Assessment of femoral artery atherosclerosis at the adductor canal using 3D black-blood MRI

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AIM: To assess whether the three-dimensional (3D) black-blood motion-sensitized driven equilibrium (MSDE) prepared rapid gradient-echo sequence (3D MERGE) magnetic resonance imaging (MRI) sequence is sensitive enough to detect differences in atherosclerotic plaque size and morphology occurring in the adductor canal and the proximal bifurcation segment.

MATERIALS AND METHODS: Fifty pairs of adductor canal and bifurcation segments from 25 patients with intermittent claudication were examined using 3D MERGE. The two-dimensional (2D) transverse section showing the largest plaque burden in each segment was chosen for comparison. Wall and lumen boundaries were segmented from each 2D section and quantified using six metrics: wall area (WA), lumen area (LA), normalized wall index (NWI), maximum wall thickness (MaxWT), minimum wall thickness (MinWT), and eccentricity.

RESULTS: The mean LA in the adductor region was significantly lower than that in the bifurcation segment ($p < 0.0001$). Mean NWI, MaxWT, and eccentricity in the adductor region were significantly higher than those at bifurcation ($p < 0.0001$, $p < 0.0021$, and $p < 0.0045$, respectively). Mean WA and MinWT of the two segments did not show a statistically significant difference. WA in both regions was positively correlated with eccentricity ($p < 0.0049$ and $p < 0.0049$, respectively). LA was negatively correlated with eccentricity ($p < 0.0017$), and NWI was positively correlated with eccentricity only in the adductor region ($p < 0.0004$).

CONCLUSION: The results suggest that compensatory enlargement was limited in the adductor canal when compared to the proximal bifurcation segment. 3D MERGE, as a fast and non-invasive sequence, may assist the evaluation of femoral atherosclerosis by assessing the size and morphology of plaques, knowledge of which can guide clinical treatment.

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Introduction

Peripheral arterial disease (PAD) is a serious worldwide health issue, affecting about 27 million people in Europe and North America,\textsuperscript{1} and about 3\% in the general Chinese population.\textsuperscript{2} PAD is characterized by the obstruction of blood flow to the limbs due to atherosclerosis, the symptoms of which range from intermittent claudication to critical limb ischaemia, which leads to non-healing wounds, gangrene, and eventual limb amputation.

Many investigations on atherosclerosis in the femoropopliteal region have found the adductor canal region of the superficial femoral artery (SFA) to be the most commonly occluded location. Lindbom\textsuperscript{3} studied 356 limbs...
angiographically and histologically after autopsy, and 295 limbs in vivo angiographically. The adductor canal was identified as one of the most occluded regions. This observation was confirmed by later angiographical studies by Dunlop and Santos and Watt. Dunlop and Santos reported that 76% of the 41 femoral arteries in their study showed obstruction in the adductor canal. Watt, in a study of 273 occluded arteries, estimated that the adductor region is the site of between 60–70% of femoropopliteal occlusion in intermittent claudication. In addition to showing the prevalence of occlusion in the adductor region, Walsh et al. studied the rate of progression of femoral artery atherosclerosis. Two angiograms of 20 arteries were collected, one at baseline and the second at a mean of 32 months later. The authors reported that lesions in the adductor canal progressed twice as fast as lesions outside the adductor region.

The tendency for superficial femoral artery stenosis in the adductor canal is thought to be the result of the restriction of compensatory enlargement that often occurs in other vascular beds to preserve lumen size. The adductor canal is completely surrounded by muscles, which apply a substantial mechanical force to the artery, limiting the extent of vessel remodelling. In a histological study of SFAs from 20 cadavers, Blair et al. found that although the adductor canal is not more prone to plaque formation than the proximal SFA, compensatory enlargement is limited in this site because of mechanical forces applied to the artery. Thus, with similar plaque burden, the adductor canal is more frequently occluded than the proximal SFA segment.

