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Mechanical stresses in carotid plaques using MRI-based fluid–structure interaction models

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Abstract

Risk assessment in patients with carotid atherosclerosis relies on the degree of luminal stenosis. Incorporating morphological information on plaque composition obtained noninvasively through the use of magnetic resonance imaging (MRI) could include other variables besides the degree of stenosis into carotid plaque risk assessment. Knowledge of the morphologic composition of the plaque allows determination of mechanic stresses exerted on the protective fibrous cap, which may be of importance in the assessment of plaque vulnerability. Based on image processing of transverse MRI scans, longitudinal 2D fluid–structure interaction (FSI) simulations of carotid atherosclerotic plaques were performed facilitating in-vivo estimation of longitudinal internal fibrous cap stresses. The FSI simulation combined finite element analysis (FEA) with computational fluid dynamics (CFD) simulations of blood-flow variables. Preliminary results from two symptomatic patients revealed longitudinal stress levels (max. 254.1 and 143.2 kPa) approaching established criteria for plaque rupture at known predilection sites of plaque rupture. Determination of longitudinal fibrous cap stresses may prove useful in assessing plaque vulnerability and improve risk stratification in patients with carotid atherosclerosis.

Keywords: Atherosclerosis; Carotid artery; Computational fluid dynamics; Fluid–structure interaction; Plaque rupture

1. Introduction

Atherothrombosis is the leading cause of death and severe disability worldwide (Rosamond et al., 2007; Yusuf et al., 2001) and atherosclerotic plaques in the carotid artery is a major cause for cerebrovascular thrombotic events including transient ischemic attacks and stroke (Babiarz et al., 2007; Fuster et al., 2005; Naghavi et al., 2003; Bamford et al., 1991). Two large studies, the North American Symptomatic Carotis Endarterectomy Trial (NASCET, 1991) and the European carotid surgery trial (ECST, 1998) have proved carotid endarterectomy to be beneficial in symptomatic patients with a luminal narrowing of 70% or greater (Rothwell et al., 2003), henceforth designated severe stenosis. The Asymptomatic Carotid Atherosclerosis Study (ACAS, 1995) and the Asymptomatic Carotid Surgery Trial (Halliday et al., 2004) demonstrated that even asymptomatic patients with severe degrees of stenosis may benefit from surgical treatment. In current clinical practice, risk assessment of carotid atherosclerotic plaques is done by evaluating the degree of

Abbreviations: MRI, magnetic resonance imaging; FSI, fluid–structure interaction; CFD, computational fluid dynamics; WSS, wall shear stress; T1W, T1-weighted scan; T2W, T2-weighted scan; PDW, proton density weighted scan; TOF, time of flight scan; TR, repetition time; TE, echo time; Inv, inversion time; RR, heart rate interval (R-peak to next R-peak); MRI-PC, magnetic resonance imaging phase contrast; Venc, velocity encoding factor; μ, initial shear modulus; κ, initial bulk modulus; ρ, density; κ–ω, κ–ε, turbulence models; ICA, internal carotid artery; ECA, external carotid artery; CCA, common carotid artery.

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luminal stenosis, as measured by imaging modalities such as conventional intra-arterial angiography, duplex ultrasound, magnetic resonance angiography, or computed tomography (Wardlaw et al., 2006; Nighoghossian et al., 2005).

While increasing degrees of stenosis carries greater risks of atherothrombotic events, most ruptured coronary plaques are in vessels less than 60% stenosed (Casscells et al., 2003). As atherosclerosis develops, arteries often dilate in an attempt to normalize elevated wall shear stresses, a process known as expansive remodelling (Pasterkamp and Smits, 2002; Glagov et al., 1987, 1988). Consequently, risk assessment based solely on the degree of luminal stenosis will tend to underestimate the severity of the atherosclerotic lesion. For these reasons, there is a need for more sensitive methods to risk stratify patients with carotid atherosclerotic disease.

Thrombosis-prone (vulnerable) atherosclerotic plaques have been determined by histological examinations to possess large lipid cores and thin fibrous caps (Naghavi et al., 2003; Carr et al., 1996; Stary et al., 1995; Falk, 1992). Since plaque rupture, the most frequent cause of thrombosis, by definition represents a structural failure of the protective fibrous cap, it seems reasonable to assume that plaque morphology as well as biomechanical properties of the atherosclerotic lesion may influence the vulnerability. An in-vitro model study (Li et al., 2006b) showed that thin fibrous caps in combination with large lipid cores generate severe internal fibrous cap stresses. In-vitro studies of coronary arteries have shown markedly elevated fibrous cap stresses in ruptured compared to stable lesions (Cheng et al., 1993). A recent publication comparing fibrous cap stress levels in asymptomatic versus symptomatic carotid patients found stresses in symptomatic patients to be nearly twice those of asymptomatic patients (Li et al., 2007).

