Cancer: brain and other. Clinical studies

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In vivo magnetic resonance spectroscopy is increasingly used to aid the diagnosis of disease, in some tumour types providing increased specificity in distinguishing malignant from benign disease, aiding the planning of treatment and providing information on response [1,2]. Mobile lipids are present in a range of disease types showing peaks at 0.9 ppm (methyl) and 1.3 ppm (methylene) in the proton spectra, when spectra are obtained at shorter echo times. Identification of such signals as lipids emanating from tumour is complex, as in many tumour types and tissues the large amount of tissue fat leads to a high likelihood of contamination in the region of interest (both with single voxel and multi-voxel techniques) leading to a requirement for lipid suppression techniques, including adjacent saturation bands. This is the case for both breast and prostate cancer, where lipid signals are generally treated as potential contamination and are not interpreted.

In short TE brain tumour spectra, evaluation of the peaks at 0.9 ppm and 1.3 ppm is helpful in diagnosing tumour type and grade [3,4], however care still has to be taken to exclude potential contamination, particularly where the volume of interest is close to the skull. In addition, macromolecules can also contribute to these two peaks in approximately equal amounts, with the potential contribution increasing as TE is reduced [5]. The peak at 1.3 ppm can also include contributions from lactate and alanine, with the lactate and alanine doublets evident as an inverted peak at a TE of 1.3ppm. Separating these contributions can be difficult without the use of spectral editing [6] or 2D techniques, and in vivo spectroscopy often reports only the sum peaks. Magic angle spinning (MAS) evaluation of intact tissue samples, or solution state extracts can aid discrimination of different metabolites, and further the understanding of mobile lipid components, but these are not routinely performed. In a range of astrocytoma samples studied by MAS, an association between lipid droplets and the size of the 1.3 ppm lipid peak has been reported [7], showing that in non-necrotic samples lipid drop concentration correlated to cell density, whilst in necrotic samples, lipid droplet number correlated with percent necrosis.

In brain tumours, the mobile lipid peaks (together with other components) are most pronounced in glioblastoma and in brain metastases, where the peak at 1.3 ppm is particularly elevated at short TE [3]. This is helpful in discriminating these two conditions from other types of brain tumour [8] and contributes to automatic analysis methods [9,10]. Other brain tumours may show a smaller peak at 1.3 ppm, often with some evidence of a doublet. Presence of a large peak at 1.3ppm is generally taken to indicate the presence of necrosis [3,4,6,11,12], although the presence of lipid peaks may also reflect other cellular processes such as proliferation, growth arrest and apoptosis [13]. The processes underlying the mobile lipid peaks seen with MRS are the subject of considerable investigation and debate [14,15,16], and the presence and changes in these peaks has to be considered in the context of the investigations. Lipid signals (methylene to water ratio) have also been reported to increase with grade,

correlating with gadolinium enhancement, and potentially providing a marker of transformation from low to high grade disease [17]. lactate or lipid levels have been reported to provide high specificity in grading glioma [18].

In addition to diagnosis, ^{1}H MRS in brain tumours is also used to help plan treatment, where aggressiveness and viability of tumour can be important, to identify residual or recurrent tumour post treatment, and to evaluate response to treatment. For example in brain tumours responding to temozolomide post resection, a reduction in the 1.3ppm peak, as well as a reduction in TCho, was seen together with an increase in NAA, suggesting that reduction in lipid signal was a feature of this response [19]. Falling lipid signals provided an early marker of response to tamoxifen in Grade III or IV glioma, while increasing lipid indicated lack of response [20]. In responders relapse was also marked by an increase in lipid signals. In radiotherapy of paediatric diffuse brain stem gliomas a fall in lactate and lipid peaks correlated with response, and stable or increasing signals correlated with relapse [21]. These changes with therapy largely appear to reflect cell death.

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