Comparison of functional MRI- and PET-techniques to assess tumor heterogeneity in malignant gliomas

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Introduction

Inherent heterogeneity of gliomas is a problem for biopsy targeting, because for correct glioma grading the biopsy should reflect the most anaplastic part of the tumor. With the advent of functional imaging modalities, these have been proposed for guiding the biopsy. However, since now several functional MRI- [1-3] and positron emission tomography (PET)-techniques [4] have been introduced that depict different pathophysiologic aspects of tumor tissue, the question remains, which of these techniques should be used for biopsy targeting. Thus, the aim of the present study was to investigate whether various functional MRI- and PET-techniques identify the same "hot spot", i.e. the most anaplastic tumor area for biopsy.

Materials and Methods

In this ongoing study, 23 patients with gliomas (7 female, 16 male; median age, 48 years) were assessed by MRI followed within one day by a PET examination. MRI was performed on a 1.5 T whole body scanner (MAGNETOM Symphony, Siemens Medical Solutions, Erlangen, Germany) equipped with a broadband transmit/receive system and with a double-resonant birdcage coil (Rapid Biomed, Wuerzburg, Germany). The MRI protocol comprised in chronological order sodium (^{23}Na)-MRI (3D-radial projection imaging, TR/TE, 4/0.2 ms), proton spectroscopic imaging (^{1}H-MRSI, point-resolved spectroscopy, TR/TE, 1000/135 ms), dynamic contrast-enhanced (DCE) MRI (TR/TE, 84/4.34 ms) and dynamic-susceptibility-weighted (DSC) MRI (TR/TE, 1440/47 ms) after a single dose each of gadobenat-dimeglumine and finally diffusion tensor imaging (DTI, TR/TE, 180/107 ms). The PET protocol comprised a 18F-fluorothymidine (FLT)- and 18F-fluorodeoxyglucose (FDG)-PET examination. FLT is a surrogate marker of tumor proliferation because its phosphorylation and thus its intracellular trapping strongly correlate with thymidine-kinase activity, while FDG evidences cellular glucose metabolism. Image analysis comprised identification of "hot spots", i.e. those tumor areas with highest values on parameter maps, e.g. maximum cerebral blood volume (CBV) or highest metabolite ratios of choline-containing compounds/*N*-acetyl-aspartate (Cho/NAA) within tumor tissue. Then co-localization of these "hot spots" was assessed.

Results

FLT- and FDG-PET, DSC- and DCE-MRI, as well as MRSI could evidence heterogeneity of gliomas that was present in all 18 high-grade gliomas but was not found in the 5 examined patients with histologically proven grade II gliomas. In our study population, tumor areas with increased thymidine-uptake and highest choline – both suggestive of increased tumor proliferation – were co-localized. Also, microcirculation was elevated in these tumor areas compared to other contrast-enhancing tumor regions as demonstrated by DSC- and DCE-MRI (Figure 1). ^{23}Na-MRI and DTI, however, were unable to depict tumor areas with increased proliferation or microcirculation. In FDG-PET, high glucose utilization of normal gray matter limited delineation of adjacent tumor tissue and made it inferior compared to FLT-PET that allowed for better delineation of tumor borders.

Discussion and Conclusion

Tumor areas with increased proliferation index also show elevated microcirculation reflecting the need of a sufficient nutrient supply for growing tumor tissue. Both MRI techniques that reflect tumor vascularity, i.e. DSC and DCE MRI, as well as MRSI and FLT-PET identified similar tumor regions. Thus, either of these techniques that reflect proliferation or microcirculation could be used for biopsy targeting, while ^{23}Na-MRI and DTI were not beneficial for this issue.

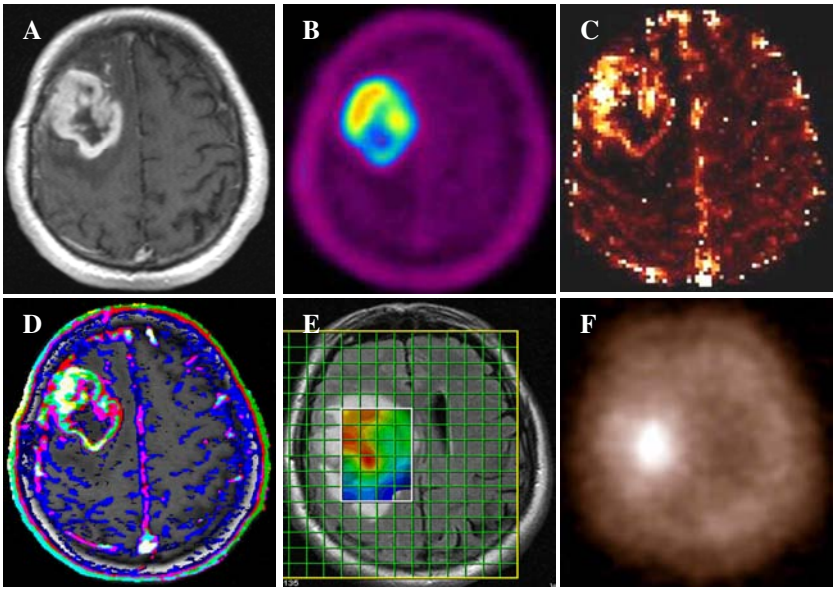

Figure 1:
Images illustrate findings in a 68-year-old man with glioblastoma in the right frontal lobe. Axial T1-weighted contrast-enhanced MRI (A), FLT-PET (B), parameter image of CBV (C), DCE parameter image reflecting degree of contrast enhancement and microvascular permeability (D), MRSI map superimposed on a FLAIR image showing Cho/NAA ratios (E), and ^{23}Na-MR image (F). FLT-PET and MRSI clearly show the higher proliferation rate in the frontal and lateral parts of the tumor (B). Higher microcirculation in these areas is depicted by the DSC and DCE MRI (C, D). ^{23}Na-MRI in contrast depicts the highest signal within the necrotic central tumor region and shows no marked difference between contrast-enhancing and hyperintense tumor areas on FLAIR images. Note strictly axial and thus slightly different orientation of MRSI and ^{23}Na-MR images.

References

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