Accuracy of diffusion weighted MRI in diagnosing cervical lymphadenopathy correlated with pathology results

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Aims and objectives

Lymphadenopathy is an abnormal increase in size and / or altered consistency of the lymph nodes. The condition is generally not a disease by itself, rather, it may be a symptom of one of many possible underlying problems and serves as an excellent clue to them. It could be due to infections, autoimmune disorders or malignancies (metastatic or lymphomas) [Sambandon et al, 2011].

The characterization of neck lymph nodes remains a difficult issue with anatomy-based imaging methods. [Abdel Razek et al, 2006].

Up to today, parameters used by conventional imaging techniques are shape, size, extracapsular spread and an abnormal inner architecture. The size is certainly the most used criterion for the diagnosis, [Perrone A et al, 2011]. Small lymph nodes with a maximum short axial diameter below 10 mm are more challenging for radiologists, because the mere use of this size criterion will result in misclassification of malignant lymph nodes as normal on MRI evaluation [Vandecaveye et al, 2009].

Diffusion-weighted magnetic resonance imaging (MRI) is an imaging technique showing molecular diffusion. Cell size, density and integrity influence the signal intensity seen on diffusion-weighted images. This technique is a helpful complementary tool to distinguish tumoral from non-tumoral tissue, and has several interesting applications in the evaluation of head and neck cancer especially in head and neck lymphadenopathy [Abdel Razek et al, 2006]. Differentiation of treatment-induced tissue changes, especially after chemo and /or radiotherapy is another area in which DWI may be very helpful .[Vandecaveye et al, 2006].

The aim is to prospectively determine the diagnostic accuracy of diffusion-weighted magnetic resonance (MR) imaging for discrimination between benign and malignant lymph nodes with histologic findings and imaging criteria as reference standards.
Methods and materials

1. Patients:

Our study cohort included 26 patients with palpable neck nodes:

7 patients (1 male and 6 females; mean age: 37 years; range: 16-55 years) that were diagnosed by histopathology as benign lymphadenopathy (1 patient with chronic granulomatous inflammation, 1 with acute lymphadenitis, 5 with reactive non-specific lymphadenitis), and 19 patients (8 males and 11 females; mean age: 48 years; range: 6-76 years) that were diagnosed by histopathology as malignant lymphadenopathy before beginning treatment (5 patients with lymphoma, 1 patient with acute lymphocytic leukemia, 9 patients with metastatic squamous cell carcinoma and 4 patients with metastatic undifferentiated carcinoma). Moreover we studied a patient with Hodgkin lymphoma after chemotherapeutic treatment.

All the patients were referred from the outpatient clinics to the radiology department in National cancer institute. 11 patients presented to ours with palpable cervical lymph nodes with no known primary. They underwent neck US or CT before MRI examination. 10 patients [known head and neck cancer] underwent MRI for staging and therapy planning. 5 patients were coming for follow up post total thyroidectomy and radioactive iodine therapy and they have undergone neck US prior to MRI neck examination.

Our patients underwent Magnetic Resonance exam from May 2012 to January 2013. Consequently, 32 neck nodes were studied, 8 nodal lymphomas and leukemia, 16 metastatic nodes and 8 benign nodes. Biopsies and histopathological analysis were done after MRI examination.

Patient preparation:

Detachable metallic implants like teeth prosthesis are considered as proportional contraindication should be removed prior to entrance to magnetic area.

For the patient needed anaesthesia, fasting four hours before the scan is required.

The patients were subjected to the followings:

1. Full clinical assessment including recording of age, sex and presentation.
2. Laboratory investigations [coagulation profile, renal function tests (blood urea and serum creatinine)]
3. MRI neck (pre- and post contrast study and Diffusion-weighted imaging) and the results were compared to histopathology results done in all patients.
4- US guided biopsies were done for the suspicious cervical lymph nodes in 22 patients in our study, only 4 patients underwent excisional biopsies. Histopathological analysis were performed in pathology department, NCI.

**2. MR technique and image analysis:**

Nearly all MR examinations (21 patients out of 25) were performed with a 1.5-T whole-body system (Intera NT; Philips Medical Systems, Best, the Netherlands) with a 30 mT/m maximum gradient capability in NCI. A standard receive-only head and neck coil was used for both conventional imaging and diffusion-weighted MR imaging to include nodes from the base of the skull to the suprasternal notch. Only 4 patients underwent their MR exam with a 1.5-T superconductive scanner (Avanto, Siemens Medical Systems, Enlargen, Germany) in the CCHE 57357.

