

Rising Signal Intensity Observed in Extra-Axial Brain Tumours – a Potential Pitfall in Perfusion MR Imaging

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ABSTRACT

Objective: Dynamic perfusion magnetic resonance (MR) techniques may be used to track the susceptibility effects of gadolinium contrast material as it passes through the brain. We describe three intracranial tumours that showed progressively rising signal intensity above the baseline during first-pass contrast-enhanced echo-planar imaging (EPI) MR imaging.

Methods: Multiphase acquisition using single-shot EPI was performed during rapid bolus contrast injection. Ten studies, using either spin-echo or gradient-echo EPI sequences, were carried out in eight patients with intracranial tumours. Time-signal intensity graphs and regional cerebral blood volume (rCBV) were reviewed.

Results: In seven studies, the signal intensity within the tumour showed initial signal drop and quick recovery to baseline and increased rCBV. Three studies revealed progressively rising signal intensity. These patients were all imaged using a spin-echo EPI method and subsequent histology revealed meningioma, hemangiopericytoma and pinealblastoma.

Conclusion: Dynamic perfusion MR methods may be used to study intracranial tumours. However, in short relaxation time spin-echo EPI, the T1-effect of gadolinium becomes noticeable during the first-pass acquisition in extra-axial tumours that lack a well-developed blood-brain barrier. Careful selection of patients and pulse sequence is essential to avoid this potential pitfall.

Keywords: magnetic resonance imaging, echo-planar imaging, brain neoplasms, perfusion, hemangiopericytoma

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INTRODUCTION

Recently, perfusion magnetic resonance (MR) imaging techniques have been developed exploiting the

susceptibility effects of intravenous paramagnetic contrast agent. When an injected bolus of gadolinium arrives in the brain, the magnetic susceptibility (T_2^*) effect results in transient signal loss, followed by rapid recovery to the baseline as the bolus leaves the brain. The change in signal intensity can be tracked by single-shot echo planar imaging (EPI) sequences, and the magnitude of the signal loss may be used to measure regional cerebral blood volume (rCBV)⁽¹⁻⁵⁾. Studies have shown that rCBV measured this way may be useful in the study of microvascular hemodynamics in intracranial tumors⁽⁶⁻¹¹⁾.

We present three cases of intracranial neoplasms that showed, instead of signal loss, rising signal intensity above the baseline during dynamic susceptibility contrast-enhanced MR imaging.

METHODS

Eight patients with brain tumours who subsequently underwent surgical biopsy or resection were included as part of a preliminary study to assess perfusion MR imaging in neuro-oncology. All patients were randomised between sequences. A total of ten studies were performed, five with spin-echo (SE) EPI sequences and five with gradient-echo (GE) EPI. Two patients were examined twice, with both SE and GE sequences. The second study was performed eight and 22 days later as part of pre-surgical functional localisation of the motor strip.

Dynamic contrast-enhanced T_2^* -weighted MR studies were performed with a 1.5-T clinical magnet (GE Medical Systems, Milwaukee, WI). Single-shot EPI parameters were set at 2000-2400/40-80 (TR/TE), 1 excitation, using a 128 x 128 matrix. For all SE sequences, the flip angle was 90 degrees, and for all GE sequences, it was 60 degrees.

Six sections were obtained to cover the entire brain with a thickness of 5 mm and interspace of 2 mm. A series of 50-60 multisection acquisitions were obtained at one-second intervals before, during and after rapid intravenous contrast injection. The first 15 acquisitions were performed before injection to establish the pre-contrast baseline signal intensity (S_0). At the 15th

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Table I. Findings on dynamic susceptibility contrast-enhanced MRI and histological diagnosis.

Study No./Sex/Age	Final histological diagnosis	EPI Pulse sequence	Signal intensity of tumour ROI over time
1/M/50	Astrocytoma (high-grade)	GE	Decrease and recovery to baseline
2/F/39	Astrocytoma (high-grade)	GE	Decrease and recovery to baseline
3/F/50	Gliosarcoma	SE	Decrease and recovery to baseline
4/M/34	Meningioma*	SE	Rising above baseline
5/F/52	Hemangiopericytoma	SE	Rising above baseline
6/M/22	Astrocytoma (low-grade) ^γ	SE	Decrease and recovery to baseline
7/M/25	Pinealblastoma	SE	Rising above baseline
8/M/34	Meningioma*	GE	Decrease and recovery to baseline
9/M/22	Astrocytoma (low-grade) ^γ	GE	Decrease and recovery to baseline
10/F/41	Oligodendroglioma (low-grade)	GE	Decrease and recovery to baseline

* = same patient

^γ = same patient

scan, gadopentetate dimeglumine (0.1 mmol/kg) was hand-injected as a bolus over five seconds through a 21-gauge intravenous catheter in an arm vein, immediately followed by a bolus of 15 ml normal saline. Conventional MR imaging sequences were also acquired, including T2-weighted (5400/105) and T1-weighted images (400-660/12-14) before and after contrast study in three planes.

