Computational Modelling of Magnetic Resonance Elastography Shear Wave Behaviour through Atherosclerotic Plaque with Disease Development

Lauren E. J. Thomas-Seale, Pankaj Pankaj, Neil Roberts and Peter R. Hoskins

Abstract—Assessment of the rupture risk of plaque is commonly made via imaging of the lumen reduction. However it is known that this is an imperfect criterion and that other features, such as plaque stiffness, may be more relevant. Magnetic Resonance Elastography (MRE) estimates the stiffness of tissues using inversion algorithms applied to the displacement of the tissue, measured in response to the induction of a shear wave from an external actuator. An idealised diseased vessel, embedded in an arbitrary tissue, was created to simulate the application of MRE to atherosclerotic plaque. The behaviour of shear waves propagating through an atherosclerotic plaque with development of the stenosis and lipid pool size was investigated. There is a local increase in wave displacement and decrease in wavelength, through a plaque containing a lipid pool compared to a purely fibrotic plaque. The amplitude of the wave through the lipid increases with lipid pool volume. This suggests that shear waves used in MRE may be able to differentiate between lipid pool sizes within an atherosclerotic plaque. The behaviour of shear waves through relatively large and small lipid pools needs further investigation. Experimental validation of the technique is required.

Index Terms—Atherosclerosis, finite element analysis, magnetic resonance elastography, plaque rupture, shear waves.

I. INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in the world (29%) and in the UK (38%) [1]. CVD is the broad title for a wide range of afflictions, including stroke and coronary heart disease, the majority of which are caused by atherosclerosis.

The most severe symptoms of atherosclerosis are a consequence of plaque rupture and the restriction of blood flow. The decision to surgically intervene is dependent on the percent stenosis, the ratio of the minimum diameter of the stenosed artery to an equivalent healthy section, measured by ultrasound or angiography. It is generally accepted that a carotid endarterectomy is beneficial for symptomatic carotid stenosis between 70-99% [2]. However studies have demonstrated that this is an imperfect criterion. The European Carotid Surgery Trail (ESCT) found that the absolute increase in benefit of surgery, for stenosis greater than 80%, was only 11.6% [3]. This translates to nine surgical interventions to allow one patient to be stroke free after 3 years [3].

The risk of plaque rupture is a trade off between the intrinsic properties of the plaque against the forces, from the blood, acting upon it [4]. It has been established that unstable plaques which are likely to rupture have the similar morphology of a thin fibrous cap and a large lipid core [5]. In these instances the lipid core is of such a low stiffness that the external forces are primarily supported by the fibrous cap and when its strength is exceeded, the plaque ruptures [5]. However composition is difficult to assess using imaging and the composition alone is not sufficient information to determine the strength of a plaque since the properties of the lipid and fibrous cap can vary [6], [7].

Magnetic Resonance Elastography (MRE) is an elasticity imaging technique, which utilizes the temporal and spatial resolution of MRI to quantitatively measure the displacement within a tissue in response to the excitation of harmonic propagating waves [8]. Phase contrast MRI measures low frequency shear waves in the region of 50-1000Hz [9]. These waves are induced in the desired tissue using external actuation, of which a range of methods may be employed [10], [11], [12]. The displacement data is then inverted into mechanical properties by a process known as wave inversion, of which again there are a range of techniques [9].

MRE has the potential to non-invasively assess the stiffness of an atherosclerotic plaque and hence provide an indication of the risk of rupture. To date there is extremely limited literature available on the application of MRE to arteries; to identify wall stiffness [13], [14], [15], [16] and stenosis size using reflected and transmitted waves [13]. There has been no research published involving MRE analysis of plaque stiffness.

An idealised computational model has been developed to investigate the concept of applying MRE to diseased arteries, in a system where all the variables may be controlled. The rationale is that the model will allow understanding of the limitations of MRE concerning quantification of plaque stiffness and provide a means of optimising the technique. The aim of this paper is to examine the change in MRE shear wave behaviour through atherosclerotic plaque, with growth of stenosis and lipid pool size.