In all patients, the protocol included:

- Fast spin echo (FSE) T2-weighted images (TR 2500-4500 ms, TE 80 ms, slice-thickness: 5 mm) in axial plane

- Fast spin echo (FSE) T2-weighted images (TR 3850 ms, TE 75 ms, slice-thickness: 5 mm), in coronal plane;

- Fast spin echo (FSE) T1-weighted images, with and without fat suppression (TR 400-650 ms, TE 14 ms, slice-thickness: 5mm) in axial plane

- Fast spin echo (FSE) T1-weighted images, with fat suppression SPAIR: (Spectral Attenuated Inversion Recovery) after contrast medium administration of 0.1 mmol/kg of gadoterate meglumine (Omniscan, GE Healthcare); in axial and coronal planes. **Diffusion-weighted MR imaging** was performed before the contrast-enhanced T1-weighted MR imaging sequence using a spin-echo single shot T2 weighted echo-planar imaging sequence with b values of 0, 500, 1000 sec/mm2. Parallel imaging with generalized auto-calibrating partially parallel acquisition (GRAPPA) with an acceleration factor of two was applied to improve image quality.

All DW imaging data were transferred to a computer workstation for determination of the signal intensity and ADC. The ADC map was automatically reconstructed by a standard software imager in the main console. The ADC was measured by manually placing regions of interest on the ADC map. In the study, we chose only the largest abnormal adenopathies and excluded from analysis the necrotic areas.

**Imaging analysis :-**

The lymph nodes were characterized on the basis of internationally accepted standards for evaluating anatomic imaging data. First, the morphological features of each lymph node of interest were recorded such as the size (in shortest axial diameter), parenchymal homogeneity, areas of necrosis and nodal contour irregularity. The above findings can
be detected in conventional T1-weighted, T2-weighted, and contrast material-enhanced T1-weighted images.

Second, the DW images and their corresponding ADC map were analysed in consensus at a picture archiving and communication system workstation. The lymph nodes were localized on the images obtained with a \( b \) value of 0 sec/mm\(^2\). For quantitative assessment, regions of interest were placed in the lymph nodes identified on the \( b \) _0 images, and the software automatically copied these regions onto the other \( b \) value images. Finally, the histopathologic and radiologic findings were correlated as a reference standard after all image interpretations had been concluded. The optimal ADCb0-1000 threshold for differentiating a benign from a malignant lymph node was determined by using receiver operating characteristic analysis. The sensitivity, specificity, and accuracy of the ADCb0-1000 were subsequently calculated.
Results

Histopathological analysis was done dividing the examined lymph nodes in our study (n = 32) into 2 categories: malignant lymphadenopathy 75% (n = 24) and benign lymphadenopathy 25% (n = 8). (figure).

DWI and ADC values revealed 27 malignant lesions (84%), 5 benign (16%). (figure). The accuracy of the MRI was 89%.

Image evaluation:

1- Conventional MRI:
   - Size Criteria among the benign and malignant LNs (in shortest axis diameter):
     The size of the examined lymph nodes (n = 32) ranged from 0.6 - 2.5 cm (mean size 1.2 ± 0.44 cm).
   - Parenchymal architecture among the benign and malignant LNs depicted on T2-weighted images.

2- Diffusion WIs & ADC: All malignant nodes (n = 24) show restricted diffusion evidenced by increased signal on increasing the b-values (b = 1000) and low signal on ADC maps. In 4/8 cases with inflammatory diseases, lymph nodes showed reduction of signal intensity on increasing b values (b = 1000) and intermediate signal intensity on ADC maps reflecting facilitated diffusion. 4/8 cases of benign lymphadenopathy, diagnosed as reactive lymphoid hyperplasia and chronic granulomatous infection show increased signal on increasing b-values (false positive).

Follow up results:

One of the patients with Hodgkin disease who received chemotherapy, had undergone follow up DW MRI, lymph nodes were hypointense on DWI (b = 1000) and intermediate signal on the ADC maps with a mean ADC value of 1.2 × 10⁻³ mm²/sec (compared to ADC 0.687 × 10⁻³ mm²/s pretreatment) indicating facilitated diffusion.

