Observation of intravascular contrast enhancement due to anesthesia in T2*-weighted imaging at 17.2 T

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Introduction MRI at ultra high magnetic field strengths allows for a dramatic increase in resolution and image contrast [1]. The gains in contrast to noise ratio are particularly important in T_2*-weighted imaging, which is sensitive to susceptibility effects caused by a variety of sources, including deoxyhemoglobin concentration, iron deposits, and tissue microstructure. The aim of the present study was to assess to what extent anesthetic drugs, which are known to interfere with hemodynamics and the vascular deoxyhemoglobin content [2], could produce observable contrast changes in images obtained *in vivo* in the rat brain at 7 and 17.2 T.

Materials and Methods
Animal Protocols and Experimental Design. All experiments were performed on Sprague-Dawley, 300 g, adult rats on two different MR systems (Bruker BioSpin, Etlingen, Germany): 7 T PharmaScan and 17.2 T BioSpec. For both systems we followed identical animal preparation and anesthesia procedures. Throughout the experiments, the animals were continuously monitored for respiration rate and body temperature. Initially, the animals were anesthetised and maintained under isoflurane (2%, within a mixture of medical air and 50% O_2) during which time a series of gradient echo images was acquired. Next, while maintained in the same position inside the scanner, the animals were injected with a bolus of medetomidine (0.3 mg/kg, i. v.) and the isoflurane was discontinued (after 5 min). A new set of gradient echo images was acquired 20 minutes after isoflurane was turned off.
MRI Acquisitions. The acquisition parameters for the gradient echo images were optimized for the two field strengths. Specifically, we used the following parameters: [TR/TE = 350/8ms, thk = 200µm] for 17.2 T and [TR/TE = 300/12ms, thk = 400µm] for 7 T, respectively. The following parameters were identical for all experiments: flip angle = 45°, FOV = 2.56 cm x 2.56 cm, matrix size: 320 x 320.
Data Processing. The MR images were analyzed in Matlab. 12 coronal slices were acquired during each scan. ROIs were selected in areas of high blood vessel density within the cortical region. For each ROI, we extracted the maximum signal intensity, and then counted the number of pixels with intensities smaller than 50% of this maximum. This 50% threshold yields good vessel identification in our experiments. In choosing the ROIs, the very bright pixels corresponding to edge artifacts were excluded.

Results The gradient echo images obtained at the two field strengths under two anesthesia conditions are presented in Fig 1. Only a slight change in contrast is observed at 7 T after the injection of medetomidine (Figs. 1a and 1b). On the other hand, at 17.2 T the change in contrast is substantial. Particularly striking is the vein-tissue contrast under medetomidine anesthesia, shown in Fig. 1d. The analysis performed on the 17.2 T data reveals a dramatic contrast increase. Specifically, in analysing the signal intensity in the cortex we found a 130% increase (average over ten slices) in the number of pixels corresponding to blood vessels when using medetomidine anesthesia versus isoflurane anesthesia. Fig. 1e shows a typical example of the pixels counted in our analysis, corresponding to the ROI displayed in Fig 1d.

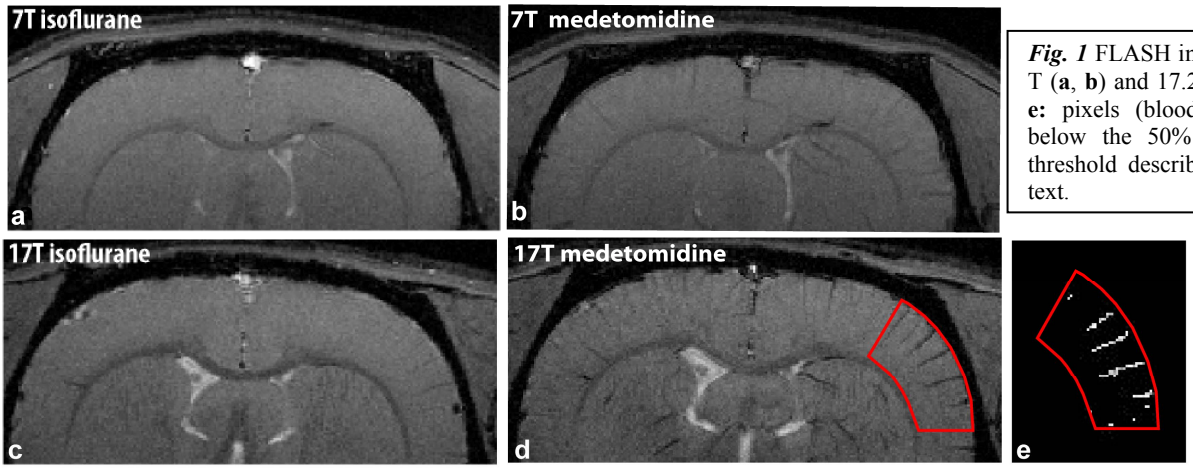

Fig. 1 FLASH images at 7 T (**a**, **b**) and 17.2 T (**c, d**); **e:** pixels (blood vessels) below the 50% intensity threshold described in the text.

The experiments were repeated using ketamine/xylazine anesthesia (100/10 mg/kg i.p.). As in the case of medetomidine anesthesia, a sizable microvascular contrast enhancement was observed when compared to the isoflurane anesthesia experiment.

Discussion We have established that the vessels/tissue contrast in T_2*-weighted images at ultra high magnetic field is greatly influenced by the anesthetic agent used. Stemming from magnetic susceptibility differences, this phenomenon is visible to a much smaller extent at lower field strengths (7 T). To our knowledge this is the first experimental observation of this effect. A plausible explanation for these results is the difference in the deoxyhemoglobin brain vascular content induced by the anesthesia. This hypothesis is supported by previous studies [3] demonstrating that the cerebral blood volume (CBV) and flow (CBF) values are increased under isoflurane anesthesia when compared to the other anesthetics used in this study.
Conclusion High contrast T_2* images of rodent brain microvasculature can be obtained *in vivo*, through the combination of high magnetic fields (17.2 T) and certain anesthetics even in the absence of contrast agents. Such capabilities open the perspectives of investigating noninvasively brain physiology during anesthesia, as well as new blood vessel growth (cerebral angiogenesis) which accompanies many types of neurological injury, such as brain tumors or stroke.

References: [1] Marques JP et al., Neuroimage 2009; 46:345- 352; Dashner RA et al J Magn Reson Imaging 2004;19:303 307; Dashner RA et al, J Magn Reson Imaging 2004; 19:303- 307, [2] Sloan HL et al., Neuroimaging 2010; 53: 399-411; [3] Lei H. et al., Brain Research (2001); 93: 174 - 179; Airaksinen AM et al., MRM (2010); 64:1191 - 1199.