Image analysis was performed off-line using Functool software (GE Medical Systems, Milwaukee, WI) on an Advantage Windows workstation. Various regions of interest (ROIs) were studied, including ROIs placed within the tumour and in the contralateral normal white matter. The dynamic image data were initially presented as signal intensity values measured over time. ROIs from tumour were directly compared with ROIs from contralateral normal white matter, and qualitatively assigned as increased or decreased rCBV, based on integral of dynamic contrast passage.

RESULTS

Eight patients (four men and four women; age range from 22 to 52 years) were successfully studied with dynamic susceptibility contrast-enhanced MR imaging. Table I summarises the final histological diagnosis and the results of the signal intensity analysis of ten dynamic contrast-enhanced MR examinations.

In seven studies (five using GE sequences, two using SE), the tumours displayed the transient decrease in signal intensity and rapid return to baseline (Fig. 1) expected of the T2* effects of gadolinium during first pass through the brain. Elevated rCBV was noted in each of the tumours compared to contralateral normal white matter.

Three SE studies (Studies 4, 5 and 7) revealed the signal intensity of tumour ROI to progressively rise above the baseline (Figs. 2c and 3c). In one

patient (Study 4), a repeat MR examination (Study 8) using the same hardware, software and scan parameters with the exception of gradient-echo EPI with a lower flip angle of 60 degrees, resulted in abolition of the rising signal intensity phenomenon.

Histological diagnosis revealed that the three tumours responsible for the rising intensity graphs to be meningioma, hemangiopericytoma, and pinealblastoma.

DISCUSSION

Dynamic contrast-enhanced MR imaging methods have been applied to the study of functional brain perfusion in neoplasms⁽⁶⁻¹¹⁾ and stroke⁽¹²⁻¹⁴⁾. rCBV maps show clinical promise in grading gliomas, guiding biopsy of the highest histological tumor grade and monitoring the results of therapy, including differentiating radiation necrosis from tumour recurrence. This technique is attractive for clinical use as it may be carried out as part of routine MR examination, requiring only an additional two to three minutes of acquisition time. Studies have shown comparable results with positron emission tomography (PET)⁽⁴⁾ but with better spatial resolution.

Various contrast-augmented MR blood volume imaging pulse sequences have been described, utilising T1-weighted sequences^(15,16), spin-echo EPI, gradient-echo EPI, non-EPI methods, and half-Fourier sequences⁽¹⁷⁾. Of these methods, EPI, with superior temporal resolution, has been the most widely used. Whereas SE EPI is sensitive only to functioning capillaries, results from GE EPI represent the total blood volume, weighing equally all vessels from capillaries to larger tumour vessel⁽⁵⁾. Although the GE sequence is more sensitive to signal attenuation for a given dose of contrast and hence has a higher contrast-to-noise ratio, it cannot assess absolute quantitative blood volume, and is

