	WML	0-2mm penumbra	2-4mm penumbra	NAWM
mean #voxels in ROI (SD)	774 (883)	2,919 (2,371)	6,087 (4,412)	228,761 (38,395)
mean #voxels for VR	229 (322)	1,075 (1,253)	2,258 (2,736)	131,654 (66,139)
n with #voxels for VR above 20th percentile of all ROI	223	377	425	456
n with >20% of ROI voxels used for VR calculation	260	324	361	399
n with both (%)	187 (40)	315 (68)	358 (77)	399 (86)

Supplemental Table 1: VR data is obtained from a subset of ROI voxels. 20th percentile, corresponding to a total of 123 activated voxels) was calculated from all 4 ROI from all subjects. The majority of voxels below this threshold were in WML. The majority of subjects have either a low number of voxels used for VR calculation or a low percent of total voxels contributing to the VR calculation.

	WML			0-2mm Penumbra			2-4mm Penumbra		
	Coefficient	SE	p value	Coefficient	SE	p value	Coefficient	SE	p value
T1	-0.0009	0.021	NS	0.47	0.019	NS	0.053	0.015	NS
T2	0.034	0.021	NS	0.12	0.016	NS	0.0062	0.011	NS
FLAIR	0.012	0.015	NS	0.0098	0.06	NS	0.086	0.00	NS
CBF	**-0.15**	**0.48**	**0.0003**	**-0.13**	**0.042**	**0.042**	**-0.012**	**0.040**	**0.002**
FA	0.0155	0.047	NS	0.0043	0.34	NS	0.039	0.32	NS
MD	0.032	0.050	NS	0.012	0.033	NS	0.0003	0.026	NS
VR	-0.014	0.061	NS	0.046	0.047	NS	0.073	0.040	0.07

Supplemental Table 2: Ordinary least squares modeling for associations between imaging parameters and number of cardiovascular risk factors (RFscore), adjusting for site, age, gender, and race. Only CBF shows significant associations with RFscore. Values are coefficient ± standard error with unadjusted p values.

WML									
	Smoking			BMI			Sedentary		
	Coefficient	SE	p value	Coefficient	SE	p value	Coefficient	SE	p value
T1	—	—	NS	—	—	NS	-0.0422	0.021	0.045
T2	—	—	NS	—	—	NS	0.0523	0.02	0.013
CBF	-0.2343	0.097	0.016	-0.124	0.05	0.013	—	—	NS

VR	-0.2606	0.123	NS	—	—	NS	—	—	NS

0-2mm Penumbra									
	Smoking			BMI					
	Coefficient	SE	p value	Coefficient	SE	p value			
T1	0.0829	0.038	0.028	—	—	NS			
CBF	—	—	NS	-0.1327	0.043	0.002			
MD	-0.1367	0.068	0.044	—	—	NS			

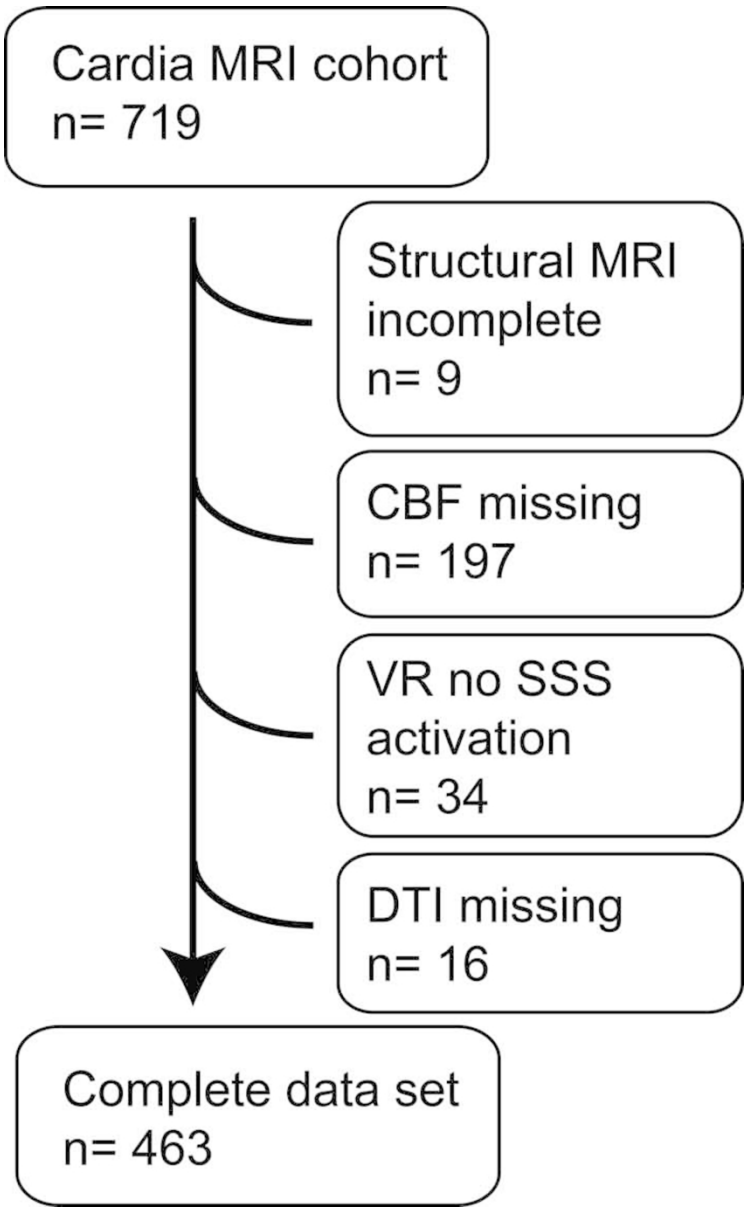
2-4mm Penumbra									
	Smoking			BMI			Sedentary		
	Coefficient	SE	p value	Coefficient	SE	p value	Coefficient	SE	p value
T1	0.0723	0.029	0.014	—	—	NS	—	—	NS
CBF	—	—	NS	-0.1398	0.041	0.001	—	—	NS
MD	-0.1331	0.052	0.011	—	—	NS	—	—	NS
VR	—	—	NS	—	—	NS	0.0948	0.04	0.018

