

## On the Generalization of Carotid Vessel Wall MRI Risk Factors across Imaging Centers

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### Introduction:

Carotid vessel wall MRI is proving to provide relevant risk stratification information over and above simple stenosis for predicting stroke in at-risk populations. Various groups have shown in prospective studies that risk factors include the presence of intraplaque hemorrhage (IPH), higher maximal vessel wall thickness (MWT), greater maximal percentage necrotic core (Max %NC), and fibrous cap (FC) thinning and rupture [1-4]. These findings have come, however, from independent research groups using differing protocols and independently customized image review criteria. Thus, the ability to generalize and combine cross-center studies is uncertain. The purpose of this investigation was to understand the cross-center similarities and differences of two independent vessel wall imaging centers.

### Materials and Methods:

Ten subjects were recruited from each of two imaging centers (20 total) with symptomatic carotid stenosis between 30-69%. Similar, but independent imaging protocols were employed on 3T MRI scanners (Philips Achieva, Best, Netherlands) at each center including T1W images before and after injection of a contrast agent, T2W, TOF, and MPRAGE (Table 1). All images were independently reviewed at both centers according to local review criteria using commercial analysis software (MRI-PlaqueView; VPDiagnostics, Inc. Seattle, WA). Reviewers interactively outlined vessel wall boundaries, NC and calcifications (CA). In addition, reviewers noted the presence/absence of IPH, FC thinning, or FC rupture. Statistical evaluations of key risk factors and general volume parameters (wall, NC, CA) were performed. Continuous variables were compared using multiple regression analysis including the imaging center as a dependent variable to investigate protocol-dependent bias. Categorical variables were compared by means of Cohen's  $\kappa$  value.

### Results:

Table 2 provides an overview of quantitative results for continuous variables. In no case was the imaging center a significant factor in the multiple regression (p value range from 0.15 to 0.84), whereas, the measurements being compared were strongly associated (p <0.005 for all). In the case of compositional measurements, intercepts significantly different from 0 were noted, indicating a reviewer dependent bias. Categorical variables showed moderate agreement with  $\kappa = 0.4$  For IPH and 0.45 for FC status. Typical review results are shown in Figure 1, which illustrates the similarity of components drawn, but comparative difference in absolute NC size.

### Discussion and Conclusions:

Overall, the data suggested considerable compatibility of carotid vessel wall MRI across centers. Relative quantities of plaque, NC and CA were consistent as were categorical assessments of IPH and FC status. No dependence on the site collecting the images was observed. Based on these findings, we conclude that similar results regarding the association of these risk factors with outcome can be expected across centers. On the other hand, considerable biases between absolute values of quantitative parameters were observed. Thus, in order for risk factors to be translated into clinical practice with appropriate risk thresholds, the source of bias must be ascertained and eliminated.

### References

1. Takaya, *Stroke* 2006 37:818-23.
2. Underhill. *AJNR* 2010 31:1068-75.
3. Altaf *J Vasc Surg.* 2008 47:337-42.
4. Kooi *ISMRM* 2011 #110.

Table 1. Imaging Parameters (Center 1/2)

| Parameter      | T1W                 | T2W                 | TOF                 | IR-TFE              |
|----------------|---------------------|---------------------|---------------------|---------------------|
| TR (ms)        | 800/1R-R            | 4800/4800           | 20/20               | 9/9                 |
| TE (ms)        | 10/10               | 50/49               | 5/5                 | 5/5.5               |
| FOV (cm)       | 14x14/<br>16x15     | 14x14/<br>16x16     | 14x14/<br>16x16     | 14x14/<br>16x12.7   |
| Matrix         | 256x250/<br>260x252 | 256x250/<br>258x258 | 256x250/<br>258x258 | 256x250/<br>206x204 |
| Thickness (mm) | 2/2                 | 2/2                 | 2/2                 | 2/2                 |

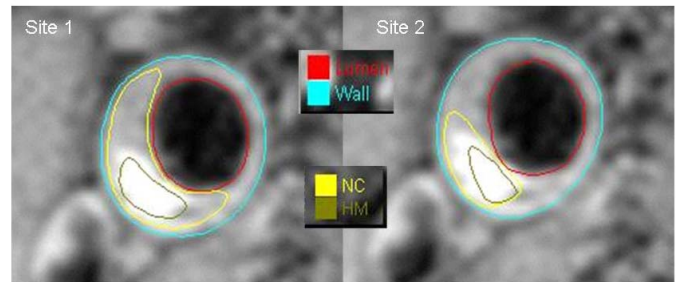


Figure 1. Comparison of review results

Table 2. Parameter agreement (volume in mm<sup>3</sup>, MWT in mm)

|                   | Wall Vol | NC Vol  | CA Vol | MWT     | Max %NC |
|-------------------|----------|---------|--------|---------|---------|
| Mean (site 1)     | 1246±526 | 205±191 | 28±48  | 4.2±1.6 | 32±20   |
| Mean (site 2)     | 1474±575 | 119±200 | 65±52  | 4.8±1.3 | 22±19   |
| P (paired t-test) | <0.001   | 0.004   | <0.001 | 0.02    | 0.01    |
| R (Pearson)       | 0.95     | 0.81    | 0.88   | 0.80    | 0.64    |