# Dynamic Changes in Murine Vessel Geometry Assessed by High Resolution Magnetic Resonance Angiography

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## Introduction

Dynamic processes of vascular remodeling in pathologic mouse models, such as the development of vessel stenosis or the initiation of neovascularization are normally evaluated by ex vivo histopathology providing information at the time of harvest only. Thus, continuous vessel analysis by non-invasive, repetitive 3D monitoring would be highly desirable. In this study we present high resolution MR angiographic images for reliable *in vivo* assessment of dynamic changes in murine vessel morphology.

## Methods

Two frequently used injury models, wire-induced denudation of the left common carotid artery (LCCA) and hindlimb ischemia by ligation of the femoral artery, were applied to mice before repetitive monitoring with TOF-MRA. All measurements were performed using flow-compensated gradient echo sequences at 9.4 T with the following parameters: LCCA: TR=30 ms, TE=2.9 ms, FA=35°, matrix 128×128×64, FOV=3×3×1.5 $cm^3$, t(acq)=4.1 min; femoral artery: TR=23 ms, TE=3.3 ms, FA=35°, matrix 256×256×64, FOV=2.56×2.56×0.64 $cm^3$, 5 overlapping slabs covering 1.92 cm in z-direction, t(acq)=5×6.2 min; brain: TR=23 ms, TE=3.3 ms, FA=30°, FOV=3×2.56×2.56 $cm^3$, matrix=256×256×128, t(acq)=12.3 min. Quantification was performed using in-house-developed software and was validated by estimation of inter- and intraobserver variabilities, reproducibility, and by correlation to histological data [1].

## Results and Discussion

Fig. 1A shows the area of the aortic arch from a mouse 8 days after wire denudation with almost no intensity for the injured LCCA. However, 1 week later the LCCA area was observed to regain intensity, and after a further week blood flow was almost completely restored with a remaining small stenosis only (arrows). In addition to these obvious dynamic changes induced by thrombus recanalization, even small changes in LCCA volumes could be detected in other mice. While measurements on these relatively large vessel structures can be obtained in a short time of 4 minutes, higher resolution and therefore longer imaging times are necessary for detection of small collateral vessels. The time course of collateral vessel formation (green) after ligation of the left femoral artery is presented in Fig. 1B showing that the vessel density is continuously increasing from day 3 to day 21. Localization and size of the new collateral vessels was validated against corrosion cast. A high resolution surface rendered MRA image of the mouse head and paws is shown in Fig. 2 which can be used to quantify vascularization and/or flow in the brain of transgenic mice compared to wildtype animals.

In conclusion, we describe high resolution MRA imaging protocols suitable to sensitively measure the extent and time course of changes in vessel morphology in mice in a repetitive manner. This provides a reliable and elegant tool for the detection of vascular lesion development, neovascularization, or simply of flow velocity alterations in transgenic mice.

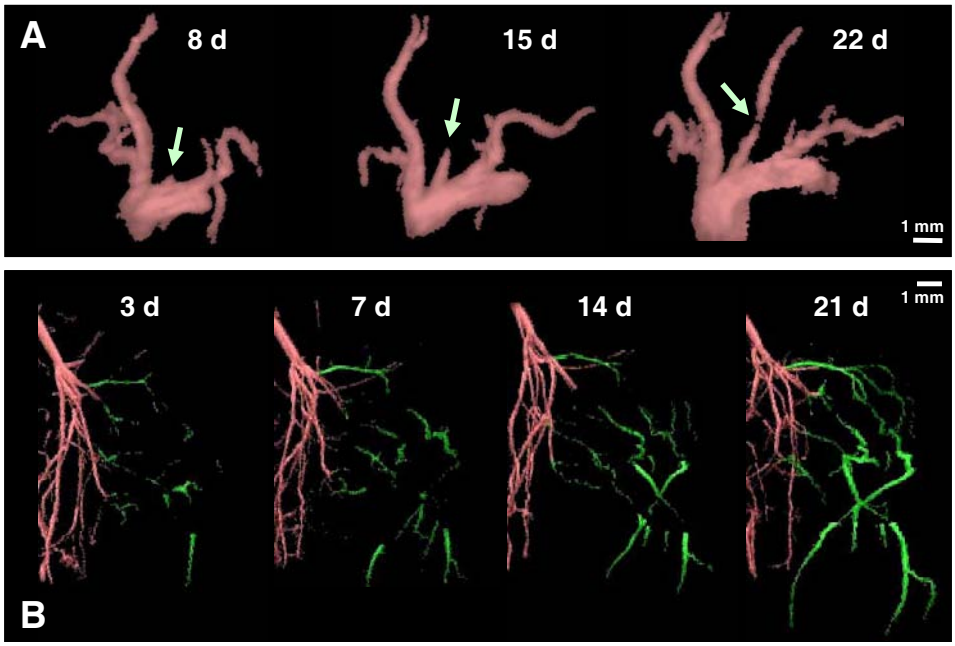


**Figure 1:** A: MRA images (MIP views) of the carotid arteries of an $ApoE^{-/-}$ mouse on days 8, 15, and 22 after wire injury. Following complete occlusion of the left common carotid artery in the beginning, blood flow is continuously restored due to thrombus recanalization. B: MRA detection of consecutive collateral vessel formation (green) after ischemia in the left mouse hindlimb (days 3, 7, 14, and 21 after ligation).

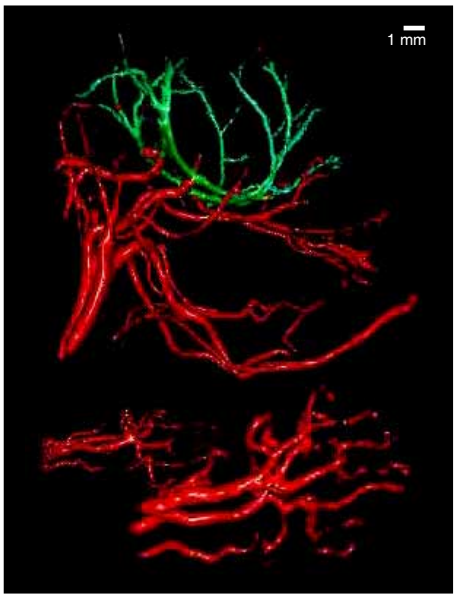


**Figure 2:** High resolution surface rendered MRA image of the mouse head and paws. The brain vessel system is shown in green.

[1] C. Jacoby, A. Zernecke, U. Flögel, Y.C. Böring, A. Beck, V. Aurich, C. Weber, J. Schrader. High Resolution 2D and 3D Magnetic Resonance Imaging of Murine Carotid Arteries In Vivo. Proceedings ISMRM Fourteenth Scientific Sessions, Seattle, May 2006. #1951