Contributions of magnetic resonance spectroscopy in brain lesions

Alberto Surur*, José Facundo Cabral*, Alberto Marangoni*, Silvio Marchegiani**, Claudia Palacios**, Enrique Herrera***, Julio Suárez***

Resumen
Introducción: La Espectroscopía por Resonancia Magnética (ERM) es una técnica no invasiva que permite un análisis del metabolismo de las lesiones o del tejido normal, aumentando la especificidad del método. De esta manera, a la información morfológica aportada por las imágenes de resonancia magnética (RM) se le suma la información bioquímica que brinda la ERM. Si bien el “gold standard” para establecer el diagnóstico definitivo de una lesión cerebral sigue siendo la biopsia, la ERM es un método no invasivo y libre de complicaciones que posibilita determinar el tipo de lesión y evitar biopsias innecesarias en procesos no tumorales. El objetivo del presente trabajo es comprobar si la ERM monovóxel protón de hidrógeno (H+) de tiempo de eco (TE) largo es capaz de discriminar la naturaleza tumoral o no de las lesiones cerebrales y clasificarlas en grados de malignidad.

Material y método: Se trata de un estudio prospectivo en el que se incluyó a pacientes de ambos sexos y de distintas edades a los que se les realizó un estudio estándar de RM completado con ERM monovoxel.

Resultados: Se analizaron 47 lesiones y se caracterizaron adecuadamente 43 (92,9%), con una sensibilidad (S) del 96,8% (IC 89-100), una especificidad (E) del 89,6% (IC 76-100), un valor predictivo positivo (VPP) del 91,1% (IC 80-100) y un valor predictivo negativo (VPN) del 96,3% (IC 87-100). Muchas son las variables que influyen en la adquisición de un espectro factible de ser analizado, pudiendo surgir de éstas diferencias inter-observador. Sin embargo, se obtuvieron resultados similares a los de otras publicaciones.

Conclusión: La ERM sumada a la RM demostró ser un método confiable para determinar la naturaleza tumoral o no de una lesión cerebral, con valores estadísticos aceptables.


Abstract
Contributions of magnetic resonance spectroscopy in brain lesions

Introduction: The Magnetic Resonance Spectroscopy (MRS) is a non-invasive technique which allows study of the metabolism of lesions or of normal tissue, increasing the method’s specificity. In this way, the biochemical information provided by MRS is added to the morphologic information provided by the Magnetic Resonance Imaging (MRI). Even though the gold standards to determine the definite diagnosis of a brain lesion is still the biopsy, the MRS is a non-invasive method, free of complications which would help determine the type of lesion and avoid unnecessary biopsies in non-tumor processes. The objective of this work is to determine if the monovoxel MRS hydrogen proton (H+) long Eco Time (TE) is capable to differentiating or not the nature of the tumor from the brain lesions and classify them into levels of malignity.

Material and Method: This is a retrospective study in which female and male patients of any ages were selected. A standard study of MRI was performed in them and it was completed with monovoxel ERM.

Results: 47 lesions were analyzed and 43 (92.9%) were adequately characterized, with a sensibility (S) of 96.8% (IC 89-100), specificity (E) of 89.6% (IC 76-100), a positive predictive value (PPV) of 91.1% (IC 80-100) and a negative predictive value (NPV) of 96.3% (IC 87-100). Many variables that can influence the acquisition of a spectrum capable of being analyzed and from them, inter-observer differences can emerge. However, our results were similar to those in other publications.

Conclusion: The MRS together with the MRI proved to be a reliable method to determine whether a brain lesion is a tumor or not, with acceptable statistic values.

Key Words: Magnetic Resonance Imaging. Spectroscopy. Monovoxel. Brain Tumors

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In recent years, the advancement of Magnetic Resonance Imaging (MRI) made it possible to make efficient diagnoses in a large number of diseases, including brain tumors (BT) with an accuracy that goes from 30 to 90% depending on the type of tumor.
Pseudotumoral Multiple Sclerosis (MS). For some years now, Magnetic Resonance Spectroscopy (MRS) has been incorporated as an auxiliary method for diagnosis to complement the MRI and increase the specificity of this method.

