

ORIGINAL ARTICLE

# Preoperative magnetic resonance spectroscopy improves diagnostic accuracy in a series of neurosurgical dilemmas

P. J. Rao<sup>1,2</sup>, R. Jyoti<sup>2,3</sup>, P. J. Mews<sup>1</sup>, P. Desmond<sup>4</sup> & V. G. Khurana<sup>1,2</sup>

<sup>1</sup>Department of Neurosurgery, The Canberra Hospital, Garran, Australia, <sup>2</sup>The Australian National University, Acton, Australia, <sup>3</sup>Department of Radiology, The Canberra Hospital, Garran, Australia, and <sup>4</sup>Department of Radiology, Royal Melbourne Hospital, Parkville, Australia

## Abstract

**Object.** The purpose of this study was to evaluate the usefulness of preoperative magnetic resonance spectroscopy (MRS) in neurosurgical patients with diagnostically challenging intracranial lesions. **Methods.** Included in this study are twenty-three consecutive patients presenting to the neurosurgery service with diagnostically challenging intracranial lesions and who were investigated by conventional MR imaging and proton (<sup>1</sup>H) MRS, followed by surgery with subsequent histopathological diagnosis. An experienced neuroradiologist (RJ) blinded to the final histopathology evaluated the imaging studies retrospectively. Provisional diagnoses based on preoperative clinical and conventional MR data versus preoperative MRS data were compared with definitive histopathological diagnoses. **Results.** Compared with preoperative clinical and conventional MR data, <sup>1</sup>H MRS improved the accuracy of MR imaging from 60.9% to 83%. We found <sup>1</sup>H MRS reliably distinguished between abscess and high-grade tumour, and between high-grade glioma and low-grade glioma, but was not able to reliably distinguish between recurrent glioma and radiation necrosis. In 12/23 cases (52%) the <sup>1</sup>H MRS findings positively altered our clinical management. Two representative cases are presented. **Conclusions.** Our study supports a beneficial role for <sup>1</sup>H MRS in certain diagnostic intracranial dilemmas presenting to neurosurgeons. The information gleaned from preoperative <sup>1</sup>H MRS can be a useful adjunct to clinical and conventional MR imaging data in guiding the management of patients with intracranial pathologies, particularly high-grade tumour versus abscess, and high-grade versus low-grade glioma. Further larger prospective studies are needed to clearly define the utility of <sup>1</sup>H MRS in diagnostically challenging intracranial lesions in neurosurgery.

**Keywords:** abscess; brain tumour; glioma; intracranial surgery; magnetic resonance spectroscopy

**Abbreviations:** Cho, Choline; Cr, Creatine; DWI, Diffusion weighted imaging; <sup>1</sup>H, Proton; MR, Magnetic resonance;

MRS, Magnetic resonance spectroscopy; ms, milliseconds; MVS, Multi-voxel spectroscopy; NAA, N-Acetylaspartate; PPM, parts per million; SD, Standard deviation; SVS, Single-voxel spectroscopy; TE, Echo time; TI, Inversion time; TR, Repetition time; WHO, World Health Organization

## Introduction

When neurosurgeons encounter patients with ambiguous imaging and clinical data, additional information is required to guide management. Often operative biopsy or debulking provides histopathological diagnosis, but even stereotactic biopsy is associated with morbidity and can be non-diagnostic in some cases.<sup>1–3</sup> Therefore, a need arises for a non-invasive tool to guide early diagnosis and management, including either prompt treatment or the avoidance of unnecessary surgery.

MRS, which evaluates the metabolite profile of the lesion when combined with conventional MR imaging, has been reported to increase diagnostic accuracy.<sup>4</sup> A number of studies have identified metabolic patterns utilizing MRS in various pathologies such as brain tumours,<sup>5–8</sup> infections<sup>9,10</sup> and inflammatory conditions.<sup>11</sup> Although a few studies have evaluated the role of MRS in differentiating brain tumours from abscesses,<sup>12,13</sup> and high-grade gliomas from low-grade gliomas,<sup>14</sup> there appears to be little information elucidating a neurosurgical perspective of the value, or otherwise, of MRS. The purpose of this study, therefore, was to evaluate the usefulness of preoperative <sup>1</sup>H MRS in neurosurgical patients with diagnostically challenging intracranial lesions.

## Methods

### Patients

Between January 2007 and July 2009, 23 consecutive neurosurgery patients who presented to the outpatient clinic

or emergency department of The Canberra Hospital with diagnostically difficult intracranial neurosurgical lesions followed by histopathological diagnosis were included in this study.  $^1\text{H}$  MRS was requested in these cases when the attending neuroradiologist felt that the lesion was diagnostically challenging on conventional MR imaging thereby generating an ambiguous or inconclusive radiology report “impression”. These cases are typically discussed with neurosurgeons at a weekly neuroradiology conference. Data from all of these patients were prospectively collected as an audit by the first author (PJR). As the number of cases accumulated, it was felt that a retrospective study would be appropriate to evaluate the diagnostic accuracy of  $^1\text{H}$  MRS versus conventional MR imaging from a neurosurgical perspective. An experienced neuroradiologist (RJ) who was blinded to the final histopathology was asked to retrospectively evaluate each patient’s clinical presentation, MR imaging and  $^1\text{H}$  MRS. Tumour “grade” refers to World Health Organization (WHO) classification. Approval was obtained from our Hospital’s Research Committee for this retrospective study.

