Technological Innovation: High Field Open Magnetic Resonance Spectroscopy

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ABBREVIATION KEY:

HMRS: Proton Magnetic Resonance Spectroscopy
MRI: Magnetic Resonance Imaging
HFO: High Field Open MRI
NAA: N-Acetylaspartate
Cr: Creatine and Phosphocreatine
Chol: Choline, phosphocholine, glycophosphocholine, and other trimethylamines

ABSTRACT:

HMRS is a useful non-invasive technique that has been used for years to aid in the early diagnosis of brain lesions, and for treatment planning. However, there is a lack of evidence in the literature of the expansion of MRS to a HFO system. Since some patients cannot undergo closed bore MRI due to claustrophobia, and body habitus development of MRS to a HFO system is a necessary step to allow access to all patients. We obtained HMRS data, using a HFO MRI, from eleven patients, eight normal and three with pathologies and compared to previously published expected values. This is a remarkable technological step since there is no data in the literature about available HMRS use with HFO.

INTRODUCTION:

Even though MRS has been used in clinical settings for over 10 years, there remains a lack of evidence in the literature exploring the use of HMRS in a HFO MRI system. An open MRI is a necessity for some patients since they cannot undergo a closed bore scan due to claustrophobia, body habitus or other individual contraindications. HMRS is a useful non-invasive technique that aids in the diagnosis of brain lesions prior to biopsy, and more recently has been used for biopsy targeting in heterogeneous tumors, evaluation of change of tumors over time, and for treatment planning. In some cases biopsies can be avoided altogether if imaging and MRS can rule out certain diagnoses, this is significant considering a reported morbidity of biopsies being 3-4%.

The utility of HMRS has been displayed in the literature, Moller-Hartmann et al showed the addition of HMRS compared to MRI alone provides a 15.4% increase in correctly diagnosing a lesion, and a 6.2% reduction in misdiagnosing a lesion. Therefore, due to the importance of MRS expansion to a HFO system to increase patient access to care, we are displaying preliminary data from a small patient sample to show its effectiveness.

METHODS:

Fletcher Allen Health Care in collaboration with Phillips®, is piloting use of HFO MRI with HMRS technology. We are under the impression that we are one of few if not the only site where this technology is currently being tested.

We obtained HMRS data from eleven patients using a HFO HMRS. Eight of the patients were considered normal controls and free of pathology; three of the patients had pathology which was later confirmed by biopsy. We compared our HMRS data to previously published normative data for both controls and pathology cases. Since the small sample size of our study we were not able to provide a statistical analysis. However, since this is a significant technological advance improving access of an important technology to more patients, we submitted a paper for publication to The American Journal of Neuroradiology as a Technological Innovation. Since we were restricted to a small sample size based on time constraints, both in this paper and our submitted publication and a relative lack of data ever published showing the
utility of this technology, we found it prudent to highlight in depth only two patient cases for our publication, one normal healthy patient and one patient with a glioblastoma multiforme, however raw data for the remaining nine patients is provided for completeness.

RESULTS:

Patient one was a healthy 28 year old female free of any pathologic processes. HMRS measurements in her right centrum semi-oval were: NAA/Cr = 2.88, Chol/Cr = 1.32, NAA/Chol = 2.18, Chol/NAA = 0.46. HMRS measurements in her left centrum semi-ovale were: NAA/Cr = 2.34, Chol/Cr = 1.10, NAA/Chol = 2.13, Chol/NAA = 0.47. Bilaterally no lactate or lipids were detected. (Figure 1)

Patient two was a 38 year old male with a glioblastoma multiforme, as confirmed post-imaging by biopsy. Measurements in the area of his lesion were: NAA/Cr = 1.89, Chol/Cr = 3.30, NAA/Chol = 0.57, and Chol/NAA = 1.75, additionally HMRS was positive for lactate and lipids. (Figure 2)

Data for patients 3-11 was within the limits of expected results based on their pathological state, or lack of pathology. (Figure 3)

DISCUSSION:

