High Resolution 2D and 3D Magnetic Resonance Imaging of Murine Carotid Arteries In Vivo

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Introduction

Wire-induced denudation of the left common carotid artery in apolipoprotein-E deficient ($apoE^{-/-}$) mice has been well established as a model to study the spontaneous development of atherosclerotic lesions and neointima formation after experimental injury. In general, such models are evaluated by ex vivo histopathology of the artery providing information on vessel morphology and stenosis at the time of harvest only. Consequently, fast, non-invasive 3D monitoring of arteries would be highly desirable for the continuous analysis of neointima and plaque formation in atherosclerotic mouse models. In the present study we have established fast 2D and 3D MR methods for non-invasive in vivo monitoring of carotid artery morphology before and at different time points after wire-induced denudation injury of the left common carotid artery. Validation of our results was achieved by correlation with histological data.

Methods

Male, 6-8 week old C57BL/6 ApoE-/- mice (n=5) were fed with an atherogenic diet containing 21% fat for 1 week before and 4 weeks after wire denudation. Imaging was performed at a vertical Bruker 9.4T DRX Wide Bore NMR Spectrometer equipped with an actively shielded 40-mm gradient set and a 30-mm birdcage resonator under isofluran anaesthesia (1.5 %) at 37 °C. 3D images were obtained using a flow compensated gradient echo (FCGE) sequence (repetition time=30 ms, echo time=2.9 ms, flip angle=35°, matrix 128x128x64, field of view=3x3x1.5 cm^3, total acquisition time=4.1 min) and segmented using self-developed software (AngioTux). Ratios between left and right carotid artery volumes were compared to ratios of luminal areas obtained by 2D high contrast images (FCGE, repetition time=80 ms, echo time=2.9 ms, flip angle=90°, matrix 128x128, field of view=2x2 cm^2, 8 accumulations, total acquisition time=1.4 min) in 2 positions. After the final MR measurements 4 weeks after injury left carotid arteries were harvested and sectioned for comparison to MR data at the same point of time.

Results and Discussion

2D and 3D MR data showed excellent agreement to morphometric data obtained in two positions (cf. Fig. 1) 4 w after injury (3D vs. Hist.: R^2=0.964 for slice 1, R^2=0.986 for slice 2; 2D vs. Hist.: R^2=0.974 for slice 1, R^2=0.970 for slice 2). Furthermore, monitoring of individual mice enabled us to detect different courses of vascular remodeling depending on the degree of injury. Quantification of both luminal areas from 2D data and volumes from 3D data led to highly reproducible results (ratio left/right: 3D: 1.1±0.06, 2D (slice 1): 1.1±0.02, 2D(slice 2): 0.92±0.06, n=6). Furthermore, intra- and interobserver variabilities are considerably low (intraobserver: 3D: 2.8±0.8 %, 2D (slice 1): 9.3±2.9 %, 2D(slice 2): 6.2±3.5 %; interobserver: 3D: 5.0±2.0 %, 2D (slice 1): 5.5±3.5 %, 2D(slice 2): 6.5±3.8 %).

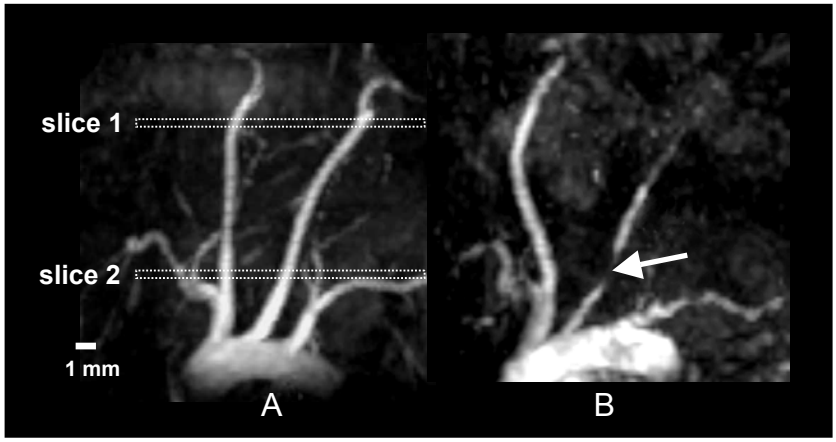

Figure 1: *In vivo* 3D (coronal view) MR images of murine carotid arteries in the same $apoE^{-/-}$ mouse. As obvious from the right image (B) arterial stenosis could be detected three weeks after injury. Slices 1 and 2 refer to 2D analyses which were compared to 3D data and correlated to histomorphometrical areas, respectively.

In conclusion, we describe high resolution 2D and 3D MR imaging techniques suitable to sensitively measure the extent and time course of changes in vessel morphology in mice in a repetitive manner. 3D data sets of excellent quality can be acquired within only 4 minutes and quantification of luminal area as a measure of vascular remodeling is highly reproducible. This provides a reliable and elegant tool for the analysis of vascular lesion development and its potential therapeutic modulation in a model of atherosclerosis in vivo.