MRS is a technique that basically produces a non-invasive analysis of the metabolism of the tissue, determining the relative concentrations of their metabolites and the interactions produced between them. Thus, the morphological information provided by MRI is combined with the biochemical information provided by the MRS.

While the “gold standard” to determine the definitive diagnosis of a brain lesion is still the biopsy, the MRS would help in certain cases to avoid unnecessary biopsies (in non-neoplastic processes or non-accessible tumors), and in other cases, it would help to lead the biopsy to the area of greatest anaplasia.

The aim of this study is to determine whether Proton Monovoxel MRS Hydrogen (H+) with long TE is able to discriminate between a brain lesion of a tumoral nature and other. To carry out this study, we calculated the sensitivity (S), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) of the lesions studied by MRS with their pathologic correlation. As secondary objectives we pose the possibility of describing the existence of characteristic spectral patterns for each group of lesions and to classify them on that basis.

MATERIAL AND METHODS

To determine the usefulness of MRS in the diagnosis of brain lesions, we performed a prospective study in which patients from both sexes and all ages with brain lesions were collected. Other patients included were those with previous surgery of known tumor pathology to investigate recurrence or response to treatment and also a normal control group. The period of time for the study was extended from March 2007 to September 2008.

To be able to make comparisons, patients underwent also a standard study of MRI. The sequences performed were T1-weighted Sequences, Spin Echo (SE) in sagittal and axial planes (TR/TE/Nex - 540/15/2), T2-Weighted sequences, TSE in axial and coronal planes (4470/110/2), and Fluid Attenuation Inversion Recovery (FLAIR) in axial plane (11000/2800/140).

It was completed with Monovoxel MRS (H+) with PRESS sequence (Point Resolved Spectroscopic Sequence) using a 20 x 20 x 20 cm3 voxel in a Philips Intera® 1.5T MRI machine. The Spectra were obtained with long echo times of 2000/288 (TR/TE). To position the voxel the images obtained in all three planes of space were taken on T2-weighted Sequences and FLAIR, trying to avoid areas of necrosis or cysts in tumor-like lesions.

Metabolites peaks; N-Acetylaspartate (NAA) at 2.0 ppm, Choline (Cho) at 3.2 ppm, Creatine (Cre) at 3.0 ppm, Lipids (Lip) between 0.9 and 1.3 ppm, Lactate (Lac) at 1.3 ppm, were analyzed as well as the relations between them.

For the spectra analysis the highest peak of each studied metabolite was considered and the relations among them were calculated, taking the Cre as reference.

The findings in both MRI and Monovoxel MRS were analyzed by two experienced radiologists who were unaware of the pathologic results. These data were matched with the pathologic findings of lesions obtained by stereotactic biopsy or surgery. No biopsy was performed on lesions that clinically and by imaging were suspected to be benign, which were controlled progressively, and no biopsies were performed among patients in the control group.

Statistical analysis of the different spectra was done using Epidat 3.1® program to determine the degree of diagnostic accuracy obtained and the capacity of the method to discriminate between lesions of tumoral and non tumoral nature through S, E, PPV, NPV variables.

Depending on the results of the pathology (P), the cases were classified into five groups: Non-Tumoral Lesions (NTL), Low-Grade Tumors (LGT) which grouped the lesions histologically classified as grade I or II, Anaplastic Tumors (AT), grade III of the pathologic classification of brain tumors, and finally, Glioblastoma Multiforme or Metastasis (GBM-MTS). The fifth group belonged to the normal control group.

Because of the variety of heterogeneous lesions that the NTL group comprises and, therefore, difficult to compare, the NTL group was divided as follows: lesions with gliosis, cystic or necrotic lesions and demyelinating or inflammatory lesions.

Regarding the groups, the average of the values for each metabolite with their standard deviations based on their relation (reason) with the Cre was calculated and the results were gathered into tables from which we obtained the respective graphs for each group.

RESULTS

A total of 67 patients (36 women and 31 men) were gathered, but only the resulting spectra of 57 patients were analyzed (47 of which presented lesions and 10 belonged to the normal control group), 33 women (57.9%) and 24 men (42.1%), aged between 12 and 81 years (35 years average). Ten patients (3 women and 7 men) were excluded, one of them had a brain tumor and we lacked the pathology results for comparison; and as for the remaining 9, a spectrum with too much artifact and poor quality was obtained, not allowing for a proper analysis.

