Hydrogen MR spectroscopy of neck masses

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Abstract
Purpose: The purpose of this study is to evaluate the role of MR spectroscopy in differentiation between benign and malignant neck masses.

Materials and methods: Thirty-two patients having neck masses underwent routine MRI of the neck as well as Hydrogen 1 (1H) MR spectroscopy with echo time of 270 ms at 1.5 T. Peak amplitudes of choline (Cho) & creatine (Cr) for each lesion as well as normal appearing muscle of the neck were obtained. Results were compared by using a nonparametric t test.

Results: Thirty-two lesions were included (14 benign) & (18 malignant). Mean value (±standard deviation) was 4.42 ± 0.83 for malignant tumors and 1.93 ± 0.74 for benign tumors. Also spectra were obtained from normal appearing muscles with average Cho/Cr ratio 1.59 ± 0.49. Differences were significant between benign & malignant tumors as well as between malignant tumors & normal appearing muscles (p value < 0.001). No significant difference could be detected between benign tumors & normal appearing muscles (p value = 0.91).

Conclusion: MR spectroscopy should be used in the future as a complementary method to routine MRI to differentiate between benign and malignant lesions.

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1. Introduction

Patients with neck masses frequently present to the radiologist for further evaluation. The main role of the radiologist is to differentiate between benign & malignant conditions using different imaging modalities such as ultrasound with color Doppler, CT and MRI. Where appropriate, the radiologist will also stage lesions for management purposes and aid in guiding aspiration or biopsy. Sometimes, it is quite difficult to discriminate benign versus malignant lesion depending on conventional radiology. Functional MRI has emerged as a new method to help in solving such problems. It has the unique ability to depict tissues at a cellular level non-invasively (1).
1H MR spectroscopy has a large potential role in oncology, including detection of malignancy, grading tumor, predicting response to treatment, monitoring treatment response, and identifying persistent or recurrent disease. The first step in this process requires the identification of spectra associated with specific cancers (2). The results of hydrogen 1 (1H) MR spectroscopy have been reported in a few articles of in vivo cancer series in the head and neck region (1).

The purpose of this study was to evaluate the role of MR spectroscopy in differentiation between benign and malignant neck masses.

2. Subjects and methods

This is a prospective study. Thirty-two patients were included in this study after taking oral approval. They were 12 females, 20 males (mean age was 37.5 years, range 1–74 years).

Patients with clinical suspicion of having neck masses, or proved by other imaging modalities to have neck masses (CT or ultrasonography), yet still need further evaluation were referred to the MRI unit Mansoura university hospital from Ear, nose and throat surgery and also to radiotherapy departments, Mansoura University Hospital. Cases who are under chemo or radiotherapy were not included in this study, also cases did biopsy after MRI examination to avoid disturbance of the lesion metabolites by hemorrhage or trauma.

2.1. Methods

2.1.1. Imaging

Magnetic resonance imaging of the neck was performed on a 1.5 Tesla at MRI Unit, Mansoura University Hospital.

All patients were examined in the same position used for routine MRI examination of the neck using head coil.

Conventional MRI sequences as well as functional MRI techniques were used for all patients.

The standard imaging protocol consisted of the following sequences: localizing sagittal T1-weighted (TR/TE/NEX: 300/14ms/1), axial T1-weighted (TR/TE/NEX: 500/15ms/1), and fast spin-echo axial T2-weighted (TR/TE/NEX: 4490/85ms/1). Post contrast axial, coronal and sagittal T1 images were obtained after manual injection of 10 mL of gadopentetate dimeglumine.

For all the above sequences, the slice thickness was 5 mm with interslice gap of 1 mm, FOV was 220–240 mm, and the matrix was 128x256.

2.2. Proton MR spectroscopy

All patients underwent Chemical shift imaging (CSI).

Localization of the ROI depended primarily on the appearance of the lesions in the preceding pre and post contrast MR images.

Water suppression of the dominant water signal by CHESS technique, outer volume fat suppression as well as magnetic shimming were performed automatically for all patients at the beginning of both SVS & CSI examinations. Curve fitting was done automatically for all obtained spectra.

The time domain signal intensity was apodized and processed to remove the residual water signal. Post-processing of the spectroscopic data consisted of frequency shift and phase and linear baseline corrections after Fourier transformation.