II. METHOD

MRE simulations were conducted using the implicit, dynamic solver of the solid modelling software ABAQUS. The simulations were run with idealised stenosis geometries of 60%, 70% and 80% and within these a variety of lipid pool volumes. The model was meshed using quadratic and linear tetrahedron, hybrid elements.
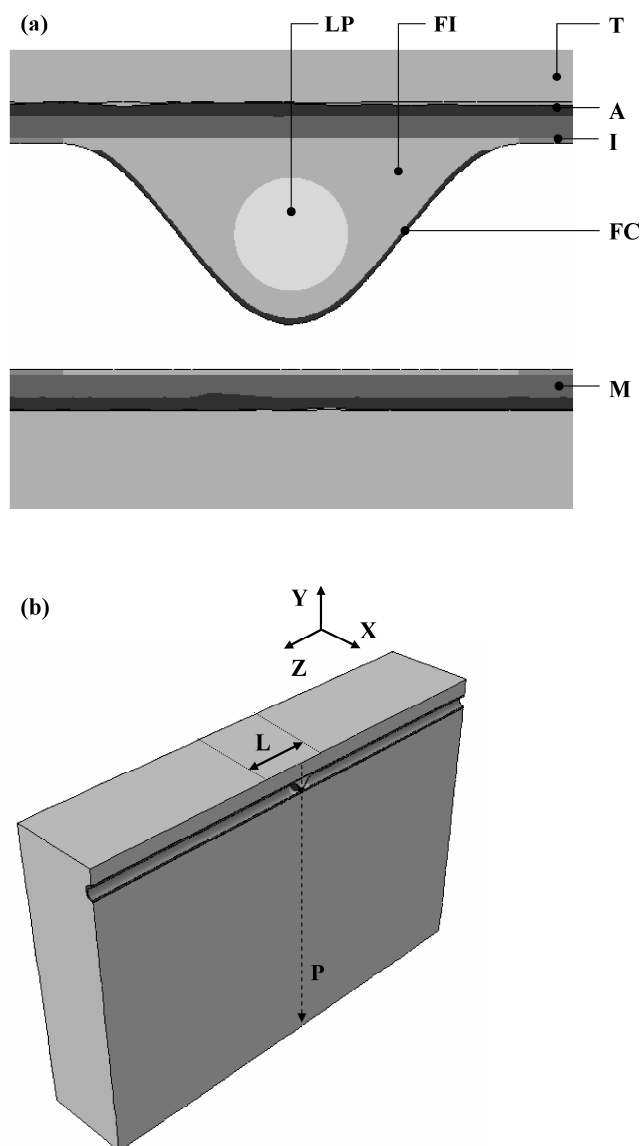

Fig. 1. (a) A sectional view of the model showing a) idealised plaque geometry; 80% stenosis and 25mm^3 lipid pool and (b) the load area, direction and analysis path. References are as follows: surrounding tissue T, adventitia A, media M, intima I, fibrotic intima, FI, fibrous cap FC, lipid pool LP, load L and the analysis path P

Idealised atherosclerotic plaque geometries were created using the computer aided design software RHINO. An idealised stenosis was implanted in an otherwise healthy three layered, straight vessel; artery layer diameters and thicknesses were taken from [17]. The 100% eccentric stenosis was modelled using the equations outlined in [18] and the length was scaled from the idealised model described in [19]. The lipid pool was modelled as a sphere surrounded by fibrotic intima and the variation in size was modelled in terms of volume. Fig. 1 (a) illustrates a sectional view through an example of the idealised plaque geometry; 80% stenosis and 25mm^3 lipid pool. The vessel was embedded in a rectangular block of tissue to replicate the transmission of MRE shear waves in-vivo.

