Vessel Wall Imaging: Thinking Outside the Lumen

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HIGHLIGHTS

- Luminal stenosis alone is not the only indicator of plaque vulnerability

- MRI allows the assessment of a wide range of large vessel atherosclerotic wall characteristics including plaque morphology, inflammation, neovascularisation and biomechanics

TARGET AUDIENCE

Scientists and Clinicians with an interest in the rationale for and methods of carotid vessel wall imaging

OUTCOME/OBJECTIVES

- Describe the main MRI techniques used for carotid vessel wall imaging

- Identify the major criteria for defining carotid plaque vulnerability

PURPOSE

In the US approximately 795,000 people experience a new or recurrent stroke each year accounting for nearly 1 in every 19 deaths (1). The majority of strokes (87%) are ischemic in origin with approximately 25-50% of these originating from carotid atherosclerosis (2). Analysis of the pooled results from the major randomised controlled trials of carotid endarterectomy have only demonstrated a significant benefit, in terms of a reduced risk of subsequent ipsilateral stroke, in participants with severe stenosis (70-99%) and only a marginal benefit in subjects with moderate

stenosis (50-69%) (3). All of these studies determined the degree of stenosis from measurements of luminal diameter using X-ray contrast angiography. However, the European Carotid Surgery Trial (ECST) found that 43.8 % of the symptomatic trial participants had a <30% stenosis (4), whilst the North American Symptomatic Carotid Endarterectomy Trial (NASCET) found that the 5 year ipsilateral stroke rate was 22.2% for subjects with a <50% stenosis (5). Hence the risk of a carotid stroke cannot be simply determined from the degree of luminal stenosis alone. Indeed, Glagov in 1987, described the phenomenon of adaptive arterial remodelling in which coronary artery plaques enlarged whilst preserving the luminal cross-sectional area (6). Since then histological analysis of carotid plaques have helped to correlate morphological features with corresponding clinical syndromes (7, 8). In addition other features of "vulnerable plaques", i.e. those at a high risk for thrombosis, rupture and embolization have been identified (9, 10). Major criteria include: active inflammation within the plaque; a thin fibrous cap overlying a lipid-rich necrotic core (LRNC) and fibrous cap disruption as well as severe stenosis. Minor criteria include intraplaque haemorrhage (IPH) and expansive remodelling. The exquisite soft-tissue contrast of MRI coupled with a range of technical developments has allowed these principal morphological features of carotid lesions to be assessed in vivo (11-16) as well as allowing functional imaging of biomarkers for plaque inflammation (17, 18), neovascularisation(19) and biomechanics (20).

METHODS

The main challenge in obtaining high quality images of the vessel wall using MRI is to obtain a sufficiently good signal-to-noise ratio (SNR). Due to their relatively superficial location it is possible to obtain very high quality images of the carotid vessel wall particularly with the use of dedicated RF receiver coils that are positioned very closely to the subject's neck (21) (see Figure 1).

In order to achieve relatively short imaging times, fast spin echo (FSE) sequences are routinely used for morphological imaging; however, the multiple refocusing pulses often result in variable signal intensities from blood depending upon the flow characteristics. This can lead to

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problems in separating slow flow effects from vessel wall pathology. Various schemes have therefore been developed to suppress the signal from flowing blood without adversely affecting the tissue contrast in the vessel wall. These include magnetisation preparation techniques such as Double Inversion Recovery (DIR) (22), Motion-Sensitized-Driven-Equilibrium (MSDE) (23, 24) and Delay Alternating with Nutation for Tailored Excitation (DANTE) (25) that are played out just prior to the imaging sequences.

Figure 1. Dedicated four channel carotid coil.

Since MRI can provide multiple contrast weightings e.g. blood-suppressed T1w, PDw, and T2w using FSE acquisitions and bright-blood gradient echo based time-of-flight (TOF) sequences it is possible to classify the various plaque constituents (26). The use of standard gadolinium-based MRI contrast agents can also help improve tissue differentiation, particularly in the identification of the LRNC (14). However, it is not possible to use DIR preparation schemes post contrast because the T_1 of blood is shortened unpredictably. Therefore techniques such as quadruple inversion recovery (QIR) were developed to allow effective blood suppression over a range of T_1 values (27). MSDE and DANTE methods are also quite robust to changes in blood T_1. Clinical examples of blood suppressed multi-contrast images obtained in a patient with a heavily calcified plaque are shown in Figure 2, whilst images from a patient with plaque containing a large LRNC are shown in Figure 3.

