Time dependence of necrotic core and fibrous cap quantitative measurements with gadobenate dimeglumine enhanced carotid plaque MRI at 3T

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Introduction The importance of accurate measurement of the lipid rich necrotic core (LR-NC) was demonstrated in a recent prospective study of 154 asymptomatic outpatients with moderate carotid stenosis on duplex ultrasound who underwent an *in vivo* 1.5T MR evaluation of their carotid plaque. The size of the LR-NC was shown to be statistically significantly associated with the occurrence of subsequent ipsilateral carotid cerebrovascular events [1]. It had been proven that contrast enhanced (CE) T1 weighted images used to depict the LR-NC demonstrate a contrast-to-noise ratio (CNR) as good or better than T2 weighted images at 1.5T MR *in vivo* [2]. The improved depiction of the LR-NC as a less enhancing structure compared to the surrounding fibrous tissue on contrast enhanced T1 weighted images (T1WI) at 1.5T with a single dose of gadodiamide was statistically significant [3]. There is no current knowledge how gadobenate dimeglumine-enhanced T1WI carotid plaque at 3T will appear and there is little information about the effect of post-injection time on the appearance of the LR-NC and fibrous cap. The aims of this study are to determine if the CNR in the LR-NC on CE T1WI obtained 5 and 10 minutes after injection of gadobenate dimeglumine at 3T are similar and if the CNR of either CE T1WI is higher compared to double inversion T2 weighted images (T2WI) as part of our on-going evaluation of patients referred with moderate to severe carotid stenosis.

Methods One hundred nine outpatient subjects were referred for 3T MR plaque evaluation of moderate to severe carotid stenosis. Dedicated 3T carotid surface coils were placed on either side of the neck at the level of the carotid bifurcations. High resolution non-contrast 3D time-of-flight MR angiographic images (3D TOF MRA), 2D non-contrast black-blood T2WI, 3D inversion recovery prepared fast spoiled gradient-recalled sequence (3D IR FSPGR), and non-contrast black-blood T1WI were obtained. Post-contrast black-blood T1WI were obtained 5 and 10 minutes after intravenous injection of 1.5x dose of gadobenate dimeglumine. Black-blood T2WI were obtained using a time-efficient multislice double inversion-recovery (MDIR) technique [4]. For pre- and post-contrast T1WI, T1-insensitive quadruple inversion-recovery (QIR) [5] black-blood preparation was used. Forty-three of the109 subjects demonstrated a moderate or large LR-NC on the MDIR T2WI and QIR T1WI. Twelve of the 43 patients subsequently underwent carotid endarterectomy (CEA). Two trained reviewers each independently reviewed the *in vivo* 3T MR carotid image data set and identified the largest region of LR-NC on MDIR T2WI and QIR T1WI. Regions of interest (ROI) were then placed within the LR-NC on MDIR T2WI as well as corresponding regions on the pre-contrast QIR T1WI, 5 and 10 minute delayed CE QIR T1WI. Additional ROI were placed in the adjacent fibrous cap region and air. The LR-NC vs. fibrous cap CNR and LR-NC SNR were calculated on the MDIR T2WI as well as the 5 and 10 minute delayed CE QIR T1WI. In addition the % signal intensity increase within the LR-NC ($\%SI_{LR\text{-}NC}$) and fibrous cap ($\%SI_{CAP}$) were calculated for the 5 minute and 10 minute delayed CE QIR T1WI.

The image data sets were divided into two groups. The first data set included the MDIR T2WI, 3D TOF MRA, 3D IR FSPGR, pre-contrast QIR T1WI as well as the 5 minute delayed CE QIR T1WI. The second data set was similar except that the 10 minute delayed CE QIR T1WI was included instead. The two data sets on all 43 outpatients are being analyzed with MRI-PlaqueView from Vulnerable Plaque Diagnostics. MRI-PlaqueView allows the reviewer to semi-automatically identify the lumen and outer wall boundary then an automated Morphology-Enhanced Probabilistic Plaque Segmentation (MEPPS) algorithm identifies the LR-NC [6]. Histological correlation of the 12 CEA specimens with *in vivo* 3T MRI is pending.

