Characterization of rat glioma models by magnetic resonance angiography

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Introduction:

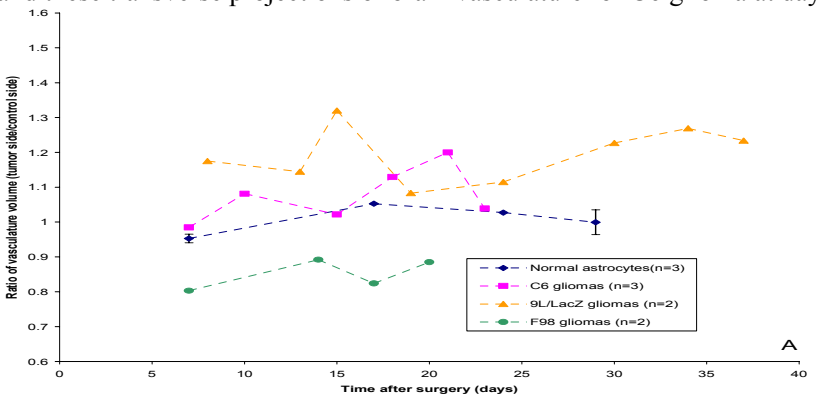
Malignant gliomas, which are the most common primary brain tumors, still lead to poor prognosis [1] because of the difficulty of an early and accurate diagnosis. One of the problems is that the presence of new blood vessels, which is an absolute requirement for tumor growth and spread [2], must be well documented. Indeed, it has been shown that a dramatically increased angiogenesis is characteristic of high-grade gliomas [3]. In this point of view, magnetic resonance angiography (MRA) can be used as a non-invasive tool to assess angiogenic behavior of gliomas and perhaps provide better diagnosis. Our aim is to use MRA to characterize specific angiogenic patterns in several glioma models generated by intracranial implantation of different cell lines (C6, F98 and 9L/LacZ) and varying in their degree of malignancy.

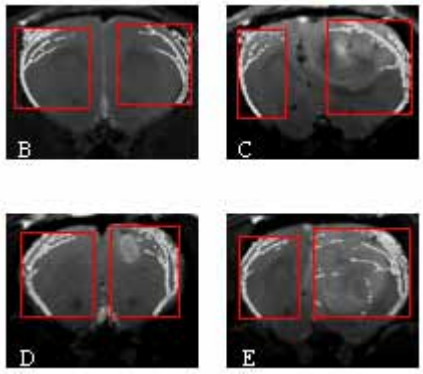
Material and methods:

C6, F98 or 9L/LacZ cells (10^4) were injected intracranially into the cortex (2mm from midline, 2mm anterior to bregma, at a depth of 3mm) of male Fischer 344 rats fed a choline-deficient diet. MRA (FLASH: 2.6 x 1.7 x 1.1 cm^3 VOI; TE 2.3 ms; TR 25 ms; 25º flip angle; 27 min acquisition) was performed on a 7 Tesla-30 cm horizontal bore magnet at day 7 after cell injection and then every 3 days until death of the rat. The MIP method was used to obtain a 3D angiogram. T1/T2-weighted images were obtained by a double-echo multi-slice spin echo method. Besides, horizontal slices were acquired by a fast low angle shot method; each region of interest (tumor area and control contralateral area) was selected on anatomical references. A Mathematica-based program was then used to quantify vasculature signals by summing all the high intensity pixels. Projections along different directions were created to superpose the brain vasculature and T2-weighted images. Finally, immunostaining assays for von Willebrand factor, a marker of endothelial cell proliferation, were conducted for each animal.

Results:

C6, F98 and 9L/LacZ gliomas showed very different angiogenesis behaviors, as illustrated by the vasculature quantification (A) and these transverse projections of brain vasculature for C6 glioma at day 7 (B) and 17 (C), and for 9L/LacZ glioma at day





5 (D) and 37 (E) after cell injection. In C6 gliomas, blood vessels are often displaced by the tumor mass and appear wider and longer (Fig.C). C6 gliomas would thus preferentially use the pre-existing blood vessels by elongating and modifying them. 9L/LacZ cells produce a very angiogenic glioma which quickly generates new blood vessels (Fig.E). F98 gliomas did not seem to induce changes in vasculature (Fig.A).

Conclusion:

Specific angiogenic patterns of different glioma models (C6, F98 and 9L/LacZ) can be revealed by MRA, which could be a useful method to differentiate gliomas in human diagnosis.

References:

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