All the studies described were either ex vivo histology studies or in vivo studies involving x-ray angiography. Although proven useful in diagnosis, angiography only provides a two-dimensional (2D) longitudinal view of the lumen and no information about the vessel wall. Therefore, its utility is restricted to measuring stenosis, and identifying surface irregularity and symmetry of the lesion. Angiography cannot be used in plaque or vessel wall area/volume studies or for assessing the extent of adaptive vessel wall enlargement. Intravascular ultrasound (IVUS) has been shown to be able to evaluate wall thickening and external compression applied to the artery. Unfortunately, both angiography and IVUS are limited by their invasive nature and, therefore, are impractical in studies of asymptomatic subjects or in longitudinal studies. Development of magnetic resonance imaging (MRI) of the vessel wall has allowed for quantification of the volumetric and morphological characteristics of plaque burden in SFA. Although 2D black-blood fast spin-echo (FSE) acquisition has been the mainstay of plaque burden analyses in many vascular beds, it is not suitable to femoral artery imaging. The SFA is much longer than the carotid and coronary arteries, and spatial resolution has to be sacrificed by prescribing thick sections (e.g., 3 mm) in order to achieve the required longitudinal coverage. Three-dimensional (3D) acquisition can provide improved signal-to-noise ratios (SNR), extended coverage, and higher resolution without increasing imaging time over 2D acquisition. 3D acquisition has been greatly improved by the introduction of blood-suppression techniques, such as the motion-sensitized driven equilibrium (MSDE), which depends on blood flow velocity instead of the outflow volume for black-blood imaging. MSDE has been integrated into a 3D black-blood imaging sequence, known as 3D MSDE, prepared rapid gradient-echo sequence (3D MERGE) and has been used to acquire SFA images with a longitudinal coverage of 50 cm and isotropic resolution of 1 mm all within 10.5 min.

The aim of the present study was to investigate whether MRI images acquired by 3D MERGE are sensitive enough to detect the differences in plaque size, morphology, and arterial stenosis of the adductor canal and the proximal femoral artery. Plaque size is quantified using parameters derived from vessel wall area and thickness, while plaque eccentricity is used to quantify the morphology of the plaque burden. A number of studies have suggested eccentricity in the coronary and carotid arteries is associated with a higher incidence of cerebrovascular events, and a rapid progression of atherosclerosis. A further aim was to investigate whether luminal narrowing is more severe in the adductor canal than in proximal SFA because of the muscular forces exerted on the femoral artery in the adductor region.

Materials and methods

Patients

Thirteen women and 12 men with symptoms of intermittent claudication but without critical limb ischaemia were recruited by the Department of Radiology, Renji Hospital (Shanghai Jiao Tong University, Shanghai, China). Levels for creatinine, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) were also collected. The numbers of patients with diabetes and gouty arthritis were also tabulated as these two diseases promote the development of atherosclerotic plaque. All patients provided written informed consent. The study protocol was approved by the ethical review board of Renji Hospital.

MRI protocol

All patients underwent MRI using a 3 T MRI system (Achieva, Philips Medical System, Best, the Netherlands) with the thigh at the centre of the magnet. A six-channel phased-array torso coil was placed over the thigh. The protocol included a multiplanar localizer and a 2D time-of-flight acquisition.
(TOF) sequence to aid in the localization of the SFA. The 3D MERGE sequence, implemented using MSDE preparation and spoiled segmented FLASH readout with centric phase encoding, was used to screen the femoral artery. The femoral artery images were acquired using three stations with a field-of-view of 400 × 40 × 250 mm to cover a longitudinal length of 50 cm with an isotropic voxel size of 0.8 mm (zero-interpolated to 0.4 mm). The imaging parameters were 9.2 ms repetition time, 4.3 ms echo time, 6° flip angle, turbo factor = 100, and one excitation.

**Image analysis**

In other vascular beds, atherosclerosis occurs predominantly at bifurcations. However, the femoral artery is unique in that stenosis is most serious in the adductor canal presumably due to the restriction of expansive remodelling due to pressure from the surrounding muscles. In this study, the bifurcation of the deep and the SFA was used as a reference to assess the plaque burden in the adductor canal. Transverse sections of the 3D MERGE images were reviewed using an Advantage Workstation (version 4.4, GE Medical System). An expert observer visually inspected the 2D transverse images of each patient and identified the femoral artery bifurcation (Fig 1b). The 4 cm segment starting from 2 cm proximal to the bifurcation (Fig 1a) and ending at 2 cm distal to the bifurcation (Fig 1c) was chosen for analysis. The adductor canal of the femoral artery is surrounded by the sartorius medially, vastus medialis anteriorly and laterally, and adductor longus and magnus posteriorly. These four muscles were used to identify the adductor segment from the MRI images (Fig 1d). The average length of the adductor canal is 7 cm.

