Journal of Clinical Neuroscience 22 (2015) 1722–1726

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Review

Magnetic resonance imaging of atherothrombotic plaques

Ammara Usman [a,*], Umar Sadat [b], Martin J. Graves [a], Jonathan H. Gillard [a]

[a] University Department of Radiology, Addenbrooke's Hospital, Post Office Box 218, Level 5, Hills Road, Cambridge CB20QQ, UK
[b] Cambridge Vascular Unit, Cambridge University Hospitals National Health Service Foundation Trust, Cambridge, UK

ARTICLE INFO

Article history:
Received 19 March 2015
Accepted 28 March 2015

Keywords:
Atherosclerosis
Imaging
MRI
Plaques
Stroke
Thrombosis

ABSTRACT

Atherosclerosis remains the leading cause of long term morbidity and mortality worldwide, despite significant advances in its management. Vulnerable atherothrombotic plaques are predominantly responsible for thromboembolic ischaemic events in arterial beds, such as the carotid, coronary and lower limb arteries. MRI has emerged as a non-invasive, non-irradiating and highly reproducible imaging technique which allows detailed morphological and functional assessment of such plaques. It also has the potential to monitor the efficacy of established and evolving anti-atherosclerosis drugs. It is envisaged that by careful identification and understanding of the underlying cellular and molecular mechanisms that govern atherosclerosis, novel treatment strategies can be formulated which may reduce the persistent high mortality and morbidity rates associated with this disease. MRI shows promise in achieving this goal.

1. Introduction

Stroke is considered to be the leading cause of death and long term disability worldwide [1]. Approximately 80% of strokes are ischaemic in origin, due to embolic events or stenosis of cerebral arteries. A specific correlation with carotid atherothrombotic plaques and luminal stenosis is seen in 20–30% of cerebral infarction patients [2]. Morphological features such as carotid artery intima-media thickness (IMT), rupture-prone plaques with thin fibrous cap (FC) and large lipid core (LC), and ulcerated plaques, are associated with an increased risk of stroke. Non-invasive radiological imaging constitutes an emerging diagnostic and prognostic tool to identify the presence and progression (or regression) of disease, as well as the vulnerability of the atherosclerotic lesions. The characterisation of the carotid artery plaque presents an opportunity to quantify the risk of cerebrovascular events and may be used to improve the therapeutic decision making for carotid endarterectomy (CEA) or angioplasty and stent placement. MRI has emerged as a promising imaging technique capable of providing detailed morphological and functional information about atherothrombotic plaques.

2. High resolution MRI

High resolution or multicontrast MRI, also known as black-blood imaging, utilises the inherent magnetic resonance relaxation properties (T1 and T2-weighted) of different plaque components and the surrounding tissue, to characterise the plaque components without contrast media (CM). The advent of fast, selective vessel wall imaging sequences allows the acquisition of high quality, morphological images using T1 and T2-weighted sequences, and proton density-weighted imaging. In addition, luminal (bright-blood) imaging can be achieved using a time-of-flight (TOF) sequence (visualisation of blood flow within a vessel without CM), which produces angiographic data. This technique has been systematically validated with histology to quantify the principal components of carotid plaques, such as the LC, plaque haemorrhage (PH), calcification and plaque rupture/erosion [3,4]. The intrareader and interreader [5], as well as the interscan reproducibility of the quantitative measures associated with both morphology and composition, have also been extensively reported [5,6].

High resolution MRI provides adequate assessment of vessel wall and atherothrombotic plaques, as described below.

3. Vessel wall assessment

3.1. Vessel wall thickness

Early disease can be detected by assessing arterial wall thickness (mean wall thickness [MWT]) using high resolution MRI, comparable to IMT measurements with B-mode ultrasound. The MWT and IMT have excellent correlation [7], further improved with the use of 3.0 T MRI in comparison with 1.5 T [8]. The characterisation of carotid MWT by MRI may have greater clinical utility compared

* Corresponding author. Tel.: +44 1223 245151.
E-mail address: au239@cam.ac.uk (A. Usman).

http://dx.doi.org/10.1016/j.jocn.2015.03.060
0967-5868/

with IMT measurements by ultrasound. MRI and ultrasound have similar repeatability for the assessment of carotid wall thickness [9]. However, unlike carotid IMT, MRI measurements of wall thickness include the adventitia, and may be sensitive to adventitial thickening which results from vasa vasorum proliferation, as a sign of early plaque development. Another merit of MRI over ultrasound is that the measurement variability is smaller, enabling smaller sample sizes and potentially shorter study durations in cardiovascular prevention trials [10]. This strongly suggests that vessel wall measurements assessed by black-blood MRI could be clinically utilised for the evaluation of plaque progression and regression.

3.2. Wall area and volume measurements

MRI is very accurate for the *in vivo* measurement of artery walls and the volume of atherothrombotic carotid plaques. Yuan et al. determined the accuracy of *in vivo* MRI for measuring the cross-sectional maximum wall area of atherosclerotic carotid arteries in a group of patients undergoing CEA, comparing it to *ex vivo* measurements [11]. The *in vivo* wall area measurements strongly agreed with those measured by the *ex vivo* MRI. Furthermore, the intraobserver and interobserver variability was minimal. However, it should be considered that *ex vivo* histology specimens undergo architectural changes during the *en bloc* atheroma resection and fixation process. Therefore, these are not a true representation of the *in vivo* tissue architecture and plaque morphology. Luo et al. used the 3D reconstruction polygonal model to obtain the vessel wall volume [12]. The measurements of carotid plaque burden (maximum wall area and wall volume) and lumen narrowing, as determined by *in vivo* black-blood MRI and *ex vivo* MRI of CEA samples, suggested that both measurements can be obtained with only a small to moderate bias.

