Diagnostic impact of echo planar diffusion-weighted magnetic resonance imaging (DWI) in musculoskeletal neoplastic masses using apparent diffusion coefficient (ADC) mapping as a quantitative assessment tool

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Purpose

To evaluate the diagnostic impact of echo planar DW Imaging in distinguishing benign from malignant musculoskeletal soft tissue masses using ADC mapping as a quantitative assessment tool.

Methods and Materials

Patients

From December 2008 to November 2010, we prospectively included 73 consecutive patients (23 women and 50 men; age range 11-70 years; median age 41 years) with clinically suspected musculoskeletal neoplasm. The patients were subjected to clinical examination, previous X ray and ultrasonographic examination. In all patients diagnosis was confirmed after MRI with histologic biopsy and/or examination of the resected specimens. We evaluated 73 tumors (27 bone tumors and 46 soft tissue tumors).

MR imaging technique:

All patients underwent MRI using a 1.5 T MR system (Magnetom Symphony ,Syngo 1.5 T Siemens ) with the following pulse sequences;

1-Standard protocols for musculoskeletal system

1)T1WI ( TR/TE/NEX;450/15/1;FOV, 20-30) in axial , coronal and sagittal planes,

2)Fast spin echo T2WI ( TR/TE/NEX ;3000-3500/100-120/2;FOV,20-30) in axial , coronal and sagittal planes,

3)Short tau inversion recovery (STIR)(TR/TE/TI/NEX;5000-5300/30-50/160/2 ; FOV ,20-30) in axial , coronal and sagittal planes,

4) Gradient Recalled Echo (GRE)(TR/TE/NEX;700-750/20-30/2;FOV ,20-30) with flip angle 15-30 degree in axial ,coronal or sagittal planes ,and

5) Post-contrast T1WI SE and T1-fat suppressed images in axial , coronal and sagittal planes using gadolinium D.T.P.A ( 0.1 mmol/kg body weight) .

6)Diffusion weighted images
A diffusion-weighted spin echo sequence with peripheral pulse triggering (TR _ 2-RR, TE _ 70, flip angle _ 90°, field of view (FOV) _ 200-300 mm, matrix size _ 51 _ 128) was used with diffusion gradient strengths yielding five b-values ranging from 0 to 701 seconds/mm² (b _ 0, 176, 351, 526, and 701 seconds/mm²)

Six slices through the tumor were acquired with a slice thickness of 5 mm and an interslice gap of 2.5 mm

Body parts containing the tumors were immobilized to prevent motion artifacts.

Arbitrarily-shaped regions of interest (ROIs) for data analysis were positioned in tumor on the basis of the T2-weighted reference image (b _ 0 seconds/mm²) and copied to all isotropic images of subsequent b-values.

When multiple tumor components (solid vs. cystic) could be identified, measurements were taken in the solid components. The mean signal intensities on five isotropic images obtained with different b-values were used to calculate the ADC values.

Differences in ADC values between malignant and benign soft-tissue masses were evaluated using Student’s t-test. P values less than 0.05 were considered a statistically significant.

**Results**

73 patients (50 males and 23 females) were included in this study. Their ages age range 11-70 years; median age 41 years. The diagnosis of the soft tissue masses was confirmed with histo-pathologic examination after excision biopsy (in 61 patients) or post-surgical excision (in 12 patients). 33 masses were benign and 40 masses were malignant. 21 bone tumors and 52 soft tissue tumors. (table 1 and 2).

<table>
<thead>
<tr>
<th>Benign lesions</th>
<th>Number</th>
<th>Main ADC value measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemangioma</td>
<td>6</td>
<td>1.4 ± 0.18 - 1.6 ±0.2×10⁻³ mm²/s</td>
</tr>
<tr>
<td>Juxtacortical enchondroma</td>
<td>2</td>
<td>2.65 ± 0.36×10⁻³ mm²/s</td>
</tr>
<tr>
<td>Ganglion</td>
<td>7</td>
<td>1.9 ± 0.21 2.8±0.23×10⁻³ mm²/s</td>
</tr>
<tr>
<td>Benign Masses</td>
<td>Number</td>
<td>Main ADC value</td>
</tr>
<tr>
<td>------------------------</td>
<td>--------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Schwannoma</td>
<td>5</td>
<td>$1.5 \pm 0.19 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Neurofibroma</td>
<td>3</td>
<td>$1.75 +/- 0.26 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Cystic neurofibroma</td>
<td>1</td>
<td>$2.5 \pm 0.04 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Aggressive fibromatosis</td>
<td>2</td>
<td>$0.37 \pm 0.05 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Osteochondroma</td>
<td>3</td>
<td>$2.1 \pm 0.34 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Elastofibroma</td>
<td>2</td>
<td>$1.9 \pm 0.24 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>PVN</td>
<td>2</td>
<td>$2.21 \pm 0.14 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>$1.86 \pm 0.67 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
</tbody>
</table>