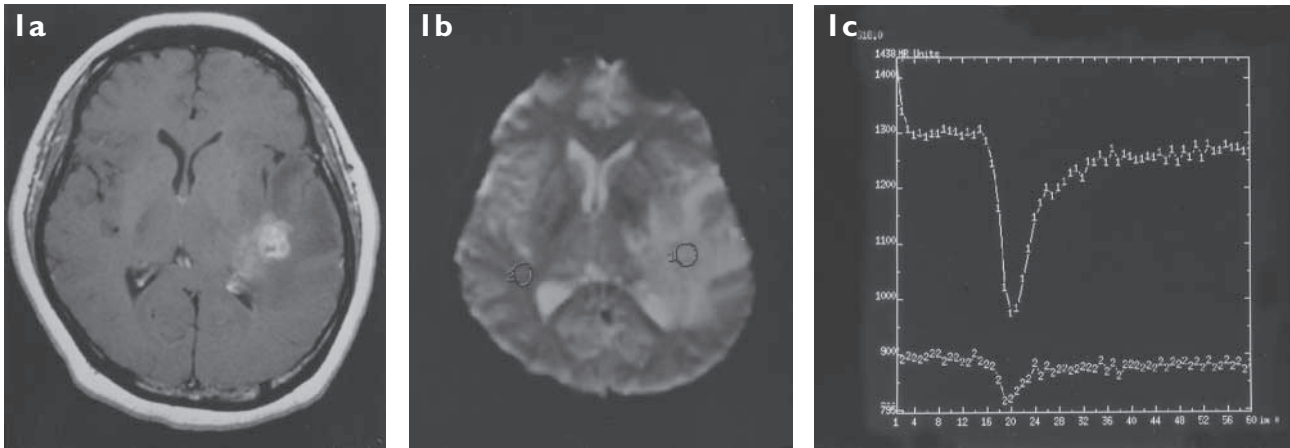


Fig. 1 Study 3: 50-year-old woman with gliosarcoma. Post-gadolinium T1-weighted image shows the enhancing gliosarcoma (a). Reference image (b) showing the regions of interest (ROIs): ROI₁ is placed within the tumour, and ROI₂ is in the contralateral normal white matter. Time-signal intensity curve (c): the vertical axis represents the signal intensity in arbitrary units, and the horizontal axis time in seconds. A transient decrease in signal intensity during transit of contrast material is followed by rapid recovery to baseline. The area under curve of the tumour (ROI₁) is greater than that of normal white matter (ROI₂) on visual inspection, representing increased rCBV in the tumour.

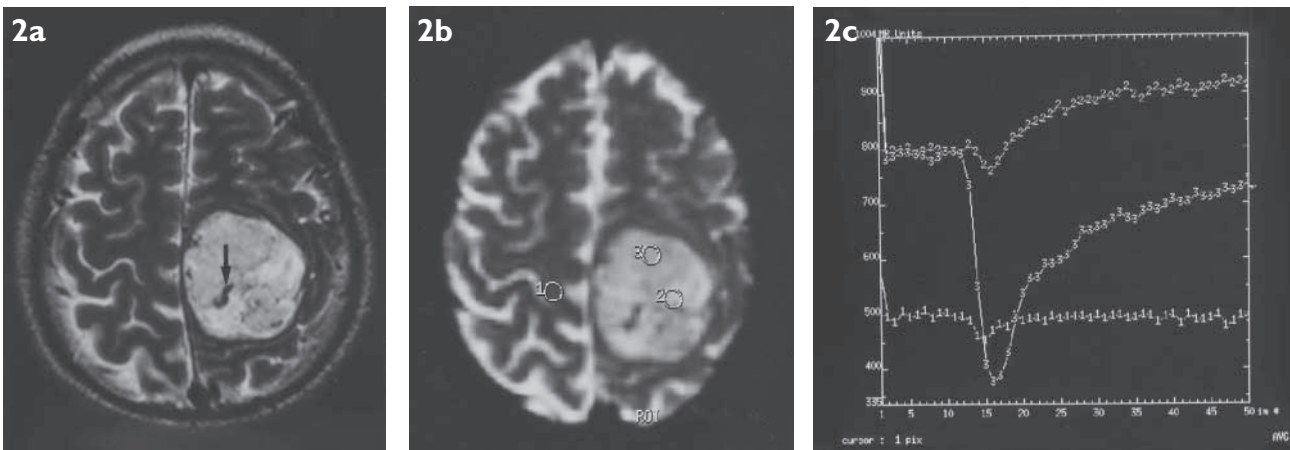


Fig. 2 Study 4: 34-year-old man with meningioma. T2-weighted image showing large meningioma with a venous flow void (arrow), confirmed at surgery (a). Reference image (b) shows ROI placement: care was taken to avoid placing ROIs in the vein. The time-signal intensity curve of the spin-echo EPI shows a rising intensity above the baseline in ROI₂ (c).

