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ARTERIAL IMAGING

Combined Transesophageal and Surface MRI Provides Optimal Imaging in Aortic Atherosclerosis

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ABSTRACT

Objective: Surface magnetic resonance imaging (MRI) for aortic plaque assessment is limited by the trade-off between penetration depth and signal-to-noise ratio (SNR). For imaging the deep seated aorta, a combined surface and transesophageal MRI (TEMRI) technique was developed 1) to determine the individual contribution of TEMRI and surface coils to the combined signal, 2) to measure the signal improvement of a combined surface and TEMRI over surface MRI, and 3) to assess for reproducibility of plaque dimension analysis. *Methods and Results:* In 24 patients six black blood proton-density/T2-weighted fast-spin echo images were obtained using three surface and one TEMRI coil for SNR measurements. Reproducibility of plaque dimensions (combined surface and TEMRI) was measured in 10 patients. TEMRI contributed 68% of the signal in the aortic arch and descending aorta, whereas the overall signal gain using the combined technique was up to 225%. Plaque volume measurements had an intraclass correlation coefficient of as high as 0.97. *Conclusion:* Plaque volume measurements for the quantification of aortic plaque size are highly reproducible for combined surface and TEMRI. The TEMRI coil contributes considerably to the aortic MR signal. The combined surface and TEMRI approach improves aortic signal significantly as compared to surface coils alone. *Condensed Abstract:* Conventional MRI aortic plaque visualization is limited by the penetration depth of MRI surface coils and may lead to suboptimal image quality with insufficient reproducibility. By combining a transesophageal MRI (TEMRI) with

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surface MRI coils we enhanced local and overall image SNR for improved image quality and reproducibility.

Key Words: Atherosclerosis; Thoracic aorta; Transesophageal MRI; Plaque volume measurements; Reproducibility.

INTRODUCTION

Atherosclerosis is the leading cause of death in the western world and its incidence is projected to increase in the future (Fuster et al., 1992; Ross, 1999). Clinicians have traditionally focused on flow-limiting stenoses originated from the atherosclerotic process. However, over the last two decades it has been shown that the process of atherosclerosis begins in the blood vessel wall as an extraluminal phenomenon (Glagov et al., 1987). Therefore, the notion of flow limiting stenoses has been challenged and studies now focus more on the vessel wall (Little, 1990). Also, it has been shown that plaques leading to mild or moderate stenoses are at least as likely to rupture as those causing more severe stenoses (Ambrose et al., 1988; Davies and Thomas, 1985; Little, 1990; Little et al., 1988; Solberg and Strong, 1983) and may be strong predictors of future stroke or cardiovascular events. (Fazio et al., 1993; Tunick and Kronzon, 2000). Thoracic aortic atherosclerosis is an important marker of systemic atherosclerosis and is correlated to cerebrovascular and coronary artery disease (Cohen et al., 1997; Kallikazaros et al., 2000). Because *aortic* atherosclerosis is a surrogate marker for coronary atherosclerosis, it is an ideal model for imaging methods that would be able to quantify the extent of plaque, differentiate between plaque components, and possibly predict the likelihood of future clinical events.

Magnetic resonance imaging (MRI) is a very sensitive technique for visualization of plaques and characterization of plaque components (Toussaint et al., 1996; Yuan et al., 1996). However, a specific limitation of surface MRI receiver coils is their trade-off between penetration depth and signal-to-noise ratio (SNR). To adequately detect and visualize such distant structures, a strong local signal could be of paramount importance. As the distance to the object of interest increases, the SNR gradually decreases (Shunk et al., 1999). In order to address the issues of reduced SNR that are encountered while imaging deep-seated structures, a novel imaging technique, transesophageal MRI (TEMRI), was developed (Shunk et al., 1999, 2001). At the cost of slightly increased invasiveness, a combined surface and TEMRI approach may lead to higher SNR in the region of interest. This enhanced SNR could subsequently be traded for improving spatial resolution for the sensitive early detection and changes in atherosclerosis, better plaque characterization, and progression or even regression of plaques.

