Diffusion-Weighted Magnetic Resonance Imaging for the Evaluation of Musculoskeletal Tumors

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MR imaging has become the diagnostic method of choice for preoperative and posttreatment staging of musculoskeletal (MSK) tumors because of the high resolution, tissue contrast, and multiplanar capability of this technique.

In addition, MR imaging offers several advantages when compared with other imaging methods in the evaluation and staging of soft tissue tumors. Several studies have demonstrated morphologic parameters such as size, margin demarcation, involvement of adjacent vital structures, homogeneity in signal intensity, and measurement of relaxation time as criteria to evaluate soft tissue tumors.1 In accordance with these criteria, malignancy can be predicted with the following parameters (Fig. 1):2:

- Heterogeneous signal intensity in a T1 scan
- Tumor necrosis
- Bone or neurovascular involvement
- Mean diameter of more than 66 mm.

However, conventional MR imaging provides low specificity in the differential diagnosis of several MSK tumors because many of the lesions exhibit nonspecific characteristics. As a result, a correct histologic diagnosis is possible in only a quarter to one-third of cases.2 Conventional MR imaging is unable to offer information about the extent of tumoral necrosis and the presence of viable cells, information that is crucial for the assessment of treatment response and prognosis. Therefore, advanced MR imaging techniques, such as diffusion-weighted imaging (DWI), are now used in association with conventional MR imaging with the objective of improving diagnostic accuracy and treatment evaluation. DWI allows quantitative and qualitative analyses of tissue cellularity and cell membrane integrity and has been widely used for tumor detection and characterization and to monitor treatment response (Fig. 2).3

The tumor tissue is usually more cellular when compared with other tissues and tends to appear at high signal intensities (restricted diffusion) when DWI is used (Fig. 3).4

The tissue contrast obtained using DWI is different from that obtained using conventional MR imaging, which facilitates the detection of soft tissue and bone tumors, particularly bone metastasis.5 In fact, previous studies have concluded that DWI is an extremely sensitive method for identifying bone metastases and is

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- Contrast enhancement
- Hyperintensity
- Musculoskeletal tumor

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superior to both positron emission tomography (PET) and scintigraphy in terms of detection capability. The detection of bone metastasis is important for cancer staging and in the determination of treatment strategy, and some reports have demonstrated whole body DWI to be highly sensitive and efficient for this purpose.

Tumors differ in cellularity characteristics, and this difference is useful in determining their histologic composition. It has been reported that DWI can differentiate benign from malignant soft tissue tumors (Fig. 4).

The malignant tumors have more cellularity than benign tumors and tend to have a more restricted diffusion (Fig. 5).

In accordance with this finding, perfusion-corrected DWI has demonstrated potential in differentiating benign from malignant soft tissue...
In addition, DWI is also used for differentiating between chronic expanding hematomas (CEHs) and malignant soft tissue tumors. CEHs are frequently misdiagnosed as malignant soft tissue tumors because of their morphologic characteristics, which include large size, slow progressive enlargement, and heterogeneous signal intensity on conventional MR imaging. DWI has also been shown to be an additional tool for differentiating vertebral fracture caused by osteoporotic collapse with bone marrow edema as well as pathologic collapse caused by tumor infiltration or metastatic disease.

On the other hand, some investigators have reported overlapping apparent diffusion coefficient (ADC) values in benign and malignant soft tissue tumors, which consequently could not be used to differentiate them. This overlapping is likely because of the fact that ADC values can be affected by cellularity and the extracellular matrix. For example, myxoid matrix is widely seen in the interstitial spaces in many soft tissue tumors, and this presence can influence the ADC values.

As a result, myxoid tumors will have significantly higher ADC values than nonmyxoid tumors. It makes no difference if the tumor is benign or malignant.