The material properties of the healthy and diseased vessel components were taken from [20]; an isotropic, hyperelastic, neo-hookean model. The lipid pool was modelled as a very low stiffness, incompressible, solid [20]. The surrounding tissue was modelled with an arbitrary stiffness and a linear elastic constitutive relationship [21]. All densities were taken as the mean value of soft tissue [21].

The replication of the waves generated by the MRE actuator was achieved by applying a 100hz sinusoidal shear load with an amplitude of 0.5N, to an area of nodes above the stenosis. The external boundary conditions were limited to fixing the surrounding tissue at the axial ends of the vessel. Fig. 1 (b) shows an isometric, axial sectional view of the model, the location of the load nodes, the global coordinate system and direction of the applied load.

III. RESULTS AND DISCUSSION

The one dimensional analysis path P, through which all the results are taken is shown in Fig. 1 (b). Results were taken whilst the simulation was in a transient state. All results are based on the component of displacement in the z direction, the direction of the applied load, and focus on the area around the plaque. At present, the fluid in the lumen has been omitted, under the assumption that fluids do not transmit shear waves [21]. The lumen is depicted in the results as an area of zero displacement.

Fig. 2 displays the z displacement of the wave through two models of a 70% stenosis with different plaque compositions. One is a fully fibrous plaque without a lipid pool and the other is a plaque containing a relatively large lipid pool of 35mm^3. The results are taken at an analysis time of 0.002s. These two models represent plaque with a high and low risk of rupture. The presence of the low stiffness lipid pool in the plaque, as opposed to the fibrotic tissue, creates an area of increased displacement in the shear wave. It appears as a local wave passing through the lipid volume, with a significantly reduced wavelength. This conforms well to MRE theory in which wavelength is dependent on local elasticity properties [9].

As the volume of the lipid pool is increased, the amplitude of this local wave increases. Fig. 3 displays the maximum amplitude of the wave as it passes through various volumes of lipid pool within an 80% stenosis. The maximum amplitude was taken as the maximum deflection of z displacement passing through the lipid pool, compared to the

wave passing through a geometrically comparable, fully fibrous plaque. The results were taken at an analysis time of 0.002s. The majority of simulations demonstrate an increase in wave amplitude as the volume of the lipid pool increases. However there appears to be threshold values above and below which this trend does not continue. At $10mm^3$ and below there is very little additional motion in the lipid pool compared to surrounding tissue. Above $35mm^3$ the amplitude of the wave begins to decrease with increasing lipid pool size.

As the volume of the lipid pool is increased, the wavelength of the local wave increases in line with the lipid pool diameter. This does not agree with MRE theory which relates wavelength to the local elasticity properties [9]. Literature suggests that MRE shear waves at relatively low frequencies limit resolution [11], [22]. Further work will be conducted at much higher wave frequencies with the aim of improving the accuracy of this technique in line with MRE literature.

The z displacement of the wave with an increasing stenosis size was also investigated. Through a stenosis of 60%, 70% and 80%, containing a similar size of lipid pool, the behaviour of the wave was relatively similar. Future development of the idealised model will include incorporating the effects of fluid in the lumen which may highlight, more realistically, the distinction between the wall and lumen and potentially allow the calculation of the stenosis size. It should be noted that during an in-vivo MRE
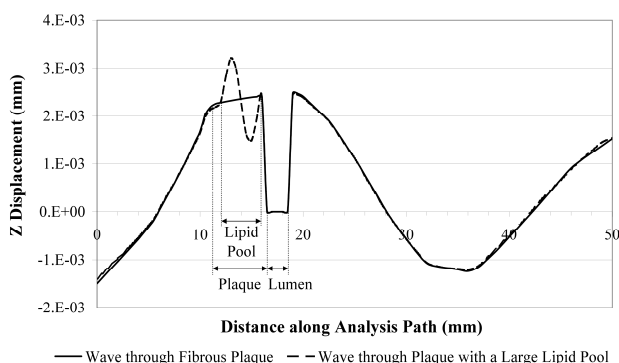
scan in addition to the phase-contrast images a structural image is also created. This may offer information about the degree of stenosis, subject to the extent of flow artefacts.