Recently, Chan et al. (2001) calculated the reproducibility of plaque area measurements from three serial two-dimensional (2D) MRI examinations performed in 16 patients and concluded that while slice-specific plaque perimeter and lumen area were highly reproducible, plaque area measurements were more subject to variability and would not be well-suited for serial MRI studies. We hypothesized that a three-dimensional (3D) method of plaque volume measurement based on the application of a modified Simpson's rule (Fleiss, 1986; Rosner, 1995; Whittaker and Robinson, 1967) to a stack of contiguous perpendicular cross-sectional images would be a more reproducible method of assessing atherosclerotic plaques that can be used for longitudinal plaque regression studies.

The aim of this study was 1) to determine the individual contribution of TEMRI and surface coil to the combined aortic signal, 2) to determine if a combination of surface and TEMRI provides improved signal over that of surface MRI alone in the imaging of aortic atherosclerotic plaque, and 3) to assess for reproducibility of plaque dimension analysis and find a reliable and highly reproducible method of plaque assessment that can be used for longitudinal plaque regression studies.

METHODS

Study participants included 24 patients who were recruited for an ongoing trial of the response of aortic atherosclerosis, as measured by combined surface and TEMRI, to simvastatin therapy. We included patients with documented atherosclerosis in at least one vascular territory: at least moderate (>3.9 mm) aortic atherosclerosis seen on transesophageal echocardiography, moderate coronary artery disease (>50% lesion) in at least one coronary artery seen at cardiac catheterization, >50% carotid lesion seen on ultrasound or documented peripheral vascular disease. We excluded patients with pacemakers, automated implanted cardioverter defibrillators, aneurysm clips, abnormal nasopharyngeal anatomy, active peptic ulcer disease, severe dysphagia, abnormally elevated baseline liver transaminases ($>2\times$normal), a clinically significant medical event within three months before study entry,

Table 1. Baseline of patients demographic data.

Age (years)	70±9
Gender	10 females
Hypertension	73%
Diabetes	13%
Smokers	15%
Stroke/transient ischemic attack	33%
Coronary artery disease	45%
Positive family history of coronary artery disease	58%

decompensated congestive heart failure, or inability to give informed consent. All patients provided written informed consent and the protocol were approved by the Johns Hopkins Committee on Clinical Investigation. The demographic data of these patients are listed in Table 1.

MRI PROTOCOL

MRI of the thoracic aorta was performed in a 1.5 T (40 mT/m) Sigma (General Electric, Milwaukee, WI) magnet using a standard flex coil (General Electric) and a specially designed two-element cardiac phased-array coil positioned on the chest wall. We used a TEMRI receiver coil (Intercept Esophageal MR Coil, Surgi-Vision, Gaithersburg, MD) in the remaining coil position. The TEMRI probe is an antenna housed inside an 8 to 12 French nasogastric tube and consists of a flexible 1.2-mm diameter loopless RF receiver constructed from a 50Ω coaxial cable with a 10-cm extension of the inner conductor at the distal end and proximally attached to an adjustable tuning and matching circuit which is connected via coaxial cable to the MRI scanner transesophageal (TE) antenna (Intercept Esophageal MR Coil, Surgi-Vision, Gaithersburg, MD) (Fig. 1). The circuitry provides high-speed diode switching to decouple the antenna during external RF pulses, preventing the patient from possibly induced unbalanced currents and allowing signal reception between pulses (Shunk et al., 1999, 2001). It was positioned in the esophagus through a small-caliber nasogastric tube by an experienced physician. Electrocardiographi-gated fast-spin echo and inversion recovery radiofrequency (RF) pulses were utilized to produce black blood double oblique sagittal images (candy-cane view) of the thoracic aorta. The thickest plaque was identified in the aorta and through this area, six *contiguous* images (to reduce submillimeter errors in matching of the images at different time points) with a 4-mm-slice thickness were obtained (1 slice/breath hold). We imaged perpendicular to the vessel wall with T2-weighted (T2W) and proton-density-weighted (PDW) techniques during breath holds (11–15 s for PDW and 15–20 s for T2W images). All the participants were able to complete the study and repetitive breath holds were not required. Additional imaging parameters were 16–24 cm field of view, repetition time (TR) = 2 RR intervals, echo delay time (TE) = 20 ms (PDW) and 65 ms (T2W), image matrix 256 × 160, echo train length (ETL) = 16–24, 1 NEX (number of excitations), no phase wrap. The total duration was about 40 min (actual scan time was about 30 min).

