MR Visualization of Tumor Angiogenesis

L. M. Brubaker[1], E. Bullitt[1], C. Yin[2], T. Van Dyke[2], W. Lin[1]

[1]Radiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, [2]Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States

INTRODUCTION:

Tumor angiogenesis, the growth of vasculature whether widespread or confined to specific regions of an individual tumor, proves an important quantifier of tumor growth and malignancy. Recent research has indicated a direct correlation between microvessel density of a tumor and its growth capacity as well as a greater tortuosity, or twisting, of intra-tumor vessels (1). However, previous studies have relied on histological results for the visualization of these vessels, making it difficult to conduct longitudinal studies and to determine the relations between microvessels and the tumors. Magnetic resonance angiography (MRA) may pose a 3D solution to visualizing tumor neovascularization with greater sensitivity to vessel location and structure.

MATERIALS AND METHODS:

Seven terminal and three subterminal mice with CPP as well as seven age-matched control mice were imaged using a 3T Siemens Allegra MR scanner. Imaging sequences included pre and post contrast 3D T1W for visualization of tumors (30mm FOV, 0.1x0.1x1.0mm voxel, 1mm slice, TR 500ms, TE 13ms, 4 averages, TA 8:46). In addition, a high-resolution 3D TOF MRA sequence was employed for acquiring MRA images ($0.1x0.1x0.1\ mm^3$) prior to the injection of contrast agent. The total acquisition time was 1.5 hrs. MRA images were co-registered with the T1-weighted images using a mutual information and affine transformation approach allowing the relation between the vessels and tumors to be investigated. Finally, the tumors and vessels were segmented, rendered, and color-coded by relation to tumor surface. Vessel segmentation was achieved using a model-based approach for the extraction of centerline of tubular objects (2).

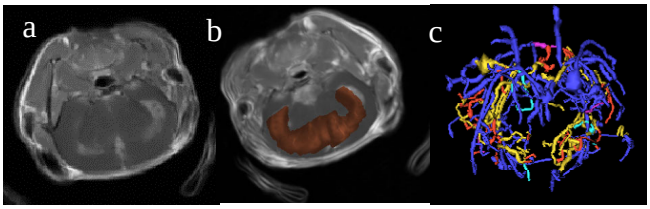

Fig. 1 Subterminal CPP Tumor Mouse: Post contrast T1 image (a) and superimposed tumor image (b). When examining the lateral ventricles by vessel analysis, a marginal increase in vessel number is noted as well as an increase in tortuosity, indicating malignant vessels. Blue vessels are outside the tumor, gold vessels transverse tumor, and red vessels are contained within the tumor.

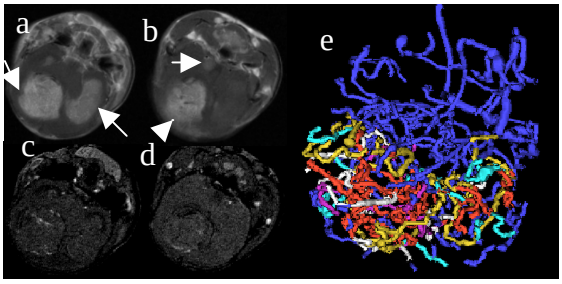

Fig. 2 Terminal CPP Tumor Mouse: Post contrast T1 images (a and b) reveal large tumors invading the lateral and third ventricles (arrows). The corresponding MRA images (c and d) indicate tumor angiogenesis, with vascular segmented result shown in e.

RESULTS:

In comparison to control mice, all seven of the terminal CPP tumor mice presented with multiple tumors, measuring approximately ~4 mm in diameter, located in the lateral and third ventricles. One of the subterminal CPP tumor mouse presented with several small tumors while the remaining two subterminal mice presented with no discernible tumors but abnormal vessels. All the major intracranial vessels are clearly visible in the normal mice (blue). In contrast, MRA images of CPP mice exhibit a substantial increase of visible vessels predominantly within the tumors as well as an increase in tortuosity of the vessels compared to control mice. Representative examples of a subterminal and a terminal mouse are shown in Figs. 1 and 2, respectively. As anticipated, the extent of tumors is less remarkable in Fig. 1 when compared with that shown in Fig. 2 (arrows). Similarly, while abnormal vessels are observed (gold and red) in Fig. 1c, a substantial increase of the number of vessels as well as tortuosity are observed in the terminal mice.

CONCLUSIONS:

Our results demonstrate that high-resolution MRA images can be obtained using the head-only 3T scanner within a reasonable time frame. In addition, the ability to segment vessels and brain tumors allow a direct analysis of the vasculature in relation to the brain tumors. While it is clear that the spatial resolution available with the MRA sequence cannot reveal capillaries, the visualization of vasculature near and within tumors may shed light on our understanding of the internal architecture of microvasculature within tumors. In addition, the ability to conduct repeated studies using MRA may offer a valuable tool for directly monitor the effectiveness of different antiangiogenic therapies without sacrificing the animals.

References

1. Bullitt E, Gerig G, Pizer S, Lin W, and Aylward S, Measuring tortuosity of the intracranial vasculature from MRA images, IEEE TMI, 2003, 22: 1163-1171

2. Aylward S and Bullitt E (2002) Initialization, noise, singularities and scale in height ridge traversal for tubular object centerline extraction. *IEEE-TMI* 21:61-75.