Journal of Cardiovascular Magnetic Resonance (2006) **8,** 529–534

ISSN: 1097-6647 print / 1532-429X online
DOI: 10.1080/10976640600675245

PERIPHERAL ANGIOGRAPHY AND ATHEROSCLEROSIS

Carotid Black Blood MRI Burden of Atherosclerotic Disease Assessment Correlates with Ultrasound Intima-Media Thickness

Venkatesh Mani, PhD,[1,2] Silvia H. Aguiar, MD,[1] Vitalii V. Itskovich, PhD,[1,2] Karen B. Weinshelbaum, BS,[1] John E. Postley, MD,[4] Erika J. Wasenda, BS,[1] Juan Gilberto S. Aguinaldo, MD,[1,3] Daniel D. Samber, PE,[1,2] and Zahi A. Fayad, PhD[1,2,3]

[1] *Imaging Science Laboratories*
[2] *Department of Radiology, Mount Sinai School of Medicine, New York, NY, USA*
[3] *The Zena and Michael A. Wiener Cardiovascular Institute, the Marie-Josée and Henry R. Kravis Cardiovascular Health Center, and Department of Medicine, Mount Sinai School of Medicine, New York, NY, USA*
[4] *College of Physicians and Surgeons, Columbia University, New York, NY, USA*

ABSTRACT

The aim of this study was to correlate carotid black blood MRI based measurements with those obtained by ultrasound intima-media thickness (IMT). Seventeen patients with intermediate to high Framingham cardiovascular risk score underwent both carotid ultrasound and rapid extended coverage double inversion recovery black blood carotid MRI. Overall, there was good correlation between wall area, wall thickness, and plaque index measured by MRI and the IMT measurements obtained from the ultrasound images (max $r^2 = 0.72$, $p < 0.05$). Patients with mean IMT $\geq$ 1.2 mm had significantly higher values of wall area, plaque index and wall thickness compared to patients with mean IMT $<$ 1.2 mm. Vessel wall measurements assessed by black-blood MRI may be potentially used clinically to evaluate plaque progression and regression.

INTRODUCTION

The Cardiovascular Health Study has shown that the incidence of myocardial infarction and stroke are correlated with ultrasound (US) intima media thickness (IMT) measurements and that increased IMT of the carotid artery is an independent risk factor and significant predictor of first myocardial infarction for older adults (1, 2). It has also been shown that increased IMT measurements in young adults are associated with unfavorable cardiovascular risk profiles and that the presence of known cardiovascular risk factors in adolescents correlate with increased IMT in adulthood (3, 4). IMT, however, can be used as a *surrogate* marker for cardiovascular diseases with the drawback that IMT measurements presuppose vessel wall to be continuously uniform.

High-resolution magnetic resonance imaging (MRI) has been used for non-invasive evaluation of arterial walls (5–7). With improvements in imaging technology, magnetic resonance (MR) is quickly becoming the preferred method for imaging the vessel wall (8–12). The use of black blood MRI to directly image atherosclerotic plaques provides the unique opportunity of measuring plaque and wall changes secondary to atherosclerotic disease with high accuracy while taking into account the intrinsic variations of the diseased arterial wall. Data are limited concerning the association between MRI and US measurements of vessel wall (13).

We hypothesize that a strong correlation exists between burden of atherosclerotic disease (BAD) derived from MRI and US IMT measurements. We therefore further hypothesize that MRI measurements may be used as an alternative to IMT measures.

Keywords: Black-Blood MRI, IMT, Atherosclerosis, Carotids.
Received 22 September 2005; accepted 11 January 2006
This study was supported partially by NIH/NHLBI RO1 HL71021.
Correspondence to:
Zahi A. Fayad, PhD, FAHA
Imaging Science Laboratories
Mount Sinai School of Medicine
One Gustave L.Levy Place
Box 1234
New York, NY 10029-6574
Fax: 212-534-2683
e-mail: zahi.fayad@mssm.edu

MATERIALS AND METHODS

Patient population

Seventeen patients (12 male, 5 female, mean age 65.6 ± 7.58 years) at moderate to high Framingham coronary heart disease (CHD) risk score underwent both carotid US and black blood carotid MRI. The Framingham 10-year CHD risk score (FCRS) was determined for each patient (14). This study was approved by the institutional review board and informed consent was obtained from all subjects.