Both of our patients displayed spectroscopic values consistent with their physiologic conditions. Patient one, a healthy 28 year old female, displayed expected HMRS results. Her NAA/Cr ratio was 2.88 and 2.34 on the right and left side respectively. This is around, but slightly above reported normal NAA/Cr ratios.\(^6,7,8\) Since NAA serves as a marker for neurons, a slightly elevated level of this metabolite most likely is a normal variation since she is a young and healthy female. All other reported ratios were within normal limits for a healthy patient. The absence of lactate and lipids was also expected since she is free of pathology.\(^6\)

Patient two presented with a depressed NAA/Cr ratio which was within the expected range for a patient with a glioblastoma multiforme\(^6,7,9\). NAA is generally regarded as a marker of healthy neurons.\(^2\) The relative decrease in NAA/Cr is seen since the patients neuronal mass is decreased in the area of his lesion and replaced by necroses and malignant cells.\(^7\) Patient two also presented with a elevated Choline/Cr ratio which was within the normal expected range for a patient with a glioblastoma multiforme.\(^6,7,9\) The observed elevation in his Choline/Cr ratio, as measured by HMRS, is also consistent with a glioblastoma multiforme. An elevation of Choline is expected since choline biomolecules are involved in lipid synthesis and breakdown, therefore an increase in choline concentration is an indication of increased cell density and proliferation, as seen in high grade tumors.\(^5,3,4\) Choline is also increased by upregulation of signaling pathways by some tumors.\(^1\) Lactate peaks were observed in patient two as well, this is expected of a patient with a GBM since lactate is a byproduct of anaerobic metabolism, and is elevated in high grade gliomas due to cellular demand overwhelming normal metabolism, and the presence of necrosis.\(^6\) Lactate peaks may be present however in any grade tumor if there are cystic or necrotic regions, however lactate peaks are not present in healthy patients.\(^4,6,10\) Finally, lipids are observed almost exclusively in necrotic regions and therefore indicator of high grade malignancy.\(^2\) Lipid peaks are not present in healthy patients.\(^6\)

Even though this is only a small sample size, HFO HMRS does show promise. Since some patients cannot undergo a closed bore MRI, due to claustrophobia or body habitus, they are not able to benefit from a more accurate diagnosis of brain lesions, superior biopsy targeting, and new developments in treatment planning using HMRS.\(^1\) Future research directions involving HFO HRMS may include a larger patient population, or direct comparisons of HMRS data from one patient population on both HFO HMRS and closed bore HMRS.
REFERENCES:

Figure 1: Healthy 28 year old female, free of pathology.
Figure 2: 38 year old male with Glioblastoma Multiforme as confirmed by biopsy.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Normal/Pathology</th>
<th>NAA/Cr</th>
<th>Choline/Cr</th>
<th>Lactate:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 3</td>
<td>Normal Right Basal Ganglia</td>
<td>2.15</td>
<td>1.65</td>
<td>Negative</td>
</tr>
<tr>
<td>Patient 4</td>
<td>Normal Right Centrum Semi Ovale</td>
<td>2.40</td>
<td>1.35</td>
<td>Negative</td>
</tr>
<tr>
<td>Patient 5</td>
<td>Normal, Left Basal Ganlia and Internal Capsule</td>
<td>1.97</td>
<td>1.18</td>
<td>Negative</td>
</tr>
<tr>
<td>Patient 6</td>
<td>Normal Left Primary Motor Strip</td>
<td>1.85</td>
<td>0.93</td>
<td>Negative</td>
</tr>
<tr>
<td>Patient 7</td>
<td>Normal Right Temporal Lobe</td>
<td>2.11</td>
<td>1.19</td>
<td>Negative</td>
</tr>
<tr>
<td>Patient 8</td>
<td>Normal Temporal Lobe</td>
<td>2.36</td>
<td>0.95</td>
<td>Negative</td>
</tr>
<tr>
<td>Patient 9</td>
<td>Normal Pons</td>
<td>2.17</td>
<td>1.49</td>
<td>Negative</td>
</tr>
<tr>
<td>Patient 10</td>
<td>Viral Encephalitis</td>
<td>0.77</td>
<td>1.73</td>
<td>Positive</td>
</tr>
<tr>
<td>Patient 11</td>
<td>Microgliosis/Astrocytosis with no malignant cells in Left Temporal Lobe</td>
<td>0.89</td>
<td>1.30</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Figure 3: Raw Data for patients 3-11.