IMAGE ANALYSIS

Data from each receiver coil (1 anterior, 2 posterior, and 1 transesophageal) were obtained individually, along with a composite image of all coils (combined). The MR images were analyzed using Scion Image 4.02 software (Scion Corporation, Frederick, MD) in a blinded manner at a different time than when the patients were imaged. The luminal and outer aortic wall boundaries were traced manually using a region of interest tool, and plaque area was calculated by subtracting the inner luminal area from the outer aortic wall area. Average plaque thickness was analyzed from six aortic images per patient (sum of the maximal plaque thickness on each of the 6 individual images/6). The average 2D plaque area (sum of all 6 individual image areas/6) was calculated by subtracting the outer aortic

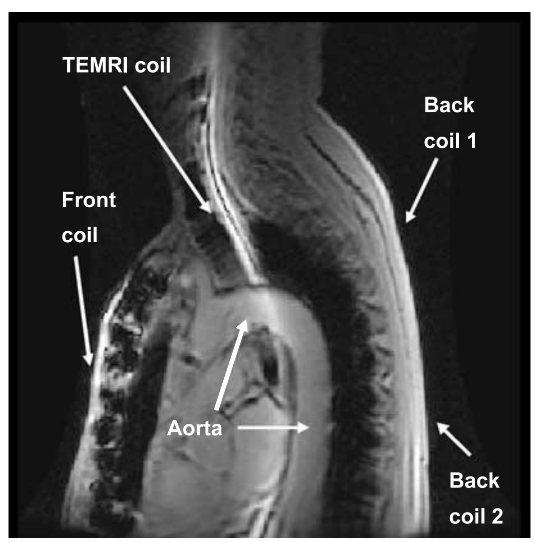

Figure 1. The TEMRI antenna is advanced through the nose and placed in the vicinity of the aortic arch and descending aorta. Note also the thoracic surface coil and the back coil signal.

wall from the inner luminal area. Three-dimensional plaque volume was calculated by integrating the area of plaque in the 2.4 cm (6 mm slices × 6 slices) region of aorta imaged using a modification of the Simpson's rule (Whittaker and Robinson, 1967): [(image 1 area + image 5 area) + 4 × (image 2 area + image 4 area) + 2 × (image 3 area)]/3 + [(image 5 area + image 6 area)/2]. This technique ensured increased emphasis on the three central slices, thus enabling superior reproducibility as it centered the slices on the same area of maximum plaque.

SIGNAL-TO-NOISE RATIO

Regions of interest (ROI) were drawn approximately 3 cm from the esophagus on the aortic wall using a mean signal ROI pixel area of 700 and mean noise ROI pixel area of 720. In order to maintain precision, the ROIs were *copied* on different images of same patient (surface MRI as well as TEMRI images) and SNR was generated for both T2W and PDW images using the following formula:

$$SNR = (\textit{Mean ROI signal intensity} - \textit{Mean background signal intensity}) / \textit{Standard deviation of background signal}$$