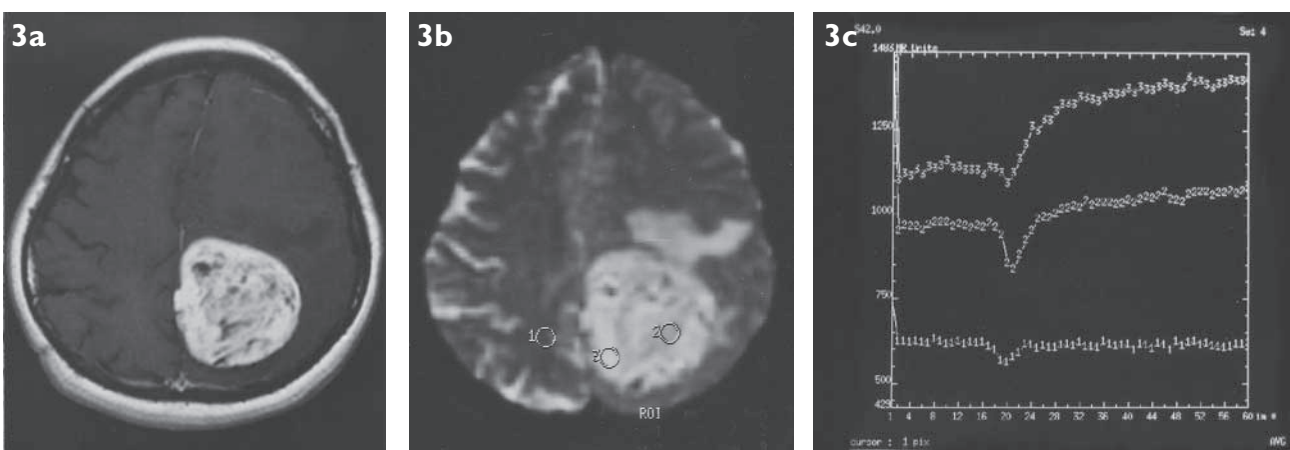


Fig. 3 Study 7: 52-year-old woman with hemangiopericytoma. Post-contrast T1-weighted image shows intense and uniform contrast enhancement of the tumour (a). Reference image (b) shows ROI placement: care was taken to avoid placing ROIs in the vein. The time-signal intensity curve of the spin-echo EPI shows a rising intensity above the baseline in ROI₂ (c).

more prone to susceptibility artifacts⁽⁹⁾. Both SE and GE methods have been proposed for study of human brain tumours^(10,11).

In our series, studies in seven intracranial tumours showed increased rCBV compared to normal brain,

consistent with published reports. In three studies, however, paradoxical rising signal intensity above the baseline was observed. These three studies were all performed with SE EPI pulse sequence, and the tumours involved were extra-axial in location;

they all lacked a well-developed blood brain barrier. In these tumours, contrast material “leaks” easily into the interstitial space, and we postulate that gadolinium accumulates outside the compartmentalised vascular space and causes detectable T1-shortening effects, even during the dynamic first pass acquisition. The T1-effect of accumulated contrast in the interstitial space overwhelms any T2* decrease in signal, leading to the observed effect of a net increase of intensity over the baseline. In effect, this violates the assumption that the paramagnetic contrast medium remains confined to the intra-vascular compartment⁽⁴⁾. Therefore, spin-echo EPI using short repetition time, which is sensitive to T1-effects, may not be the appropriate pulse sequence to study “leaky” extra-axial tumours.

To decrease the T1-sensitivity of a pulse sequence, measures such as decreasing the flip angle or increasing the relaxation time (TR) may be helpful. Compensation for diminished first pass T2* effects using mathematical algorithms have also been proposed by other authors to correct for T1-effects⁽⁵⁾. Finally, a purely intravascular macromolecular contrast medium or one that has minimal T1-effect, such as superparamagnetic iron oxides (SPIO), would also abolish the phenomenon of rising intensity entirely and give a true picture of the T2* rCBV⁽¹⁸⁾.

The phenomenon of contrast leakage into the interstitial space may have important pathophysiological significance⁽¹⁹⁻²¹⁾. Using a T1-weighted non-EPI method, Roberts et al showed that estimates of microvascular permeability were predictive of pathologic grade in brain tumours⁽²²⁾. Further studies are needed to determine if meningiomas and hemangiopericytomas, as a group, are different in their “leakiness” and if this difference can aid in grading or in differential diagnosis. Controlled studies comparing spin-echo and gradient-echo pulse sequences may also assess which methods are appropriate for studying these tumours.

The phenomenon of rising intensity from T1-effects was most pronounced in the patient with hemangiopericytoma. Hemangiopericytoma is a rare, highly vascular tumour that used to be classified as angioblastic meningioma, but is now recognised as a distinct pathological entity with different clinical behaviour, ultrastructural features and immunohistochemical characteristics. It arises from pericytes, which are cells with smooth muscle characteristics found in close association with small blood vessels. This aggressive neoplasm has a poor prognosis with a high recurrence rate and a propensity to metastasize⁽²³⁾.

On CT and conventional MR imaging, a hemangiopericytoma has similar characteristics to a large, extremely vascular angioblastic meningioma^(24,25),

with intense contrast enhancement. It might also be expected to have increased leakage of contrast, causing the overwhelming T1-relaxation effects as observed in our study. To our knowledge, ours is the first MR perfusion description of this rare tumour.

CONCLUSION

Dynamic susceptibility contrast-enhanced MR studies utilising short TR spin-echo EPI may not be appropriate for studying the rCBV of extra-axial brain tumours. A thorough understanding of post-processing methods is essential; and caution and experience are invaluable in the selection of cases and pulse sequence in perfusion MR study of intracranial neoplasms.

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