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Recurrent brain tumor versus radiation necrosis; can dynamic susceptibility contrast (DSC) perfusion magnetic resonance imaging differentiate?

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ABSTRACT

Background: Assessment of treatment response in patients with a brain tumor is paramount, as true tumor recurrence and radiation necrosis are similar looking on conventional MRI.
Purpose: To evaluate the role of dynamic susceptibility contrast (DSC) perfusion magnetic resonance imaging in the differentiation between recurrent brain tumors and radiation necrosis.
Material and Methods: Twenty patients with a history of operated primary brain tumors and postoperative radiotherapy with or without chemotherapy were enrolled in this prospective study having conventional MRI findings of enhancing lesion suspicious of being recurrence or radiation necrosis. All patients were examined by DSC-perfusion MRI. Definitive diagnosis was reached through either subsequent surgical biopsy or follow up over 6-12 months.
Results: Fifteen patients (75%) were diagnosed as tumor recurrence and 5 patients as radiation necrosis (25%). The relative cerebral blood volume (rCBV) and relative peak height (rPH) were significantly higher ($P < 0.05$) in recurrent tumors than in radiation necrosis lesions. The rCBV and rPH thresholds in differentiating between them were 1.8 and 1.22 respectively with 87%, 93% sensitivity and 100% specificity for each respectively.
Conclusions: DSC-perfusion MRI is a valuable non-invasive tool besides conventional MRI whenever available to differentiate between radiation injury changes and tumor recurrence.

1. Introduction

The current standard management for high-grade gliomas, especially glioblastoma, comprises surgical resection followed by adjunctive chemoradiotherapy. These adjuvant treatments improve the adequacy of tumor therapy, nonetheless, it may also increase the risk of radiation necrosis [1].

The distinction between radiation necrosis and tumor recurrence presents usually a diagnostic dilemma as they usually show similar conventional MRI features (contrast-enhancing lesions with mass effect) [2]. Correct diagnosis of both entities is critical and would largely affect the management plan. Radiation necrosis usually requires conservative management with steroids, whereas tumor recurrence implies a change in the chemotherapy protocol and possible surgical re-intervention [3].

Currently, surgical biopsy or excision is the only definitive discriminative method. This surgery would be beneficial for patients with recurrent tumors, however, it would lead to further damage to adjacent normal cerebral parenchyma in cases of radiation necrosis in deep-seated or eloquent cortical locations [4].

Increased both microvascular density and capillary permeability are the histopathologic markers that discriminate neoplastic brain lesions from irradiated necrotic brain parenchyma. Perfusion MR imaging is currently a promising tool to quantify a tumor's hemodynamic properties and microvasculature [5].

Depending upon the use of exogenous contrast agent, two main perfusion MRI techniques have been developed. The first group includes T2* based dynamic susceptibility contrast (DSC)-MRI and T1 based dynamic contrast-enhanced (DCE)-MRI; while the second group is known as arterial spin-labeling (ASL) [6].

DSC MRI technique is based on the rapid injection of intravenous contrast with serial measurement of signal loss during the bolus passage through the tissue, using T2*-weighted images. The signal drop correlates with concentration of the contrast agent and is used to measure

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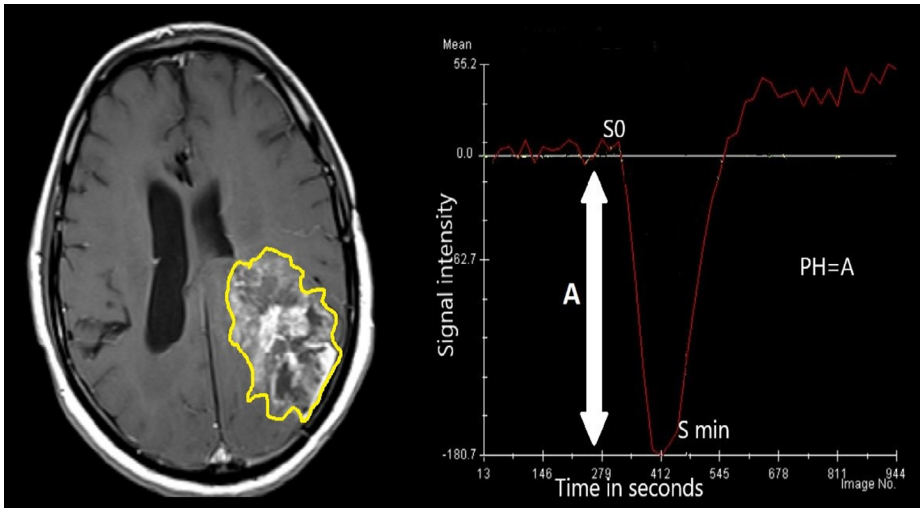

Fig. 1. Left: T1-weighted axial MR with GAD image showing an enhancing lesion at the operative bed of surgically excised GBM proved to be recurrence by histopathology (outlined in yellow). Right: T2*-weighted signal intensity–time curve. Peak height (PH) was calculated as follows: $PH = S_0 - S_{min}$, where S_0 is pre-contrast signal intensity and S_{min} is minimum signal intensity. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

different hemodynamic parameters. The hemodynamic characteristics of the tissue could be quantified by several parameters, the relative cerebral blood volume (rCBV) and relative peak height (rPH) are of our concern [6].

