each step of arterial remodelling we can estimate disease progression in an individual.

Conclusions
We have developed a computational model of the propagation of pulmonary arterial pressure pulses in anatomically based models of the lungs of an individual. This model includes a staged progression of blood vessel remodelling typical in pulmonary hypertension. The model predicts significant increases in arterial pulse pressure and mean wall shear stress in the peripheral arteries with remodelling. As arterial remodelling is associated with both shear stress magnitude and oscillatory changes in shear this suggests that vessel remodelling in early stages of pulmonary hypertension contribute to a transmission of shear stress proximally in the arterial tree and so to a ‘vicious cycle’ of remodelling.

Our model predictions can be related to an individual patient’s state via clinical measurements made routinely in patients with pulmonary hypertension, hence providing the potential to assess the level of vessel remodelling in an individual when planning therapies.

References & Acknowledgements
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