Diffusion-weighted imaging in the characterization of superficial lymph nodes: effect of b-value

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Aims and objectives

For two decades diffusion-weighted (DW) magnetic resonance imaging (MRI) has predominantly been applied to investigate intracranial alterations. Technological advances have recently made it possible to obtain high-quality DW images also in extracranial compartments, prompting studies of the method's diagnostic accuracy in detecting and assessing superficial and deep lymph nodes [1-10].

A 2012 meta-analysis documented that DW imaging (DWI) is more sensitive than conventional MRI, positron emission tomography (PET), computed tomography (CT) and ultrasound (US) in detecting lymph nodes in patients with head and neck cancer [11]. However, there is still no single established b-value for DWI of lymph nodes-the parameter expressing the degree of diffusion weighting, which closely correlates with scanner hardware and software.

This study was undertaken to investigate the ability of DWI to differentiate malignant from benign lymph nodes using two different b-values, 600 s/mm$^2$ vs. 1000 s/mm$^2$. 
Methods and materials

The Diagnostic Imaging and the Oncohaematology Department of our Institution participated in this prospective study.

From January to September 2012, all patients presenting with clinically suspicious lymph nodes ascribable to haematological disorder or to a reactive/inflammatory process based on clinical, laboratory, and imaging findings (US, echo-colour-Doppler sonography, contrast-enhanced CT, or CT-PET) obtained at our or other institutions were enrolled in the study. Exclusion criteria were essentially those related to MRI contraindications, i.e. pace-makers, protheses, or other devices incompatible with magnetic fields, claustrophobia and obesity.

The 28 patients who were eligible were informed of the scientific goals of the DW-MRI study and were assured that the additional information obtained from the DW study would not affect the diagnostic work-up as laid down in our Institution's guidelines for the investigation of clinically suspicious lymph nodes. Our protocols envisage lymph node dissection in case of suspected haematological disease, and clinical and instrumental follow-up after pharmacological treatment in case of superficial lymph node enlargement due to a reactive or inflammatory process.

This study was approved by the local ethics committee. Patients were asked to sign an informed consent form to document their willingness to participate in the study.

Seven patients were eventually excluded: 3 because they did not complete the DW-MRI examination due to claustrophobia; 2 because of artefacts; a young woman referred for a suspected haematological neoplasm was found on MRI to have multiple neurofibromatosis in the cervical region; finally the 7th patient was excluded because although he had undergone axillary lymph node dissection the DWI study had erroneously been aimed at the neck. This left 21 subjects whose mean age was 55.6 years ± 22.7 standard deviation (SD); range 12.4-85.4 years. The clinical and pathological characteristics of the patients are reported in table 1.

All patients underwent DW-MRI in a 1.5 Tesla scanner (Signa Excite HD; GE Healthcare, Milwaukee, WI, USA) with 33mT/m gradients using an FSE T2-weighted sequence with FAT SAT and an axial DWI sequence centred on the lesions; b-values were 0 s/mm², 600 s/mm² and 1000 s/mm². All DWI parameters are reported in table 2.

Image analysis
Examination of the DWI scans focused on the lymph nodes whose topographic and imaging features (morphology, size, vascularisation pattern, increased carbohydrate metabolism) were suspicious for a malignancy or a reactive/inflammatory process.

All images were transferred to a workstation (Advantage Windows version 4.2; GE Healthcare) and the DWI sequence was post-processed using a commercial software (Functool GE Healthcare) to obtain apparent diffusion coefficient (ADC) maps.

The mean ADC value at a b-values of 600 s/mm$^2$ and 1000 s/mm$^2$ was manually recorded on the ADC map by placing three circular region of interest (ROIs) in the target lymph node in the same location. Mean ROI area was 15 mm$^2$. The position of each ROI was selected avoiding areas with a necrotic appearance or containing cysts on FSE T2-weighted images.

Scans were reviewed by consensus by two radiologists (E.C. and L.A.) experienced in DWI of intra- and extracranial compartments. The gold standard was pathological examination of excised nodes (15 patients) and clinical and US follow-up after drug treatment in the other cases (6 patients).

Statistical analysis

The limited sample size required use of non-parametric tests.

The difference in ADC value between patients with a diagnosis of benign and malignant disease was analysed using Wilcoxon’s test; a p value <0.05 was considered significant.