### Imaging

All patients were examined by using a 1.5 Tesla superconducting MR scanner (Magnetom Avanto 76 × 32; Siemens, Erlangen, Germany) with a standard circularly polarized head coil. In each participant, axial and sagittal T1-weighted (400/8.1 ms [TR (repetition time)/TE (echo time)]) spin-echo (SE), T2-weighted (4590/123 ms) turbo SE, and fast fluid-attenuated inversion recovery (FLAIR) (8200/2500/110 ms [TR/TE/TI (inversion time)]) images were obtained by using 5 mm section thickness, 210 mm field of view (FOV), and 160 × 256 matrix size. After intravenous administration of 20 mL gadolinium (Magnevist; Schering, Germany) contrast-enhanced T1-weighted SE sequences were obtained in 3D magnetization prepared rapid gradient echo (MPRAGE) sequence.

In most of the cases single-voxel  $^1\text{H}$  MRS (SVS) measurements were performed with the point-resolved spectroscopy double-spin echo localization sequence. Spectra were obtained at TE 136 ms and TR 1500 ms by using 192 averages to get acceptable signal: noise ratios. The size of the target volumes ranged from 4 to 20 mL, adapted to the individual lesions. Voxel positioning avoided susceptibility effects by covering most of the lesion and avoiding partial volume effects of surrounding structures like CSF space, bone and fat. If the centre of the lesion was necrotic or cystic then we included only the homogenous solid edge of the lesion. In a few lesions which were inhomogeneous, multi-voxel  $^1\text{H}$  MRS (MVS) was performed which were 2D and voxels of 1 mL each (TR 1700/TE 136, delta frequency 0.003). In these cases the mean of the metabolite values in the voxels of the solid edge was utilized. In some cases both were performed if there was any doubt about the spectrum obtained. Pre scan automatic shimming was performed to yield a full width half maximum of water < 10 Hz. The spectra were evaluated through simple peak integration after increasing the line width by approximately 2 Hz by using commercially available Siemens software, which analyses the spectra as a linear combination of different model spectra.

### Spectroscopy

Cho/NAA or Cho/Cr ratio greater than 1 was considered abnormal. Abscess was identified by presence of acetate, succinate or amino acids at TE 136 ms. Differentiation of high grade glioma from high low grade glioma was done with Cho/Cr ratio or Cho/NAA ratio > 1.5 or by presence of lactate or lipid resonances.

### Evaluation

Patients underwent stereotactic-guided aspiration (in case of an abscess) or debulking as deemed appropriate by the attending neurosurgeon. Final histopathology was subsequently correlated with the clinical data, conventional MR imaging and  $^1\text{H}$  MRS.

Final histopathology of the entire lesion was correlated with SVS or mean of the abnormal voxels of the MVS. Conventional MR imaging was determined by the histopathology-blinded neuroradiologist (RJ) as being: (i) “definitive” if he felt one of the differential diagnoses was highly probable and the remainder were of low probability; (ii) “equivocal” if two differential diagnoses were equally probable; or (iii) “inconclusive” if more than two diagnoses were equally probable.

$^1\text{H}$  MRS impact on clinical decision was deemed as ‘positive’ if the clinical decision was completely changed (for example observation to surgery) and it was a correct decision based on histopathology. The impact was ‘negative’ if the clinical decision was completely changed but the final histopathology did not support the  $^1\text{H}$  MRS findings.

### Statistics

For statistical purposes a commercially available software package (SPSS 17.0) was utilized and Kruskal–Wallis Test was performed to compare the Cho/NAA and Cho/Cr ratios between different grades of glioma. Mann–Whitney U-test was performed to compare the Cho/NAA and Cho/Cr ratios between abscess and high-grade tumour, low-grade and high-grade glioma, benign lesion and glioma, and recurrent tumour and radiation necrosis. *P* values below 0.05 were regarded as statistically significant.

### Results

Twenty-three consecutive patients (11 males, 12 females) were included in the study. Age ranged from 23 years to 74 years (mean 54 years; standard deviation 13 years). In this cohort of patients, grade 4 astrocytoma was the single most common pathology (*n* = 5).

#### Diagnostic accuracy of conventional MR imaging versus $^1\text{H}$ MRS

Clinical data combined with conventional MR imaging were deemed by the neuroradiologist to be definitive in 2 (9%) patients; however,  $^1\text{H}$  MRS had been requested by the neurosurgery team owing to a difference of opinion at the multidisciplinary meeting. Of the remaining 21 patients, the neuroradiologist found the clinical data and conventional MR imaging to be equivocal in 16 (70%) and inconclusive in 5 (21%) (Table I). Compared with the final histopathology, the neuroradiologist was found to be 60.9% accurate using

Table I. Data showing the diagnostic difficulty of clinical data and MR imaging in various pathology subsets. Conventional data were ambiguous in abscess and radiation necrosis (100% of cases, respectively).

Final histopathology	Preoperative MR imaging and clinical data		
	Definitive	Ambiguous	Inconclusive
Abscess	0 (0%)	3 (100%)	0 (0%)
Low grade glioma	1 (33.3%)	1 (33.3%)	1 (33.3%)
High grade glioma	1 (11%)	6 (66.7%)	2 (22.2%)
Recurrent glioma	0 (0%)	3 (100%)	0 (0%)
Other	0 (0%)	3 (60%)	2 (40%)
Total	2 (9%)	16 (70%)	5 (21%)

clinical data and MR imaging versus 83% accurate using  $^1\text{H}$  MRS as an adjunct (Table II).