To estimate the amount of contribution of SNR by TEMRI and the surface coils, we imaged the ascending aorta in nine patients, the descending thoracic aorta in 13 patients, and the aortic arch in eight patients and used the following formulas:

$$\%\ \textit{contribution by surface coil to the combined image signal} = (\textit{Surface coil } SNR^2 \times 100\%)/\textit{Combined image } SNR^2$$

and the % contribution by TEMRI coil to the combined image signal

$$= (\textit{TEMRI coil } SNR^2 \times 100\%)/\textit{Combined image } SNR^2$$

SIGNAL INTENSITY GAIN OF TEMRI VS. SURFACE COILS

In six patients, we compared the total signal intensities for PDW images for both approaches (surface alone and combined surface and TEMRI) in three anatomical locations of the aorta (ascending aorta, aortic arch, and descending aorta). This was achieved by obtaining images with and without activating the TEMRI coil during scan acquisition. The % signal gain by using the combined approach was derived from the following formula (Fig. 2):

$$\textit{Combined (TEMRI + Surface coils)} SNR^2 \times 100\%/\textit{Surface coils } SNR^2$$

INFLUENCE OF DISTANCE TO THE TEMRI COIL ON SNR

As seen from Fig. 3A, the signal intensity of the aortic vessel wall near the TEMRI probe is more enhanced than in wall segments far from the probe.

To investigate the heterogeneity of the aortic vessel SNR of the descending aorta and the aortic arch, we subdivided aortic vessel circumferences per slice into quartiles (segments 1 to 4). In six patients with PDW weighting, in the resulting 144 segments (6 pts. with 6 slices and 4 segments per slice) we individually generated SNR values as described above and compared them to the overall signal intensity gain of the combined surface and TEMRI coil approach..

REPRODUCIBILITY OF PLAQUE SIZE MEASUREMENTS

We repeated the combined MRI in 10 patients within one week of the index exam to assess for inter- and intraobserver variability. Reproducibility measurements were performed by two independent observers (WPW, SG). The follow-up MR images of the same patient, were reproduced using imaging planes with various identical anatomical landmarks (e.g., pulmonary arteries).

STATISTICAL METHODS

For regional signal contribution of transesophageal versus surface coils, significance was determined using 95% confidence intervals (CI). Inter- and intraobserver variability was measured using Pearson's correlation coefficient (r). Reproducibility was calculated using the intra-class corellation coefficient R and the coefficient of variation (Fleiss, 1986; Rosner, 1995).