For each of the two segments of a patient, the expert observer scanned through the 2D transverse images with an intersection distance 0.4 mm and visually located the image with the largest plaque burden for analysis. In each selected image, the wall and lumen boundaries were manually outlined. The lumen area and total wall area were obtained from the segmented wall and lumen boundaries on each 2D transverse image. The total wall area included the lumen, intima, media, and adventitia. The wall area was computed by subtracting the total wall area by the lumen area. The normalized wall index (NWI) was calculated by dividing the vessel wall area by the total wall area. The NWI normalizes the wall area to the total wall area, thereby taking the anatomical difference between the adductor canal and the bifurcation segment into account. The maximum (MaxWT) and minimum wall thickness (MinWT) measurements were also taken based on the wall and lumen boundaries. The eccentricity index was calculated for each image using the equation: (MaxWT−MinWT)/MaxWT. For the whole study, 50 2D images in the bifurcation segment (25 patients × 2 sides (left/right)) and 50 images in the adductor canal were segmented. Each image had six measurements: wall area, lumen area, NWI, MaxWT, MinWT, and eccentricity index.

**Statistical analysis**

Statistical analysis was performed using GraphPad Prism version 4.01 for Windows (GraphPad Software, San Diego, CA, USA) and MATLAB (Version R2010b). Measurements obtained from the bifurcation and adductor canal of the same artery were paired. Then, paired t-tests were performed to compare each of the six measurements associated with the bifurcation and the adductor canal. The effects of plaque eccentricity on plaque size were investigated by computing the correlation coefficients (r) between eccentricity and each of the area-based metrics — wall area,
Results

Comparison between plaque burden characteristics in the adductor canal and the proximal segment

Table 2 shows the average and standard deviation of lumen area, wall area, NWI, MaxWT, MinWT, and eccentricity in the bifurcation and the adductor canal. Paired t-tests show that although the differences in wall area and MinWT between the bifurcation segment and the adductor canal were not statistically significant, the differences in lumen area, NWI, MaxWT, and eccentricity were.

Fig 2 shows the Bland–Altman plots displaying the difference between the measurements obtained in the adductor canal and in the bifurcation segment against the mean of the measurements. A Bland–Altman plot was generated for each of the six measurements: lumen area, wall area, NWI, MaxWT, MinWT, and eccentricity. Each data point in the Bland–Altman plots represents the measurement obtained in one of the 50 arteries.

In the present cohort, the vessel wall area in the adductor canal was almost exactly the same as in the bifurcation (p = 0.98), suggesting that the adductor canal was not more prone to plaque formation. However, the lumen area in the adductor canal was significantly smaller in the adductor canal than at the bifurcation (p < 0.0001), suggesting that the remodelling capability of the adductor canal was reduced. Fig 3 shows the transverse images chosen from the bifurcation segment and the adductor canal for three patients. In each of these patients, the wall area measurements in the adductor canal and in the bifurcation segment were similar, whereas the difference between the lumen area in the adductor canal and the bifurcation segment ranged from 23.5 mm² in patient A to 3.7 mm² in patient C. Patient B was associated with a difference of 11 mm², which was approximately the mean difference as shown in the Bland–Altman plot displayed in Fig 2a.

The NWI in the adductor canal was significantly higher than that at the bifurcation (p < 0.0001). This observation is the direct effect of the more significant luminal narrowing in the adductor canal. With equivalent vessel wall area in the adductor canal and at the bifurcation, the narrower lumen produces a smaller total wall area (lumen area + wall area). The equivalent wall area divided by a smaller total wall area gives a higher NWI in the adductor canal. The plaque eccentricity in the adductor canal was significantly higher than that at the bifurcation (p = 0.045). This result is directly related to the maximum thickness being significantly higher in the adductor canal (p = 0.0021). The results suggest that the plaque tends to have a more irregular shape in the adductor canal.

Correlation between eccentricity and plaque size/degree of luminal narrowing

Fig 4 shows the plots of the wall/lumen area and NWI against eccentricity of the adductor canal and the bifurcation segment. Table 3 shows the correlation coefficients between plaque eccentricity and the three measurements obtained in the adductor canal and the bifurcation segment. The 95% confidence intervals of the correlation coefficients are also shown.