MR imaging system and pulse sequences

All MRI images were obtained on a 1.5T whole body MR imaging system (Siemens Sonata, Erlangen, Germany) that was running Numaris 4.0 operating system. The system had a maximum gradient amplitude of 40 mT/m and a slew rate of 200 mT/m/ms. The integrated body coil was used for transmission and a custom built 4-channel carotid array (11) was used for signal reception.

Twelve to 24 non-overlapping cross sectional slices centered around the carotid bifurcation were obtained using the rapid extended coverage double inversion recovery turbo spin echo black blood (REX) pulse sequence (12). Imaging parameters were as follows: proton density weighted (PDW) non-gated sequence imaging 12 slices simultaneously (TR/TE = 2130/ 5.6 ms), with a field of view of 12 × 12 cm, bandwidth of 488 Hz/pixel, matrix size of 256 × 256, a turbo factor of 15 and 2 signal averages. A chemical shift suppression pulse was used to suppress signal from perivascular fat, not affecting the signal from intraplaque lipids. Each scan of 12 slices lasted 1 minute 17 seconds. The total examination time was approximately 15 minutes.

MRI measurements

The outer wall, inner wall, carotid arterial wall thickness at 4 locations (12, 3, 6, 9 o'clock positions), and the lumen diameter on two perpendicular axes were traced on all images by an expert human observer for both the left and right common carotid arteries. A second observer verified these results concurrently, and discrepancies were settled by mutual agreement. Sample MR image measurements are shown in Fig. 1. The wall area was calculated for all the slices as determined by the number of pixels contained within the outer and inner wall traces. The traces and measurements were done using Image Pro Plus Version 5.0 (Media Cybernetics Inc, Silver Spring, MD, USA).

IMT measurements

The US images were obtained using a Sonosite Titan modular US system (Sonosite Inc, Bothell, WA, USA). Images were stored as bitmap files, and then the IMT measurements were performed using SonoCalc Version 1.41 (SonoSite INC. Bothell, WA, USA), an US IMT off-line edge-detection computer software. The IMT sonographic interfaces were outlined automatically by a computer program that defined and joined regions of maximal signal intensity change between lumen/intima and media/adventitia tissue interfaces. Thus defined boundaries were subjected to the best-fit algorithm criteria. One expert observer verified that the automated IMT trace was accurate. If the trace was not satisfactory, it was manually adjusted.

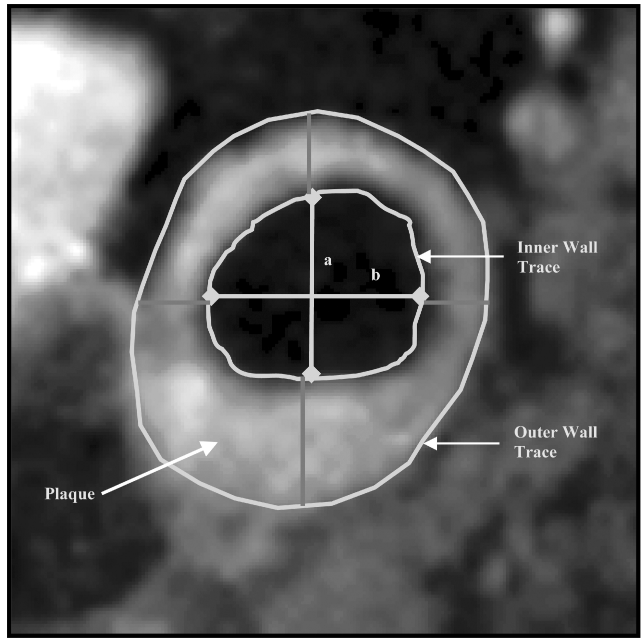


Figure 1. Manual tracing of a cross sectional MR image of right carotid artery of a 59-year-old patient with atherosclerosis. The lines indicate wall thickness at 12, 3, 6, and 9'o'Clock positions: A and B represent lumen diameters on two perpendicular axes. Inner and outer wall tracing can also be seen. Wall area is computed based on the number of pixels present between the inner and outer wall trace.