Table 1 revealed the number and ADC value of benign masses

<table>
<thead>
<tr>
<th>Malignant Tumors</th>
<th>Number</th>
<th>Main ADC value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low grade sarcoma</td>
<td>6</td>
<td>$1.1 \pm 0.22 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Intermediate liposarcoma</td>
<td>2</td>
<td>$1.4 \pm 0.21 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>High grade liposarcoma</td>
<td>2</td>
<td>$0.97 \pm 0.18 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Intermediate fibrosarcoma</td>
<td>3</td>
<td>$1.0 \pm 0.2 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>High grade fibro sarcoma</td>
<td>2</td>
<td>$0.78 \pm 0.14 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Malignant histiocytoma</td>
<td>2</td>
<td>$0.81 \pm 0.18 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Neurofibrosarcoma</td>
<td>1</td>
<td>$0.96 \pm 0.17 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Metastatic deposits</td>
<td>6</td>
<td>$0.9 \pm 0.18 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Ewings sarcoma</td>
<td>4</td>
<td>$1.1 \pm 0.9 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Giant Cell tumour</td>
<td>6</td>
<td>$1.1 \pm 0.5 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>5</td>
<td>$0.9 \pm 0.6 \times 10^{-3} \text{ mm}^2/\text{s}$</td>
</tr>
</tbody>
</table>
Table 2 revealed the number and ADC value of malignant masses

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Number</th>
<th>ADC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesenchymal chondrosarcoma</td>
<td>1</td>
<td>2.1±0.32×10⁻³ mm²/s</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>0.97±0.35×10⁻³</td>
</tr>
</tbody>
</table>

The average ADC of benign cases was 1.86±0.67×10⁻³ mm²/s, and that of malignant soft tissue tumors was 0.97±0.35×10⁻³ mm²/s. ADC value of malignant tumors was significantly lower than that of the benign tumor group (p<0.0001). The highest ADC value was seen in the case of ganglion cyst (2.8±0.23×10⁻³ mm²/s) (figure 1), juxta cortical enchondroma (2.65±0.36×10⁻³ mm²/s) (figure 2) and cystic neurofibroma (2.5±0.04×10⁻³ mm²/s) (figure 3) while the lowest one was seen in aggressive fibromatosis (0.37±0.05×10⁻³ mm²/s) (figure 4). For malignant soft tissue masses, the highest ADC value was seen in mesenchymal chondrosarcoma (2.1±0.32×10⁻³ mm²/s) and liposarcoma (intermediate grade) (1.4±0.21) (figure 5) while the lowest ADC value was seen in fibrosarcoma (high grade) (0.78±0.14) (figure 6). GCT (figure 8), osteosarcoma (figure 9), and Ewing’s sarcoma (figure 10), showed intermediate ADC.

**Discussion:**

Magnetic resonance imaging has an important role in diagnosis, staging and follow up of soft tissue masses owing to its precise visualization of degenerative changes, tumor and inflammatory disease.

Tissue contrast attained by using diffusion-weighted magnetic resonance (MR) imaging is different from that attained by using conventional MR techniques. The diffusion technique involves the diffusion motion of water protons in the tissues, and this technique produces different contrast in different kinds of tissue. Therefore, the findings of this procedure can provide different information about diseased tissues (4). Recently DWi was used to characterize soft tissue tumour, differentiate between benign and malignant soft tissue masses.

Our results demonstrate increased apparent diffusion coefficients in benign soft-tissue masses compared to malignant soft tissue masses where the main ADC value of all benign soft tissue masses was 1.86±0.67 while the main ADC value for all malignant soft tissue masses was 0.97±0.35. This may be attributed to increased diffusion of water molecules in the extracellular spaces in benign lesions as compared to that of malignant soft tissue masses. These results were comparable to those of Nagata et al (10) who stated that the size of the extracellular space is the most important component of the true diffusion measurement in soft-tissue tumors. A larger or less restricted extracellular space, allowing spin dephasing and loss of signal on diffusion-weighted images, is the...
most likely explanation for the increased diffusion of most benign soft-tissue tumors. Malignant soft-tissue tumors tend to have lower true diffusion measurements due to increased tumor cell packing in the majority of the malignant soft-tissue tumors, resulting in restriction of Brownian motion in the extracellular space(11-12).