A significant difference between benign and malignant cervical nodes on diffusion-weighted imaging and on ADC maps is reported and a threshold ADC value equal to 1.005 × 10⁻³ mm²/s was identified in our study the results obtained 24 true positive, 4 false positive, 4 true negative yielding 100% sensitivity, 62.5% specificity. The difference between the mean ADC value between benign and malignant lesions was statistically significant (p < 0.0001).
Fig. 2: Histopathological diagnosis into benign (blue) and malignant (green) groups
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Fig. 3: DWI and ADC diagnosis into benign (blue) and malignant (green) groups
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### Fig. 4: Size criteria among benign and malignant lymph nodes:

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<table>
<thead>
<tr>
<th>Size groups</th>
<th>Benign</th>
<th>Malignant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 cm</td>
<td>2</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>1 cm or more</td>
<td>6</td>
<td>17</td>
<td>23</td>
</tr>
<tr>
<td>TOTAL</td>
<td>8</td>
<td>24</td>
<td>32</td>
</tr>
</tbody>
</table>

### Fig. 5: Parenchymal architecture among benign and malignant LNs

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<table>
<thead>
<tr>
<th>Parenchyma</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homogenous</td>
<td>8 (100%)</td>
<td>19 (79.2%)</td>
</tr>
<tr>
<td>Heterogenous</td>
<td>0</td>
<td>5 (20%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>8</td>
<td>24</td>
</tr>
<tr>
<td>ADC value</td>
<td>Range</td>
<td>Mean</td>
</tr>
<tr>
<td>-----------</td>
<td>-------------</td>
<td>-------</td>
</tr>
<tr>
<td>Malignant</td>
<td>0.567 - 0.98</td>
<td>0.774</td>
</tr>
<tr>
<td>Benign</td>
<td>0.712 - 1.3</td>
<td>1.019</td>
</tr>
</tbody>
</table>

**Fig. 6:** Comparison of ADC values among benign and malignant LN groups

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<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>True positive</td>
<td>24</td>
<td>75</td>
</tr>
<tr>
<td>False positive</td>
<td>4</td>
<td>12.5</td>
</tr>
<tr>
<td>True negative</td>
<td>4</td>
<td>12.5</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>100</td>
</tr>
</tbody>
</table>

**Fig. 7:** ADC - pathology correlation

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**Fig. 8:** CASE 1: 49 y female, insidious left neck swelling: axial T2 WIs

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Fig. 9: CASE 1: DWIs b0-1000 (restricted suggesting malignant lymphadenopathy)

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**Fig. 10:** CASE 1: ADC value: 0.57 x 10^{-3} \text{ mm}^2 /\text{sec} (Non Hodgkin lymphoma)

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Fig. 11: CASE 2: A 55 Y male, left sided retromolar malignant mass of insidious onset, Axial T2: Left upper deep cervical LN: Ib

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Fig. 12: CASE 2: DWIs: b0 & b1000 (restricted suggesting malignant lymphadenopathy)

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**Fig. 13:** CASE 2: ADC value: 0.834 x 10⁻³ mm²/sec (metastatic SCC)

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Conclusion

Head and neck lymphadenopathy is divided into benign and malignant lymph nodes. The benign group includes infection and inflammation while the malignant group includes primary as lymphoma and secondary as metastatic.

Diffusion gives good support or exclusion of the nature of the lymph nodes either benign or malignant. DWI is able to characterize tissue based on differences in water mobility. Hypercellular tissue, such as occurring within malignant lymph nodes, will show restricted diffusion and low ADC values. The benign lymph node that shows non-tumoral tissue changes such as oedema, inflammation, fibrosis, and necrosis is expected to show low cellularity, in strong contrast with viable tumour. This results in facilitated diffusion and a high ADC.

The higher accuracy of DW imaging (b 0-1000), as compared with TSE MR imaging was most beneficial in the detection of not only the enlarged but also the sub-centimeter metastatic lymph nodes in patients with HNSCC suggesting that DW imaging can be complementary to conventional MR imaging regarding its size and morphologic criteria. It can also be used as an indicator for improvement and recurrence post chemo and radiotherapy.


3. **Sambandan T, Christefi Mapel R,** Review of cervical lymphadenopathy, January -March 2011, JIADS volume 2 Issue 1, pages 31-33