IMT measurements were recorded from 12 different locations on the near and far walls of the left and right common carotid artery, and the mean IMT was determined (15, 16). Figure 2 shows the IMT measurements from an image of a 57 year-old patient.

Comparison of IMT with MRI data

The mean IMT obtained was compared with average wall area, an MRI based plaque index (PI) and the average wall thickness of MRI measurements obtained from both the left and right common carotid arteries. This measurement included atherosclerotic plaque if any was present. The PI was determined by normalizing the wall area to the average of the lumen diameters. The formula is given below:

$$PI = \sum_{1}^{n} \frac{WallArea}{(a+b)/2}, \qquad [1]$$

where a and b are the lumen diameters of the vessel wall on two perpendicular axes, and n is the total number of images analyzed for the patient. The purpose of the plaque index was to normalize the values of the wall area measured by MR for individuals of different size and between sexes.

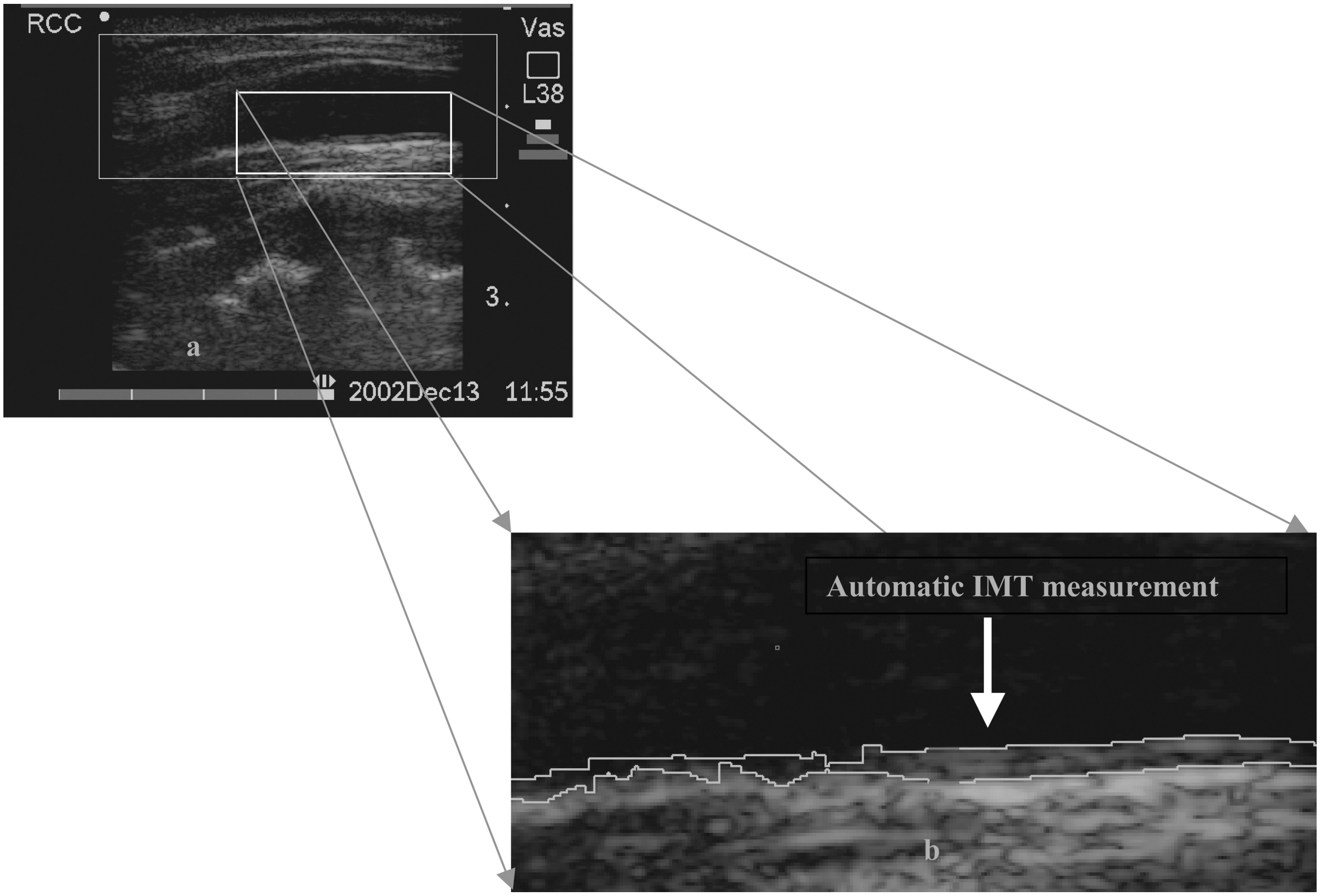


Figure 2. Ultrasound of right common carotid artery of a 57-year-old female patient at risk for atherosclerosis. Panel (B) shows zoomed image of panel (A) as shown by the arrows. The automated IMT trace is shown by the gray lines.

A mean IMT values of 1.2 mm has been shown by several studies as the number associated with elevated risk for cardiovascular disease (17). Patients with mean IMT values $\geq$1.2 mm were compared with patients with mean IMT values <1.2 mm in terms of wall area, plaque index and wall thickness measured by MRI.

The mean value of carotid wall thickness $\leq$2 mm as measured by MRI was considered to be normal. Wall thickness >2 mm was considered to be abnormal and therefore said to exhibit signs of atherosclerosis.

Statistics

Spearman's correlation was used to compare the MRI and IMT data. A two-sample t-test was used to compare the values of MR parameters for values of IMT $\geq$1.2 and <1.2 mm. A p value <0.05 was considered statistically significant. Scatter plots showing the correlation between various parameters were done using Excel 2000 (Microsoft Corp, Seattle, WA, USA), and statistical analysis was performed using NCSS software (NCSS Statistical Software, Kaysville, UT, USA).

RESULTS