43 of 47 brain lesions (92.9%) were properly characterized, with 3 false-positive findings and 1 false-
ative, yielding the following statistical values: S of 96.8% (CI 89-100), E of 89.6 (IC 76-100), PPV of 91.1% (CI 80-100) and a NPV of 96.3% (CI 87-100) (Graphic 1).

NTL group was composed of a total of 18 patients: 8 in the subgroup of lesions with gliosis, 4 in the cystic-necrotic lesions and 6 in the inflammatory demyelinating lesions (most did not undergo biopsy but just progressive control because its appearance and evolution were benign and showed no change except a necrotic lesion and a progressive multifocal leukoencephalopathy (PML), which were false-positive findings). In the LGT group, 15 patients were included (Ganglioglioma (n=1); TNED (n=1), Hamartoma (false positive) (n=1), grade I Astrocytoma (WHO) (n=2); Grade II Astrocytoma (n=5), Oligodendroglioma (n=4) and Oligoastrocytoma (n=1)). The AT group was composed of 6 patients (Anaplastic Astrocytomas (n=3) and Anaplastic Oligodendroglioma (n=3)). GBM-MTS group was consisted of 8 patients (GBM (n=5) and MTS (n=3), melanoma (false negative), lung and breast). Lastly the normal control group was composed of 10 patients (Tables and Graphics 2 to 9).

In the gliosis cases a mild increase in Cho was identified together with a decrease of NAA, and a slight increase in Lac was observed in one case.

In necrosis or cystic lesions, a marked decrease of all peaks was measured with a significant increase of Lip and Lac (Fig. 1).

In the group of demyelinating or inflammatory lesions, in most cases, a slight increase in the Cho peak was observed while the NAA peak remained slightly decreased and, in about half of the cases, a slight increase Lip and Lac was shown (Fig. 2).

In the group of LGT, it was found that most lesions had an increase of Cho and a decrease of NAA in relation to neoproliferation and cell injury respectively; significant Lip and Lac peaks were not identified (Fig. 3).

In contrast, in the AT a significant increase of Cho was noticed as well as a significant decrease of NAA; elevated peaks in the spectrum for Lip and Lac were also observed (Fig. 4). Finally, in the GBM-MTS group a significant increase in Cho was not always found, probably due to a larger component of necrosis, though it did show a marked decrease of NAA and a significant increase of the peaks in the area of Lip and Lac (Fig. 5 a-b).

DISCUSSION

Obtaining a spectrum, that will analyzed, is influenced by many factors, namely the physical and chemical characteristics of each metabolite and the compounds in which they are located; the selection of the area to study (cystic, solid, homogeneous, heterogeneous) together with the homogenization of the area (homogenization of the field and the sample, suppression of water signal), choice of the type of technique to be employed (monovoxel or multivoxel) and of the sequence to be used (PRESS, DRESS, SPARS, STEAM) and the choice of the echo time (short or long). Obtaining a spectrum adequate for analysis depends on the correct choice or application of all the above mentioned parameters, plus an appropriate cooperation on the part of the patient; this could give rise to differences observed by different researchers.

In material and methods the various parameters used in obtaining the spectrum were mentioned; however, it is worth pointing out that the spectra obtained at long TE were mainly analyzed due to:

- the spectrum obtained is simpler to analyze, quantify and interpret, making the technique more reproducible in daily practice;
- at long echo times the resulting peak at 1.3 ppm is mainly composed of lactates because lipids have a short echo time and therefore, they would become saturated. In addition, some authors suggest that the presence of lipids in long echo times have stronger predictive value for malignancy than those observed in short echo times 
- we know that because not performing spectroscopy in short echo times, some valuable information is missed, such as the values of Myo-Inositol (MI); however, it is important to mention that the use of both echoes doubles the scan time, producing patient motion artifacts, and that the main objective of this study is to determine whether or not a lesion is tumoral and correlate the findings of long echo time with the pathology.