DWI can also be used to monitor tumor response to treatment, most likely because effective anticancer therapy results in changes in the tumor microenvironment, resulting in an increase in the tumor's signal intensity on DWI.
in the diffusion of water molecules and a consequent increase in the ADC value (Fig. 7).4

Furthermore, DWI has been used to provide information regarding cellular changes related to cytotoxic treatment in soft tissue sarcomas.12 Some investigators have suggested that it could be possible to evaluate the response of osteosarcoma to chemotherapy using DWI, considering that the ADC values of viable tumor tissue and tumor necrosis differ significantly.9,13 This information is a crucial prognostic factor for patients with osteosarcoma.

This article provides a short discussion of the technical aspects of DWI, particularly the quantitative and qualitative interpretation of diffusion-weighted (DW) images in MSK tumors. The clinical application of DWI for tumor detection, characterization, differentiation of tumor tissue from non-tumor tissue, and assessment of treatment response are emphasized.

TECHNICAL ASPECTS

Herein, the authors briefly discuss some important concepts regarding the specificity of DWI in the MSK system. However, for a detailed explanation of the physics of DWI see the article elsewhere in this issue. See the article by Figueiredo and colleagues elsewhere in this issue for further exploration of this topic.

DWI exploits the random motion of water molecules in the body, which is classically called the Brownian motion. In biologic tissues, the movement of water molecules is restricted because their motion is modified and limited by their interactions with cellular membranes and macromolecules.14 The DWI signal in vivo is therefore derived from the motion of water protons in extracellular, intracellular, and intravascular spaces.15

DWI yields qualitative and quantitative information that reflects tissue cellularity and cell membrane
Fig. 6. A huge myxoid liposarcoma in the posterior muscular compartment of the thigh. (A) Sagittal short tau inversion recovery (STIR) image. The tumor looks like a cystic lesion on the STIR sequence, but (B) axial T1-weighted fat suppression postcontrast image shows contrast enhancement. (C) Axial ADC map. The tumor tissue has facilitated diffusion on the ADC map, with PIDC = 2.56 × 10⁻³ mm²/s, probably because of the myxoid matrix in the extracellular space. These types of tumors will have significantly higher ADC and PIDC values than nonmyxoid malignant solid tumors. (D) On histologic evaluation, the final diagnosis was a myxoid liposarcoma (Hematoxylin-eosin [H&E], original magnification ×100).

Fig. 7. Evaluation of response to mesenchymal chondrosarcoma using DWI. (A) Axial T1-weighted fat suppression postcontrast image. There is a big mass with heterogeneous contrast enhancement located inside the muscle in the thigh. (B) Axial ADC map (before treatment). The tumor presents very low signal intensity on the ADC map (restricted diffusion) and PIDC value = 0.89 × 10⁻³ mm²/s. (C) Axial ADC map (3 months later). The tumor presents areas of intermediate to high signal intensity (facilitated diffusion) inside the tumor (red arrow) and a few areas of low signal intensity (restricted diffusion) (blue arrow) suggesting viable cells. (D) Axial ADC map (9 months later). The tumor presents high signal intensity on the ADC map (facilitated diffusion) and PIDC value = 2.8 × 10⁻³ mm²/s suggesting good response to the treatment.
integrity, which complements the morphologic information obtained by conventional MR imaging. Thus, the data obtained from DWI must be interpreted using qualitative and quantitative approaches.

Qualitative analysis is achieved via visual assessment of the relative tissue signal attenuation of both the DW image and the ADC parametric map. The visual assessment of DW image enables tissue characterization based on differences in water diffusion and is performed by observing the relative attenuation of the signal intensity of images obtained at different b values. In a heterogeneous tumor, for instance, the more cystic or necrotic fraction of the tumor will show greater signal attenuation on high-b value images because water diffusion is less restricted, whereas the more cellular solid tumor areas will continue to show a relatively high signal intensity (Fig. 8).

