Quantitative Contrast Enhancement Maps of the Carotid Atherosclerotic Plaque In-vivo: Methodology and Clinical Assessment

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Introduction: Carotid atherosclerotic disease is one of major sources of stroke. In addition to plaque composition, neovasculature and inflammation are important determinants of plaque vulnerability [1]. Contrast enhancement (CE) patterns of the atherosclerotic plaque are indicative of neovasculature and inflammation. Black-blood contrast-enhanced MRI (CE-MRI) has the potential to provide a comprehensive assessment of plaque burden and compositional information, in addition to CE information. To date, studies on plaque CE-MRI have been limited to qualitative analysis of CE. Quantitative CE maps (QCEM) of the entire atherosclerotic plaque may provide additional markers of plaque vulnerability.

Aim: To obtain QCEM of the carotid atherosclerotic plaque in-vivo and to compare normalized CE histograms between plaques with low and high plaque burden.

Materials and Methods:

Imaging: Twenty four patients underwent CE-MRI according to institutional review board guidelines. Patients were scanned on a GE 3T Signa scanner with a four-element bilateral phased array carotid coil. Pre-contrast black-blood T1w images of bilateral carotids were obtained using a quadruple inversion recovery (QIR) [2] sequence with the following imaging parameters: TR(msec)/TE(msec)/echo train length/FOV(cmxcm)/Matrix/NEX/Slice-thickness(mm) of 800/9/11/14x14/256x256/1/2. Gadodiamide (Omniscan, GE Healthcare, Milwaukee, USA) was then injected intravenously at a dose of 0.1 mmol/kg. Post-contrast T1w images were obtained using identical QIR parameters. **Image analysis:**.A reader matched pre and post-CE images based on the location of the flow divider. Lumen and outer wall boundaries of bilateral carotid arteries were outlined. Pre and post-CE images were registered by an active edge map registration method [3]. Plaque area was divided into four subregions: lumen surface, outerwall surface, shoulder of the plaque and core of the plaque (Figure 1, inset). Lumen and outerwall surface were defined as a 3 pixel wide region around lumen/outerwall contours. The shoulder was defined as the region where the bulk of plaque abuts the adjacent normal wall. The remainder of the plaque was considered to be the core region. All regions were segmented using appropriate morphological image operators. Contrast enhancement was defined as post-CE signal intensity (SI) – pre-CE SI / pre-CE SI. The normalized wall index (NWI), defined as ratio of plaque area to vessel area, was also measured. Locations with NWI<0.5 were considered to have a low plaque burden while locations with NWI>0.8 were considered to have a high plaque burden. CE histograms of plaque subregions were compared between the two groups. Mean, standard deviation (SD), skewness and kurtosis of the CE histograms were tested for difference between the two groups using the Mann-Whitney non-parametric test.

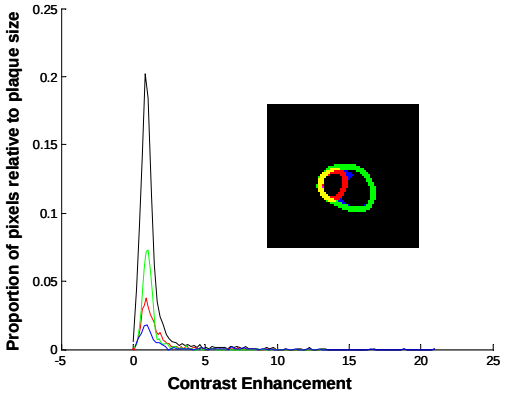

Figure 1: Representative artery based histogram from QCEM and plaque subregions from one image location (inset). Luminal surface (red), outerwall surface (green), shoulder region (blue). Overall plaque histogram is shown in black. Area under plaque CE curve was normalized to one and other histograms scaled proportionally.

Results: QCEM of high quality were generated by this method. The maps clearly show the differences in CE due to plaque composition (figure 2). Group histograms of high and low NWI locations (figure 3) showed significant differences of core CE in mean (P<0.01), SD (P<0. 01), kurtois (P<0.4) and skewness (P<0. 01). The increase in skewness with higher NWI is likely due to increased neovasculature and inflammation associated with a necrotic core, as opposed to small hypoenhancing lipid cores in plaques with low NWI. Overall mean plaque CE was greater with NWI<0.5 (P<0.01) which can be accounted for by a larger proportion of lipid cores in higher NWI. Luminal surface CE did not differ significantly between the two groups. The mean, SD, skewness and kurtosis of outerwall CE were greater with NWI<0.5 (All P<0.01) indicating a less homogenous enhancement in low NWI. Mean shoulder CE was greater with NWI>0.8 indicating increased shoulder inflammation in large plaques.

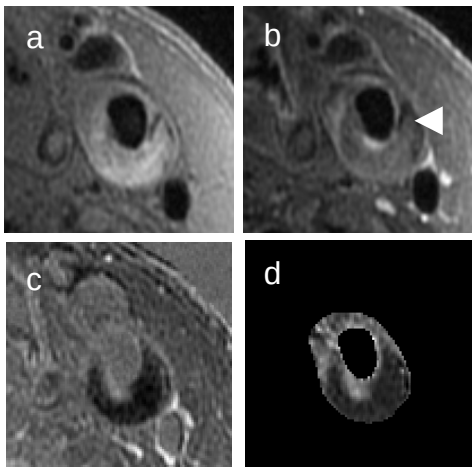

Figure 2) QCEM showing compositional CE a) Pre-contrast QIR b) Post-contrast QIR with hypoenhancing lipid-rich necrotic core (arrow) c) CE map clearly delineating margins of the necrotic core d) QCEM of segmented plaque region.

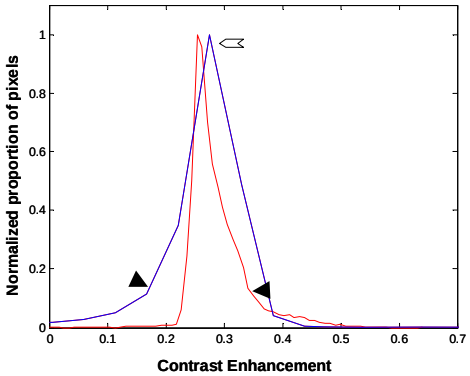

Figure 3: Group histograms showing difference in core CE between low and high plaque burden: Histograms of core CE with NWI > 0.8 (Red) and < 0.5 (Blue). The modes of both histograms were normalized to one to illustrate the difference in histogram shape. Low NWI shows a negatively skewed histogram compared to high NWI (solid arrows). The relative shift of the two histograms (chevron) was reflected by a significant difference in mean core CE.

Conclusions: Accurate QCEM can be obtained in-vivo using our method and CE of subregions of interest in the plaque can be quantitatively compared. Our method is semi-automated and provides a fast, accurate and objective measure to analyze black-blood CE-MRI of plaque. QCEM of good quality were generated in all 24 patients. Analysis of plaque CE revealed significant differences between plaques with low and high plaque burden showing that QCEM analysis can be used effectively in clinical studies. Possible applications of this method include clinical trials where changes in QCEM could be used to monitor the efficacy of statin treatment.

References: [1]Saam T et al, Radiology. 2007, 244:64-77. [2] Yarnykh VL et al, MRM. 2002, 48:899-905. [3] Kerwin WS et al, Topics in MRI, In Press.