Plaque eccentricity was positively correlated with the wall area in both the bifurcation (r = 0.39) and the adductor canal (r = 0.28). The correlations were statistically significant with p = 0.0049 and 0.049 in the bifurcation segment and the adductor canal, respectively. Fig 5 shows examples of a highly eccentric vessel wall and one with low eccentricity. Lesions with high eccentricity were typically associated with a larger wall area compared with lesions of lower eccentricity. In the bifurcation segment, the eccentricity is not significantly correlated with the lumen area, whereas the lumen area in the adductor canal was negatively correlated with the lumen area and the correlation was statistically significant (p = 0.017). In the adductor canal, the wall area increase is accompanied by a significant luminal narrowing, whereas the luminal area preserves at the bifurcation. The eccentricity had a statistically significant positive correlation with the NWI in the adductor canal (r = 0.48, p = 0.0004), whereas the correlation between the eccentricity and NWI at the bifurcation was not statistically significant (p = 0.28).

Discussion

Many in vivo and ex vivo studies have found that stenosis in the adductor region of the femoral artery is the most severe. 3–6 The in vivo studies on plaque distribution were generally based on x-ray angiography. 3–6 However, although useful in assessing luminal narrowing, angiography provides no information regarding the vessel wall,
and therefore, regarding the relationship between plaque size and luminal narrowing. Several IVUS investigations have been performed to study the remodelling mechanism of the femoral artery; the results of these studies have been mixed. Losordo et al. concluded that compensatory enlargement occurs in atherosclerotic regions of the femoral artery, but is not present in normal vessel segments immediately adjacent to them. Pasterkamp et al. suggested that the remodelling response to plaque growth ranges from no remodelling, in which case the plaque encroaches upon the lumen, causing luminal narrowing, to compensatory enlargement that preserves the luminal area, or even luminal enlargement. The mechanisms underlying the different remodelling models are unclear, and constrictive and expansive remodelling can occur in one arterial segment. However, these studies are common concluding that compensatory enlargement of the femoral artery is a focal process. Although the adductor canal is the area in which stenosis most frequently occurs, arterial remodelling is seldom studied at that location using IVUS, possibly due to the fact that the exact location of the adductor canal cannot be determined using IVUS.

The introduction of improved blood-suppression techniques has made 3D MRI acquisition a viable alternative to the conventional 2D FSE protocol. The 3D MERGE sequence was developed by integrating the flow-sensitive MSDE technique with the 3D spoiled segmented fast low angle shot (FLASH) readout sequence. This sequence has been shown to enable fast, accurate, and reproducible plaque assessment in the carotid artery. Compared to IVUS, 3D MRI is non-invasive. The adductor canal can also be clearly visualized (Fig 1d), making 3D MRI a valuable imaging tool to investigate localized atherosclerosis in this region. The purpose of the present study was to evaluate whether 3D

**Figure 2** Bland–Altman plots of the mean differences between measurements obtained in the adductor canal and in the bifurcation segment versus the mean measurements obtained at these two regions. Bland–Altman plots for six measurements are displayed: (a) lumen area, (b) wall area, (c) NWI, (d) maximum thickness, (e) minimum thickness, and (f) eccentricity.
MERGE was sensitive enough to identify the distinct morphological characteristics of plaque burden in the adductor region.

In other vascular beds, atherosclerosis is localized at the bifurcations. Thus, in this study, a 4 cm segment centred at the bifurcation and the SFA was used as a reference to assess the plaque burden in the adductor canal. Because the bifurcation and the adductor canal in the same artery of the same patient were compared in this study, the bifurcation measurements of patients served as the control for the adductor canal measurements, avoiding the comparisons of measurements between patients and limiting the effects of potential confounders that may have contributed to the differences. Based on the bilateral measurements obtained for 25 patients with atherosclerotic SFA, the vessel wall area in the adductor region was not significantly greater than that in the bifurcation, suggesting that the adductor region was not more prone to plaque formation. However, the lumen was significantly narrower in the adductor canal. These two results are consistent with the observation obtained in the ex vivo histological studies of Blair et al. Although the present study involves only atherosclerotic patients, the study by Blair et al. provided evidence that the lumen area in the proximal SFA and the adductor canal is the same for normal subjects. The evidence provided in the present study for atherosclerotic patients together with that from the study of Blair et al. in normal subjects, suggest that the difference between lumen area in the adductor canal and proximal SFA is due to the limited ability of arterial enlargement as plaque grows in the adductor region. The limited compensatory enlargement explains the prevalence of severely stenosed lesions in the adductor canal.

Eccentricity has been proposed as a parameter characterizing high-risk plaques, and has also been linked with an increased plaque progression rate. Clinical studies have also shown that the incidents of cerebrovascular and coronary events are significantly higher in patients with eccentric plaques. In the present study, wall area had a significant positive correlation with plaque eccentricity in the adductor canal.