Patient distribution was 29% female, 38% family history of heart disease, 6% history of stroke, 24% history of CHD, 35% hypertension, 6% diabetic and 69% on lipid lowering treatment. The FCRS for this patient population was 14.6 $\pm$ 0.94% (ranged from 8% to 31%).

For all 17 patients, MRI measurements showed average carotid wall area of 40.40 $\pm$ 14.27 mm^2, a PI of 5.91 $\pm$ 1.82 mm, average wall thickness of 2.60 $\pm$ 0.69 mm. The mean IMT was 1.16 $\pm$ 0.32 mm.

Overall, there was good correlation between MRI vascular profile measurements and IMT data. Figure 3A shows a plot of the correlation between the mean IMT and the average wall thickness of the carotid. Figure 3B shows the correlation between the wall area of the carotids and the mean IMT, and Fig. 3C shows the correlation between the PI and the mean IMT. The highest correlation was observed between the mean IMT and wall area measured by MRI ($r^2 = 0.72$).

Table 1 shows the comparison of wall area, plaque index and wall thickness measured by MRI between patients with mean IMT <1.2 mm and those patients with mean IMT $\geq$1.2 mm.

Table 1. Comparison of wall area, plaque index and wall thickness of common carotid arteries with mean IMT

Parameter	Mean IMT < 1.2 mm (n =12)	Mean IMT ≥ 1.2 mm (n = 5)	p value
Wall Area, mm^2	33.02 ± 7.00	58.11 ± 11.16	0.002
Plaque Index, mm	5.00 ± 0.95	8.07 ± 1.56	0.004
Thickness, mm	2.29 ± 0.41	3.34 ± 0.69	0.011

All values are expressed as Mean ± Standard Deviation. Bold p value indicates significant difference.

Patients with mean IMT ≥1.2 mm had significantly higher values of wall area, plaque index and wall thickness compared to patients with mean IMT <1.2 mm.

DISCUSSION

The results of the present study show a strong correlation between common carotid MRI burden of atherosclerotic disease (wall area, plaque index and wall thickness) and mean carotid IMT obtained by US. As IMT measurements have been linked to increased risk of acute cardiovascular events, our results may substantiate the clinical use of black blood MRI in monitoring plaque burden and directing therapy in selected cohorts. The high spatial resolution and low variability as demonstrated by lower values of standard deviations of MRI measurements allow recognition of significant clinical variations in a small sample of population. MRI's unique features also permit direct visualization of the plaque and arterial wall changes facilitating an objective profile of the disease. IMT, on the other hand, is only a surrogate marker for atherosclerotic disease.

