COMPARISON BETWEEN THREE T1-WEIGHTED SEQUENCES FOR DETECTION AND AREA MEASUREMENT OF INTRAPLAQUE HEMORRHAGE IN CAROTID ATHEROSCLEROTIC PLAQUE IMAGING AT 3 TESLA.

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Introduction: Carotid intraplaque hemorrhage (IPH) demonstrated by *in vivo* 1.5T MR imaging has shown associations with recent and future cerebral ischemic events and plaque progression [1-3]. Typically, T1-weighted (T1W) sequences, black-blood fast spin-echo (FSE) and bright-blood spoiled gradient-echo (SPGR), are used for IPH imaging, since formation of methemoglobin within IPH results in shortening of T1 [1,2]. An alternative technique based on a heavily T1-weighted 3-dimensional magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence (originally termed as "direct thrombus imaging") was also proposed for IPH detection [3] and subsequently extended for use at 3.0T [4]. Recently introduced high-resolution carotid imaging at 3.0T demonstrated a significant improvement in signal to noise ratio (SNR), contrast to noise ratio (CNR) and image quality compared to 1.5T [5]. However, increased susceptibility of paramagnetic ferric iron in hemorrhage may degrade quantification and/or detection of IPH [6]. It is important therefore to identify an optimal technique for IPH imaging at 3.0T.

Purpose: To compare the detection and area measurement of IPH among three T1W sequences (FSE, SPGR, and MPRAGE) at 3.0T using histology of carotid endarterectomy specimens as the gold standard.

Materials and Methods: Twenty patients scheduled for carotid endarterectomy were recruited. Consent forms were obtained and the study was approved by the institutional review board. All patients underwent a carotid MR scan within 4 week prior to endarterectomy on a clinical 3.0T scanner (General Electric) using a custom-made four-channel carotid coil. Three different T1W sequences were acquired: 2D quadruple inversion-recovery [7] FSE (TR/TE=800/11 ms, scan time 6 min), 3D SPGR (TR/TE=23/3.5 ms, flip angle 20°, scan time 4 min), and 3D MPRAGE (TR/TE/TI=13.2/3.2/304-357 ms, flip angle 15°, scan time 4 min). Images were acquired in the axial plane and centered at the carotid bifurcation on the side of planned surgery. All images were obtained with an in-plane resolution 0.63x0.63 mm^2, longitudinal coverage 36 mm, and slice thickness 2 mm for 2D FSE or 1 mm for 3D scans. For each T1W sequence, an experienced radiologist identified IPH blinded to histology and the images and results from the other T1W sequences. IPH was identified as an area of hyperintense signal compared to fibrous tissue. Presence/absence and area of IPH were documented on each slice. Mean values of signal intensities (SI) within IPH and fibrous tissue (FT) were used to calculate %-contrast, which was determined as $(SI_{IPH}-SI_{FT})/SI_{FT}$ *100.

Carotid endarterectomy specimens were fixed in 10% neutral buffered formalin, decalcified in 10% formic acid, and embedded en bloc in paraffin. Sections (10 µm thick) were taken throughout the length of the specimen and stained with hematoxylin-eosin and Mallory's trichrome stains. Morphological features of lumen, vessel wall, and calcifications were used for co-registration between MRI and histology. In corresponding sections, a trained histologist blinded to the MRI findings determined the presence/absence of IPH and, when present, area of IPH.

Across all matched locations, the sensitivity, specificity, and Cohen's kappa value were evaluated using histology as the gold standard for each T1W sequence. To evaluate detection statistics as a function of IPH size, kappa values were also calculated after exclusion of slices where the area of IPH by histology was smaller than a specified cut-off value. Cut off values were calculated as the area of a circle where the radius was an increment of the acquired spatial resolution: area = $\pi*(0.63X)^2$ where X was 1, 1.5, 2 or 2.5 (cut-off value, 1.25, 2.81, 4.99, or 7.79 mm^2). Repeated measure ANOVA was used to compare %-contrast of IPH among 3 image weightings. Pearson's correlation was used to determine associations between MRI and histology measurements of IPH. Mean hemorrhage areas per artery were compared between each MRI sequence and histology by the paired student's t-test.