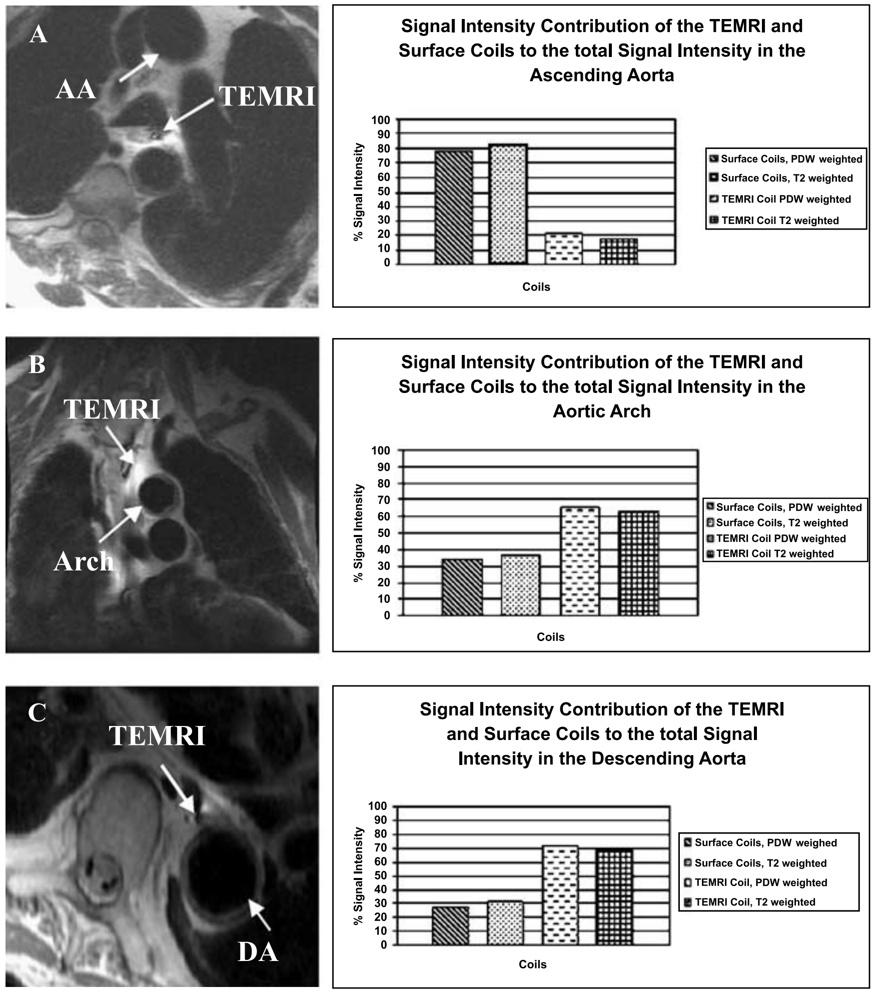

Figure 2. Signal intensity contribution of the transesophageal coil in the ascending (A) and descending (C) aorta as well as in the aortic arch (B). Abbreviations: AA = ascending aorta, DA = descending aorta, Arch = aortic arch.

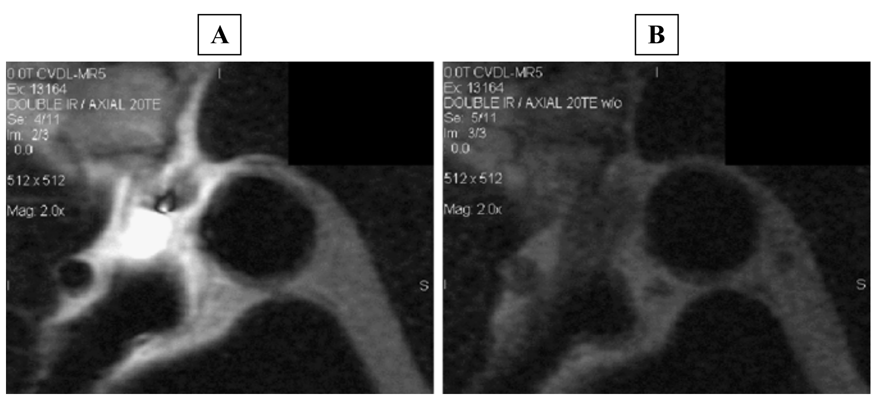

Figure 3. MR image of the aortic arch with (A = left) and without (B = right) the transesophageal coil activated.

RESULTS

Contribution of Surface MRI and TEMRI Coil to the Total Signal

For all measurements, we found a very strong correlation between T2W and PDW images ($r = 0.97$). In the descending aorta, the TEMRI coil SNR was 72% of the combined SNR for PDW images (95% CI, 60–83%). The surface coils accounted for 28% of the combined SNR (95% CI 18–35%). For T2W images in the descending aorta, the TE coil SNR was 67% (CI 57–78%), while the surface coil SNR was 33% (CI 22–43%) of combined image SNR. In the aortic arch, the TEMRI coil SNR was 64% (CI 44–83%) of combined SNR for PDW and 53% (CI 28–79%) for T2W images. In the ascending aorta, the TEMRI coil contributed <25% to the combined SNR. Surface coils accounted for 78% (CI 65–80%) and 82% (CI 66–90%) of combined image SNR for PDW and T2W images respectively. Interobserver and intraobserver agreement were high (both $r = 0.96$).