Supplemental Table 3: Ordinary least squares modeling for associations between imaging parameters (mean T1, T2, FLAIR, MD, FA, CBF, and VR) and individual cardiovascular risk factors: hypertension, hypercholesterolemia, diabetes, BMI, sedentary behavior, and smoking history. Models were adjusted for site, age, gender, and race. Only significant parameters from the models are shown; coefficients for all other parameters and risk factors were not significant and are not shown.

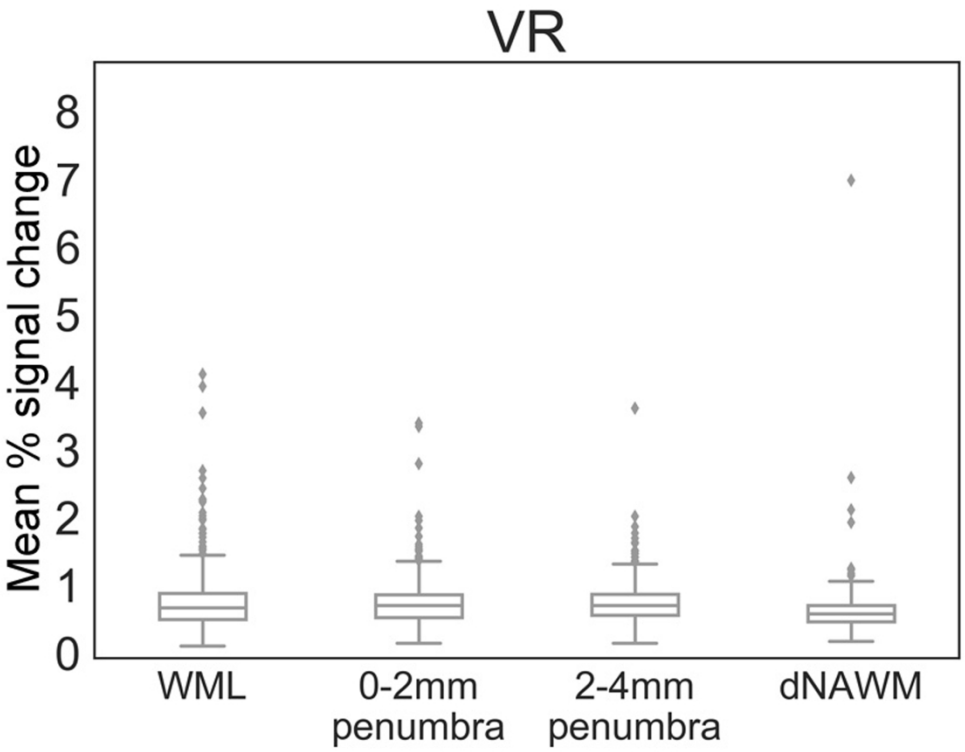
Supplemental Figure 1: Only subjects with all MRI parameters available are included for analysis. CBF data from one CARDIA study site were technically inadequate and could not be processed, leading to the largest exclusion of subjects.

Supplemental Figure 2: Box plots of mean percent change of vascular reactivity for each region, with outliers included.

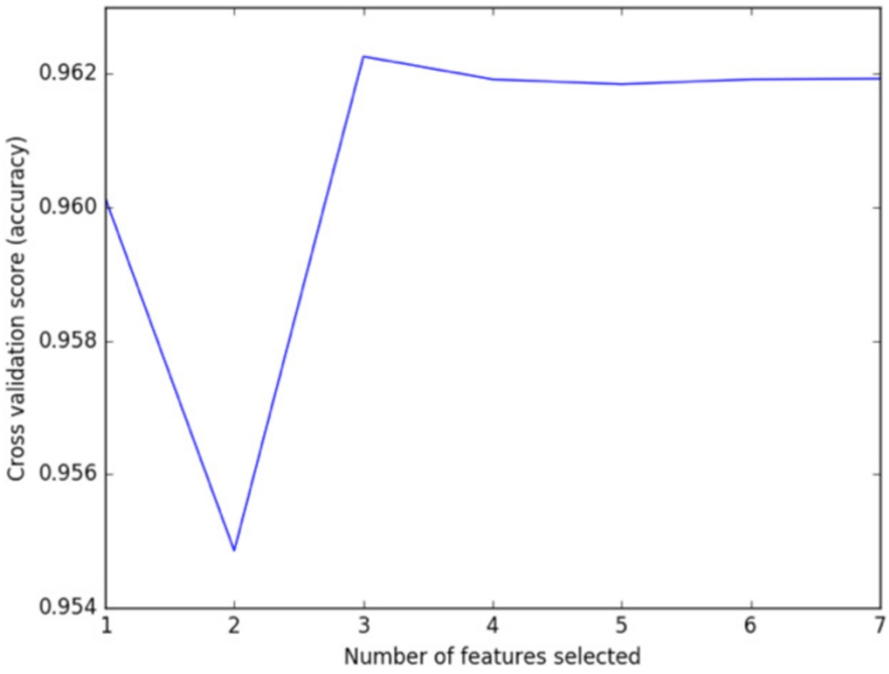
Supplemental Figure 3: Cross validation scores as a function of number of feature selected.



Supplemental figure 2 TIFF



Supplemental figure 2 TIFF



Supplemental figure 3 TIFF