The choice of monovoxel technique in this work, it was made taking into account various factors. Although the multivoxel technique allows assessment of the metabolic characteristics of multiple voxel at a time, it also presents some disadvantages such as: the larger the area of study the more the technical difficulties to obtain a quality registration, not only in the relation signal-noise but also in the homogeneity of the magnetic field and in the definition of the peaks; in second place, the acquisition time is significantly higher and the data processing is longer. Another lim-
Table 1: Normal group (values corresponding to the Cre relation to the different metabolites, average and standard deviation).

<table>
<thead>
<tr>
<th></th>
<th>NAA/Cre</th>
<th>Cho/Cre</th>
<th>Cho/NAA</th>
<th>Lip/Cre</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2,4</td>
<td>1,7</td>
<td>0,74</td>
<td>-</td>
</tr>
<tr>
<td>X</td>
<td>2,34</td>
<td>1,33</td>
<td>0,58</td>
<td>0,5</td>
</tr>
<tr>
<td>DS</td>
<td>0,39</td>
<td>0,34</td>
<td>0,11</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 2: Demyelinating/inflammatory non neoplastic lesions.

<table>
<thead>
<tr>
<th></th>
<th>NAA/Cre</th>
<th>Cho/Cre</th>
<th>Cho/NAA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1,6</td>
<td>0,7</td>
<td>0,47</td>
</tr>
<tr>
<td>X</td>
<td>1,56</td>
<td>1,33</td>
<td>1,19</td>
</tr>
<tr>
<td>DS</td>
<td>0,36</td>
<td>0,34</td>
<td>0,41</td>
</tr>
</tbody>
</table>

Fig. 1. Normal group: Normal relation between the Cho, Cre and NAA peaks.

The contribution of magnetic resonance spectroscopy in brain lesions...
Table 3: Non Neoplastic Necrotic / Cysts Lesions (values corresponding to the Cre relation to the different metabolites, average and standard deviation).

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Ratio</th>
<th>Average</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAA/Cre</td>
<td>0.83</td>
<td>1.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Cho/Cre</td>
<td>1.3</td>
<td>2.9</td>
<td>1.4</td>
</tr>
<tr>
<td>Cho/NAA</td>
<td>1.6</td>
<td>1.7</td>
<td>1.4</td>
</tr>
<tr>
<td>Lip/Cre</td>
<td>0.87</td>
<td>7</td>
<td>3.3</td>
</tr>
<tr>
<td>X</td>
<td>1.50</td>
<td>2.2</td>
<td>1.4</td>
</tr>
<tr>
<td>DS</td>
<td>0.96</td>
<td>1.29</td>
<td>0.12</td>
</tr>
<tr>
<td>X</td>
<td>5.29</td>
<td>1.4</td>
<td>1.57</td>
</tr>
<tr>
<td>DS</td>
<td>4.02</td>
<td>1.28</td>
<td></td>
</tr>
</tbody>
</table>

results. In this section there are several points to consider:

a) Brain tumors can be very heterogeneous and, within the same tumor, various types of tissue may be found: viable tumor cells, necrosis areas, cystic areas, normal tissue, infiltrated tissue. Each compartment provides different information that will end up conditioning the diagnosis depending on the location of the voxel;

b) Cells with different tumor grades can coexist in the same tumor, therefore, a voxel of a certain size will yield the average spectrum of that volume, while the pathology diagnosis will consider the highest tumor grade detected in the sample;

c) The histopathological diagnosis of a small tumor sample obtained by stereotactic biopsy may not be representative of the entire lesion; in this case, it is not about a limitation of the MRS, but of the technique used for biopsy and of the P, which will negatively condition the diagnosis made by MRS and which will be different from the P and therefore considered as incorrect.

d) Finally there is another limitation of the P is the discrepancy that may exist in the diagnosis made by different pathologists for the same sample, which will condition the results obtained by the MRS.

These limitations partly justify the discrepancies observed between different studies, when trying to classify or perform a grading of tumoral lesions. Despite this, the MRS has proved to be useful in distinguishing between normal brain tissue or non tumoral lesions and brain tumors. The main features described in brain tumors are: marked decrease of NAA, slight decrease of Cre, marked increase of Cho, and presence of Lac and Lip in different proportions in some cases (6-11).

