12-2019

MR perfusion imaging, techniques and role in differentiating radiation necrosis and tumor recurrence

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Abstract

High grade brain tumours are treated with surgery, chemotherapy and radiation therapy and despite such aggressive treatment, can recur in a short span of time. MRI scan has been the conventional diagnostic modality to diagnose recurrence, although at times it becomes difficult for the neuroradiologists to differentiate between tumour recurrence and radiation necrosis. Herein lies the emergent need to explore the efficacy of functional imaging to assist in this diagnostic challenge.Recent studies have sought to do so with promising implications, which we have attempted to summarize in this review.

Keywords: Functional imaging, neuro-oncology; tumor recurrence; treatment necrosis; perfusion.

Introduction

Despite aggressive treatmenrt regimes for high grade brain tumours, recurrence remains inevitable.[1] For a considerable amount of time, conventional contrast enhanced MR imaging has been the mainstay of assessing post treatment tumour recurrence, especially in CNS neoplasms.The usual indicators of a recurrent tumour on follow up MRI include progressive enlargement of lesion, causing mass effect and infiltration of corpus callosum; whereas the enhancement pattern following a Swiss cheese or spreading wavefront pattern is more indicative of radiation necrosis.[2] Over the years considerable overlap between these two types has been observed which has prompted new research efforts into investigating advanced non-invasive imaging methods measuring physiological tumour properties.[3] Novel modern day research centers on bringing forth the capabilities of MR perfusion in exploiting the functional differences at the cellular level between recurrent or progressive tumour

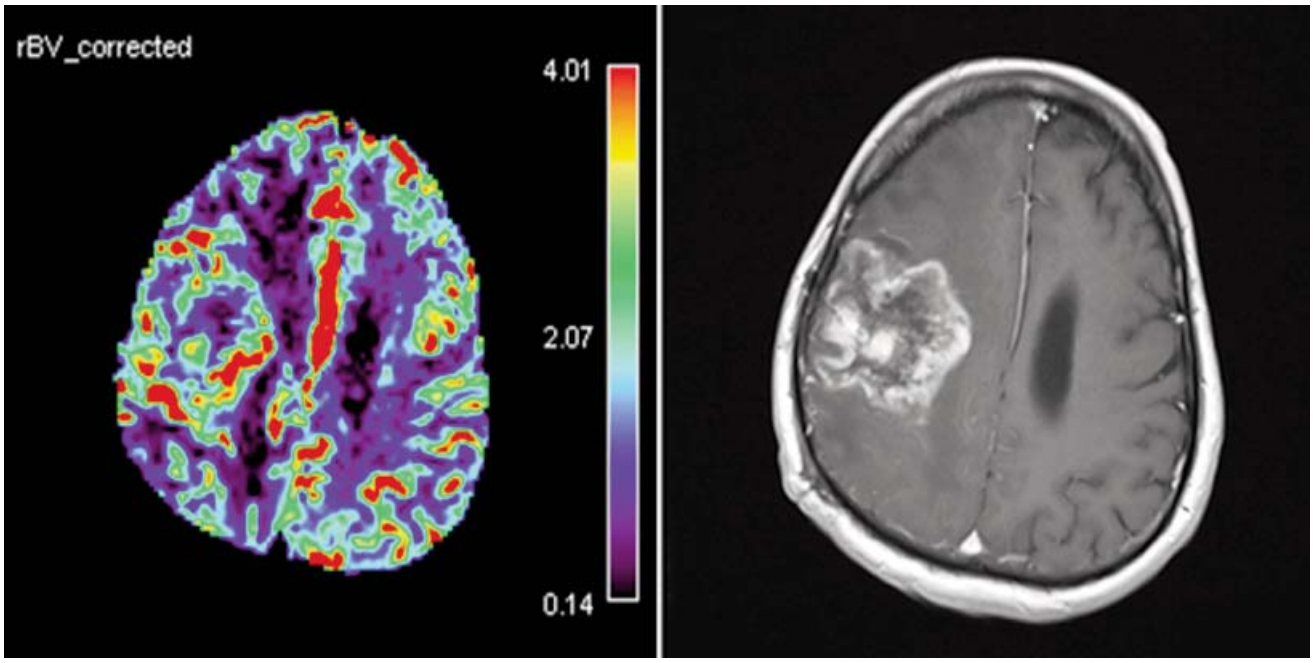

Figure : Enhancing right frontal lobe lesion with perfusion showing raised CBV along medial margins and center representing viable tumour, supporting a diagnosis of recurrence.