By contrast, on the ADC parametric map, visual assessment reveals a trend opposite to that of DW images: areas of restricted diffusion in highly cellular areas appear as low signal intensity areas compared with less cellular areas, which have a higher signal intensity (see Fig. 5). Quantitative analysis is performed by calculating the conventional ADC value and/or perfusion-insensitive diffusion coefficient (PIDC) value. The conventional ADC value is calculated using a biexponential function from DWI, which includes low b values \((b = 0–600 \text{ s/mm}^2)\), or can be obtained alternatively by drawing regions of interest (ROIs) on the ADC map. However, an exponential function fitted only through the high b values \((b = 300, 450, \text{ and } 600\text{s/mm}^2)\) can be used to describe the PIDC value. This measurement excludes the initial reduction of signal intensity that is probably caused by vascular capillary perfusion. Consequently, for large b values, perfusion effects tend to be canceled out. The PIDC map may provide more accurate information about tumor tissue cellularity by minimizing vascular contributions, which are higher in malignant tumors (Fig. 9). The two most important components of signal attenuation on DWI in soft tissue tumors are diffusion of water molecules in the extracellular space and the perfusion fraction. The latter tends to be higher in malignant tumors than in benign tumors and has more influence on the ADC values in malignant soft tissue tumors than in benign tumors. Based on this, the PIDC value is routinely calculated to differentiate benign from malignant solid soft tissue tumors, considering that the size of the extracellular space is the most important component influencing this measurement in soft tissue tumors.

To maximize lesion visualization and characterization, diffusion-weighted MR imaging should be performed with sufficient degrees of diffusion weighting (by appropriate choices of b values), with consideration given to the anatomic region, tissue composition, and pathologic processes, which may require the customization of DW MR imaging protocols for different tumor types and locations. Indeed, in the MSK system, the geometric parameters of the imaging sequence must be flexible in terms of image positioning and field of view (FOV) to compensate for the great variety of tumor shapes and sites in the extremities and trunk.

Several types of DW sequences have been described (Table 1). The range of imaging techniques includes conventional spin-echo (SE) and stimulated echo, fast SE, gradient-echo (eg, steady-state free precession), echo planar imaging (EPI), and line scan diffusion imaging. Each of these techniques has its advantages and limitations. The SE method has been studied extensively in phantom experiments, animal models, and brain imaging and allows for a precise

![Fig. 8](image-url)  
Fig. 8. (A–E) Signal attenuation of a heterogeneous tumor, with necrotic portion on axial diffusion images with different b values. The more cystic or necrotic fraction of the tumor (long arrows) shows greater signal attenuation on high—b value images because water diffusion is less restricted, whereas the more cellular solid tumor areas (arrowhead) will continue to show relatively high signal intensity.
calculation of the ADC value. The disadvantages of the SE method are long acquisition times and vulnerability to motion artifacts. The most commonly used acquisition strategy for DWI is single or multishot EPI because of its efficiency in terms of scan time. The rapid acquisition of this technique makes it less sensitive to patient motion while allowing for large volume coverage. EPI sequences usually achieve a comparably high signal-to-noise ratio. However, echo planar (EP) DW images are prone to artifacts, particularly magnetic susceptibility artifacts, especially at tissue interfaces such as those encountered between air and soft tissue or bone and soft tissue. The EP DW images are also prone to geometric distortions created by eddy currents, particularly in large FOVs.

There are some practical aspects to be considered at the workstation when analyzing soft tissue tumors. First, depending on whether the tumor being evaluated is solid, cystic, or necrotic, there are some technical differences concerning the placement of the ROI for quantitative analysis. On predominantly solid tumors, the ROI must be placed in the most solid and homogeneous portion of the lesion, as selected from corresponding morphologic imaging, and cystic and necrotic areas should be avoided. The evaluation of cystic and necrotic lesions must be performed differently, taking into account the tumor content.

**CLINICAL APPLICATION**

Multiple studies have described the potential application of DWI in tumor detection, characterization, and assessment of treatment response. First, the authors emphasize the usefulness of this technique.
in tumor characterization, particularly in differentiating benign from malignant MSK tumors.

DWI has previously been used to differentiate benign from malignant soft tissue tumors by analyzing perfusion-corrected DW MR images, and a significant difference between the true diffusion coefficients of benign and malignant tumors was found \( P < .05 \).\(^8\) However, this study also noted that not all benign tumors have a large extracellular space and not all malignant soft tissue tumors are more cellular than benign soft tissue tumors.