Our results revealed that ganglion and cystic neurofibroma (fig-1 and 3) and juxtacortical enchondroma (fig-2) had higher ADC values than those other benign soft tissue lesions (table-1). For malignant soft tissue masses, the highest ADC value was seen in mesenchymal chondrosarcoma (2.1±0.32×10-3 mm2/s) and liposarcoma (intermediate grade) (1.03 +/-0.21). These results were comparable with those of Nagata et al (10) who stated that ADC values of myxomatous, cystic, and cartilaginous components are significantly higher than those of other tumors and even malignant cartilaginous tumor ADC values are higher than those of benign tumors.

Previous studies reported that not all benign soft-tissue tumors have a large extracellular space, and not all malignant soft-tissue tumors are more cellular than benign soft-tissue tumors. There was a considerable variation in true diffusion values within a group of liposarcomas and between the high- and low-grade myxofibrosarcomas. A possible explanation may be related to the various histologic subtypes and variation in the degree of tumor differentiation. Another explanation that the ADC value is affected not only by cellularity but also by the amount and type of extracellular substance. Soft tissue tumors, as opposed, for example, to brain tumors, are a highly heterogeneous entity as regards extracellular matrix. Both benign lesions and sarcomas exhibit such heterogeneity as may explain the overlapping of ADC values(13,14,15).

In the current study the two patients with benign lesions, demonstrating very low ADC value (0.37+/-0.05) similar to ADC values of malignant soft-tissue tumors, had aggressive fibromatosis (figure 4). This can be explained by the fact that, histologically, aggressive fibromatosis consists of relatively uniform spindle-shaped cells surrounded and separated from each other by collagen fibers. However, fibrosarcoma is also composed of a relatively uniform population of spindle cells, demonstrating variable anaplasia. Fibrosarcoma is differentiated from aggressive fibromatosis by increased collagen and the absence of atypia in the latter, which is beyond the reach of diffusion-weighted MRI (16).

Several techniques have been used to obtain diffusion-weighted MR images (13). We used a peripheral pulse-triggered conventional spin-echo sequence that corrects for, or minimizes the effects of vascular pulsation on MR images in the extremities, and which was described previously as a successful sequence for diffusion measurements (17,18). The main disadvantage of the spin-echo sequence is the long acquisition time, and the subsequent increased sensitivity to motion artifacts. Faster imaging sequences, such as echoplanar techniques, are available and have been used for diffusion measurements.
in human brain (17), hepatic lesions (19), and in the pelvis (20,21). Steady state free precession (SSFP) techniques have also been used in the musculoskeletal system for diffusion weighted MRI, with reported adequate image quality, SNRs, and relatively short acquisition times. The main disadvantages of the SSFP technique are the difficulties in quantifying diffusion, T2-contamination, and other confounding relaxation effects. Apparently, further studies are warranted to achieve faster diffusion-weighted spin-echo and/or EPI sequences with adequate image quality for diffusion measurements in the musculoskeletal system (22,23).

Limitations in our study were that our study not included some of the musculoskeletal tumour histology to know if our results are applicable to all tumors or not, and difficult comparison of our results with those of others due to differences in imaging sequences and differences in b-values.

Images for this section:

![Fig. 1: Ganglion cyst on the lateral aspect of the wrist. ADC Value 2.6 +/-0.45](image_url)
Fig. 2: Juxtacortical Enchondroma of the shoulder ADC Value 2.65 +/- 0.36
Fig. 3: Cystic Neurofibroma ADC Value 2.5+/-0.04
Fig. 4: Aggressive fibromatosis of the foot. ADC Value 0.32 +/- 0.07
**Fig. 5:** Mesenchyma chondrosarcoma of the foot ADC Value 2.1±/0.32.
**Fig. 6:** Liposarcoma of the thigh. ADC Value 1.1+/−0.13
Fig. 7: GCT .ADC Value 1.1+/-0.5
Fig. 8: Osteosarcoma of the femur. ADC Value 0.9+/−0.6.
Fig. 9: Ewing's sarcoma of the fibula. ADC Value 1.1+/-0.9
Conclusion

In conclusion, Diffusion measurements of soft tissue masses has potential as a noninvasive tool in differentiation of benign and malignant soft tissue lesions. It provides important additional information, but does not serve as a substitute for the routine MRI sequences. Further prospective studies with larger patient populations are required.

References


3- Rubesova E, Grell AS, De Maertelaer V, et al. Quantitative diffusion


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