

Gadofluorine-Enhanced Magnetic Resonance Imaging of Atherosclerotic Plaque in Swine

I. Koktzoglou¹, K. R. Harris¹, B. J. Kane¹, R. Tang¹, A. Nagaraj¹, B. Lu¹, B. Misselwitz², H-J. Weinmann², T. J. Carroll¹, D. D. McPherson¹, D. Li¹
¹Northwestern University, Chicago, IL, United States, ²Schering AG, Berlin, Germany

Introduction: Gadofluorine is a newly developed targeting contrast agent which has been shown to enhance atherosclerotic plaques in rabbits, and appears promising for detection of non-stenotic plaques and sub-clinical atherosclerotic disease [1,2]. This study sought to investigate whether Gadofluorine enhances atherosclerotic lesions in balloon injured carotid arteries of Yucatan miniswine.

Materials and Methods: Atherosclerotic plaques were induced in the left carotid (LC) arteries of three female Yucatan miniswine with balloon injury and high cholesterol diet. Twelve weeks after balloon injury, MRI of the carotid artery wall was performed in a 1.5T scanner (Sonata, Siemens Medical Systems, Erlangen, Germany) with a 6-channel phased-array cardiac coil. In each pig, MRI of the carotid wall was performed before and 24 hrs after Gadofluorine injection (100 micromole/kg) with two segmented sequences: 1) dark-blood T1-weighted turbo spin-echo (DB-TSE); and 2) inversion-recovery diffusion prepared [2] fast low-angle shot (IR-D-FLASH). Imaging parameters were: TR/TE = 600/10 ms, matrix = 384×384, FOV = 20×20 cm², slice thickness = 3 mm, echoes = 9, NEX = 13, BW = 200 Hz/pixel, TA = 5m35s (DB-TSE); TR/TE = 623/2.4 ms, matrix = 384×384, FOV = 20×20 cm², slice thickness = 3 mm, number of segments = 15, NEX = 32, inversion time = 540 ms, flip angle = 20°, BW = 345 Hz/pixel, TA = 8m37s (IR-D-FLASH). MR wall imaging was performed on two slices perpendicular to the LC artery: 1) a 'disease' slice through atherosclerotic wall as determined based on location of the injury site; and 2) a 'control' slice through healthy wall. Care was taken to match the imaging slices before and 24 hrs after injection. In each image a cross section through the right carotid (RC) artery wall was also captured. Signal-to-noise ratio (SNR) was measured in both LC (SNR_{left}) and RC (SNR_{right}) artery walls. In each slice the relative SNR (RSNR) of the LC artery was defined as SNR_{left}/SNR_{right}. Finally, the enhancement ratio (ER) was defined as: ER = RSNR_{post}/RSNR_{pre}. A t-test was used to determine whether the ER was greater than 1 in both the control and disease slices.

Results: MRI of the carotid walls were successfully completed in all swine both before and 24 hrs after Gadofluorine injection. No control slice was imaged in the LC artery of the third pig since the LC artery was severely diseased over its entire length. Good blood suppression was achieved with both DB-TSE and IR-D-FLASH. Results for RSNR and ER are listed in Table 1. The mean enhancement ratio in the control slices (n = 4) was 1.02 ± 0.16 (not significant; p = 0.80) and 1.21 ± 0.10 (significant; p < 0.01) in the disease slices (n = 6). Images of the acquired slices in pig 1 are shown in Figure 1.

Conclusion: Gadofluorine selectively enhanced carotid artery atherosclerotic plaques in miniswine. Statistically significant signal enhancement was observed in diseased (injured) portions of the left carotid artery wall. Enhancement was not observed in healthy portions of the left carotid artery wall and the right carotid artery wall. Gadofluorine is a promising contrast agent for determining the presence of atherosclerotic plaques.

Table 1. Carotid Signal Measurements

Pig	Slice	Sequence	RSNR _{pre}	RSNR _{post}	ER
1	disease	TSE	1.08	1.47	1.36
	control	TSE	0.96	1.01	1.06
	disease	FLASH	0.92	1.17	1.19
	control	FLASH	0.98	0.89	1.15
2	disease	TSE	1.03	1.21	1.17
	control	TSE	1.05	0.82	0.79
	disease	FLASH	1.04	1.32	1.28
	control	FLASH	0.82	0.89	1.09
3	disease	TSE	1.83	2.12	1.16
	disease	FLASH	1.56	1.72	1.10

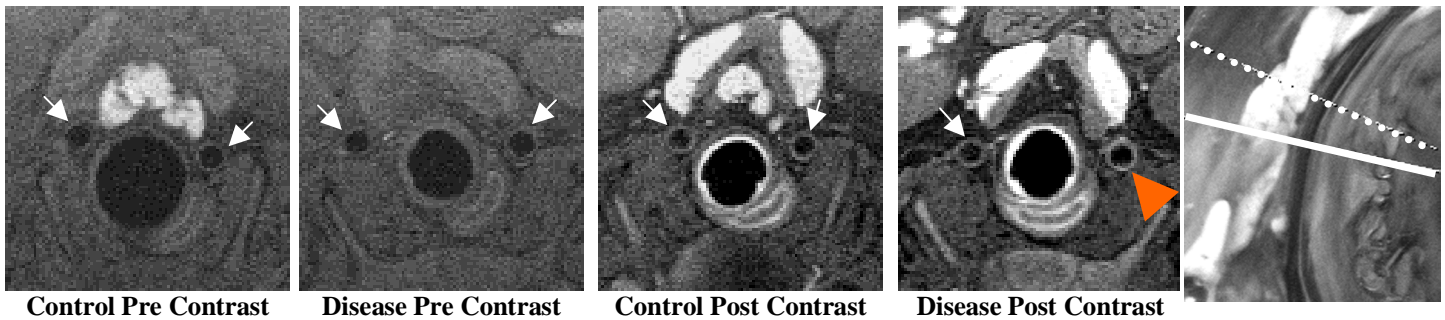


Figure 1. Close-up of images acquired before and after Gadofluorine injection with inversion-recovery diffusion prepared FLASH. The left and right carotid arteries are shown in each image (arrows). Atherosclerotic thickening in the left carotid artery is enhanced in the post contrast image (thick arrow) while no enhancement is seen in healthy portions of the left and right carotid artery walls. In-plane image of the left carotid artery (right) shows the position of the disease (dotted line) and control (solid line) slices.

References:

- [1] Barkhausen J et al. Circulation 2003; 108:605-9
- [2] Sirol M et al. Circulation 2004; 109:2890-6