The authors performed a study between January 2006 and August 2007, which was presented at the meeting of the Radiological Society of North America, 2007, in which 44 patients with MSK tumors (Table 2) with no previous surgical procedures or adjuvant treatment underwent MR examination, and the lesions were biopsied. The exclusion criteria were lesions with classic appearances on MR images (lipomas, hemangiomas, ganglions, and synovial cysts) and highly necrotic lesions surrounded by edema because edema likely contaminates the tumor tissue and consequently increases the diffusion coefficient value. Qualitative (ADC map) and quantitative analyses (PIDC value) of these tumors were obtained. A significantly increased PIDC value was obtained in benign tumors \((1.67 \pm 0.18) \times 10^{-3} \text{ mm}^2/\text{s}\) compared with malignant tumors \((1.07 \pm 0.46) \times 10^{-3} \text{ mm}^2/\text{s}\), \( P = .0011 \). These findings are consistent with previous work (Fig. 10).\(^8\)

A type of border for PIDC values of approximately \(1.1 \times 10^{-3} \text{ mm}^2/\text{s}\) was observed, which separated malignant from benign solid tumors. Together with morphologic characteristics analyzed using conventional MR imaging, this border has been useful in differentiating these tumors in the authors’ clinical practice.

Based on the literature and their own clinical routine, the authors discuss the DWI characteristics of various types of MSK tumors.

### Myxoid Tumors

In the authors’ study, among benign and malignant tumors, the highest PIDC values were obtained from myxoid tumors (myxoma, myxoid liposarcoma, and low-grade myxofibrosarcoma), with a mean PIDC value of \(2.92 \times 10^{-3} \text{ mm}^2/\text{s}\). These values reflect the high mucin and low collagen contents of the tumor, representing a lesion composed of a large amount of water, which has been confirmed by histologic analyses.\(^7\) Many investigators have observed that the diffusion coefficients of these tumors are higher than those of nonmyxoid tumors because the myxoid matrix influences the diffusion coefficient in both benign and malignant soft tissue tumors.\(^5,7,8,18\) Maeda and colleagues\(^7\) concluded that ADC values overlap greatly between benign and malignant soft tissue tumors, so these values might not be useful for differentiating these tumors. Consequently, myxoid tumors, particularly myxoid liposarcomas, should be considered the main diagnostic hypothesis whenever an MSK tumor with the noncontrast conventional MR imaging characteristics of a cystic lesion is encountered and in which the contrast-enhanced MR images demonstrate a solid lesion and the DWI analyses show high PIDC values with facilitated diffusion on the ADC map.