Other areas of development will include incorporating the variation of tissue density, fluid in the lumen and realistic geometry. It would be desirable to apply a wave inversion technique to the simulated data and investigate how changes in size, composition and stiffness affect the value of stiffness yielded by this algorithm.

IV. CONCLUSIONS

The rupture risk of atherosclerotic plaque is related to plaque composition and stiffness properties of the lipid pool and fibrous cap. It has been demonstrated that shear waves can differentiate between lipid pools of different sizes, allowing identification of plaques with large volumes of low stiffness lipid that are more vulnerable to rupture. This would suggest that applying MRE to atherosclerotic disease may identify plaque stiffness and hence provide an indication of rupture risk. Further developments to this study will include incorporating an appropriate method of wave inversion and experimental validation.

Fig. 2, Z displacement of the wave along the analysis path, through a 70% stenosis containing either a fully fibrous plaque or a plaque with a large lipid pool.
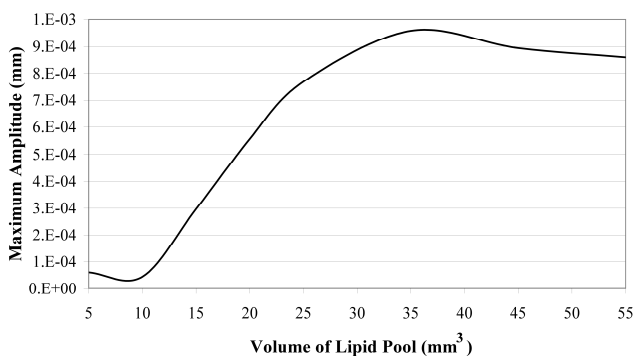

Fig. 3. Maximum amplitude of the local wave within lipid pools of varying volume, in an 80% stenosis.

REFERENCES

[1] C. D. Mathers, C. Bernard, K. M. Iburg, M. Inoue, D. Ma Fat, K. Shibuya, et al, "Global burden of disease in 2002: data sources, methods and results," *World Health Organization*, Dec. 2003.

[2] P. M. Rothwell, S. A. Gutnikov and C. P. Warlow, "Reanalysis of the final results of the European carotid surgery trail," *Stroke*, vol. 34, pp. 514-523, Jan. 2003.

[3] B. Farrell, A. Fraser, P. Sandercock, J. Slattery and C. P. Warlow, "Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European carotid surgery trail (ECST)," *Lancet*, vol. 351, pp. 1379-1387, May 1998.

[4] E. Falk, P. K. Shah and V. Fuster, "Coronary plaque disruption," *Circulation*, vol. 92, pp. 657-671, Aug. 1995.

[5] R. T. Lee and P. Libby, "The unstable atheroma," Arterioscler. Throm. Vasc. Biol., vol. 17, pp. 1859-1867, Oct. 1997.

[6] H. M. Loree, B. J. Tobias, L. J. Gibson, R. D. Kamm, D. M. Small and R. T. Lee, "Mechanical properties of model atherosclerotic lesion lipid pools," *Arterioscler. Throm. Vasc. Biol.*, vol. 14, pp. 230-234, Feb. 1994.

[7] C. L. Lendon, M. J. Davies, G. V. R. Born and P. D. Richardson, "Atherosclerotic plaque caps are locally weakened when macrophages density is increased," *Atherosclerosis*, vol. 87, pp. 87-90, Mar. 1991.

[8] R. Muthupillai, D. J. Lomas, P. J Rossman, J. F. Greenleaf, A. Manduca and R. L. Ehamn, "Magnetic resonance elastography by direct visualization of propagating acoustic strain waves," *Science*, vol. 269, pp. 1854-1857, Sep. 1995.