### MRS spectra by final histopathology

There were several different histopathological diagnoses encountered in our series of 23 patients. Their MRS spectra are as follows:

(i) *Grade 2 glioma*: All the 3 cases were astrocytomas with a mean Cho/NAA ratio of  $1.1 \pm 0.5$  (standard deviation) and Cho/Cr ratio of  $1 \pm 0.1$ . Lipids and lactate were absent in all.

(ii) *Grade 3 glioma*: Of the 4 cases, one was an oligodendroglioma and the others astrocytoma. Mean Cho/NAA ratio was  $2 \pm 0.6$  and Cho/Cr ratio was  $1.6 \pm 0.7$ . Lipids were present in 2 of 4 patients and lactate was present in 1 of 4 grade 3 glioma patients.

(iii) *Grade 4 glioma*: There were 5 cases of astrocytoma in this group. Mean Cho/NAA ratio was  $5.1 \pm 6.7$  and mean Cho/Cr was  $2.2 \pm 1$ . Amino acid spectra at 0.9 parts per million (ppm) at 136 ms TE were absent in these patients. Lactate was present in 4 of 5 (80%) while lipids were present in 40% (2 of 5) patients. Acetate, succinate and alanine were absent in all.

(iv) *Abscess*: *Streptococcus milleri* was the etiologic organism in all the three cerebral abscesses and in one of them mixed anaerobic organisms were also present. Mean Cho/NAA ratio was  $1.4 \pm 0.4$  while mean Cho/Cr was  $2.2 \pm 0.6$ . Amino acid spectra at 0.9 ppm at 136 ms TE were present in all abscesses, as were lactate and lipids. Acetate was present in 1 of 3 patients and alanine in 2 of 3. Succinate was absent in all.

(v) *Recurrent tumour*: There were 2 cases of recurrent grade 4 astrocytoma and one recurrent medulloblastoma. Mean Cho/NAA was  $2.3 \pm 1.4$  and mean Cho/Cr was  $2.2 \pm 0.5$ . Lactate was present in all of them while lipids were present in one of them.

(vi) *Radiation necrosis*: There were 2 patients, with one having had radiation for metastatic breast carcinoma and the other for grade 4 astrocytoma. Mean Cho/NAA ratio was  $1.7 \pm 0.0$  and Cho/Cr ratio was  $1.6 \pm 0.2$ . Both cases had lipid peaks and one had an additional lactate peak.

(vii) *Nonspecific pathology (benign, non-infective lesion)*: Of the two benign lesions, one had a Cho/NAA ratio of 2.5 and Cho/Cr ratio of 1.9 with absent lipids and lactate. In the other benign lesion, Cho/NAA ratio was

Table II. Comparing the accuracies of MR imaging and clinical data impression and  $^1\text{H}$  MR spectroscopy in pathology subsets.  $^1\text{H}$  MR spectroscopy increased diagnostic accuracy from 60.9% to 83%.

Definitive pathology	MR imaging and clinical data	$^1\text{H}$ MR spectroscopy
Cerebral abscess	1/3 (33.3%)	3/3 (100%)
Low grade glioma	2/3 (66.7%)	2/3 (66.7%)
High grade glioma	6/9 (66.7%)	9/9 (100%)
Recurrent tumour	3/3 (100%)	3/3 (100%)
Other	2/5 (40%)	2/5 (40%)
Total	14/23 (60.9%)	19/23 (83%)

0.5 while Cho/Cr was 0.9. Both were nondiagnostic on final histopathology.

### Clinical dilemmas

In this series of 23 patients, we identified four major clinical dilemmas that led to further radiological evaluation via the addition of  $^1\text{H}$  MRS to the preceding conventional MR imaging sequences. The dilemmas and imaging results are as follows:

(i) *High-grade tumour versus abscess*: In 7 patients presenting with ring-enhancing lesions, the dilemma was distinguishing between abscess and high-grade tumour. Compared with the final histopathology, clinical data and conventional MR imaging correlated in 4/7 (57%), while  $^1\text{H}$  MRS was accurate in all seven (100%) cases. In light of the final histopathology, the following could be gleaned: the mean Cho/NAA ratio was  $1.4 \pm 0.4$  (standard deviation) in abscess while in high-grade tumour [including grade 3 and 4 glioma, lymphoma and recurrent high-grade tumours (glioma, metastasis and medulloblastoma)] it was  $2.1 \pm 0.9$ . Mean Cho/Cr was  $2.2 \pm 0.6$  in abscess and  $2.0 \pm 0.8$  in high-grade tumour. When these ratios were compared between abscesses and high-grade tumour patients, no statistically significant difference was found ( $p = 0.15$  for Cho/NAA and  $p = 0.5$  for Cho/Cr). Amino acid spectra at 0.9 ppm at 136 ms TE were present in all abscesses but absent in high-grade tumours. Lactate was present in all abscesses and in 9 of 13 high-grade tumours. Lipids were present in all abscesses but in only 5 of 13 high-grade tumours. In patients with abscesses, acetate and alanine were present in 2 of 3 cases while succinate was absent in all of them. Acetate and alanine were absent in high-grade tumours.

(ii) *Glioma versus benign (non-infective) lesion*: These 8 cases presented with non-specific clinical symptoms and MR imaging findings of a hypointense lesion on T1-weighted imaging, with minimal mass effect and minimal or no contrast enhancement. The dilemma was distinguishing between benign (non-neoplastic) lesion and glioma. The differential diagnoses for benign causes considered included infarction (4 cases), benign cyst (1 case) and demyelination (3 cases). WHO grade 2 glioma was the tumour differential considered for these cases. The  $^1\text{H}$  MRS diagnosis correlated with the final histopathology in 6 (75%) of these 8 cases. Amongst gliomas, only one case was missed on MRS and this was a multicystic parenchymal lesion that was non-enhancing

on contrast MR imaging. In this patient, Cho/NAA was 0.6 and Cho/Cr ratio was 1.1 with absent lactate and lipids. On comparing non-infective benign lesions and tumours, Cho/NAA and Cho/Cr ratios were not significantly different.