### Table 2

<table>
<thead>
<tr>
<th>Malignant Tumors (n = 21)</th>
<th>Benign Tumors (n = 23)</th>
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</thead>
<tbody>
<tr>
<td>Malignant fibrohistiocyтома</td>
<td>1</td>
</tr>
<tr>
<td>Nondifferentiated sarcoma (high grade)</td>
<td>3</td>
</tr>
<tr>
<td>Myxoid liposarcoma (low grade)</td>
<td>1</td>
</tr>
<tr>
<td>Myxofibrosarcoma (low grade)</td>
<td>1</td>
</tr>
<tr>
<td>PNET</td>
<td>1</td>
</tr>
<tr>
<td>Lymphoma non-Hodgkin</td>
<td>2</td>
</tr>
<tr>
<td>Clear cell sarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Metastasis (prostate, stomach)</td>
<td>2</td>
</tr>
<tr>
<td>Ewing sarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Osteosarcomas</td>
<td>3</td>
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<tr>
<td>Leiomyosarcoma</td>
<td>1</td>
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<tr>
<td>Epithelioid sarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Synoviosarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Ossificans myositis</td>
<td>1</td>
</tr>
<tr>
<td>Benign schwannoma</td>
<td>2</td>
</tr>
<tr>
<td>Calcified fibrous tumor</td>
<td>1</td>
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<tr>
<td>Hematoma (chronic)</td>
<td>1</td>
</tr>
<tr>
<td>Neurofibroma</td>
<td>2</td>
</tr>
<tr>
<td>Myxoma</td>
<td>1</td>
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<tr>
<td>Benign fibrous histiocytoma</td>
<td>1</td>
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<tr>
<td>Benign leiomyoma</td>
<td>1</td>
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<tr>
<td>Desmoid tumor</td>
<td>7</td>
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<tr>
<td>Hemangioma</td>
<td>4</td>
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<tr>
<td>Fibrous dysplasia</td>
<td>1</td>
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<tr>
<td>Giant cell tumor</td>
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Abbreviation: PNET, primitive neuroectodermic tumor.
Myxoid liposarcomas account for 50% of all liposarcomas. Histologic evaluation has demonstrated that these tumors contain less than 10% mature fat, which accounts for their low signal intensity on T1-weighted sequences and differentiates them from the high signal intensity encountered in other liposarcomas. From August 2007 until the present, the authors have performed quantitative and qualitative DWI analyses of several myxoid liposarcomas, and all of them demonstrated high PIDC values (mean PIDC value $= 2.82 \times 10^{-3}$ mm$^2$/s) and high facilitated diffusion on the ADC map. An understanding of the MR image appearances and DWI characteristics of these tumors may permit it to be considered in the differential diagnosis of the indeterminate soft tissue mass (Fig. 11).

Small Round Blue Cell Tumors

Small round blue cell (SRBC) tumors are a group of undifferentiated aggressive embryonal tumors, which include neuroblastoma, rhabdomyosarcoma, non–Hodgkin lymphoma, and the Ewing family of tumors. These tumors have similar histologic features and immunochemistry, so alternative techniques are required to diagnosis them. Accurate diagnoses of these cancers is critical for the correct administration of therapy and for avoiding unnecessary patient procedures. At present, there is no readily available tool for real-time diagnosis.

Malignant lymphomas have characteristically low ADC values in the brain, head and neck, and retroperitoneal regions. Nagata and colleagues have shown that soft tissue tumors have this property as well. Because of their high cellularity and nucleocytoplasmic ratio, lymphomas have a high signal intensity on DW images. In addition, lymphomas have lower ADC values than other tumor types in different body regions (Fig. 12). In the authors’ experience, these tumors also tend to have lower PIDC values and restricted diffusion on the ADC map than other malignant MSK tumors (Fig. 13).

The authors studied 15 patients with histologically proven SRBC soft tissue and bone tumors (trunk and extremities) and 15 patients with malignant non-SRBC (NSRBC) tumors with no previous surgical procedures or adjuvant treatment. All the patients underwent MR examination, and lesions were biopsied (Table 3). Malignant NSRBC tumors had significantly increased PIDC values (mean PIDC $= [0.98 \pm 0.21] \times 10^{-3}$ mm$^2$/s) when compared with SRBC tumors (mean PIDC $= [0.64 \pm 0.18] \times 10^{-3}$ mm$^2$/s). In addition, it was observed that SRBC tumors tend to contain tissue with a relatively uniform population of SRBCs, which have less extracellular space and typically smaller PIDC values than other NSRBC malignant tumors. In conclusion, in the differential diagnosis of a tumor with restricted diffusion on the ADC map and very low PIDC value, SRBC tumors should be the main diagnostic hypothesis. However, this conclusion must be corroborated by morphologic characteristics obtained using conventional MR imaging and other imaging methods.
Fibroblastic/Myofibroblastic and Fibrohistiocytic Tumors

Of the soft tissue tumors, benign fibrous and fibrohistiocytic tumors are the most commonly encountered tumors in clinical practice and are seen in all age groups.2 These tumors usually have typical morphologic characteristics on conventional MR imaging. For example, MR imaging findings in aggressive fibromatosis typically include bands of low signal intensity across all sequences and uniform to moderate contrast enhancement after gadolinium administration, but sometimes a benign lesion can be misdiagnosed as a malignant tumor (Fig. 14).25