4. Plaque assessment

4.1. Lesion type

Since *in vivo* and *ex vivo* MRI can characterise components of carotid atherothrombotic plaques, a modified American Heart Association classification for MRI of carotid atheroma has been proposed [13] (Table 1).

The MRI characteristics of plaque components at different contrast weightings are shown in Table 2 and Supplementary Fig. 1. The sensitivity and specificity of high resolution MRI in detecting various plaque components has been reported as very high in *ex vivo* imaging studies on CEA specimens (median sensitivity and range: LC 100% (95–100), FC 100% (95–100), calcification 100% (95–100) and thrombus 84% (73–90); specificity: 100% for all above components) [14]. Similar results have been reported by Fabiano et al [15]. Excellent results have been reported with *in vivo* imaging using the standard multicontrast carotid MRI protocol (LC sensitivity: 85%, specificity: 92% [16]; PH sensitivity: 90%, specificity: 74% [17]).

4.1.1. Fibrous cap

More than 75% of major thrombotic events are precipitated by atherosclerotic plaque ruptures, which results in the exposure of thrombogenic subendothelial plaque constituents [18]. MRI can detect the FC status (thick, thin, ruptured) [19,20]. The 3D TOF pulse sequence is able to distinguish intact, thick FC from intact thin and ruptured caps, with a high level of agreement between MRI and histology (89% agreement; k = 0.83) [21]. MRI-identified ruptured FC has a strong association with recent [19] and subsequent cerebrovascular ischaemic events [20].

Table 1
American Heart Association classification for atherosclerotic plaques

Conventional[a]	Modified for MRI of carotid atheroma[a]
Type I: initial lesion with foam cells Type II: fatty streaks with multiple foam cell layers	Type I–II[b]: near normal wall thickness, no calcification
Type III: preatheroma with extracellular lipid pools	Type III: diffuse intimal thickening or plaque with small LC, no calcification
Type IV: atheroma with confluent extracellular LC	Type IV–Va[c]: plaque with a large LC, covered by a FC, possible small calcification
Type Va: fibroatheroma	
Type Vb: calcified plaque with LC or fibrotic tissue, with large calcification	Type Vb: plaque with a LC or fibrotic tissue, with large calcification
Type Vc: fibrotic plaque with large fibrous tissue, no LC	Type Vc: plaque with fibrotic tissue, no LC, possible small calcification
Type VI: complex plaque with haemorrhage or thrombus	Type VI[d]: plaque with haemorrhage or thrombus
Type VII: complex plaque with extensive calcification	Type VII[d]: complex plaque with extensive calcification
Type VIII: complex with extensive fibrosis	Type VIII[d]: complex with extensive fibrosis

[a] The classification obtained by MRI and the American Heart Association classifications showed good agreement, with Cohen's κ of 0.74 and weighted κ of 0.79 [13].
[b] Types I and II of the classification were combined into Type I–II. The current resolution of MRI does not allow for the differentiation of discrete foam cells in Type I and the multiple foam cell layers of the fatty streak in Type II.
[c] Types IV and V were combined into Type IV–V because the ability of MRI to distinguish the proteoglycan composition of the Type IV cap *versus* the dense collagen of the Type V cap has not been demonstrated.
[d] Type VI, VII and VIII are easily distinguishable on MRI and remained separate classifications.
FC = fibrous cap, LC = lipid core.

4.1.2. Lipid core

LC has been proposed to represent a phenotype of atherosclerotic disease with a high risk for future cardiovascular events [22]. The identification and quantification of LC with multicontrast carotid MRI has been histologically validated [23], with low interscan variability in a multicentre trial setting [24]. The presence of LC, as identified by carotid MRI, is a predictor of the future development of cerebrovascular ischaemic events [25,26]. A study of 108 patients with 50–79% stenoses revealed that the size of the LC relative to plaque size was the strongest predictor of new FC rupture or ulceration after 3 years of follow-up [27]. TOF and T1-weighted images can help differentiate LC from PH [16].

4.1.3. Plaque haemorrhage

PH, due to its proinflammatory properties, results in carotid plaque destabilisation [28]. The detection of PH by carotid MRI is predicted on the degradation of haemorrhage into methaemoglobin, which shortens the longitudinal relaxation time of T1 of surrounding protons. The consequent imaging effect in carotid MRI is a bright signal on T1-weighted sequences such as TOF, and standard T1-weighted fast spin echo sequences. These sequences have been validated with histology [16,17,29], with TOF particularly useful for identifying the relationship of PH with the FC, for example, to differentiate juxtaluminal haemorrhage/thrombus with ruptured FC from intraplaque haemorrhage with intact FC [29].

Multicontrast MRI-identified PH, either alone or in combination with other plaque features such as FC rupture, has a strong correlation with subsequent cerebrovascular events [20,25,30] and the progression of carotid plaque size [31]. Altaf et al. used a T1-weighted 3D magnetisation-prepared direct thrombus imaging pulse sequence to detect carotid PH [32] (Fig. 1). A further improvement in detection of PH has been reported recently, using new MRI pulse sequences [33,34].