(iii) *Low-grade glioma versus high-grade glioma*: There were 3 cases with this dilemma and <sup>1</sup>H MRS was accurate in all of these. Although there was gradation of Cho/NAA and Cho/Cr levels with increasing grade of glioma, it was not statistically significant ( $p = 0.19$  for Cho/NAA and  $p = 0.08$  for Cho/Cr). Comparing these ratios between low-grade and high-grade gliomas also showed no significant difference ( $p = 0.1$  for Cho/NAA and  $p = 0.06$  for Cho/Cr). With caution, we may interpret these values as showing a trend. Presence of lactate or lipids indicated high-grade tumour.

(iv) *Recurrent tumour versus radiation necrosis*: <sup>1</sup>H MRS was accurate in 3/5 (60%) of these cases. The metabolite profile was very similar between recurrent tumours and radiation necrosis in our series. Both the cases of radiation necrosis were erroneously termed as recurrent tumours. On comparing radiation necrosis with glioma, Cho/NAA and Cho/Cr ratios were not significantly different.

### Impact of <sup>1</sup>H MRS on clinical decisions

In 12/23 cases (52%) the <sup>1</sup>H MRS findings positively altered our clinical management (Table III). In three cases elective surgery was converted to urgent surgery, as they were cases of brain abscesses with obvious clinical implications. A case of multifocal glioblastoma multiforme underwent surgery in a controlled fashion instead of urgent surgery (illustrative case 2). Four cases underwent surgery instead of conservative non-operative management as they were correctly identified as gliomas on <sup>1</sup>H MRS. Two cases of radiation necrosis and 2 cases of benign lesions (non-diagnostic) underwent

surgery but histopathology did not support <sup>1</sup>H MRS findings (Table III).

### Two illustrative cases demonstrating the adjunctive value of <sup>1</sup>H MRS

*Case 1.* A 52-year-old female presented with acute-onset headache and confusion but with no lateralizing signs. She was afebrile and inflammatory markers were negative. MR imaging showed two ring-enhancing lesions (Fig. 1) while chest imaging showed a mass lesion that on biopsy was positive for adenocarcinoma. Diffusion weighted imaging showed restriction in one lesion but not in the other. <sup>1</sup>H MRS showed features of cerebral abscess and stereotactic biopsy of the lesions were therefore carried out early, revealing *Streptococcus milleri* abscesses. Without <sup>1</sup>H MRS, the expected diagnosis would have been multiple metastases from the lung and the patient would likely have deteriorated more rapidly without appropriate antibiotics.

*Case 2.* A 65-year-old male presented with dense left hemiplegia on a background of previous ischaemic strokes. While investigating episodes of respiratory desaturation, he was found to have pulmonary emboli. He was commenced on anticoagulation. He intercurrently developed high fever and raised inflammatory markers. Brain MR imaging was performed for evaluation of the stroke and showed ring-enhancing lesions with surrounding edema (Fig. 2). Blood cultures were negative. The clinical consensus was septic emboli causing brain abscesses necessitating urgent stereotactic-guided aspiration of the lesions. However, the added concern was the procedural morbidity as the patient was on anticoagulation for the pulmonary emboli. <sup>1</sup>H MRS revealed features of high-grade glioma with a high Cho/NAA ratio of 3.2 and with lactate and lipid peaks. The patient was managed conservatively for a few days during

Table III. Impact of <sup>1</sup>H MRS on clinical decisions.

Case	Clinical decision prior to MRS	MRS diagnosis	Impact on clinical decision	Altered management
1	Radiotherapy	Abscess	Positive	Urgent surgery
2	Elective resection	Abscess	Positive	Urgent surgery
3	Elective resection	Abscess	Positive	Urgent surgery
4	Resection	Low grade glioma	None	No
5	Observation	Low grade glioma	Positive	Surgery
6	Resection	Low grade glioma	None	No
7	Observation	High grade glioma	Positive	Surgery
8	Observation	High grade glioma	Positive	Surgery
9	Resection	High grade glioma	None	No
10	Observation	High grade glioma	Positive	Surgery
11	Resection	High grade glioma	None	No
12	Aspiration	High grade glioma	Positive	Delayed surgery
13	Surgery	High grade glioma	None	No
14	Surgery	High grade glioma	None	No
15	Aspiration	High grade glioma	None	No
16	Observation	Recurrent high grade glioma	Positive	Surgery
17	Observation	Recurrent high grade glioma	Positive	Surgery
18	Observation	High grade glioma	Negative	Surgery
19	Observation	High grade glioma	Negative	Surgery
20	Observation	Recurrent high grade tumour	Negative	Surgery
21	Observation	Recurrent high grade glioma	Negative	Surgery
22	Observation	Recurrent high grade glioma	Positive	Surgery
23	Observation	High grade tumour	Positive	Surgery