Signal Intensity Gain of Combined Approach Over Surface MRI

In the descending aorta, the mean SNR of combined surface and TEMRI was 54 ± 6 and that of surface MRI was 24 ± 1.4. The mean noise was 4 ± 0.7 and 4 ± 0.85. Hence, the mean gain in signal intensity due to combined MRI was 225% over surface MRI. Similarly, in the aortic arch, the mean SNR of combined surface and TEMRI was 83 ± 7 and that of surface MRI was 53 ± 13. The mean noise was 9 ± 1 and 13 ± 2. Hence, the mean gain in signal intensity due to combined MRI was 157% over surface MRI.

Influence of Distance to the TEMRI Coil on SNR

SNR measurements could be obtained in all segments. In the aortic arch, in the two segments nearest to the TEMRI coil the average SNR was 26% (20–52%) higher than the mean SNR gain of the circumferential vessel wall SNR. In the descending aorta the mean SNR was 32% (27–56%) higher than the mean SNR gain of the circumferential vessel wall.

In the aortic arch as well as the descending aorta the segments further away from the TEMRI coil showed a mean SNR decrease of 28% (10% and 44%) when compared to the SNR gain of the circumferential vessel wall.

MEASUREMENT OF REPRODUCIBILITY

For plaque thickness, intraclass correlation coefficient was 0.82 and 0.90 and coefficient of variation was 18.9% and 18.2% for PDW and T2W images, respectively. For plaque area, intraclass correlation coefficient was 0.90 and 0.91 and coefficient of variation was 21.3% and 23.9% for PDW and T2W images, respectively. Plaque volume had an intraclass correlation coefficient of 0.95 and 0.97 and coefficients of variation of 5.7% and 4.8% for PDW and T2W images, respectively. The correlation of plaque volume was excellent between PDW and T2W images ($r = 0.97$). The variability range was 4.5–5.3% while intraobserver and interobserver concordances were 0.91 and 0.81, respectively. Based on this, we concluded that >4.6% changes in aortic plaque volume could be considered as accurately measured by MRI.

DISCUSSION

MRI is a very sensitive technique for visualization of atherosclerotic plaques and characterization of plaque components (Toussaint et al., 1996; Yuan et al., 1996). However, a specific limitation for surface MRI receiver coils is their trade-off between penetration depth and signal-to-noise ratio (SNR). The distal portion of the aortic arch and the descending aorta are situated ''deep'' in the thoracic cavity, which necessitates that in order to image them, surface coils with sufficient penetration depth are required. This would make them very large in size, which in turn reduces their SNR. Thus, one way to circumvent this potential pitfall is to bring smaller coils with high SNR close to the object of interest. With this idea in mind, TEMRI, a novel imaging technique, was developed (Shunk et al., 1999, 2001). This study demonstrates the potential role that a combined surface and TEMRI approach might play in the MR imaging of aortic atherosclerosis. We were able to demonstrate that the TEMRI coil contributes significantly to the signal attained from the arch and descending aorta. In fact, the contribution of the TEMRI coil to the total signal was about 67–72% in the descending aorta and 53–64% in the aortic arch. As one might expect (because of the relatively anterior location), the TEMRI coil contributed to <25% of the combined signal for the ascending aorta. Furthermore, addition of the TEMRI coil increased the signal by 157–225% in the aortic arch and descending aorta over and above that attained by surface coils alone. In the near vicinity of the TEMRI coil, the SNR gain was even more pronounced.

For imaging purposes, the additional signal intensity could be converted into improved spatial resolution and abbreviated scanning times. Thus, we optimized our TEMRI imaging protocol from 1.5×4.0 mm to a biplanar isotropic resolution of 0.6×4.0 mm, which could potentially aid in getting more detailed information about the vessel wall. Finally, in the case of the loopless antenna coil (like the TEMRI coil), the drop in the signal is a linear inverse of the distance as opposed to a receiver coil where the signal decreases with the inverse square of the distance from the coil (Shunk et al., 1999). Thus, by utilizing the combination approach to image deep-seated structures like the thoracic aorta, we can maintain a high enough (and a relatively lesser drop) signal, which could increase the sensitivity of plaque assessment.

