Design of a 3D-Phantom to evaluate optimized imaging parameters for Time-of-Flight Angiography in mouse glioblastoma models

Carly Warren[1], Michael Bock[1], Jochen Leupold[1], and Wilfried Reichardt[1,2]
[1]*Department of Radiology Medical Physics, Universitiy Medical Center Freiburg, Freiburg, Germany,* [2]*German Cancer Consortium (DKTK), German Cancer Center (DKFZ), Heidelberg, Germany*

Introduction

Glioblastomas are heterogeneous and diffusely growing malignant tumors of the brain which express vascular endothelial grow factors (VEGF) to initiate and maintain angiogenesis. The suppression of the VEGF signal cascade is currently a target for therapeutic approaches. Additionally, other kinds of vasculoactive drugs, such as nitricoxide (NO)-donors are currently under evaluation. To assess drug-induced changes of the vascular architecture, non-invasive imaging methods to study changes of the neo-angiogenic vasculature are urgently needed. Time-of-Flight (TOF) MR angiography can depict the pathologic vasculature in glioblastomas [1,2]. TOF-MRA makes use of the signal difference between flowing blood and saturated stationary tissue, however, this difference is highly dependent on imaging parameters and vascular geometry [3], and the TOF-MRA needs to be optimized to provide useful diagnostic information. In particular, the TOF-signal is dependent on the geometry and sensitivity of the imaging RF coil, which can be a high-SNR cryogenically cooled surface coil in studies of mouse models. In this study a 3D-phantom is constructed to simulate the vascular tree in a mouse to analyze the effects of TOF-MRA sequence parameters on the signal intensity in the vicinity of a glioblastoma.

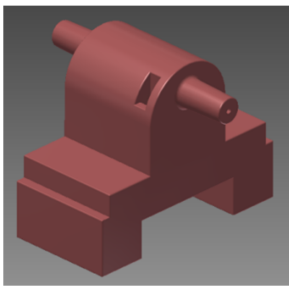

Figure 1: CAD 3D-model (AutoDesk Inventor) of the designed phantom

Methods

A 3D-phantom was designed using AutoDesk Inventor Professional 2013® to simulate the vasculature tree in a mouse brain. The simplified vasculature model consisted of a series of branching tubes starting with a diameter of 0.75 mm and decreasing by 0.15 mm down to 0.30 mm (Fig. 2a), which is the lowest diameter that can be realized by the 3D printing process used.

TOF-MRA images of the phantom were acquired using a cryogenically cooled surface coil at a 7T Bruker Biospec 70/20 small animal scanner. To examine the inner structure, the phantom was filled with a contrast agent solution (10µmol/ml Gadopentetate Dimeglumine, Gd-DTPA) in order to characterize its form (Fig. 2b), and a T1-weighted 3D-FLASH acquisition (40µm isotropic resolution, TE/TR/FA: 7ms/25ms/25°) was performed. Next, a TOF-MRA was performed (50µm isotropic resolution) while a solution of distilled water and 0.1 % Triton X-100 was pumped through the structure at a rate of 8ml/h which would theoretically result in a flow speed of 5 mm/s in the largest tube, which is in good accordance with the flow speed in mouse capillaries [4]. The Triton was added to improve bubble tolerance [5]. TOF-MRA data sets were acquired for different TR between 20ms and 55 ms, with a flip angle of 40° and TE = 3.4 ms. Next, the flip angle was altered between 20° and 40° at constant TR = 40 ms. From the 3D data maximum intensity projections (MIPs) were calculated (Fig. 2c.), and the MRA signal was measured in the source images in the left and right branches of the middle vasculature layer.

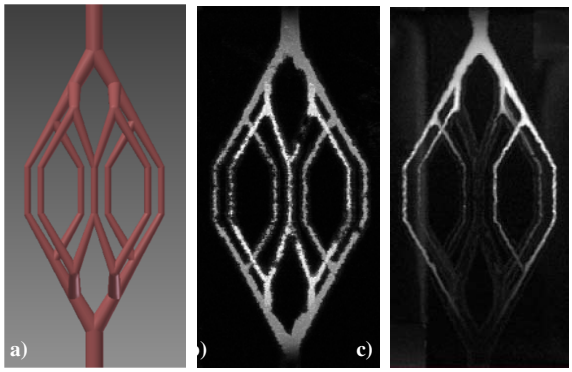

Figure 2: a) CAD model of inner structure of phantom b) 3D FLASH image with contrast agent c) TOF-MRA image

Results

The 3D FLASH image acquired using contrast agent showed a strong similarity with the inner structure of the design model; however, some small blockages or narrowing of the tubes could be seen. In the MIP one can clearly identify the decrease in signal intensity from the inlet at the top of the image towards the outlet at the bottom, which is a well-known saturation phenomenon seen in TOF-MRA (Fig. 2c). In the TOF-MRA images the signal increased with increasing TR (Fig. 3), and it decreased with increasing flip angle (Fig. 4).

Discussion

The contrast-enhanced FLASH data clearly showed the inner structure of the phantom. It is likely that unexpected narrowing or blockages of the tunnels were caused by remnants of wax support material used during the 3D printing process that was not be removed in the subsequent cleaning process. The initial data from the TOF-MRA measurement showed that it is possible to detect the changes of different parameters and their contribution to the TOF-MRA signal, that would important for the detection of the pathological changes in the vasculature that are present in glioblastoma mouse models [6].

In conclusion, it is possible to create a flow phantom to detect the alteration of specific parameters of the TOF-MRA sequence in a highly defined setting, which would be impossible in vivo, due to limited imaging time and ethical considerations. In the next step we will use the phantom to optimize further parameters, develop a postprocessing strategy for B1 field correction and work on the TOF-MRA sequence to further improve its sensitivity.

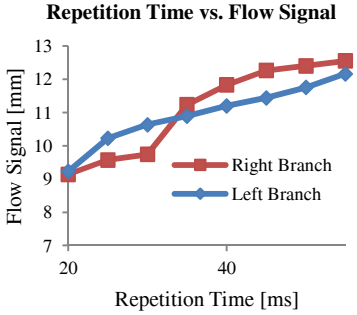

Figure 3: Plot of repetition time verses flow distance in the left and right branches of the phantom

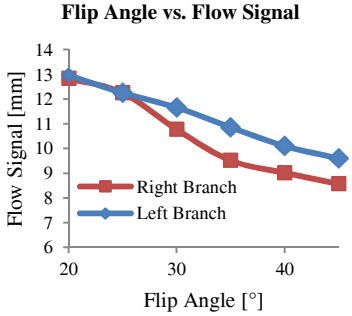

Figure 4: Plot of flip angle verses flow distance in the left and right branches of the phantom

References

[1] Kadota, T, et al. Acta Radiol 1998
[2] Gerik, L, et al. ISMRM 2010
[3] Morelli, J, et al. JMRI 2013
[4] Hudetz, AG. Microcirculation 1997
[5] Pečar, B, et al. Inform Midem. 2013
[6] Kording, F. JMRI 2014