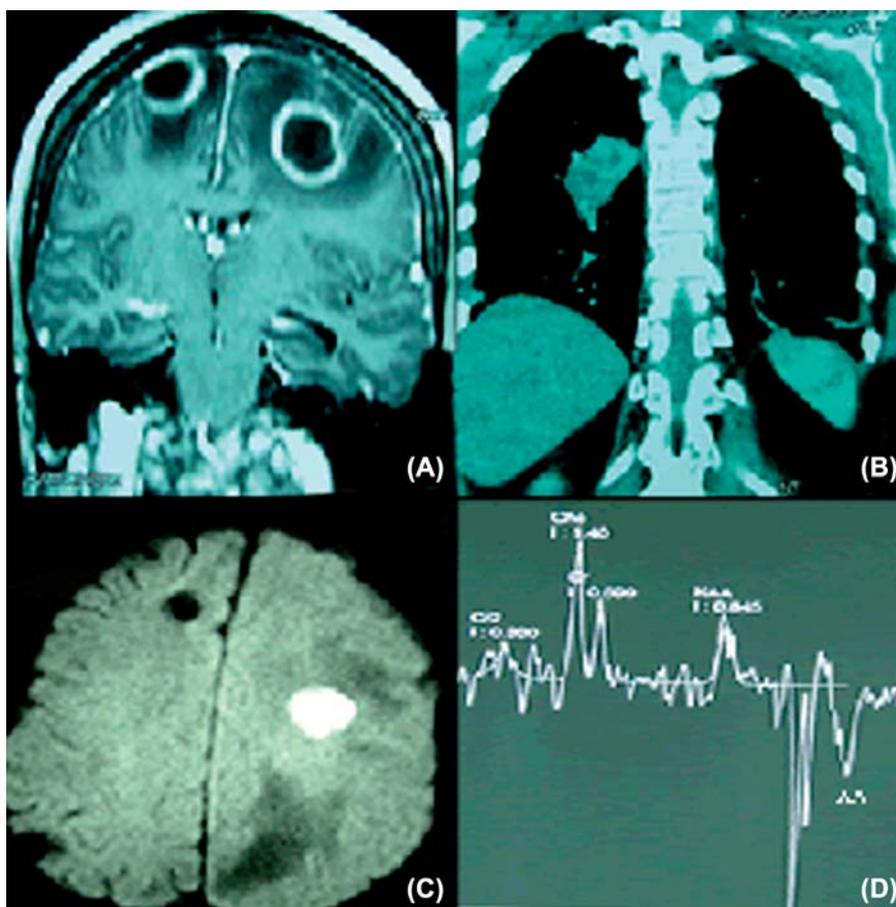


Fig. 1. *Cerebral abscess*. (A) Coronal T1 weighted MR image with contrast of a patient who presented with acute onset of headache and confusion with no lateralizing signs. Inflammatory markers were negative. (B) CT chest showing a mass lesion that on biopsy was positive for adenocarcinoma. (C) Diffusion weighted image showing restricted diffusion in one lesion only. (D)  $^1\text{H}$  MR spectroscopy (TE 136 ms) reveals spectra of an abscess including Cho/NAA ratio of 1.7, Cho/Cr ratio of 2.9 with inverted lactate peak at 1.3 ppm and amino acids (AA) at 0.9 ppm.

which his fever subsided and his respiration stabilized. An inferior vena cava filter was also inserted. Once medically stable, the patient underwent stereotactic debulking of these lesions which revealed multifocal glioblastoma multiforme. We believe that information derived from  $^1\text{H}$  MRS in this patient allowed for the safer planning and delivery of care.

## Discussion

Although MR imaging has tremendously improved diagnostic accuracy, neurosurgeons frequently encounter diagnostically challenging clinical scenarios. The sensitivity of MR imaging varies from 55% to 83%.<sup>4,14</sup> According to Moller-Hartmann et al.,<sup>4</sup> addition of  $^1\text{H}$  MRS has been associated with a 15.4% increase in the number of correct diagnoses, 6.2% fewer incorrect diagnoses, and 16% fewer equivocal diagnoses when compared with conventional MR imaging alone. The common diagnostic dilemmas include high-grade tumour versus low-grade tumour, abscess versus high-grade tumour, benign versus malignant lesion and radiation necrosis versus recurrent tumour.<sup>4</sup> While a number of studies have evaluated the role of  $^1\text{H}$  MRS in diagnosing tumours, grading tumours, and differentiating between tumours and abscesses, to the authors' knowledge, this is the first study

to evaluate its accuracy in a diverse series of diagnostically difficult lesions presenting to a neurosurgical service.

Preoperative histological diagnosis of brain tumours by  $^1\text{H}$  MRS is imperfect,<sup>15</sup> although a few studies such as by Preul et al.<sup>16</sup> have shown promising results. Preul et al.<sup>16</sup> found that  $^1\text{H}$  MRS could correctly classify 99% of the most common brain tumours using resonance profiles across 6 metabolites improving preoperative diagnosis from 77% with conventional MR imaging alone to 99%. Although it is useful to know preoperatively the type and grading of a brain tumour, from a clinical perspective the information needed may also concern whether there is any need to operate at all and, if so, whether a biopsy versus debulking would be more appropriate, and when. For example, if the lesion is deemed to be an abscess, aspiration of the lesion is done early rather than via a routine elective list. Similarly, if the lesion is deemed to be radiation necrosis, treatment may initially be via medical or conservative measures, rather than by surgery.