Lower correlation between carotid wall thickness by MRI and IMT can be explained by the fact that MRI images incorporate adventitia as compared to US, which measures only the intima and media. This phenomenon can also explain consistently higher values of MR measurements compared to those obtained by IMT. Another drawback of IMT measurements is that excessive arterial wall calcification may cause artifacts obscuring US signal. Transition studies have been performed to assess carotid artery atherosclerosis by measuring plaque area and plaque volume using 3D US (18).

MRI also allows assessment of plaque thickness, extent, and composition (19) and can be performed in different vascular sites in the same session. It compares well with transesophageal echocardiography (TEE) in aortic plaque detection and can be safely completed without the use of contrast agents or exposure to ionizing radiation (6). Both MRI and IMT are methods for assessing burden of atherosclerosis, which may determine the probability of cardiovascular events in humans, and since neither of these two different methods is considered a "gold standard", the correlation values between them shown in this study need not approach unity.

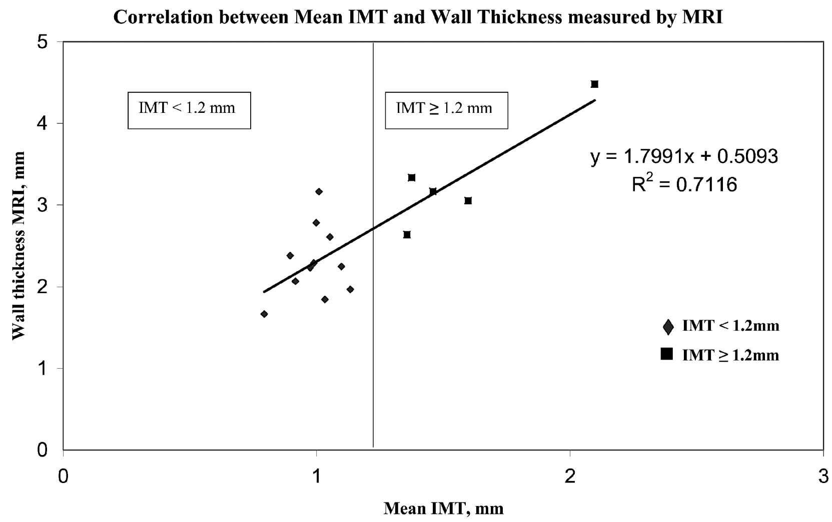
The effects of statins on vessel wall thickness have been studied by MRI (20) and by US carotid IMT data (21). The Rotterdam study showed that predictive value is not substantially increased when adding IMT to a risk assessment for coronary heart disease and cerebrovascular disease (22). A follow-up of the Rotterdam study found that "relatively crude" measurements of atherosclerosis such as direct assessment of plaques through US or x-ray were as predictive of incidence of myocardial infarction as was the precise measurement of IMT (16). The high correlation with IMT found in this study shows that black blood MRI of carotid arteries may possibly be used as a predictive tool for cardiovascular events. Prospective studies are currently being conducted by our group to further assess this possibility. The meaning of an increased IMT in healthy subjects without evidence of atherosclerotic plaques have been object of studies (23).

Although the value of IMT as an useful predictor for risk screening is unclear, it is well established that carotid artery IMT is strongly predictive of incidence of cardiovascular disease, and it is widely used for serial measurements and as an end point in clinical trials (24, 25). The mean IMT values of 1.2 mm have been shown by several studies as the number associated with elevated risk for cardiovascular disease (17). In our study, we observed that patients with elevated mean IMT (≥1.2 mm) had significantly higher values of wall thickness, wall area and plaque index as measured by MRI. On going studies are looking at relationships between subclinical atherosclerotic measures in different major vascular beds (26–28) and measures of atherosclerosis using different imaging modalities in asymptomatic and asymtomatic subjects across global CHD risk categories. IMT is also easy to perform and is relatively inexpensive. MRI on the other hand require more complicated hardware (MR scanners) and are therefore more expensive.