In a patient study by our group (Shunk et al., 2001), we compared the TEMRI approach to that of conventional transesophageal echocardiography (TEE). Although the SNR of the TEMRI probe decreased linearly with radial distance, it maintained its SNR along its longitudinal axis of about 20 cm. Therefore, investigations of the aortic arch and the descending aorta could be accomplished without repositioning of the device and without anesthesia, as in TEE studies. According to the combined surface and TEMRI coil approach even the ascending aorta where the TEMRI coil has no effect on additional SNR, the aortic vessel wall could be imaged with high quality because of the anterior surface coil position.

Secondly, TEE is hampered by near-field limitations inherent to the ultrasound technique that could potentially lead to misdiagnosis of the atherosclerotic disease. The combined approach of surface and TEMRI coils provides a more accurate measure of the entire aortic circumference, especially in the aortic arch, where in ultrasound the lung-tissue interface often leads to severe artifacts. As shown in a cadaver study (Shunk et al., 2001), TEE led to relative underestimation of the atherosclerotic extent with less detailed morphological information, especially in more severe stages of the disease.

In this study, we also investigated the reproducibility of this combined MR imaging approach. Similar to the findings by Chan et al. (2001) (using standard surface coil MRI), we found significant variability in one- and two-dimensional measurements of plaque size (i.e., plaque thickness and area). Because of the sudden alterations of regional plaque surfaces, the thickness and area measurements are less accurate and more vulnerable to anatomic mismatches because only a single slice is measured and an entire anatomical rematch of the patient prior scanning position is virtually impossible. By applying the modified Simpson's rule (Fleiss, 1986; Rosner, 1995; Whittaker and Robinson, 1967) (where the emphasis is predominantly on the middle and lesser on the outer slices) we are able to demonstrate that plaque volume measurements are significantly more reproducible ($r = 0.95-0.97$ and coefficients of variation ranging from 4.8–5.7%) than plaque thickness or area analysis. Thus, assessment of plaque volume appears to be significantly more precise in quantification of changes in atherosclerotic plaques. Our data suggest that this parameter could be used beneficially for further longitudinal pharmacological studies of plaque regression.

We feel that this combination approach with a potential for improved visualization of atheromata can aid in greater understanding of mechanisms and different processes related to plaque progression and might play a role in the longitudinal follow up of plaque regression induced by therapeutic interventions. This technique is also advantageous because an internal MR coil is placed without invading the vascular space. Also, the entire apparatus (coil and the nasogastric tube) can be inserted without any sedation or topical anesthesia, thus minimizing any further risks related to medications. Finally, no major hardware modification is required for this combination approach.

LIMITATIONS

The TEMRI technique is a semiinvasive procedure and therefore demands further safety considerations, operator skills, and exclusion criteria, although none of the patients experienced any adverse effects and all tolerated the procedure well without any sedation or anesthesia. The field of view, although large (16–24 cm), was individually adjusted per patient according to their body habitus and remained consistent for the same patients during follow-up imaging. The reproducibility of plaque volume assessment was excellent ($r=0.95-0.97$); however, in coronary vasculature using intravascular ultrasound, it has been suggested that this variation could still be in the realm of statistically important events in patients with less severe disease.

CONCLUSIONS

This study demonstrates that the measurement of plaque volume by combined surface and transesophageal MRI is a highly reproducible parameter of plaque size assessment that could further increase the accuracy of measurement in longitudinal plaque regression studies.

In this regard, the TEMRI coil contributes substantially to the signal emanating from the aortic arch and descending aorta. Using a combination of surface and TEMRI coils, there is a significant improvement in the aortic signal as compared to the surface coils alone, which leads to improved image quality with enhanced spatial resolution.

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