In our study, the overall diagnostic accuracy of  $^1\text{H}$  MR spectroscopy was 83%. This is in agreement with Moller-Hartmann et al.,<sup>4</sup> who evaluated the utility of  $^1\text{H}$  MRS in 176 focal intracranial lesions and found 70.5% accuracy as compared to 55.1% with conventional MR imaging alone. Their study included various pathologies such as glioma, infarction and cerebral abscess. In contrast, Lin et al.<sup>17</sup> found the accuracy

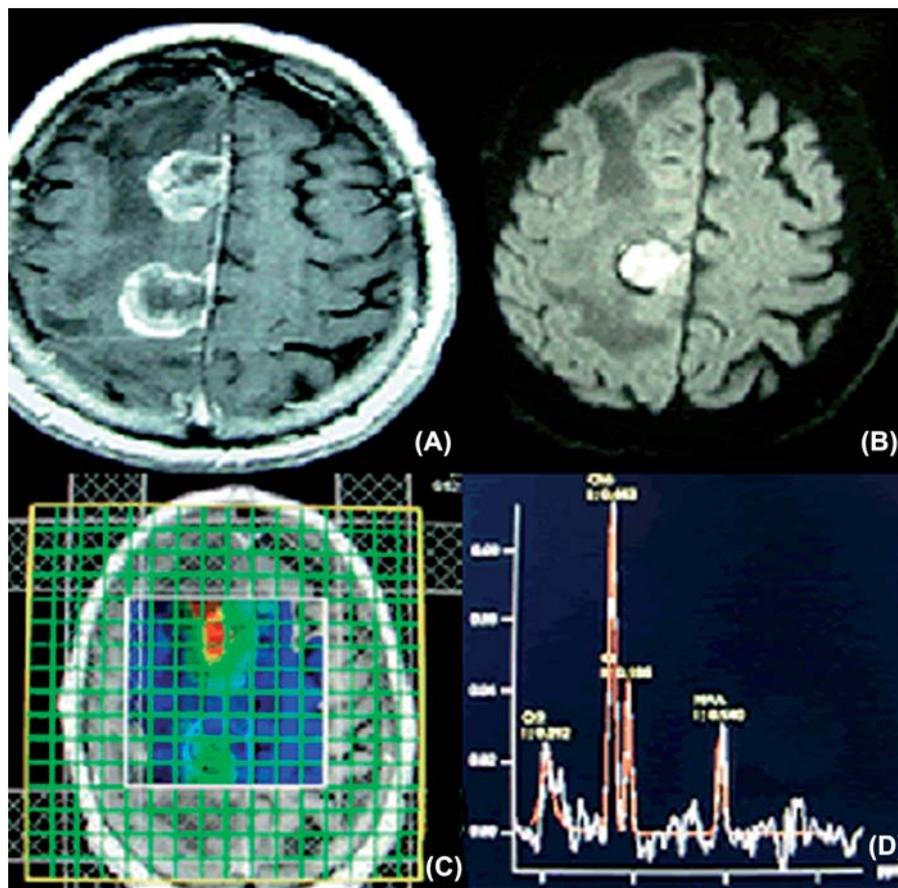


Fig. 2. Multifocal astrocytoma WHO grade 4. (A) Axial T1 weighted MR image with contrast of a patient who presented dense left hemiplegia, pulmonary emboli, fever and raised inflammatory markers. (B) Diffusion weighted image shows restricted diffusion of one of the lesions. (C) Multi-voxel  $^1\text{H}$  MR spectroscopy spectral map of Cho/NAA ratio with highest ratio shown in red. (D) Spectrum of a high-grade glioma showing high Cho/NAA ratio of 3.2, Cho/Cr ratio of 2.7, lipid and small inverted lactate peak (TE 136 ms).

of  $^1\text{H}$  MRS in distinguishing tumour from non-neoplastic lesions to be 96%. The aim of their study was to identify the need for biopsy of the lesion to determine malignancy and included 10 known tumours and 5 suspected tumours. Seven of these cases had histological confirmation and the remainder, clinical and radiological follow-up. In our study, histological diagnosis was obtained in all 23 cases.

#### High-grade tumour versus abscess

Conventional MR imaging can be very similar in high-grade tumours (with cystic or necrotic centers) and abscesses, both presenting as ring-enhancing lesions. Although hyperintensity on diffusion-weighted imaging (DWI) and low apparent diffusion coefficient (ADC) values are highly suggestive of brain abscesses,<sup>18</sup> we had two patients in this series where the results of these sequences were confusing. Both patients had two ring-enhancing lesions and in each patient, one lesion was hyperintense and the other hypointense on DWI. The pathology of one patient turned out to be multifocal abscesses, while the other patient had multifocal glioblastoma multiforme (GBM; Fig. 2). In our study, abscesses were accurately identified by  $^1\text{H}$  MRS in all instances. The presence of amino acid spectra at 0.9 ppm detected at 136 ms TE and varying presence of acetate and alanine were the main features allowing them to be distinguished from high-grade tumours. Cho/NAA and Cho/Cr ratios in abscesses and high-

grade tumours were not significantly different. Grand et al.<sup>12</sup> performed *in vitro* and *in vivo* biochemical analyses of cerebral abscesses, non-cerebral abscesses and necrotic brain tumours. As in our study, they found all abscesses (cerebral and others) had lactate and amino acid spectra around 0.9 ppm at 136 ms TE. In their study, although acetate and succinate were specific for cerebral abscesses, they were not universally present (88% and 35% of cases, respectively). Similar findings have been reported in other studies.<sup>12,13,18,19</sup>