Many published papers have described a direct correlation between the increase of the Cho and tumoral grade in glial tumors. Even when this can not be verified in all studies, the increased levels of Cho in Anaplastic Astrocytomas (AA) is a constant fact in relation to the low grade tumors; however, some authors have found lower levels of Cho in GBM than in AA (as in our series). This may be due to the fact that the AA have less amount of necrosis in its composition with greater areas of proliferative tissue (viable) in contrast to the GBM, in which the necrotic areas predominate or where the average volume of the necrotic areas are greater than viable tissue. Therefore,
the positioning of the voxel in these cases is crucial in order to obtain the real metabolism of the lesion. This point would also explain the differences observed between the different studies, depending on the voxel size, positioning strategy and employed sequences, as well as studies made “in vitro”, where only viable tissue is considered (12).

Another metabolite used by many authors for the grading of tumors is the Lac, its presence being an indicator of high-grade tumor, since it is assumed that increased tumoral metabolic activity will displace cell metabolism towards anaerobic tract leading to accumulation of this metabolite. The Lip has been associated with necrosis areas, so it would be present in high-grade tumors (GBM, MTS), in non-tumor necrosis and infectious diseases (13).

The findings described by different authors in other frequent brain lesions such as the MTS include reduction of NAA and Cre, with an increase of Cho, these findings are similar to what has been observed

Table 4: Non Neoplasic Lesions with gliosis (values corresponding to the Cre relation to the different metabolites, average and standard deviation).

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>0.96</th>
<th>1.7</th>
<th>0.7</th>
<th>0.7</th>
<th>0.6</th>
<th>0.9</th>
<th>0.9</th>
<th>0.6</th>
<th>2.2</th>
<th>0.3</th>
<th>0.9</th>
<th>2</th>
<th>2.2</th>
<th>X=1.12</th>
<th>DS=0.65</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAA/Cre</td>
<td>2</td>
<td>2.1</td>
<td>1.3</td>
<td>2.9</td>
<td>2.7</td>
<td>1.6</td>
<td>2.6</td>
<td>2.2</td>
<td>1.6</td>
<td>0.36</td>
<td>1.5</td>
<td>X=1.89</td>
<td>DS=0.73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cho/Cre</td>
<td>1</td>
<td>2</td>
<td>1.4</td>
<td>1.5</td>
<td>2.8</td>
<td>1</td>
<td>1.4</td>
<td>0.75</td>
<td>2</td>
<td>1.3</td>
<td>0.84</td>
<td>X=1.45</td>
<td>DS=0.61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cho/NAA</td>
<td>0.4</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>1.1</td>
<td>0.65</td>
<td>0.48</td>
<td>0.24</td>
<td>1.2</td>
<td>3.3</td>
<td>0.37</td>
<td>X=0.93</td>
<td>DS=0.85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lip/Cre</td>
<td>0.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.65</td>
<td>0.4</td>
<td>0.4</td>
<td>-</td>
<td>X=0.48</td>
<td>DS=0.11</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5: Low Grade Malignancy Lesions (I-II) (values corresponding to the Cre relation to the different metabolites, average and standard deviation).

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>2.2</th>
<th>0.9</th>
<th>4</th>
<th>2.5</th>
<th>7</th>
<th>2.1</th>
<th>2.9</th>
<th>3.2</th>
<th>1.6</th>
<th>13</th>
<th>2.8</th>
<th>1.8</th>
<th>0.64</th>
<th>X=2.63</th>
<th>DS=1.66</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAA/Cre</td>
<td>2</td>
<td>1.5</td>
<td>2.9</td>
<td>3.9</td>
<td>1.8</td>
<td>2.6</td>
<td>1.9</td>
<td>3.7</td>
<td>4</td>
<td>2.3</td>
<td>4.2</td>
<td>2.5</td>
<td>1.6</td>
<td>X=2.63</td>
<td>DS=0.99</td>
</tr>
<tr>
<td>Cho/Cre</td>
<td>2.2</td>
<td>0.9</td>
<td>4</td>
<td>2.5</td>
<td>7</td>
<td>2.1</td>
<td>2.9</td>
<td>3.2</td>
<td>1.6</td>
<td>13</td>
<td>2.8</td>
<td>1.8</td>
<td>0.64</td>
<td>X=2.63</td>
<td>DS=1.66</td>
</tr>
<tr>
<td>Cho/NAA</td>
<td>2.1</td>
<td>0.33</td>
<td>0.53</td>
<td>0.36</td>
<td>0.41</td>
<td>0.65</td>
<td>0.16</td>
<td>0.15</td>
<td>0.53</td>
<td>0.9</td>
<td>0.16</td>
<td>1.3</td>
<td>0.48</td>
<td>X=0.61</td>
<td>DS=0.54</td>
</tr>
<tr>
<td>Lip/Cre</td>
<td>2.1</td>
<td>0.33</td>
<td>0.53</td>
<td>0.36</td>
<td>0.41</td>
<td>0.65</td>
<td>0.16</td>
<td>0.15</td>
<td>0.53</td>
<td>0.9</td>
<td>0.16</td>
<td>1.3</td>
<td>0.48</td>
<td>X=0.61</td>
<td>DS=0.54</td>
</tr>
</tbody>
</table>