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Recent developments in three-dimensional (3D) acquisition techniques allow high quality blood-suppressed imaging of the vessel wall with near isotropic sub-millimetre voxel sizes (28). A clinical example of a 3D FSE acquisition with 0.6mm isotropic resolution is shown in Figure 4.
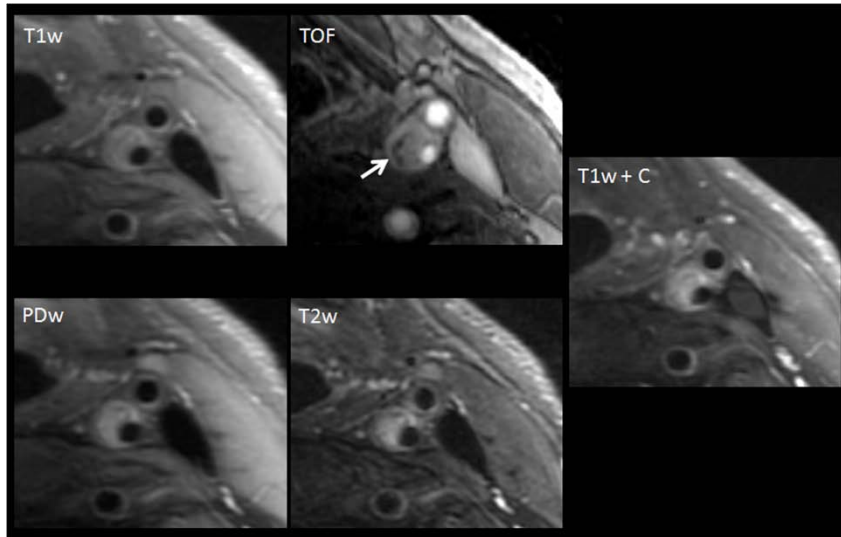

Figure 2. Multi-contrast, motion-sensitised driven equlibrium (MSDE) prepared 2D fast spin echo and 3D time-of-flight (TOF) images obtained in a patient with a heavily calcified plaque. The calcification is best seen in the TOF image (arrow).
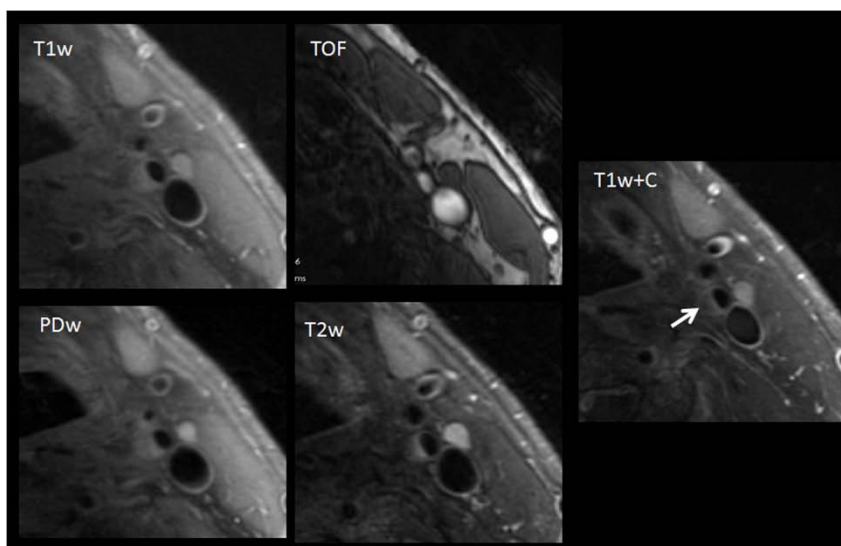

Figure 3. Multi-contrast, motion-sensitised driven equlibrium (MSDE), prepared 2D fast spin echo and 3D time-of-flight images mages obtained in a patient with a large lipid rich necrotic core (LRNC). The LRNC is best seen in the post contrast T1w image (arrow).

