MRI of brain tumour

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Introduction

Contrast-enhanced MRI has become the mainstay of clinical brain tumour imaging, for diagnosis, neurosurgical guidance for biopsy and resection, radiotherapy planning and subsequent evaluation of treatment response and progression. Although widely-used T1-weighted, T2-weighted and gadolinium-enhanced sequences provide exquisite anatomical detail and improved tissue characterisation compared with CT, the biological specificity of the signal is limited. Distinguishing brain tumours from other non-neoplastic diseases, tumour characterisation and grading, delineation of aggressive components and tumour margins, and the evaluation of treatment response, present real challenges in clinical management. Advances in physiological MRI techniques now allow non-invasive in vivo evaluation of tumour microvasculature, cellularity, ultrastructure and metabolic profile. This provides quantitative data that complements the structural information provided by conventional MRI. Measurement of such physiological parameters can add specificity and sensitivity to the overall MRI examination, particularly where appearances on standard sequences are equivocal, and can aid diagnosis, surveillance and therapeutic evaluation.

Conventional MRI

Although some space occupying lesions have characteristic appearances on conventional MRI, in general, conventional MRI has limited specificity for distinguishing brain tumours from other non-neoplastic space occupying lesions. For example, a peripherally enhancing mass may represent a high-grade tumour (figure 1), metastasis, inflammatory lesion, demyelinating lesion or infection. Great emphasis is placed on contrast enhancement as an indicator of aggressive lesion behaviour but it is worth noting that comparison of T1-weighted images before and following contrast administration gives only a crude indication of local blood-brain barrier integrity, which is a limited surrogate of tumour activity. Up to one third of malignant gliomas due not enhance, and certain subtypes of low-grade gliomas can demonstrate enhancement. Multifocal enhancement and satellite lesions make tumour assessment and therapeutic evaluation challenging. Radionecrosis following therapy can cause oedema and enhancement that may be impossible to distinguish from residual or aggressive tumours using conventional MRI. Pseudoprogression refers to an apparent increase in tumour size and enhancement following aggressive chemoradiotherapy, while pseudoregression or pseudoresponse refers to reduced enhancement following steroid or anti-angiogenic therapy. These phenomena can cause false positive and false negative results respectively, when assessing response to treatment using MRI.

Spectroscopy

Magnetic resonance spectroscopy (MRS) techniques allow non-invasive in vivo analysis of major brain metabolites. The protons of different metabolites have different chemical environments due to differences in surrounding electron clouds. This results in the protons from different metabolites resonating at different frequencies (chemical shift effect). Metabolite data can be averaged from single-voxel or multivoxel techniques; the latter are particularly useful in tumour imaging because metabolite maps can be produced which will indicate tumour heterogeneity. These maps may guide stereotactic biopsies to the most aggressive areas of a heterogeneous tumour and could be also be used for radiotherapy planning.

MR spectroscopy of the same patient in figure 1. (A) demonstrates elevated choline levels (high choline levels displayed as red on the metabolite map) in keeping with high cellular turnover. Elevated choline at the periphery of the tumour extends beyond the enhancing margin demonstrated on the structural image in figure 1. (B) Elevated lipid levels (high lipid levels displayed as red on the metabolite map) indicate central necrosis, characteristic of glioblastoma.

High choline (figure 2, figure 4), low NAA and high lipid (figure 2) and lactate levels are established markers of high grade gliomas (HGGs; malignant gliomas; WHO grade III and IV). High myo-inositol levels are associated with low grade gliomas (LGGs; WHO grade I and II). The peritumoural choline/creatine ratio has been found to be higher in HGGs than metastases, and in conjunction with rCBV measurements, can help discriminate between infiltrative, non-enhancing tumour and vasogenic oedema. MRS can help differentiate pyogenic abscesses from other tumours by demonstrating evidence of bacterial metabolism from peaks in succinate, acetate and cytosolic amino acids. MRS may
Dynamic susceptibility contrast enhanced MRI (DSC-MRI) is the most common perfusion method used in clinical practice. It involves acquiring time-resolved images during the transit of exogenous gadolinium chelate contrast agent. The most widely used method is blood oxygen level dependent (BOLD) MRI which exploits differences between local tissue signal caused by oxygenated and deoxygenated haemoglobin. Task-evoked signal changes are processed using statistical models and ‘activation areas’ superimposed onto structural brain images. This can help identify the relationship between tumour and adjacent, functionally-eloquent white matter tracts and provide useful information for deciding the feasibility of potential surgical resection.

Diffusion weighted imaging and diffusion tensor imaging

Diffusion weighted imaging (DWI) measures the Brownian motion of water. The apparent diffusion coefficient (ADC) is determined by the barriers to free diffusion, predominantly of extracellular tissue water; the signal in brain tumours is principally determined by tumour cellularity and extracellular matrix composition. Studies have found reduced ADC measurements in cellular tumours such as lymphoma or medulloblastoma. However, overlap in ADC values between different types of tumours generally limits its role to narrowing potential differentials rather than making a firm diagnosis. DWI shows greater promise for assessing treatment response, and ‘functional diffusion maps’ from quantitative voxel longitudinal ADC measurements provide early indicators of response to radiotherapy.

Diffusion tensor imaging (DTI) is based on the same principles as DWI but is acquired in multiple directions to determine the degree of directionality of diffusion restriction (quantified as fractional anisotropy; FA) and dominant direction of water diffusion. DTI gives additional information on white matter ultrastructure and integrity, because myelin limits extracellular diffusion. DTI may therefore demonstrate tumour microinfiltration into white matter tracts better than conventional imaging and there is some evidence that it may be able to discriminate tumour infiltration from areas of vasogenic oedema. Diffusion tractography uses additional mathematical modelling to ‘connect’ the dominant diffusion directions in adjacent voxels to visualise the positions of white matter tracts, and the resulting maps can be superimposed onto structural brain images. This can help identify the relationship between tumour and adjacent, functionally-eloquent white matter tracts and provide useful information for deciding the feasibility of potential surgical resection.

Functional MRI

Functional MRI (fMRI) uses regional blood flow and oxygen extraction as a surrogate marker of local brain activation. The most widely used method is blood oxygen level dependent (BOLD) MRI which exploits differences between local tissue signal caused by oxygenated and deoxygenated haemoglobin. Task-evoked signal changes are processed using statistical models and ‘activation areas’ superimposed onto structural brain images.
on structural brain images. This technique is particularly useful for demonstrating eloquent areas of the brain, which are identified by asking the patient to perform motor or language tasks in the MRI magnet. The accuracy of cortical localisation is generally higher with low grade tumours and more reliable with motor tasks compared with language tasks. fMRI is increasingly used in combination with tractography to provide the neurosurgeon and clinical oncologist with additional information about the relationship between the tumour and functionally important brain structures to maximise treatment efficacy and minimise deficit, when planning treatment.

Conclusion
A range of quantitative MRI techniques which reflect different molecular and cellular processes relevant to brain tumour physiology are now available. A multimodal approach to tumour characterisation and monitoring synthesises the information from these individual methods with that from structural MRI; there is evidence that combining physiological MRI with conventional MRI increases diagnostic accuracy, and multimodal algorithms may help in the investigation of an unknown intra-axial lesion. These methods are also likely to play an increasing role in response evaluation, both with current treatments and in future therapeutic trials. While physiological MRI may lack some of the exquisite molecular specificity and sensitivity of some advanced PET-based methods, it may be performed as part of an MRI examination at relatively low cost, and is hence more accessible to wider clinical neuro-oncology practice.

References