Fig. 2. Inflammatory lesion temporal of the Cho, Cre and NAA peaks. Right: increased Cho peak and a slight decrease in the NAA peak.
in Astrocytomas. As with high-grade glial tumors, MTS may also contain Lip and Lac. Numerous study methods have been developed and different signs were proposed to differentiate these lesions from primary tumors, without detecting any significant differences to date (14).

In our series we had three false positives cases; one was a PML in a patient with no history of HIV at the time of the test, which was confirmed later. Spectrum obtained was of good quality, showing a not very marked increase of the peak of Cho, with a decrease the peaks of NAA and Cre and presence of two small peaks in the area of Lip and Lac. The analysis of the images posed a differential diagnosis between a neoproliferative lesion and a demyelinating lesion with pseudo tumoral aspect, given the mild mass effect that it presented.

Reviewing the literature it was found that in this entity moderate astrogliosis with atypical appearance of astrocytes exist, simile neoplastic with large nuclei. If the biopsy sample includes the edges, this does not represent a problem for diagnosis; however before a biopsy with cellular atypia, as in the case of LEMP, the pathologist can interpret it as oligodendrogial or astrocytic glioma, revealing the difficulties that its characterization presents also in pathology (15).

Another case was a patient with a history of low-grade tumor who had a brachytherapy seed implanted and we wished to evaluate the response to treat-
Contributions of magnetic resonance spectroscopy in brain lesions

**Table 6:** Anaplastic Lesions (III) (values corresponding to the ratio of the Cre with different metabolites, average and standard deviation).

<table>
<thead>
<tr>
<th>Metabolets</th>
<th>Ratio 1</th>
<th>Ratio 2</th>
<th>Ratio 3</th>
<th>Ratio 4</th>
<th>Ratio 5</th>
<th>Average (X)</th>
<th>Standard Deviation (DS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAA/Cre</td>
<td>0.57</td>
<td>0.4</td>
<td>1.7</td>
<td>1.3</td>
<td>2.3</td>
<td>0.7</td>
<td>X=1.16 DS=0.74</td>
</tr>
<tr>
<td>Cho/Cre</td>
<td>2</td>
<td>2.5</td>
<td>1.2</td>
<td>12.3</td>
<td>1.7</td>
<td>3.1</td>
<td>X=3.8 DS=4</td>
</tr>
<tr>
<td>Cho/NAA</td>
<td>3.3</td>
<td>6.8</td>
<td>0.63</td>
<td>9</td>
<td>0.75</td>
<td>4</td>
<td>X=4.08 DS=3.32</td>
</tr>
<tr>
<td>Lip/Cre</td>
<td>0.26</td>
<td>0.4</td>
<td>0.47</td>
<td>1</td>
<td>0.52</td>
<td>0.21</td>
<td>X=0.47 DS=0.28</td>
</tr>
</tbody>
</table>