Analysis of receiver operating characteristics (ROC) was also applied, to assess the diagnostic ability of ADC values and determine the cut-off differentiating benign from malignant nodes in DW images obtained with b-values of 600 and 1000 s/mm$^2$.

**Table 1.** Characteristics of the 21 patients

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>21</td>
</tr>
<tr>
<td>Mean age ± standard deviation</td>
<td>55.6 ± 22.7 years</td>
</tr>
<tr>
<td>Age range</td>
<td>12-4-85.4 years</td>
</tr>
<tr>
<td>Men (n)</td>
<td>11 (52.4%)</td>
</tr>
<tr>
<td>Neck lymph nodes (n)</td>
<td>13</td>
</tr>
</tbody>
</table>
Axillary lymph nodes (n) 4  
Inguinal lymph nodes (n) 4  
Mean node diameter (mm) 22  
Diameter range (mm) 9-58

**Table 2. DWI parameters**

<table>
<thead>
<tr>
<th>DWI parameters</th>
<th>Body region</th>
<th>Axilla</th>
<th>Groin</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR (ms)</td>
<td>5000</td>
<td>6000</td>
<td>4500</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>Minimum</td>
<td>Minimum</td>
<td>Minimum</td>
</tr>
<tr>
<td>Matrix</td>
<td>128x128</td>
<td>128x128</td>
<td>96x128</td>
</tr>
<tr>
<td>Nex</td>
<td>6.00</td>
<td>4.00</td>
<td>6.00</td>
</tr>
<tr>
<td>Slice thickness (mm)</td>
<td>4.0</td>
<td>3.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Spacing (mm)</td>
<td>3.0</td>
<td>0.6</td>
<td>1.0</td>
</tr>
<tr>
<td>Scan time (min)</td>
<td>2.00</td>
<td>3.12</td>
<td>3.36</td>
</tr>
<tr>
<td>b-value (s/mm²)</td>
<td>0, 600, 1000</td>
<td>0, 600,1000</td>
<td>0, 600,1000</td>
</tr>
<tr>
<td>Coil</td>
<td>Multichannel phased-array</td>
<td>8 channel (upper body)</td>
<td>8 channel (lower body)</td>
</tr>
</tbody>
</table>
Results

The pathology findings and clinical evolution after medical treatment showed that 11 patients (52.4%; mean age 46.3±24.6 years) had benign lymphadenopathy (BD) related to an ongoing reactive or inflammatory process; in particular 9 patients had reactive hyperplastic lymphadenitis; 1 had granulation lymphadenitis, and another had pyogenic granuloma. The other 10 patients (47.6%; mean age 65.8±15.7 years) were diagnosed with a haematological malignancy (MD): 3 had B-cell chronic lymphocytic leukaemia; 2 had follicular lymphoma; 2 had Hodgkin’s lymphoma; there was also one case each of large B-cell lymphoma, small lymphocytic lymphoma, and lymphoplasmacytic lymphoma.

BD patients with were younger (mean age, 46.3 ± 24.6 years) than MD subjects (65.8 ± 15.7 years), but the difference was not significant (p=0.09). In contrast, the two b-values yielded significantly different mean ADCs in the two sets of patients (600 s/mm²: 1.50x10⁻³ vs. 0.97x10⁻³ mm²/s; p=0.033; 1000 s/mm²: 1.21x10⁻³ vs. 0.91x10⁻³ mm²/s; p=0.021). These data are reported in table 3. The cut-off values differentiating BD from MD nodes with 80% sensitivity (SE) and specificity (SP) were 0.92x10⁻³ mm²/s (600 s/mm²) and 0.93x10⁻³ mm²/s (1000 s/mm²).

Figure 1 shows the ROC curves of the ADC values used to differentiate benign from malignant lymph nodes. The area under the curve (AUC) is 0.800 for 600 s/mm² and 0.823 for 1000 s/mm²; the difference is not significant (p=0.40).

Finally, a similar image quality was provided by the two b-values (Figure 2.a,b).