To estimate stress levels in the fibrous cap, fluid–structure interaction (FSI) analysis has emerged as a tool combining blood-flow simulation through computational fluid dynamics (CFD) with finite element analysis (FEA) of the corresponding stress levels in the surrounding tissues (Tang et al., 2004; Ivankovic et al., 2002; Zhao et al., 2002). Magnetic resonance imaging (MRI) is an ideal imaging modality for providing geometric models for FSI simulations given its unique in-vivo soft tissue imaging capabilities (Saam et al., 2005) combined with the ability to determine blood velocities (Chai and Mohiaddin, 2005), wall shear stress (Oyre et al., 1997), and vessel wall compliance (Metafratzi et al., 2002) noninvasively.

Performing 3D simulations of fibrous cap stresses is time consuming, so simulations in 2D cross-sections corresponding to either histological data (Cheng et al., 1993) or MRI scans (Li et al., 2006a) have been suggested. Even though the use of cross-sectional data matches the orientation of the available morphologic data, this approach precludes examinations of the longitudinal stress distribution. A previous study (Lovett and Rothwell, 2003) determined carotid plaque ruptures to be asymmetrically distributed longitudinally with a majority of ruptures occurring on the upstream side of the plaques. Furthermore, histological examinations of the longitudinal distribution of cell-types indicate differences in smooth muscle cell and macrophage content between upstream and downstream parts of the plaque (Dirksen et al., 1998). In this study, we present a semi-automated method of creating longitudinal 2D FSI models from MRI scans. This allows simulations of longitudinal stress distributions and blood pressure levels to be performed, enabling predictions of plaque rupture risk and examinations of correlations between local stress variation and morphology.

2. Methods

The protocol was approved by the local ethics committee. Informed consent was obtained prior to patient enrollment.

2.1. Magnetic resonance imaging

Two non-consecutive males (ages 69 and 79) awaiting operation for symptomatic carotid stenosis were scanned using a validated MRI protocol (Yuan and Kerwin, 2004) on a Philips 1.5 T scanner equipped with a C-4 circular surface coil (diameter = 8 cm, Philips Intera Achieva 1.5 T R1.5.4, Philips Inc., Best, The Netherlands). The symptomatic carotid plaque was scanned using four different MRI contrast weighted scans. These will exhibit different image intensities depending on the contrast weighting employed allowing segmentation of the individual plaque components including lipid, fibrous cap, and calcifications as well as normal vessel wall (Saam et al., 2005). A T1-weighted scan (T1W), T2-weighted scan (T2W), proton-density weighted scan (PDW), and time-of-flight (TOF) scan were used. Sixteen transverse slices centered on the carotid flow divider were acquired using cardiac-gated turbo spin echo sequences: T1W (TR/TE/Inv: 1RR/8 ms/650 ms), T2W and PDW scans with TR = 3RR and TE = 40 ms/20 ms, and a TOF sequence (TR/TE 34.9 ms/2.4 ms). All sequences covered a field of view of 16 cm × 12 cm using a 256 × 256 matrix yielding a raw resolution of $0.6 \times 0.6\,mm^2$ with 2 mm slice thickness. Flow velocities were measured in the transverse plane 2 cm up- and downstream from the flow divider using a phase-contrast (MRI-PC) turbo field echo sequence (TR/TE/Venc: 4.84 ms/2.90 ms/150 cm/s). Vessel wall deformation during a cardiac cycle (20 heart phases), in the common carotid artery below the plaque was evaluated using a balanced gradient echo sequence (B-TFE) with an in-plane resolution of $0.6 \times 0.6\,mm^2$, 2 mm slice thickness, TR = 7.63 ms, and TE = 3.8 ms.

2.2. Model generation

The image intensities of each carotid plaque scan were analyzed using Cascade (Vascular Imaging Lab, Seattle, WA, USA), a dedicated semi-automated segmentation tool, allowing segmentation into lipid core, fibrous cap, vessel wall, and blood stream (Liu et al., 2006) (Fig. 1A). The components in each slice were exported as a collection of spline curves which were imported into Matlab® R2006b (The MathWorks Inc., Natick, MA, USA) and converted to 2D grayscale images (Fig. 1B). The images were upscaled to an in-plane resolution of 0.078 mm in order to preserve fine details from the spline curves. From the 2D images, a region-of-interest was selected and collected into a single 3D matrix describing the spatial distribution of segmented tissue within the scanned volume. Due to the large difference between the final in-plane resolution of 0.078 mm and slice thickness of 2 mm, the dataset was resampled using linear interpolation to obtain a uniform voxel size of $0.3125 \times 0.3125 \times 0.3125\,mm^3$ followed by Gaussian smoothing (voxel size = 2 voxels, standard deviation = 15 voxels). From this isotropic dataset, isosurfaces