**Table 7:** High-Grade Malignancy Lesions (GBM-MTS)

<table>
<thead>
<tr>
<th>Metabolets</th>
<th>Ratio 1</th>
<th>Ratio 2</th>
<th>Ratio 3</th>
<th>Ratio 4</th>
<th>Ratio 5</th>
<th>Average (X)</th>
<th>Standard Deviation (DS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAA/Cre</td>
<td>0.4</td>
<td>1.3</td>
<td>1.9</td>
<td>2.1</td>
<td>1.7</td>
<td>0.78</td>
<td>X=1.36 DS=0.66</td>
</tr>
<tr>
<td>Cho/Cre</td>
<td>2.5</td>
<td>1.7</td>
<td>3</td>
<td>1.5</td>
<td>2.9</td>
<td>1.6</td>
<td>X=2.2 DS=0.68</td>
</tr>
<tr>
<td>Cho/NAA</td>
<td>4.6</td>
<td>1.3</td>
<td>1.5</td>
<td>0.7</td>
<td>1.7</td>
<td>2</td>
<td>X=1.96 DS=1.36</td>
</tr>
<tr>
<td>Lip/Cre</td>
<td>5.2</td>
<td>1.4</td>
<td>2.1</td>
<td>-</td>
<td>5</td>
<td>0.15</td>
<td>X=2.77 DS=2.23</td>
</tr>
</tbody>
</table>

**Fig 4.** Anaplastic Tumor: similar finding as in Figure 3, but with the appearance of Lac peaks.

On the tests made, a specter of a very heterogeneous tissue was obtained, difficult to assess and somewhat artifact, which may have influenced the final interpretation, however it presented low peaks of Cre, NAA, with relative increase of Cho over the other peaks, and a significant increase of the peaks of Lip and Lac, which could suggest a tumoral nature, masked in an inflammatory/necrotic context. A stereotactic biopsy showed necrosis and reactive inflammatory tissue, and a test run five months later, showed almost complete disappearance of the lesion which confirmed its reactive inflammatory nature.

The last was a lesion that was interpreted as tumor and it actually was a Hamartoma, where an increase in the peak of Cho, with a slight decrease of the peaks of NAA and Cre and some small peaks of Lip and Lac, was visualized. Hamartomas correspond to undifferentiated dysplastic tissue areas, that both in MRI and in the MRS may have a behavior similar to the LGT.

The case of a false-negative reported in our work...
was a Meningeal Melanoma MTS, where the small size and location of the lesion in proximity to the bone (dural) complicated the MRS performance. The positioning of the voxel was contaminated with signals coming from the bone and normal brain tissue, yielding an artifact spectrum in one opportunity and later, something similar to a benign lesion, even though the patient history and radiological features drove us to think about MTS. These difficulties were encountered in several studies with very small lesions. Different authors propose, as a solution, to decrease the voxel size and adjust its position to avoid contamination of the tissue which does not correspond to the lesion, but sometimes in the daily practice this is not so easy to obtain. In our work, due to protocol, the voxel size was maintained in all cases, which may be the cause of the false negative.

Concerning the spectra removed from the work, most were from motion artifacts caused either by the patient or by presence of postoperative ferromagnetic material near the exploration area which made the area to explore very inhomogeneous, or because of a poor calibration of the equipment during the acquisition, perhaps due to non homogeneity of the area to explore. This usually occurred in brain regions close to the base of the skull, all of them corresponding to limitations of the method.

To summarize, in our work as in the majority of the different revised bibliography, an adequate characterization of tumoral and non tumoral lesions was obtained with very acceptable statistical values that proves the method to be an excellent pre surgery alternative. Even though the goal of the work was not to try to make a classification of brain tumor lesions with MRI and MRS as many publications have done, we feel -as most of the authors- that the distribution of metabolites within each group have similar behavior with some exceptions; therefore, the graphs obtained correlate well with those observed in the worldwide literature. We only obtained lower values of Lac in the AT group with a not so marked increase compared with other authors, this may be due to the TR/TE employed.

CONCLUSION

Monovoxel MRS combined with MRI proved to be a reliable method to determine the tumoral or non tumoral nature of a brain lesion, with very acceptable statistical values.

While there are some exceptions, the majority of brain lesions can be sorted into different groups according to the type of spectral behavior for a better categorization of the lesions, with the possibility of differentiating benign and malignant lesions and, among these last ones, in low and high grade.

Bibliography


Fig 5. a) Glioblastoma Multiform; b) Metastases. a) and b) show increased Cho, low NAA and frank elevation of the peaks corresponding to Lip and Lac.