CBV is the blood volume in a given region of brain tissue (measured in milliliters per 100 g of brain tissue) [4]. It is the most commonly used hemodynamic parameter obtained from DSC-perfusion MRI showing well studied correlation with the microvascularity and grade of brain glioma [7]. The PH is the maximal signal intensity drop from pre-contrast baseline during the first-pass bolus phase of gadolinium contrast. Correlation between rPH and tumor capillary blood flow has been previously documented [7].

We herein try to evaluate the usefulness of the DSC perfusion to discriminate between tumoral recurrence and radiation necrosis.

2. Material and methods

The study was approved by our institutional ethical committee. All patients signed informed consent before the MRI study

2.1. Patients

Between January 2016 and February 2017, we included patients referred to the MRI unit of our university hospital for imaging of the brain, presenting with a history of operated brain tumors followed by radiotherapy with or without chemotherapy and who showed suspicious enhancing lesion at their initial follow up conventional MRI. We excluded patients with non-enhancing suspicious lesions. We ended with 20 patients (14 males and 6 females) aged from 15 years to 85 years with mean age of 49.4 ± 15.67 years presenting with 20 enhancing brain lesions who were enrolled in this prospective study.

2.2. MRI imaging protocol

MRI examinations were obtained with a 1.5 T closed MRI scanner (Siemens, Avanto, Germany) using an 8-channel head coil. The contrast material used in the study was Gadolinium diethylene triamine pentacetic acid (Gad-DTPA) (Dotarem) in a dose of 0.1 mmol/kg body weight. MR images were acquired with the following protocols: (a) Pre-contrast series included axial and sagittal T1-weighted spin echo (repetition time msec/echo time msec, 600/15), axial and coronal T2-weighted turbo spin echo (4000/100), axial FLAIR(repetition time msec/echo time msec/inversion time msec, 11,000/140/2200), Diffusion-weighted imaging (DWI) with diffusion gradient b values of 0 and 1000 s/mm2, along three orthogonal axes (x, y, and z directions) over (TR = 5072; number of sections = 16–22), (b) Dynamic Susceptibility Weighted contrast-enhanced (DSC) gradient echo echo-planar imaging (TR/TE;1250 ms/54 ms, flip angle: 35°). A series of gradient- echo echo-planar images were taken immediately before, during, and after bolus injection of the contrast agent. The T2*-weighted DSC perfusion MR images were used in the creation of CBV maps and corresponding T2*-weighted susceptibility signal intensity–time curves. (c) Post-contrast series included axial, coronal and sagittal T1-weighted spin echo.

2.3. Image processing and evaluation

The DSC and the conventional MRI data were transferred to an off-line workstation where T2*- weighted signal intensity–time curves were generated on a basis of voxel by voxel. CBV maps were calculated, and displayed as overlay image with the contrast T1-weighted images. ROI analysis for CBV was done. First, the control CBV_{NAWM} ROI was drawn in the normal appearing white matter contralateral to the enhancing lesion. Two to three circular ROIs (about 0.5 mm^2) were then placed in the enhancing lesion in the CBV map targeting areas of visually highest CBV. Cystic or necrotic changes as well as areas containing blood vessels, hemorrhage, or other susceptibility artifacts were eliminated. ROI with the maximal CBV abnormality measured was selected as the CBV_{lesion}. Dividing the CBV_{lesion} by the CBV_{NAWM} yielded the relative CBV_{lesion} ($rCBV_{lesion}$). Two variables were obtained from the signal intensity–time curve, which were S0 (denoting pre-contrast baseline signal intensity) and S_{min} (denoting minimum signal intensity at the peak of contrast bolus). Both S0 and S_{min} were calculated for the NAWM and the enhancing lesion, then these values were used to calculate the relative peak height (rPH) by the following equation: $rPH = [S0_{(lesion)} - Smin_{(lesion)}]/[S0_{(NAWM)} - Smin_{(NAWM)}]$ (Fig. 1).

2.4. The final diagnosis

The final diagnosis of the examined brain lesions was established either by histopathological analysis of the surgically excised lesions or by serial MRI examinations performed every 3 months over a period of 6–12 months. Recurrence was diagnosed if there was an increase in the size of the lesion by at least 25% (according to RANO criteria for response assessment in neuro-oncology) [8] while radiation necrosis/pseudoprogression was diagnosed if there was stationary size, shrinkage or total vanishing during 6 months or longer.

2.5. Statistical analysis

Data were fed to the computer using IBM SPSS (Statistical Package for the Social Sciences) software package, V20 (SPSS Inc., Chicago,

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