

Dynamic Contrast-Enhanced T_1 -Weighted Perfusion MRI differentiates Tumor Recurrence from Radiation Necrosis: relative Cerebral Blood Volume Measurements and FDG-PET Validation

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INTRODUCTION: Magnetic resonance imaging plays an important role in the detection and evaluation of brain tumors. Conventional contrast-enhanced MRI delineates areas of blood brain barrier (BBB) leakage, but is less reliable in assessing tumor grade and distinguishing radiation-induced necrosis (RN) from tumor recurrence. The gold standard for distinguishing RN from tumor recurrence is ¹⁸F fluorodeoxyglucose positron emission tomography (FDG-PET), which provides a measure of the rate of glucose metabolism. A high metabolic rate of glucose indicates active tumor tissue. Since MRI is used for the routine evaluation of brain tumors and is less expensive and less time-consuming than FDG-PET, the development of a MR technique that could help distinguish RN from tumor recurrence would be an advance. It is generally agreed that there is an association between microvascular density and tumor energy metabolism meaning estimates of cerebral blood volume (CBV) provided by MR perfusion imaging should provide information similar to FDG-PET. Dynamic susceptibility contrast (DSC) perfusion imaging is confounded by the BBB deficiency of brain tumors, due to a change of T_1 and T_2^* relaxation and sampling of the extravascular space. Recently, a T_1 weighted MR perfusion imaging method has been developed (1), where the BBB deficiency can be readily incorporated in the tracer kinetic modelling (2,3). Thus, T_1 weighted perfusion imaging can estimate the CBV of brain tumors, without a pre-bolus of contrast (4) or additional corrections for contrast agent extravasation (5). Here, we investigate whether T_1 weighted perfusion is able to distinguish RN from tumor recurrence using FDG-PET as a reference.

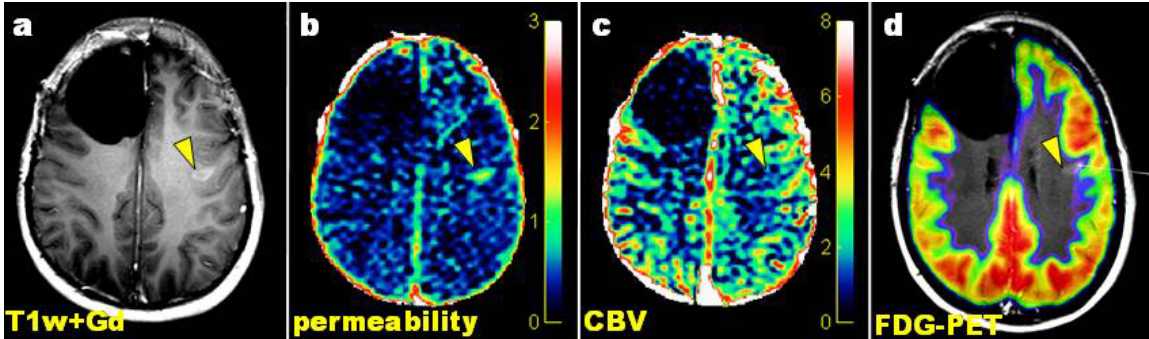


Figure 1. Images from a single patient obtained 3 months after surgery and radiation treatment. a) T_1 weighted post contrast image with an enhancing lesion (arrow). b) Permeability map with an enhancement at the lesion, c) CBV map, which does not show an increase at the site of the lesion. d) FDG-PET overlaid on MR image.