![Fig 3](image-url)

**Figure 3** Transverse images chosen at the bifurcation segment and the adductor canal for three patients. Each column represents images for the same patient (denoted as patient A, B, and C as labelled). Rows i and ii show the same transverse image selected from the bifurcation segment with and without wall and lumen boundaries, respectively. Rows iii and iv show the same transverse image chosen in the adductor canal with and without wall and lumen boundaries, respectively. In each of these patients, the wall areas are similar in the bifurcation segment and the adductor canal. Patient A has the largest difference between the lumen area in the adductor canal and in the bifurcation segment. Patient B is associated with the mean difference (Fig 2a), and the difference is smallest in Patient C.
both the adductor and the bifurcation segments. However, although eccentricity had a significant negative correlation with the lumen area in the adductor canal, this correlation was not significant in the bifurcation segment. These results provide evidence that as plaque size increased, plaque eccentricity also increased. As eccentricity increased, the luminal area in the adductor canal became narrower, whereas the luminal area in the bifurcation segment was preserved. In the bifurcation segment, as the eccentricity increased, the vessel wall size also increased, but the increase in vessel wall area was not enough to produce a significant positive correlation between eccentricity and NWI. In the adductor canal, the increase in eccentricity was associated with a significant vessel wall increase and luminal narrowing, and as a result, there existed a significant positive correlation between eccentricity and NWI.

One limitation of this pilot study is that only one transverse image was chosen from each of the bifurcation and adductor segments for analysis. The measurements from one section with the largest plaque burden may not be representative enough for the whole segment under investigation as the plaque burden and the morphological characteristics may vary along the length of the lesion. To address this issue, the present authors are currently analysing the femoral 3D MERGE images in a cohort consisting of diabetic and non-diabetic patients using the 3D fast segmentation and an editing tool recently developed by our group. This tool allows us to segment the wall and lumen boundaries for the whole superficial femoral artery in 8 min. With the segmented contours, the wall and lumen surfaces can be reconstructed using a 3D surface reconstruction technique previously developed for carotid artery analysis. The wall thickness of the arteries can be evaluated on a point-by-point basis and displayed as a 3D wall thickness distribution map. To facilitate interpretation of the distribution, the 3D map can also be cut and unfolded to

### Table 3

Correlation coefficients between plaque eccentricity and three measurements [lumen area, wall area, and normalized wall index (NWI)] obtained in the bifurcation segment and the adductor canal.

<table>
<thead>
<tr>
<th></th>
<th>Bifurcation</th>
<th>Adductor</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r_{bf} (95% CI)</td>
<td>p-Value</td>
</tr>
<tr>
<td>Lumen area (mm²)</td>
<td>0.18 (−0.10, 0.44)</td>
<td>0.21</td>
</tr>
<tr>
<td>Wall area (mm²)</td>
<td>0.39 (0.13, 0.60)</td>
<td>0.0049</td>
</tr>
<tr>
<td>NWI</td>
<td>0.16 (−0.13, 0.42)</td>
<td>0.28</td>
</tr>
</tbody>
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Each p-value represents the probability of obtaining a correlation coefficient as large as the observed value by chance, if the true r is 0.
produce a 2D flattened map. These maps will provide much more detailed information regarding the spatial distribution of plaques as well as patterns of luminal narrowing in relation to surrounding muscular structures.

The second limitation of the present study was the unavailability of follow-up measurements. A longitudinal study of plaque burden and lumen area would provide more insights on the change of eccentricity and lumen area in relation to plaque progression/regression in the adductor canal as compared to more proximal segments of the femoral artery. Nevertheless, in the present cross-sectional study, it was shown that (1) compensatory enlargement is limited in the adductor canal; (2) plaque eccentricity is positively correlated with plaque size; (3) plaque eccentricity is only positively correlated with luminal narrowing in the adductor canal.

Unlike the two most commonly used techniques in PAD assessment, x-ray angiography and IVUS, 3D MRI acquisition is non-invasive. This non-invasive imaging tool enables more practical monitoring of symptomatic PAD patients, which is particularly important considering that symptomatic PAD is predictive of cardiovascular events and death. This study has demonstrated the utility of the 3D MERGE sequence for localized arterial assessment. In particular, it has confirmed the unique characteristics of plaque burden development in the adductor canal. The capability of localized assessment will prove useful in future longitudinal studies for clarifying the roles of plaque size, morphology, and location in relation to PAD symptoms.

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