MAGNETIC RESONANCE MICROSCOPY OF HUMAN BRAIN TUMOR BIOPSIES

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Purpose/Introduction:
Brain tumors afflict a larger percentage of the population as lifespan increases. In general, in western developed countries, brain tumors represent between 1.4% and 2% of all neoplasms. The current gold standard classification of a brain tumor is histopathological analysis of a biopsy. Histopathological analysis is the standard procedure routinely used to reveal the contribution of necrosis, proliferative regions, collagen and vascularity within the tumor area. However, it is very difficult to determine a priori regions of interest inside the tissue or a preferred orientation for slicing before processing it. High resolution MRI (resolution lower than 100 μm) is called Magnetic Resonance Microscopy (MRM). MRM of excised tissue provides a detailed functional and anatomical picture of identical nature to those obtained by MRI and of higher resolution, which may be used as a bridge between histopathology and clinical MRI. The aim of this study was the characterization by MRM of specific morphological features of the tumor. With this purpose, we performed MRM imaging and correlative histopathology in 30 biopsies from brain tumor patients. The correlation between MRM and histopathology images allows the determination of MRI parameters for critical microstructures of the tumor. The MRM analysis of meningioma and glioma biopsies revealed microstructural details of these tumors, which may add some information for clinical MRI images interpretation. We believe that our results have also potential pathobiological significance as MRM is capable of exploring the biopsy before processing it.

Subjects and methods
Samples: MR microscopy images at 14 Teslas and correlative histopathology images were obtained for 10 meningioma, 10 glioma biopsies, 2 cavernomas and 1 sample of normal brain tissue from the Hospital Clinico Universitario de Valencia. Samples were fixed in 4% paraformaldehyde, marked for geometrical referencing, embedded in an agarose matrix and subjected to high resolution MRM at 14 Teslas.
MR microscopy: The whole study was performed at room temperature of 20C. The images were recorded in a Bruker-AVANCE600 system equipped with a 10mm microimaging 1H coil and 210 gauss/cm maximum gradient strength (80% of maximum nominal strength). Images acquired included T1, T2 and T2* weighted images, T2-multiecho images (16 echo times) and Difussion Coefficient Images (16 B values).
Data analysis: All images were converted to DICOM standard format and transferred to MATLAB for further image analysis. T2 and Diffusion coefficients were calculated using in-house MATLAB scripts.

Results and discussion
MRM of brain tumor biopsies provided images with high contrast and high geometrical resolution (35 to 40 microns). Examples of MRM images for some brain tumors, brain lesions and healthy brain are shown in Figure 1. Our results show that the spatial organization of microstructural elements within the biopsy is preserved despite agarose embedding and the high magnetic field. MRM allowed, for example, the observation of peritumoral regions in glioma (Figure 1D), the distinction between gray and white matter in healthy brain tissue (Figure 1E), the observation of capillaries in meningioma (Figure 1C) or the identification of caverns in cavernomas (Figure 1A). Among the different types of meningiomas, fibroblastic and translational meningiomas appear largely homogeneous whereas microcystical and meningiothelial meningioma exhibit some. Collagen structures, which are the most extensive microstructural features in MRM images of meningioma, have different appearance in different meningioma subtypes. On the other hand, all glial tumors appear with higher intensity than agarose exhibiting some hypo-intense heterogeneous elements. Microvasculature, as determined by correlative histopathology, appears highly hypo-intense in these images. The combination of T1 and T2-weigthed images together with ADC maps reveals some microstructural elements otherwise hidden, like blood breakdown foci, capillaries, collagen large bands, calcium deposits, necrotic foci and peritumoral areas.

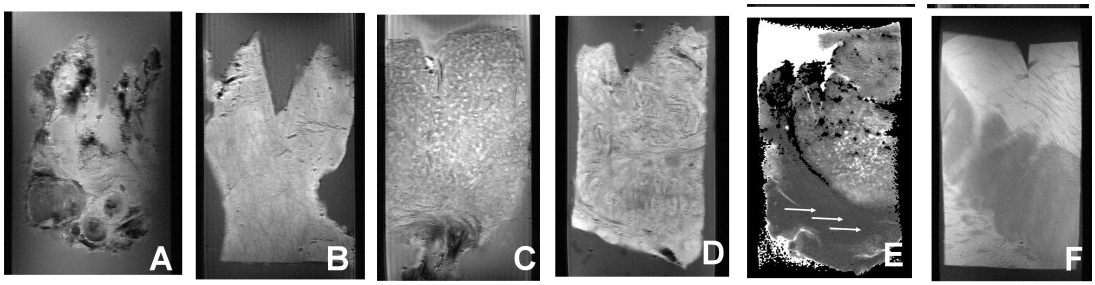

Figure 1. MRM images of different human brain excised tissue A) PD image of human cavernoma B) T2-weighted image of human fibroblastic meningioma C) T2-weighted image of human meningothelial meningioma D) T2-weighted image of human gliosarcoma E) ADC map of human oligoastrocytoma showing peritumoral region (white arrows) F) T1-weighted image of human healthy brain showing the differences between gray (hyper intense) and white (hypo intense) matter.

Conclusion
The MRM analysis of meningioma and glioma biopsies revealed microstructural details of these tumors, which may add some information for clinical MRI images interpretation. The correlation between MRM and histopathology images allowed the determination of MRI parameters for critical microstructures of the tumor, like necrotic foci, vascular patterns, collagen bands and hemorrhage among others. To our knowledge, this is the first MRM structural characterization of human brain tumor samples. The findings reported here provide a new and unique microstructural view of intact human brain tumor tissue. At this point, our approach and results allow the identification of specific tissue types and pathological features in unprocessed tumor samples.

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