Results All 43 patients have undergone ROI analysis of the LR-NC and fibrous cap with calculation of CNR, %SI, and SNR (Table 1). The CNR of LR-NC was significantly higher on both CE QIR T1WI compared to MDIR T2WI (*P*=0.001). There is no statistically significant difference in the CNR of LR-NC between the 5min and 10min delay CE QIR T1WI (*P*=0.849). Figure 1 shows similar CNR in LR-NC on both the 5min and 10 delay T1WI. The SNR of LR-NC was also significantly higher on the 10 minute delayed CE QIR T1WI compared to both the 5 minute delayed CE QIR T1WI and T2WI. The % SI increase in the LR-NC is lower than fibrous tissue at 3.0T at both time points. Interestingly, the % SI increase in the LR-NC was statistically significantly higher on the 10 minute delayed CE QIR T1WI compared to 5 minute study (*P*=0.001), so is the fibrous tissue (*P*=0.048). These results indicate that the LR-NC is slowly enhancing over time, but so is the fibrous cap. Preliminary quantitative plaque analysis in the first 5 patients using MRI-PlaqueView from VPD demonstrated no significant difference in the measurement of LR-NC volume and % LR-NC using either the 5min delayed or 10min delayed CE QIR T1WI (n=5, P=0.898). Quantitive analysis of the LR-NC volume and % LR-NC in the remaining patients is on going as is histological correlation of LR-NC size from 12 CEA specimens.

	T1WI	T2WI	CE1	CE2
$CNR_{LR\text{-}NC}$	2.49±1.4	4.06±1.9	11.8±1.5	12.0±2.0
$\%SI_{LR\text{-}NC}$	n/a	n/a	0.327±0.1	0.470±0.1
$\%SI_{Fibrous}$	n/a	n/a	1.07±0.1	1.17±0.1
$SNR_{LR\text{-}NC}$	31.9±2.4	33.3±2.4	34.8±2.6	41.1±3.6

Table 1. Mean errors of CNR, SNR and % SI with different sequences CE1 = 5 min delay CE QIR T1WI. CE2 = 10 min delay CE QIR T1WI

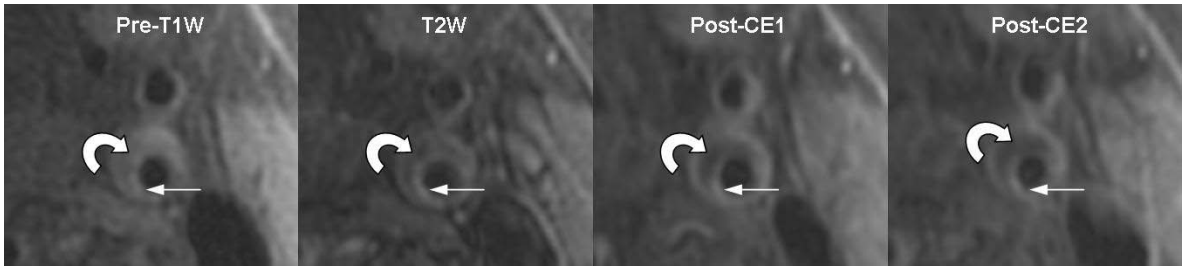

Figure 1. Pre T1W, T2W, and 2 time point post-contrast T1W show deep necrotic core (curved arrow) and fibrous cap (straight arrow) on *in vivo* high resolution 3T MR imaging. Notice similar high CNR on both post-contrast T1W

Conclusion These preliminary findings suggest that the CE QIR T1WI can begin between 5 and 10 minutes after injection of gadobenate dimeglumine at 3T with similar CNR of the LR-NC compared to the fibrous cap. The LR-NC was shown to slowly enhance between 5 and 10 minutes as did the fibrous cap when measured by % signal intensity increase. The SNR of the post-contrast QIR T1WI increases with the time delay and was statistically significantly higher for the 10 minute delay study compared to the 5 minute delay. The effect of the 5 and 10 minute delay on post-contrast QIR T1WI in the measurement of % LR-NC and total LR-NC volume as detected by MRI-PlaqueView was not statistical different in the first 5 patients reviewed. Quantitative LR-NC volume measurements using MRI-PlaqueView in the remaining patients are on going. Histological correlation of the LR-NC size from 12 CEA specimens in this group of 43 patients compared with the *in vivo* 3T MR measurements from both time points is pending.

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