In most cases, these processes were automatic. Frequency domain curve was fitted to Gaussian line shape by using the software provided by the manufacturer to define choline-containing components (Cho), and creatine and phosphocreatine (Cr) peaks.

Metabolic peak used in the differentiation of different tissue types was that of Cho at 3.22 ppm.

2.2.1. Pathological examination

Surgical excision was done for 20 cases, FNAC was done for the remaining 12 cases.

2.2.2. Statistical analysis

Statistical analysis was done using SPSS for windows version 17.

The level of significance was set at $P \leq 0.05$.

3. Results

Tables 1–3.

Cho/Cr ratios were obtained in 32 lesions, with a mean value ($\pm$ standard deviation) of 4.42 ± 0.83 for malignant tumor, 1.93 ± 0.74 for benign tumors. Also spectra were obtained from normal appearing muscles in 32 patients with average Cho/Cr ratio 1.59 ± 0.49. Differences were significant between benign & malignant tumors as well as between malignant tumors & normal appearing muscle. No significant difference could be detected between benign tumors & normal appearing muscles.

There was mild overlap between benign mixed salivary gland tumor and one case of adenoid cystic carcinoma of the parotid gland. Cutoff value in our study was 3 with sensitivity of 94% and specificity 86%.

High Lipid peaks were detected in both malignant and benign lesions, we did not include their values in the statistics of this study as we thought they represent contamination from adjacent tissue.

Also we were not able to separate Lipid from Lac peaks owing to software defect in our device.

3.1. Case 1

Female patient aged 47 y with history of cancer breast, presenting with left orbit metastatic deposit (Fig. 1a and b).

3.2. Case 2

Female patient aged 67 y with SCC of the base of the tongue (Fig. 2a and b).

3.3. Case 3

Male patient 37 y with malignant minor salivary gland tumor (Fig. 3a and b).

3.4. Case 4

Female patient aged 65 y with DM who had extensive right masticator space chronic non specific infection (Fig. 4a and b).
3.5. Case 5

Male patient aged 17 y with nasopharyngeal angiofibroma (Fig. 5a and b).

3.6. Case 6

Male patient aged 7 y with left bacterial non specific parotitis (Fig. 6a and b).

4. Discussion

Head and neck region comprises a variety of anatomic sites. For example, tumors such as neurogenic tumors and paragangliomas are all included in the head and neck region. The pre-operative information on whether a tumor is benign or malignant may be helpful to prevent treatment delay in the case of malignant tumor and in patient counseling as to likely treatment and possible sequels (3).

For this purpose, in many instances, the conventional imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI) and ultrasonography (US) are of limited accuracy (4). Consequently, there is a great need for a high technology noninvasive imaging method that allows the detection of head and neck malignancy more accurately.

$^{1}$H MR spectroscopy has the potential to become another tool in differentiating malignant from benign tumors. It has already an established technique for brain tumors and breast and prostate cancer (5–7). Because this technique measures the presence of specific metabolites, it is independent of anatomic information and may be used to characterize lesions that are indeterminate on standard anatomic studies (8).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Different types of malignant and benign lesions included in this study and their corresponding Cho/Cr ratio.</th>
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</thead>
<tbody>
<tr>
<td>Type of lesion</td>
<td>Number</td>
</tr>
<tr>
<td>A-malignant</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>5</td>
</tr>
<tr>
<td>Adenocarcinoma of the minor salivary glands</td>
<td>5</td>
</tr>
<tr>
<td>Nasopharyngeal carcinoma</td>
<td>4</td>
</tr>
<tr>
<td>Adenocarcinoma of the ethmoid sinus</td>
<td>1</td>
</tr>
<tr>
<td>Cystic adenoid carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Metastases from cancer breast</td>
<td>1</td>
</tr>
<tr>
<td>SCC of the tongue</td>
<td>1</td>
</tr>
<tr>
<td>Mean</td>
<td>4.42 ± 0.83</td>
</tr>
<tr>
<td>B-benign lesions</td>
<td></td>
</tr>
<tr>
<td>Benign mixed salivary gland tumor</td>
<td>4</td>
</tr>
<tr>
<td>Nasopharyngeal angiofibroma</td>
<td>3</td>
</tr>
<tr>
<td>Non specific inflammation</td>
<td>2</td>
</tr>
<tr>
<td>Thyroglossal duct cyst</td>
<td>2</td>
</tr>
<tr>
<td>Inflammatory LNs</td>
<td>2</td>
</tr>
<tr>
<td>Schwannoma</td>
<td>1</td>
</tr>
<tr>
<td>Mean</td>
<td>1.93 ± 0.74</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Table 2</th>
<th>mean Cho/Cr ratio for each group of lesions.</th>
</tr>
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<tbody>
<tr>
<td>Group</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Malignant</td>
<td>4.42 ± 0.83</td>
</tr>
<tr>
<td>Benign</td>
<td>1.93 ± 0.74</td>
</tr>
<tr>
<td>Normal appearing muscles</td>
<td>1.59 ± 0.49</td>
</tr>
</tbody>
</table>