#### Glioma versus benign non-infective lesion

In our study, the sensitivity of  $^1\text{H}$  MRS in detecting glioma of any grade or recurrence was 94%. In the detection of gliomas, various studies have reported sensitivities of 90%–97% and specificities of 85%–88%.<sup>5,14,17,6,20</sup> Floeth et al.<sup>20</sup> evaluated the role of [ $^{18}\text{F}$ ] fluoroethyl-L-tyrosine (FET)-positron emission tomography (PET) and  $^1\text{H}$  MRS in detecting glioma in 50 consecutive patients. In detecting gliomas they found the sensitivity was 100% and specificity was 81% with  $^1\text{H}$  MRS, and 88% each with FET-PET. In the present study, the only patient in which  $^1\text{H}$  MRS failed to identify malignancy was a multi-cystic non-enhancing lesion. Chang et al.<sup>18</sup> found  $^1\text{H}$  MRS to be of limited value in cystic tumours. Our study concurs with other studies in that if the metabolic profile on  $^1\text{H}$  MRS is non-neoplastic, the likelihood of a glioma on histopathology is remote.<sup>5,14,6,14,20</sup>

### Low-grade glioma versus high-grade glioma

Grading of gliomas has been shown to be reliably predicted by  $^1\text{H}$  MRS.<sup>4,16</sup> In the present study,  $^1\text{H}$  MRS was 100% accurate in the 3 instances of dilemma we encountered relating to the grading of glioma. Our results are similar to Moller-Hartmann et al.<sup>4</sup> and Law et al.<sup>14</sup> with Cho/NAA and Cho/Cr ratios increasing commensurate with the grade of the glioma, but in our study this was not statistically significant despite the observed trend. In our study, as in others,<sup>4,16</sup> the presence of lipid and lactate indicated a higher pathological grade.

### Recurrent glioma versus radiation necrosis

In our series  $^1\text{H}$  MRS was not accurate in the 2 cases of radiation necrosis. Although the sample size is too small to draw conclusions, both radiation necrosis and recurrent high-grade gliomas had similarly high Cho/NAA and Cho/Cr ratios and varying amounts of lactate and lipids. Rock et al.<sup>21</sup> elucidated the correlations between  $^1\text{H}$  MRS and image-guided histopathology, with special attention to radiation necrosis. They found that while  $^1\text{H}$  MRS was useful in detecting pure tumour and differentiating normal tissue from radiation necrosis, it was limited in differentiating between tumour-with-necrosis, radiation necrosis and mixed lesions. After radiation and chemotherapy, the radiological lesion may have different degrees of tumour and necrosis and the spectrum is dependent on the predominant tissue. This feature can also make histopathological diagnosis difficult.<sup>21</sup> MR perfusion imaging in addition to MR imaging and MRS have been found to be useful in distinguishing radiation necrosis and tumour recurrence in a few studies.<sup>23,24</sup>

### Impact of $^1\text{H}$ MRS on clinical decisions

The key issue for neurosurgeons and radiologists is 'does  $^1\text{H}$  MRS alter clinical decisions? Although it is difficult to completely base decisions on  $^1\text{H}$  MRS results alone, in our case series  $^1\text{H}$  MRS had positive impact on clinical decisions in 52% of cases. In a small series of 15 patients, Lin et al.<sup>17</sup> found  $^1\text{H}$  MRS positively impacted clinical decisions in 12/15 cases (80%) while altering surgical planning in 7/15 (47%). But this series included known tumours (10) or presumed tumours (5). Harada et al.,<sup>19</sup> in 100 consecutive cases, found 26 cases where preoperative diagnosis was uncertain and in 6 (6%) of these cases MRS could have made significant contribution if added preoperatively. In our series  $^1\text{H}$  MRS was not used routinely in all neurosurgical cases but was instead utilized to resolve clinical dilemmas.

### Limitations of this study

Although data from these 23 cases were logged prospectively as an audit, this study is retrospective and largely descriptive owing to the paucity of numbers in each category. As the study was retrospective, the technique of MRS was not precisely the same for all patients in whom it was used. Our centre has more experience with SVS and hence it was the preferred technique as SVS is regarded as providing a detailed and reliable qualitative and quantitative spectrum.<sup>17</sup> Furthermore, spectroscopic analysis itself can have its limitations. A poor spectrum is obtained in instances where a lesion lies close to bone or CSF pathways. As SVS provides an average

over the region of interest, it can lead to misinterpretation in lesions that are multicystic, large, and/or radiologically inhomogeneous.<sup>16,21</sup> Hence, on some occasions we also utilized MVS in addition to SVS.

### Future directions

Currently, the interpretation of  $^1\text{H}$  MRS spectrum is done manually by experienced neuroradiologists and physicists. Utilizing automated pattern-recognition techniques and maintaining local and international databases of MRS spectra of various lesions, as performed by the European Union project entitled International Network for Pattern Recognition of Tumours using Magnetic Resonance (INTERPRET; <http://azizu.uab.es/INTERPRET/index.html>), may help to consolidate the knowledge and lead to optimization of the diagnostic approach to patients utilizing MRS.<sup>22</sup>

### Conclusion

$^1\text{H}$  MRS can add critical information in certain clinical dilemmas faced by neurosurgeons, and we found its use improved the diagnostic accuracy from 60.9% (conventional MR imaging) to 83%. In this series,  $^1\text{H}$  MRS was able to reliably distinguish between high-grade tumour and cerebral abscess, and between high-grade and low-grade glioma. However, it was not found to reliably diagnose radiation necrosis. Further larger prospective studies are needed to clearly define the role of  $^1\text{H}$  MRS in neurosurgery.

### Acknowledgements

The authors wish to thank Ms Dianne Lane, senior radiographer at The Canberra Hospital, for her technical expertise during this study. We also wish to thank Dr Bruce Shadbolt for the assistance with statistics.