METHODS: 9 patients were recruited following surgery and radiation therapy for a brain tumor (all were gliomas, 2 were WHO grade II, 1 grade III and 6 grade IV). All patients had contrast enhancing lesions, which during the standard MRI examination could not be exclusively determined as tumor recurrence or radiation necrosis. MRI was performed on a 3 T Philips Achieva (Philips Healthcare, The Netherlands) equipped with an eight-element receive head coil. The perfusion imaging (2) and an initial T_1 measurement utilized a saturation recovery gradient echo sequence. Dynamic image parameters were: saturation delay 120 ms, flip angle 30° , TR=3.9 ms, TE=1.9 ms, centric phase ordering, SENSE factor 2, matrix 96×61 (reconstructed to 256×256), FOV 230×182 mm², 4 or 5 slices, slice thickness 8 mm, dynamic image time 1.0 s or 1.25 s, 180 frames. The Gd bolus (Magnevist or Dotarem; 0.05 mmol/kg bodyweight) was injected after the 10th frame. The procedure was repeated, if necessary, to cover the lesion(s) of interest. The voxel in the internal carotid artery (or in some cases the anterior cerebral artery) with maximal signal change during the bolus passage was chosen for the arterial input function. MR signal curves were converted to contrast agent concentration and CBV and BBB permeability were determined from a Patlak plot (2,6). Cerebral blood flow was also quantified, using model-free deconvolution (1), but the results will not be discussed here. For all patients, 1-5 ROIs were placed in enhancing areas, and 1-2 reference ROIs were placed in normal appearing white matter contralateral to the lesion. Relative CBV (rCBV) for enhancing areas was calculated by normalizing to the reference CBV. All subjects underwent FDG-PET within 2 months of the MRI, and lesions were judged metabolically active (tumor) or inactive (RN). The perfusion analysis was performed without knowledge of the PET result.

RESULTS: 1 patient had 2 enhancing lesions. Of the total of 10 lesions, 2 were judged RN and 8 were judged tumor by the FDG-PET examination. Absolute CBV of tumor, RN and white matter was 9.0 ± 6.0 , 1.3 ± 1.0 and 1.5 ± 0.7 ml/100g, respectively. The corresponding values for the permeability were 3.6 ± 2.8 , 0.9 ± 0.1 , and 0.3 ± 0.2 ml/100g/min. Fig. 1 shows an example of a contrast enhancing lesion contralateral to the primary tumor and the cavity resulting from surgery. The lesion shows an increased permeability. However neither the blood volume, nor the metabolism is increased from normal white matter values, thus indicating that the lesion results from radiation damage. The results for the relative blood volume are summarized in Fig. 2. All necrotic areas have rCBV less than 1.7, whereas all tumor lesions have rCBV larger than 2.0. Absolute CBV did not show an equally well defined distinction of RN and tumor values (data not shown).

DISCUSSION: The present preliminary study strongly indicates that it is possible to distinguish RN from tumor tissue by a measurement of relative CBV provided by T_1 weighted perfusion imaging. The data presented in Fig. 2 shows a clear separation of rCBV from necrotic and metabolically active tissue implying a 100% sensitivity and specificity for detection of tumors if choosing a rCBV threshold of 2.0; though a larger number of patients is needed to confirm this. The methodology for calculating CBV used here provides a measure of the intravascular blood volume directly (2,6), and hence does not need a correction for extravasation of contrast agent in case of a deficient BBB. A half or full dose of Gd was used, whereas for DSC perfusion imaging often double or even triple dose is employed including pre-bolus. A further advantage of T_1 weighted perfusion imaging compared to DSC imaging is a decreased sensitivity to susceptibility artefacts, which can occur near the base of the brain or indeed close to areas of surgery or biopsy. A potential disadvantage of T_1 perfusion is the limited coverage. However, we obtained a satisfactory coverage of lesions by acquiring a dataset once or twice. Additionally, techniques like k-t SENSE have shown potential to speed up acquisition and increase coverage (7).

REFERENCES: (1) Larsson H, et al., JMIR 27:754 (2008); (2) Larsson H, et al., MRM 62:1270 (2009); (3) Sourbron S, et al., MRM 62:205 (2009); (4) Hu LS, et al., AJNR 30:552 (2009); (5) Boxerman JL, et al., AJNR 27:859 (2006); (6) Patlak CS, et al., JCBFM 5:584 (1985); (7) Pedersen H et al., Proc. of ISMRM (2009), 124.

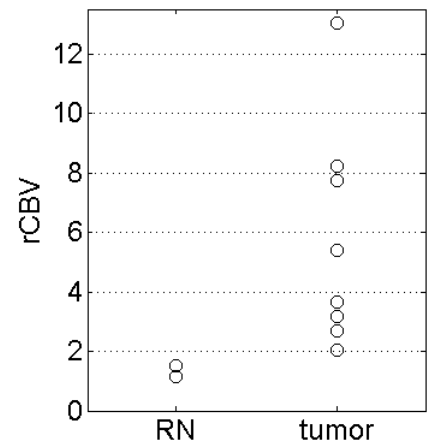


Fig. 2. Values of rCBV from contrast enhancing lesions. All 8 tumors have rCBV larger than 2.0, whereas 2 necrotic lesions (RN) have rCBV less than 1.7.