Mechanical Characterisation and Modelling of Thrombus Material

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Abstract

The enormous prevalence of vascular disease and stroke, has fueled the development of minimally invasive treatments. Mechanical thrombectomy, where the thrombus is removed from the diseased site, is becoming the new standard of care for stroke recovery.

Defining the material properties of thrombus material has many potential benefits for the development of treatment devices. To-date, this material definition has not been adequately investigated. The aim of this research is to generate a better understanding of the biomechanical properties and viscoelastic behaviour of thrombus material. It also explores the use of finite element analysis to create a viscoelastic model of thrombus material.

1. Introduction

A thrombus or blood clot is a solid mass, made up of a network of fibrin, platelets and other blood components [1]. Blood clots can form in the heart or blood vessels through various pathways, for example as a result of exposed tissue factor from vascular injury, as a result of low flow/stasis, or in very high shear flow conditions. Embolization of cardiac or vascular originating blood clots causing an occlusion of the neurovasculature is the major cause of stroke, accounting for 85% of all stroke.

The composition of blood clots (e.g. the fibrin:cellular ratio) will vary depending on the conditions in which the clot is formed, or the age of the clot before it embolizes.

The enormous prevalence of vascular disease has led to the development of minimally invasive treatments such as stent angioplasty, where the implanted stent scaffolds the occluded artery and restores patency [2], and embolic filtration, where the filter captures embolic (thrombus) material in the blood stream and thereby minimises stroke risk.

Mechanical thrombectomy, where the thrombus is removed from a vessel, is becoming the new standard of care in stroke therapy [2]. Therefore, defining the material properties of thrombus has obvious implications for the development of treatment devices. To-date, this material definition has not been adequately investigated.

Thrombus material has been found to be incompressible, non-linearly elastic and inhomogeneous [3]. It has been shown to be highly heterogeneous, with both fibrous regions and cellular regions [4]. Although some experimentation has been performed, the viscoelasticity and rupture behaviour of the material is still not fully understood and model development has been extremely limited. Therefore, the aim of this research is to generate a better understanding of the biomechanical properties and viscoelastic behaviour of thrombus material. This data will be used to formulate an accurate material (constitutive) model for thrombus.

2. Methods

2.1. Experimental Methods

Thrombus analogue material was generated (performed in collaboration with Neuravi Ltd, using their recently developed thrombus analogue generation protocols) [5]. The analogue material samples were generated to represent a range of overall thrombus tissue types, with varying red blood cell content.

Uniaxial unconfined compression testing was used to carry out a range of experiments to determine the viscoelasticity and rate-dependence of the material (Figure 1). The testing was performed using a 10N load cell on a Zwick biaxial testing machine.

![Figure 1: Image illustrating the compression test setup](image)

Firstly, stress-relaxation testing of the material was carried out to determine if the material was viscoelastic. A strain of 30% was applied to the material and it was held constant for 1000s. Secondly, the rate-dependence of the material was investigated by applying a strain of 30% at strain rates of 1%, 5%, 10% and 15% per second (Figure 2).

Uniaxial tensile testing was also carried out. Dogbone-shaped specimens of the analogue clot material were produced. A 100N load cell was used and samples
were loaded at a strain rate of 10mm/min. The test was run until failure occurred.

2.2. Computational Methods

The experimental results were used to develop a constitutive model for the material for finite element analysis (FEA). A two-arm generalized Maxwell model, also known as the Wiechert model, was selected to represent the material’s viscoelasticity. The stiffness of the material, $E(t)$, is defined as the sum of the stiffness of the isolated spring plus the stiffness of each of the Maxwell spring-dashpot arms:

$$E(t) = E_\infty + \sum_j E_j e^{-t/\tau_j}$$

(1)

where $E_\infty$ is the long-term modulus of the material once it is completely relaxed, and $\tau_j$ is the relaxation time.

The model was calibrated to the experimental stress-relaxation results by determining appropriate values for the material constants $E_0$, $E_3$, $E_2$, $\tau_1$ and $\tau_2$. The model was then related to a Prony series, so that stress relaxation experiment could be simulated in Abaqus using Prony series viscoelasticity.

A two-parameter Mooney-Rivlin model was also used to capture the hyperelasticity of the material. The Cauchy stress for a Mooney-Rivlin hyperelastic material under uniaxial compression is given by:

$$\sigma = C_{10}(\lambda^2 - \lambda^{-1}) + C_{01}(\lambda - \lambda^{-2})$$

(2)

where $C_{10}$ and $C_{01}$ are the material constants and $\lambda$ is the stretch.

An inverse FE method, as proposed in [6], was used to optimise the constitutive parameters. An FE simulation replicating the experiment, using a single-element unit cube model, was performed and the net force–displacement curve was computed after each simulation. A least-squares regression method was implemented in MATLAB to minimise the error between the FE and experimental force-displacement curves until a good fit was achieved.

3. Results

Figure 2: Plot of Stress versus Strain comparing the experimental results with the results from the FE simulation.

Figure 3 shows that the optimised constitutive parameters accurately captured the experimental results.

4. Discussion

The thrombus material was found to exhibit a viscoelastic response. Therefore, a combined hyperelastic and viscoelastic constitutive model was implemented to predict the material behaviour.

The optimised material parameters accurately captured the material response under compressive loading and unloading conditions. This indicates that the constitutive model is suitable for implementation in other geometries.

The results from the uniaxial tensile testing indicate that the material is highly elastic as it can reach very high strains before failure. There is also little plasticity indicated.

Clot types also vary depending on their constituents. The results above illustrate the behavior of one type of clot analogue. In the future, the properties of a range of clot types with varying constituents will be investigated and compared.

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6. References