RESULTS

MRI has been used in a number of clinical trials evaluating morphological changes in carotid plaques. Plaques containing large LRNC have been postulated as inferring a greater risk of

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plaque rupture. A three-year, 108 subject, observational study by Underhill et al showed the proportion of wall volume occupied by the LRNC was the strongest predictor of subsequent 'surface disruption' (29). A three year randomised, double-blind, placebo controlled study by Zhao et al showed a significant reduction in LRNC volume with intensive lipid-lowering therapy (30).
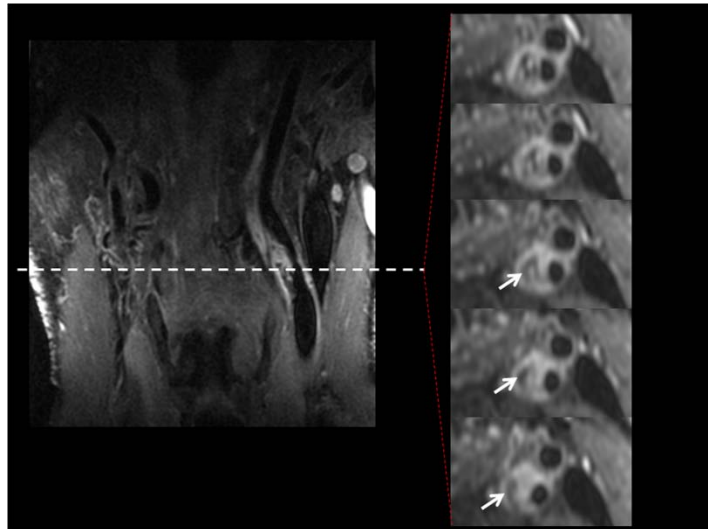

Figure 4. Three-dimensional, coronally acquired, isotropic (0.6x0.6x0.6mm) voxel fast spin echo acquisition in a patient with a large lipid rich necrotic core (LRNC). The LRNC is best seen on the axial reformats (arrows).

Intraplaque haemorrhage (IPH) also confers a greater risk. In an 18 month, prospective study of 29 asymptomatic patients Takaya reported a significant increase in wall volume and LRNC in subjects with IPH compared to those without (31) . Underhill et al also found that the presence of IPH altered the remodelling pattern (32).

Macrophage infiltration and neovascularisation have been identified as two potential markers of inflammation and hence plaque vulnerability. Tang et al used ultrasmall superparamagnetic iron oxide (USPIO) nanoparticles in 47 asymptomatic patients, randomised to high and low dose statins (33). A significant reduction in USPIO uptake was identified in the high dose group as early as 6 weeks after treatment. Kerwin et al used DCE-MRI with pharmacokinetic modelling of the contrast agent uptake to investigate plaque neovascularisation (34). Whilst DCE-MRI correlated with histological evaluation of plaque neovascularisation there was also a correlation with macrophage content (18).

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Biomechanical modelling of the forces acting upon atherosclerotic plaques can also be performed using data obtained from multi-contrast MRI images. Examples include: Trivedi et al showed a difference in plaque tensile stresses between symptomatic and asymptomatic patients (35);Sadat et al reported that plaques with IPH have significantly higher stresses than non-IPH plaques (36);Li et al demonstrated a reduction in arterial wall strain following aggressive lipid lowering therapy (37).

DISCUSSION

MR imaging of morphological plaque features has been shown to be reproducible and correlates well with histological examination of plaques excised at endarterectomy. MRI derived measures of plaque volume have been successfully used in a number of longitudinal and interventional studies.   MRI also offers the capability to imaging molecular processes such as inflammation and neovascularisation that are highly related to plaque vulnerability.

CONCLUSION

Multi-contrast carotid MRI allows a wide range of plaque characteristics to be imaged in vivo and is an important contributor to atherosclerosis research. The pathophysiological information that can be obtained has great potential for improving the selection criteria for vascular intervention.

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