[9] A. Manduca, T. E. Oliphant, M. A. Dresner, J. L. Mahowald, S. A. Kruse, E. Amromin, et al, "Magnetic resonance Elastography: non-invasive mapping of tissue elasticity" *Med. Image Anal.*, vol. 5, pp. 237-254, 2001.

[10] I. Sack, J. Rump, T. Elgeti, A. Samani and J. Braun, "MR elastography of the human heart: non-invasive assessment of myocardial elasticity changes by shear amplitude variations," *Magn. Reson. Med.*, vol. 61, pp. 668-677, Mar. 2009.

[11] R. Sinkus, J. Lorenzen, D. Schrade, M. Lorenzen, M. Dargatz and D. Holz, "High-resolution tensor MR elastography for breast tumour detection," *Phys. Med. Biol.*, vol. 34, pp. 1649-1664, Nov. 2000.

[12] S. A. Kruse, J. A. Smith, A. J. Lawrence, M. A. Dresner, A. Manduca, J. F. Greenleaf and R. L. Ehman, "Tissue characterization using magnetic resonance elastography: preliminary results," *Phys. Med. Biol.* vol. 45, pp. 1579-1590, Jun. 2000.

[13] D. A. Woodrum, A.J. Romano, A. Lerman, U. H. Pandya, D. Brosh, P.J. Rossman, et al, "Vascular wall elasticity measurement by magnetic resonance imaging," *Magn. Reson. Med.*, vol. 56 pp. 593-600, Aug. 2006.

[14] D. A. Woodrum, J. Herrmann, A. Lerman, A. J. Romano, L. O. Lerman and R. L. Ehman, "Phase contrast MRI-based elastography

technique detects early hypertensive changes in ex vivo porcine aortic wall," *J. Magn. Reson. Imaging*, vol. 29, pp. 583-587, 2009.

[15] Y. Zheng, Q. C. C. Chan and E. S. Yang, "Magnetic resonance elastography with twin drivers for high homogeneity and sensitivity," *in Proc. 28th IEEE EMBS Annual Int. Conf.*, New York, 2007, pp. 1916-1919.

[16] A. Kolipaka, D. A. Woodrum, K. R. Gorny, O. I. Garcia Medina, A. J. Romano and R. L. Ehman, "MR elastography of the in vivo abdominal aorta: feasibility study," in *Proc. Int. Soc. Mag. Reson. Med.* 18, Stockholm, 2010, pp. 1257.

[17] C. A. J. Schulze-Bauer, C. Mörth and G. A. Holzapfel, "Passive biaxial mechanical response of aged human iliac arteries," *J. Biomech. Eng*., vol. 125, pp. 395-406, Jun. 2003.

[18] D. Tang, C. Yang, S. Kobayashi and D. N. Ku, "Effect of a lipid pool on the stress/strain distributions in stenotic arteries: 3-D fluid-structure interactions (FSI) models," *J. Biomech. Eng*., vol. 126, pp. 363-370, Jun. 2004.

[19] M. Li, "Numerical simulation of blood flow and vessel wall stresses in stenosed arteries," Ph.D dissertation, Dept. Medical Physics, Edinburgh Univ., Edinburgh, UK, 2006.

[20] G. A. Holzapfel, M. Stadler and C. A. J. Schulze-Bauer, "A layer-specific three-dimensional model for the simulation of balloon angioplasty using magnetic resonance imaging and mechanical testing," *Ann. Biomed. Eng*., vol. 30, pp. 753-767, Jun. 2002.

[21] P. R. Hoskins, K. Martin and A. Thrush, Diagnostic ultrasound: physics and equipment, 2nd ed. Cambridge Univ. Press, 2010.

[22] K. J. Parker, L. S. Taylor, S. Gracewski and D. J. Rubens, "A unified view of imaging the elastic properties of tissue," *J. Acoust. Soc. Am*., vol. 117, pp. 2705-2712 , May 2005.