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growth from treatment-induced necrosis after radiation therapy.These include increased cell proliferation with neo-angiogenesis in case of tumour; and liquefactive necrosis, vascular hyalinization and endothelial damage in case of radiation induced changes.[4] The observed clinical symptoms vary from none to significant neurological deficit predominantly affecting the white matter. Vermaet al.,[5] reported an incidence of 3–24% for radiation necrosis, showing a direct correlation with the dose of radiation, duration and volume of targeted brain parenchyma.

Technique

In perfusion scanning, successive images are obtained during the first pass of contrast. There are two methods of obtaining perfusion sequences namely dynamic susceptibility-weighted contrast-enhanced (DSC) and dynamic contrast-enhanced (DCE) imaging. In DSC-MRI, the susceptibility effect of contrast causes a T2 signal drop in DSC-MR thus allowing measurement of haemodynamic parameters: relative cerebral blood volume (rCBV), relative peak height (rPH), and percentage of signal-intensity recovery (PSR). Higher rCBV indicates highly permeable blood vessels as in the case of tumour neo-angiogenesis whereas lower values stipulate treatment necrosis reducing blood flow.[5] CBV data is compared with the contralateral side for normalization hence the term relative.[6] In DCE-MRI, rapid sequence T2 imaging is used to measure signal intensities of contrast bolus which reflects lesion perfusion, permeability and extracellular volume. However very few precedents are found in literature that show compelling results in application of DCE-MRI to the question of tumour recurrence versus radiation necrosis.[5]

Review of Evidence

Prager et al.[7], conducted perfusion analysis in post treatment enhancing lesions for patients with primary high grade gliomas. They reported lower rCBV values in treatment related changes, rCBV lesion ($P = 0.003$) and rCBVROI (region of interest) ($P = 0.011$). An optimized rCBV lesion threshold of ≥1.27 had 86.5% sensitivity and 83.3% specificity with AUC (area under curve) of 0.863 for the diagnosis of recurrence.Barajas et al.[8], performed a retrospective review of 27 patients that underwent gamma knife radiosurgery for metastatic lesions of the brain.Upon follow up patients that presented with enhancing lesions on conventional imaging were selected and ROI were drawn around the entire contrast-enhancing region.Their observations stipulated lower rCBV ($P <0.01$) in lesions with necrosis. A cutoff rCBV value of 1.52 in enhancing lesions withstood cross-validation with a sensitivity of 91.30% and specificity of 72.73 for tumour recurrence.

Sugahara et al.[9], were amongst the initial investigators to pave the way for future research efforts that may solidify the role of MR perfusion in this area. In their landmark paper they reported higher normalized ratios of rCBV in the tumour recurrence group compared to those of the non-neoplastic group. The differences between the two groups reached statistical significance, P value 5.03 and 0.02, respectively. A sensitivity of 50% and a specificity of 90% for perfusion-sensitive contrast-enhanced MR imaging at a cutoff value of 1.0 for normalized rCBV ratios was reported.They also presented a detailed overview of overlap in normalized rCBV ratios between the two groups. According to them, the factors that may have affected the ratios include coexisting neoplastic and necrotic tissue, the affected vessels in irradiated tissue being prone to vascular phenomena such as formation of aneurysmal or telangiectatic collaterals resulting in larger rCBV ratios, and finally post radiation petechial haemorrhages that reduce the rCBV when occurring in areas of tumour recurrence.Young et al.[10],also reported that patients in their study group comprising of treated glioblastoma with progressive disease demonstrated significantly higher median rCBV with P=0.009.

In a recently published meta-analysis, Chuang MT et al.[11], reviewed 13 articles that encompassed a total of 397 patients not restricted by tumour type as these included primary plus metastatic lesions providing a bigger picture to comprehend the versatile role of MR perfusion in lesion characterization.They concluded that average rCBV was significantly higher in tumour recurrence compared with radiation injury (all $P < 0.05$).Bobek-Billewicz et al.[12], compared the efficacy of MR perfusion over MR spectroscopy in differentiating true recurrence from radiation injury. They made observations that show statistically significant difference in terms of rCBV between tumour recurrence and radiation injury group ($rCBVmax\ p < 0.001$, $rCBVmean\ p < 0.005$) with mean rCBV being more plausible as a differing factor than max rCBV.

Conclusion:

In the light of available evidence as briefed in our review, it would be safe to conclude that functional MR imaging has far progressed over the years as a potential non-invasive tool for differentiating between tumour recurrence and radionecrosis.MR perfusion has been consistently reported as a promising adjunct for the distinction between recurrent tumour and radiation

injury.

Disclaimer: None to declare.

Conflict of Interest: None to declare.

Funding Disclosure: None to declare.

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