Table 3. Mean values of the apparent diffusion coefficient (ADC) calculated for each b-value

<table>
<thead>
<tr>
<th>b-value (mm²/s)</th>
<th>Malignancy</th>
<th>Patients (n)</th>
<th>Mean ADC</th>
<th>SD</th>
<th>P value (Wilcoxon’s test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>600</td>
<td>NO</td>
<td>11</td>
<td>0.0015053</td>
<td>0.0006519</td>
<td>0.033</td>
</tr>
<tr>
<td></td>
<td>YES</td>
<td>10</td>
<td>0.0009702</td>
<td>0.0007536</td>
<td></td>
</tr>
<tr>
<td>1000</td>
<td>NO</td>
<td>11</td>
<td>0.0012100</td>
<td>0.0003953</td>
<td>0.021</td>
</tr>
<tr>
<td></td>
<td>YES</td>
<td>10</td>
<td>0.0009087</td>
<td>0.0007888</td>
<td></td>
</tr>
</tbody>
</table>

SD, standard deviation
Fig. 1: Figure. 1a,b The relation between the ROC curves: AUC dwi_600 (a)=0.800 vs AUC dwi_1000(b)=0.823 Pvalue=0.40 (no significative)

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**Fig. 2:** Fig. 2a,b - DWI b-value 600 s/mm² (a) and DWI b-value 1000 s/mm² (b). Right inguinal lymphadenopathy (Non-Hodgkin lymphoma). The two b-values provided a similar image quality.

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Fig. 3: Fig. 2a,b - DWI b-value 600 s/mm2 (a) and DWI b-value 1000 s/mm2 (b). Right inguinal lymphadenopathy (Non-Hodgkin lymphoma). The two b-values provided a similar image quality

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Conclusion

This study investigates the ability of DWI in differentiating benign from malignant superficial lymph nodes using two different b-values.

Clinical examination and laboratory tests have demonstrated poor specificity in detecting and characterising lymph nodes [12]. A number of diagnostic criteria including size, morphology, margins, structure, hilar vascularity, microcalcification, necrosis, tendency to confluence, perilesional oedema, vascular pattern, and rim enhancement have been suggested to help differentiate benign from malignant lymph nodes on US, CT and conventional MRI [13,14]. The one currently affording the highest accuracy is the increase in minimum axial diameter, which is suspicious if it exceeds 10 mm [14]. However, reactive benign lymph nodes may also be enlarged, whereas small metastases may not involve a clear size increase. It has been reported that 58% of metastatic lymph nodes examined by fine needle aspiration cytology have a minimum axial diameter <10 mm [15]. The functional information provided by approaches such as SPECT (Single Photon Emission Computed Tomography) and PET is also affected by limitations like low spatial resolution, high cost and poor availability [8].

A recent meta-analysis of the value of conventional MRI [11] in detecting lymph nodes in head and neck cancer patients has evidenced an SE of 76% and an SP of 86%, which are not significantly different from the performance of PET, CT or US. Interestingly, SE was 86% in the subgroup undergoing DW-MRI.

The diffusion of water molecules, a biological parameter correlating with the structural characteristics of tissues both in physiological and pathological conditions, is mainly influenced by cell size and density and by membrane integrity [16]. DWI is sensitive to microscopic changes and is capable of differentiating healthy tissue from tissue affected by inflammatory changes, tumour lesions and necrotic degeneration [17]. The ADC value is commonly lower in malignant than in benign lesions [1,4,5,7-9,18]. However, little information is available as to the optimal b-value for ADC calculation in normal vs. pathological lymph nodes.

The b-value—the parameter expressing the degree of diffusion weighting of a sequence—is related to gradient amplitude and duration and to the time interval between the activation of the two diffusion gradients. It therefore closely correlates with scanner hardware and software. Higher b-values are generally associated with decreased node signal intensity (reduction of signal to noise ratio), increased magnetic susceptibility artefacts, and greater SP [12]. In this study, as in the literature, a higher mean ADC value was found in lymphadenopathy ascribable to reactive or inflammatory processes. In addition, the ADC cut-off values associated with 80% SE and SP were not significantly different between the two b-values. Finally, the two b-values provided a similar image quality.
In conclusion, despite limitations due to sample size, these findings confirm the ability of DW-MRI to differentiate benign from malignant superficial lymph nodes and document that b-values of 600 s/mm\(^2\) and 1000 s/mm\(^2\) do not involve significant differences. However the non-optimal SE and SP values and the broad SD range associated with the mean ADC values of benign and malignant lymph nodes prevent the adoption of DW-MRI to replace pathological examination in clinical practice.