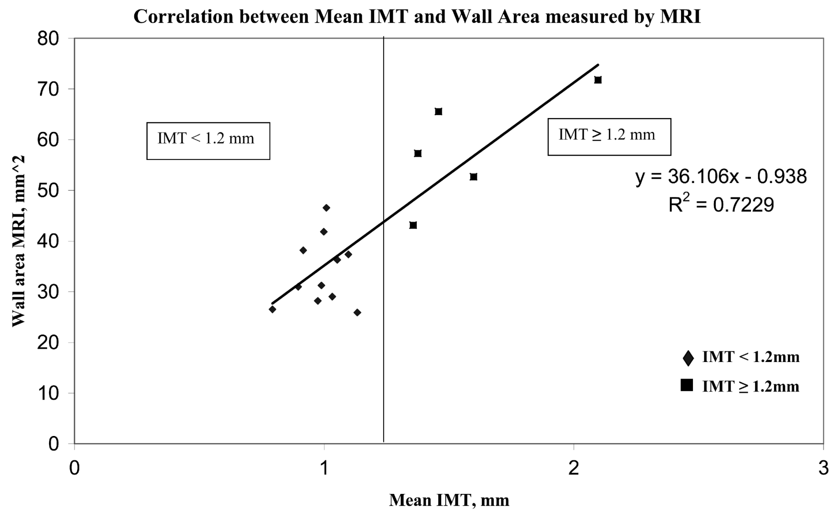
In summary, the assessment of atherosclerotic disease and vessel wall measurements by non-invasive black blood MRI may be used for a thorough clinical evaluation of patients in a selected risk distribution, thereby allowing the estimation of total burden of atherosclerotic disease in different vascular beds. The results presented in this study indicate that black blood MRI may be comparable to carotid ultrasound measurements and provide information about atherosclerotic plaque composition, extent and size. This in turn can be used to direct clinical decisions regarding patient treatment such as surgical intervention or pharmacological therapy (statins). It is important, however, to keep in mind that, in search for the paradigm of atherosclerosis evaluation, techniques are limited by cost and availability.

ABBREVIATIONS

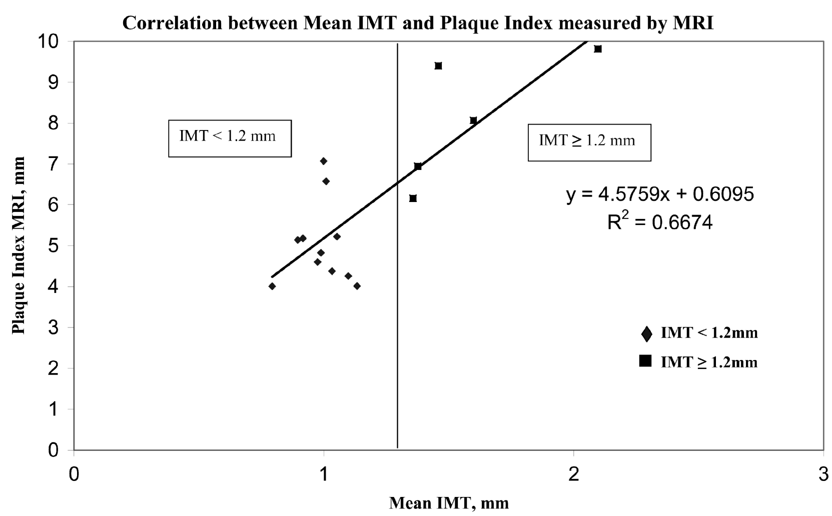
US Ultrasound
MRI Magnetic Resonance Imaging
IMT Intima Media Thickness
CHD Coronary Heart Disease
REX Rapid Extended Coverage
DIR TSE Double Inversion Recovery Turbo Spin Echo
PI Plaque Index
TEE Trans Esophageal Echocardiography



(a)



(b)



(c)

Figure 3. (A) Correlation between the Wall Thickness of the carotids and the Mean IMT. (B) Correlation between the Wall area of the carotids and the Mean IMT. (C) Correlation between the plaque Index (PI) of the carotids and the Mean IMT. ♦ – IMT $<$ 1.2 mm, ■ – IMT $\geq$ 1.2 mm.

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