In a study that the authors conducted between January 2006 and January 2008, 21 patients with histologically proven fibroblastic/myofibroblastic and fibrohistiocytic soft tissue tumors (trunk and extremities), who had received no previous adjuvant treatment, underwent MR examination. In accordance with the World Health Organization classification, tumors were classified as benign (n = 5), intermediate (n = 9), or malignant (n = 8). The mean PIDC value of benign/intermediate tumors (mean ± standard deviation [SD] = [1.56 ± 0.25] × 10^{-3} mm²/s) was significantly different from that of malignant tumors (mean ± SD = [0.89 ± 0.15] × 10^{-3} mm²/s) (P<.001) (Fig. 15).

It was also found that there was no significant difference (P>.01) between the mean PIDC values of benign and intermediate tumors. Benign and intermediate tumors presented with facilitated diffusion, whereas malignant tumors presented with restricted diffusion on the ADC map. When used alongside conventional MR imaging, these parameters are useful in the differential diagnosis of an indeterminate mass

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**Fig. 11.** Follow-up examinations of two different patients after myxoid liposarcoma surgery on the hip. (A, C) Axial T1-weighted fat suppression contrast-enhanced images. (B, D) Axial ADC map. There are two solid nodules on the surgical site in (A, C; arrows) with contrast enhancement. Analyzing the ADC map, both lesions have facilitated diffusion (B, D; arrows), but the PIDC value of the tumor in (D) is 3.1 × 10^{-3} mm²/s and in (B) is 1.9 × 10^{-3} mm²/s. The histopathologic analysis showed tumoral recidive in (D) and postsurgical neuroma in (B). The myxoid tumor had very facilitated diffusion with a PIDC more than 2.5 × 10^{-3} mm²/s.

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with morphologic characteristics of a fibrous tissue tumor (Fig. 16).

**Necrotic Lesions**

Necrotic masses can either be malignant tumors or benign masses, such as abscesses and/or hematomas. Therefore, care must be taken during imaging to differentiate a hemorrhagic malignant soft tissue tumor from a hematoma. Previous work concluded that it is possible to differentiate CEHs from malignant soft tissue tumors using DWI.\(^9\) The authors think that it is not possible to differentiate abscesses and/or hematomas from malignant tumors using PIDC values from the solid parts of tumors. This inability to differentiate is probably because of the edema that surrounds necrotic lesions, which likely contaminates the tumor tissue. Previous reports have shown that DWI analysis of brain abscesses usually reveals a markedly reduced ADC in the necrotic center.\(^26,27\) For this reason, ADC maps are of great value in distinguishing abscesses from neoplasms. Neoplasms have more facilitated diffusion compared with abscesses, which tend to have more restricted diffusion in their necrotic portions. In addition, the authors have observed that highly malignant tumors tend to have more restricted diffusion on the ADC map in the solid wall of the tumor, which has higher cellularity. On the other hand, acute and subacute hematomas have typical morphologic characteristics on conventional MR imaging and present with restricted diffusion on the ADC map in the central portion of the lesion. Therefore, the authors think that it is possible to differentiate abscesses and hematomas from malignant tumors using the ADC value from the necrotic portion of the tumor (Fig. 17).

**Cartilaginous Lesions**

Previous reports indicate that malignant cartilaginous tumors have higher ADC values than benign tumors.\(^18\) The authors have found high PIDC values and facilitated diffusion on the ADC map in benign and malignant cartilaginous tumors, likely because of the high chondroid matrix content of these tumors (Fig. 18).

The authors have observed only one type of cartilaginous tumor, the mesenchymal chondrosarcoma, with a low PIDC value \((0.89 \times 10^{-3} \text{ mm}^2/\text{s})\) and restricted diffusion on the ADC map (see Fig. 7). Histopathologically, this tumor has
cellular zones composed of undifferentiated small cells and chondroid zones with a bimorphic appearance that is virtually pathognomonic in most cases. However, the usefulness of diffusion in the diagnosis of cartilaginous tumors requires further validation.