**Declaration of interest:** The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

### References

- Bernstein M, Parrent AG. Complications of CT guided stereotactic biopsy of intra-axial brain lesions. *J Neurosurg* 1994;81:165–8.
- Air EL, Leach JL, Warnick RE, McPherson CM. Comparing the risks of frameless stereotactic biopsy in eloquent and noneloquent regions of the brain: a retrospective review of 284 cases. *J Neurosurg* 2009;111:820–4.
- Field M, Witham TF, Flickinger JC, Kondziolka D, Lunsford LD. Comprehensive assessment of hemorrhage risks and outcomes after stereotactic brain biopsy. *J Neurosurg* 2001;94:545–51.
- Moller-Hartmann W, Herminghaus S, Krings T, et al. Clinical applications of proton magnetic resonance spectroscopy in diagnosis of intracranial mass lesions. *Neuroradiology* 2002;44:371–81.
- Dowling C, Bollen AW, Noworolski SM, et al. Preoperative proton MR spectroscopic imaging of brain tumors: correlation with histopathologic analysis of resection specimens. *AJNR* 2001;22:604–12.
- McKnight TR, von dem Bussche MH, Vigneron DB, et al. Histopathological validation of a three-dimensional magnetic resonance spectroscopy index as a predictor of tumor presence. *J Neurosurg* 2002;97:794–802.

7. Murphy M, Loosemore A, Clifton AG, *et al.* The contribution of <sup>1</sup>H MRS to clinical brain tumour diagnosis. *Br J Neurosurg* 2002;16:329-34.
8. Sibtain NA, Howe FA, Saunders DE The clinical value of proton magnetic resonance spectroscopy in adult brain tumours. *Clin Radiology* 2007;62:109-19.
9. Garg M, Gupta RK, Husain M, *et al.* Brain abscesses: etiologic categorization with in vivo proton MR spectroscopy. *Radiology* 2004;230:519-27.
10. Rémy C, Grand S, Lai ES, *et al.* <sup>1</sup>H MRS of human brain abscesses in vivo and in vitro. *Magn Reson Med* 1995;34:508-14.
11. Aydin K, Tatli B, Ozkan M, *et al.* Quantification of neurometabolites in subacute sclerosing panencephalitis by <sup>1</sup>H -MRS. *Neurology* 2006;67:911-3.
12. Grand S, Passaro G, Ziegler A, *et al.* Necrotic tumor versus brain abscess: Importance of amino acids detected at <sup>1</sup>H MR Spectroscopy - initial results. *Radiology* 1999;213:785-93.
13. Lai PH, Ho JT, Chen WL, *et al.* Brain abscess and necrotic brain tumor: discrimination with proton MR spectroscopy and diffusion-weighted imaging. *AJNR* 2002;23:1369-77.
14. Law M, Yang S, Wang H, *et al.* Glioma grading: sensitivity, specificity, and predictive values of perfusion MR imaging and proton MR spectroscopic imaging compared with conventional MR imaging. *AJNR* 2003;24:1989-98.
15. Demaerel P. In vivo localized single-voxel proton magnetic resonance spectroscopy of intracranial tumors. *Int J Neuroradiol* 1997;3:94-110.
16. Preul MC, Caramanos Z, Collins DL, *et al.* Accurate, noninvasive diagnosis of human brain tumors by using proton magnetic resonance spectroscopy. *Nat Med* 1996;2:323-5.
17. Lin A, Blumi S, Mamalak AN. Efficacy of proton magnetic resonance spectroscopy in clinical decision making for patients with suspected malignant brain tumours. *J Neurooncol* 1999;45:69-81.
18. Chang KH, Song IC, Kim SH, *et al.* In vivo single-voxel proton MR Spectroscopy in intracranial cystic masses. *AJNR* 1998;19:401-5.
19. Harada M, Tanouchi M, Miyoshi H, Nishitani H, Kannuki S. Brain abscess observed by localized proton magnetic resonance spectroscopy. *Magn Reson Imaging* 1994;12:1269-74.
20. Floeth FW, Pauleit D, Wittsack HJ, *et al.* Multimodal metabolic imaging of cerebral gliomas: positron emission tomography with [<sup>18</sup>F]fluoroethyl-L-tyrosine and magnetic resonance spectroscopy. *J Neurosurg* 2005;102:318-27.
21. Rock JP, Hearshen D, Scarpace L, *et al.* Correlations between magnetic resonance spectroscopy and image-guided histopathology, with special attention to radiation necrosis. *Neurosurgery* 2002;51:912-20.
22. Tate AR, Underwood J, Acosta DM, *et al.* Development of a decision support system for diagnosis and grading of brain tumours using in-vivo magnetic resonance single voxel spectra. *NMR Biomed* 2006;19:411-34.
23. Prat R, Galeano I, Lucas A, *et al.* Relative value of magnetic resonance spectroscopy, magnetic resonance perfusion, and 2-(<sup>18</sup>F) fluoro-2-deoxy-D-glucose positron emission tomography for detection of recurrence or grade increase in gliomas. *J Clin Neurosci* 2010;17:50-3.
24. Kim YH, Oh SW, Lim YJ, *et al.* Differentiating radiation necrosis from tumor recurrence in high-grade gliomas: assessing the efficacy of <sup>18</sup>F-FDG PET, <sup>11</sup>C-methionine PET and perfusion MRI. *Clin Neurol Neurosurg* 2010;112:758-65.