Dynamic Contrast-Enhanced MRI model parameters from different regions within the vascular wall of carotid plaques: comparison with histology

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Target Audience: Researchers interested in non-invasive measurement of microvasculature in carotid plaques

Introduction: Interest in atherosclerotic plaque microvasculature, a hallmark of plaque vulnerability, has greatly increased in recent years. Several studies have shown a correlation between quantitative perfusion parameters (e.g. K^{trans}) derived from pharmacokinetic modelling of Dynamic Contrast-Enhanced (DCE-)MRI with microvasculature as assessed by histology[1, 2], and other features of plaque vulnerability[3-5]. However, these studies focused on only a single region of the vascular wall (i.e. either the entire vessel wall or, adventitial region) using various descriptive statistics (mean, median, or 75th percentile), which makes direct comparison between studies and interpretation difficult. Therefore, we aim to systematically investigate the agreement between K^{trans} parameters from the various regions of the vascular wall (entire vessel wall, adventitia, or plaque) using different descriptive statistics and their correlation with the microvasculature on histology as gold standard.

Methods: *MRI Acquisition.* 45 symptomatic patients with 30-99% carotid stenosis underwent MRI[6], including ECG-gated 3T DCE-MRI (T1w 3D FFE) on a 3T Achieva TX whole body MRI system (Philips, The Netherlands) using a dedicated 8-channel carotid RF coil. At the third time frame (≈ 60 s), 0.1 mmol/kg Gadobutrol (Bayer Healthcare, Germany) was injected at 0.5 ml/sec followed by a 20 ml saline chaser. *MR Image Analysis.* Luminal and outer vessel wall contours were drawn manually. Adventitial and plaque contours were determined automatically from the vessel wall contours[3]. Voxel-wise pharmacokinetic analysis was performed using the Patlak model[7] in the entire wall, adventitia, or plaque region separately, and using various descriptive statistics. *Histology.* Carotid endarterectomy was performed in 12 patients and specimens were collected. Specimens were fixed and further processed into 4-µm-thick slices. Plaque microvasculature was detected with CD31 immunohistochemistry and assessed using morphometric analysis software (Leica, England). Endothelial microvessel perimeter was determined and correlated to K^{trans} parameters using Pearson's correlation coefficient. Two patients were excluded for analysis with histology because of poor MRI (n=1) or histology (n=1) quality.

Results: *MR Parameter Agreement.* A strong correlation was found between K^{trans} determined as mean, median, or 75th percentile from one vascular region (Table), although absolute values differed. Adventitial K^{trans} showed a weak correlation with plaque K^{trans} (r=0.54, p=0.05), but stronger with entire wall K^{trans} (r=0.78, p=0.007, Table). Adventitial K^{trans} was substantial higher compared to that of the plaque (17.3%, p<0.001) and the entire wall region (13.9%, p<0.001). The uncertainty in K^{trans} model parameter estimation was significantly higher for plaque and entire wall compared to adventitia (p=0.015 and p=0.018 respectively). *Correlation of MRI with Histology.* A significant positive correlation was found between K^{trans} determined from either the entire wall (r=0.65, p=0.045) and the adventitial region (r=0.85, p=0.002), but not for the plaque region (r=0.44, p=0.2).

Discussion and Conclusion: K^{trans} determined as mean, median or 75th percentile from one vascular region have a strong mutual correlation. Although K^{trans} values assessed over various regions within the vascular wall are correlated, the absolute values are different. More importantly, adventitial K^{trans} seems to be a better measure for plaque microvasculature compared to other regions of the vascular wall, coinciding with a lower uncertainty in the parameter estimation. Comparison with histology in a larger number of patients is recommended for definitive recommendations for standardization.

		Group average	Pearson's correlation coefficient			
	K^{trans}, adventitia	mean ± SD [min^{-1}]	median§	mean§	75th percentile§	histology#
A	median	0.062 ± 0.018	-	0.93***	0.91***	0.85**
	mean	0.088 ± 0.028	0.93***	-	0.98***	0.72*
	75th percentile	0.110 ± 0.036	0.91***	0.98***	-	0.73*
	K^{trans}, median	mean ± SD [min^{-1}]	entire wall§	adventitia§	plaque§	histology#
B	entire wall	0.055 ± 0.014	-	0.76***	0.97***	0.65*
	adventitia	0.062 ± 0.018	0.76***	-	0.63***	0.85**
	plaque	0.053 ± 0.014	0.97***	0.63***	-	0.44

Table: Correlation of A) adventitial K^{trans} parameter mutually using different statistical descriptives and with endothelial microvessel perimeter determined with histology and B) median K^{trans} values from the three vascular regions mutually and with histology. *p<0.05, **p<0.01, ***p<0.001, §n=45, #n=10.

References: [1]Kerwin et al., Circulation 2003;107:851-6, [2]Gaens et al., Radiology 2013;266:271-9, [3]Sun et al., Stroke 2013;44:1031-6, [4]Truijman et al., Stroke 2013;44:3568-70, [5]Calcagno et al., EJNMMI 2013;40:1884-93, [6]Truijman et al., Int J Stroke 2013;10.1111, [7]Patlak et al., JCBFM 1983;3:1-7. **Acknowledgements:** This research was performed within the framework of CTMM, project PARISk (grant 01C-202), and supported by the Netherlands Heart Foundation.