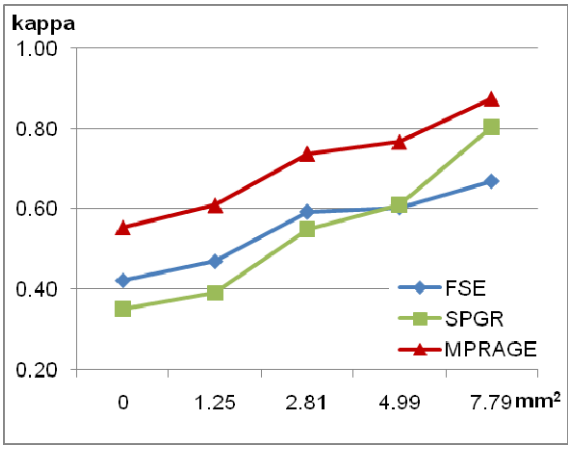
Results: Two arteries out of 20 were excluded due to disrupted histology specimens. The remaining 18 arteries yielded 198 MRI cross-sections matched to histology. Out of 198 slices, 85 slices had IPH by histology. Table 1 details the sensitivity and specificity for the detection of IPH for each T1W sequence. When slices with IPH smaller than each cut-off value were excluded, kappa values increased along with the increment of the cut-off values for all the 3 weightings (Fig. 1). MPRAGE consistently demonstrated the highest kappa at each cut-off point (Fig. 1). Pearson's correlation coefficients for mean IPH area between MRI and histology was the highest for MPRAGE (r=0.843; p<0.001) Mean IPH area imaged by SPGR was significantly smaller than that of histology (p=0.020), whereas those of MPRAGE and FSE were not significantly different from histology. In twenty-four locations where IPH was depicted on all sequences and histology, the %-contrast for IPH was determined (Table1). MPRAGE demonstrated significantly higher %-contrast than FSE (p=0.001) and SPGR (p<0.001) (Fig. 2).

Table 1. IPH detection statistics, area measurement agreement, and contrast properties for three T1W sequences.

	FSE	SPGR	MPRAGE
Sensitivity,% †	63.0	50.0	70.4
Specificity,% †	92.9	98.2	98.2
% contrast (SE)	55.9 (10.8)	60.3 (12.1)	118.1 (10.0) *
Pearson's r‡	0.662	0.737	0.843

† for IPH > 2.81 mm^2; ‡mean hemorrhage area per artery, MRI vs. histology; *p<0.05

Figure 1. Kappa values for three T1W sequences as a function of the hemorrhage area cutoff value (mm^2)



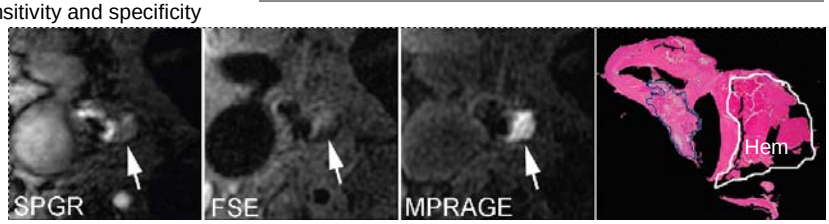


Figure 2. Hyperintensity area (arrows) corresponds to hemorrhage outlined by the white line on the histology image (Hem). MPRAGE showed marked improvement of hemorrhage visualization.

Conclusions: The MPRAGE sequence at 3T has the highest diagnostic capability for the detection and quantification of hemorrhage among 3 different T1W techniques. This study validates the use of MPRAGE as a fast and reliable hemorrhage-specific sequence for 3.0T carotid plaque MRI.

References:

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