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<tr>
<th>Table 3</th>
<th>$P$ values of Cho/Cr ratio between malignant, benign lesions and muscles.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparison group</td>
<td>$P$ value</td>
</tr>
<tr>
<td>Benign lesions versus normal appearing muscles</td>
<td>0.91</td>
</tr>
<tr>
<td>Malignant lesions versus normal appearing muscles</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Benign versus malignant</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Statistically significant difference ($P < .05$).

Fig. 1  (a) Coronal post contrast fat suppressed T1 W1 revealed; a large well defined heterogeneously enhanced mass is seen infiltrating the left greater wing of sphenoid bone with both intra-orbital & intra-cranial extensions. (b) MRS revealed: high Cho peak (7.75) detected at (3.2 ppm), white arrow points to Cho peak, thick arrow points to Cr peak.
In the current study we did not limit case selection to certain pathological entities in the neck region. We aimed to evaluate the ability to use proton MR spectroscopy as a differentiating tool as a general, based upon the idea that a high Cho/Cr ratio is tied to a high cellular membrane turnover in malignant lesions.

Typical spectral patterns associated with cancer include an increase in the total choline (Cho, 3.2 ppm) signal intensity (SI) relative to creatine (Cr, 3.0 ppm), often coupled with the presence of other metabolites, including lactate (Lac, 1.3 ppm)(1–5). Both diagnostic and oncologic applications may be offered by allowing for discrimination between regions of healthy tissue, necrosis, and new growth or recurrence (9).

Choline and its derivatives are thought to originate from phospholipid metabolism of cell membranes. The finding of higher Choline metabolite levels indicates an increase in cell proliferation and membrane biosynthesis in tumors. Similar results have been obtained from prostate, brain, colon, breast, thyroid, adrenal and neck masses (7,10–13) and it is possible that it can be used as a marker for active cellular proliferation. The high Cho/Cr ratio of cancer compared with that of normal muscle has also been observed in cases of squamous cell carcinoma of the extracranial head and neck (14). On the other hand it was suggested that there is a possible decrease in the creatine levels consistent with an increased rate of metabolism (i.e., an increased energy consumption) in tumors that are highly aggressive (14).

We found that Cho/Cr ratio was significantly higher in malignant tumors than in muscles and benign lesions as well. Malignant lesions showed a mean value (± standard deviation) of 4.42 ± 0.83, as compared with 1.93 ± 0.74 for benign tumors and 1.59 ± 0.49 for normal appearing muscles. Similar results were obtained in other studies by Mukherji et al. (1) (Cho/Cr ratio of 0–1.16 at TE 136) and Star-Lack et al. (15) (lymph node Cho/Cr = 2.9 ± 1.6, muscle Cho/Cr = 0.55 ± 0.210 at TE 144). The high Cho/Cr ratio of cancer compared with that of normal muscle has also been observed in cases of squamous cell carcinoma of the extracranial head and neck (1,14,16–18), with a reported Cho/Cr range of 1.8–7.2. High Cho values were also noticed in nodal metastases (18,19).

Fig. 2  (a) Axial fat suppressed T2 WI revealed a large irregular lobulated mass of high SI infiltrating the right posterolateral aspect of the tongue. (b) MRS revealed: high Cho peak (9.36) detected at (3.2 ppm), white arrow points to Cho peak, thick arrow points to Cr peak.

Fig. 3  (a) Axial post contrast fat suppressed T1 WI revealed; a large well defined heterogeneously enhanced mass in the left parapharyngeal space. (b) MRS revealed: high Cho peak (9.36) detected at (3.2 ppm), white arrow points to Cho peak, thick arrow points to Cr peak.
Tse et al. (18) beside reporting high Cho/Cr for head and neck squamous cell carcinoma and metastatic lymph nodes (2.23 and 2.34, respectively), have also reported significant correlation between these ratios and certain biomarkers such as epidermal growth factor receptor (EGFR) and cyclo-oxygenase 2 (COX-2).

On the contrary other studies reported higher Cho/Cr in benign tumors than in muscle and malignant lesions (8,20). As Maheshwari et al. (8) found that the average Cho/Cr ratio for benign lesions was 3.92 (TE = 136) and 6.11 (TE = 272) while it was 1.16 and 1.31 for muscles at TE 136 & 272 respectively, whereas for SCCA the average Cho/Cr ratio at TEs of 136 and 272 was 1.67 and 2.45, respectively. Also King et al. (20) reported higher Cho/Cr in benign salivary gland tumors as compared to malignant ones. They have attributed these results to the fact that an elevated Cho level, which is a marker of membrane turnover, is found not only in malignant tumors but also in benign tumors that are hypercellular and in inflammatory processes (20).

In our study there was mild overlap between benign mixed salivary gland tumor and one case of adenoid cystic carcinoma of the parotid gland which could be explained by hypercellularity of benign mixed salivary gland tumors as previously reported by King et al. (20). Cutoff value in our study was 3 with sensitivity of 94% and specificity of 86%.

Other researchers found difficulty in detecting Cr peak, and attained other methods to differentiate lesions. Gupta et al. (13), focused their study on detecting high Cho peak only. They have found high Cho peak in all malignant follicular carcinomas that were included in their study, and only one case of benign follicular adenoma with sensitivity of 100%, while the specificity was 94.11%. Others tried to measure Cho/noise ratio and used it instead of Cho/Cr ratio, like Yua et al. (21) and Bartella et al. (10). Yua et al. (21) who had classified lesions into three categories: type1; lesions with the absence of Cho signals, type 2; lesions with Cho signals and a Cho/noise ratio <3, and type 3; lesions with Cho signals and a Cho/noise ratio >3. They had a sensitivity of 76.5%, specificity of 100%, positive predictive value of 100%, negative predictive value of 63.6%, and accuracy of 83.3% on considering type 3 lesions as malignant tumors.

Other researchers (22) had connected high Cho peak detected in SCC lesions with grave tumor response to therapy.
which by indirect way indicates a high grade of malignancy. They have suggested that MR spectroscopy may be a simple method for predicting tumor behavior. In our study we did not follow malignant cases to verify this issue.

In addition to Cho and Cr peaks, broad lipid signals were also detected in most malignant as well as benign masses spectra. This copes with Smith et al. (23) who reported that the significance of these lipid peaks is uncertain because they are associated not only with malignancy but also with necrosis, inflammation, and benign cellular processes. It is unclear whether the bulk of these detected lipids originated from within the cancer or was caused by signal intensity contamination from adjacent fatty tissues (23).

As regard using Lactate peak to differentiate abscess from malignant lesions, it was not applicable in this study for several reasons. First lactate resonates (1.32 ppm) in the same region as lipids (0.90–2.02 ppm), and, since these fatty acid signals were very broad (12.2 Hz ± 2.4) and intense, weak signal contribution from lactate might have been overshadowed by that from lipids (20). Also there was a defect in our software made it inefficient in detecting and separating lactate and aspartate peaks.

On the other hand controversial results were reported as regard lactate. Le et al. (24) reported that the lactate SI could not be used as hypoxia indicator as it did not correlate with tumor pO2, treatment response, or locoregional control. While Star-Lack et al. (15) stated that tissue hypoxia and pO2 levels were correlated with tumor lactate indicating the use of 1H MRS in monitoring oxygenation of head and neck tumors and squamous cell carcinoma tumors.

Beside inability to detect aspartate and lactate peaks in inflammatory lesions, there were other technical difficulties and limitations in this study. First of all a small number of lesions were included in the study as compared to the large pathological entities present in the neck region. Unavoidable inclusion of adjacent bony and air-containing structures in the large VOI which reduced the likelihood of obtaining an adequate shim and resulted in decreased spectral resolution.

The presence of high lipid concentrations could have corrupted metabolite intensity measurements. Also we did not examine the technique on small volume lesions (< 1 cm³).

5. Conclusion

MR spectroscopy is a useful non-invasive imaging modality which can aid in the differentiation between benign & malignant neck masses.

References