**Giant Cell Tumors**

Nagata and colleagues found low ADC values in giant cell tumors (GCTs) of the tendon sheath and diffuse-type GCTs. GCTs of the tendon sheath contain histiocytic mononuclear cells, multinucleated giant cells, xanthoma cells, and collagenous strands. The diffuse-type GCT is characterized by synovial villonodular proliferation with hemosiderin pigmentation and stromal infiltration of histiocytes and giant cells. In bone GCTs, histologic features include a moderately vascularized network of round, oval, or spindle-shaped stromal cells and multinucleated giant cells. These characteristics probably contribute to reducing the extracellular space and the concomitant decrease in ADC value. In the authors’ experience, soft tissue and bone GCTs tend to have low PIDC values and restricted diffusion on the ADC map. These

![Fig. 13.](image)
parameters could be useful in the diagnosis of these tumors and in the management of local recurrence after surgery by allowing for the differentiation of postsurgical fibrosis from reciditive tumor (Fig. 19).

**MALIGNANT BONE DISEASE**

DWI performed regionally or as whole body imaging has been shown to have a high diagnostic accuracy for the identification of bone metastases.
when combined with conventional MR imaging. Goudarzi and colleagues\(^6\) concluded that DWI could visualize more metastatic lesions and detect smaller metastases that PET or bone scintigraphy. The detection of bone metastasis is crucial for cancer staging and to determine the appropriate treatment strategy.\(^6\)

Acute vertebral collapse is a common clinical problem in elderly patients and usually results from osteoporosis or metastasis.\(^{16}\) Previous reports have concluded that both qualitative and quantitative DW MR imagings are effective additional tools for differentiating malignant from benign vertebral fractures.\(^{16}\)

In osteosarcoma and Ewing sarcoma, the degree of necrosis after a course of induction chemotherapy is a prognostic factor for an event-free survival.\(^{34}\) Consequently, a noninvasive

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Fig. 15. Fibrous and fibrohistiocytic tumors. Tumor characterization. (A, D) Coronal T1-weighted fat suppression contrast-enhanced images and (B, C) axial ADC maps. There are two different fibrous tumors with similar characteristics on conventional MR imaging (A, D). The tumor on the left presents facilitated diffusion in (B, arrow) and a PIDC \(= 1.65 \times 10^{-3} \text{ mm}^2/\text{s}\), suggesting benign tumor (desmoid tumor). The tumor on the right presents restricted diffusion on the ADC map (C, arrow) and PIDC \(= 0.89 \times 10^{-3} \text{ mm}^2/\text{s}\) (malignant fibrous histiocytoma).

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Fig. 16. Two similar painless palpable masses in the elbow of a 5-year-old boy on the right and a 7-year-old girl on the left. (A) Coronal and (D) axial T1-weighted images show intramuscular tumors isointense to muscle (A, D; arrows). (B, E) Axial T1-weighted contrast-enhanced images show homogeneous contrast enhancement in both tumors (B, E; arrows). (C, F) Sagittal ADC maps show that the tumor on the left presents facilitated diffusion (C, circle) and its PIDC \(= 1.6 \times 10^{-3} \text{ mm}^2/\text{s}\) (desmoid tumor) and the tumor on the left presents restricted diffusion (F, circle) and its PIDC \(= 0.68 \times 10^{-3} \text{ mm}^2/\text{s}\) (rhabdomyosarcoma).
method of assessing the presence of intracellular necrosis and viable cells is crucial for the evaluation of treatment response (Fig. 20).

In terms of osteosarcomas, tumor size does not diminish significantly with successful chemotherapy because therapy has a limited effect on the mineralized matrix of the tumors. In these tumors, the treatment response is considered effective if more than 90% of the tumor cells show necrosis histologically. The use of conventional MR imaging is limited to the assessment of tumoral viability because in T2-weighted images, both viable and necrotic tumor tissues show high signal intensities. Morphologic changes induced by chemotherapy may be associated with hemorrhage, necrosis, edema, and inflammatory fibrosis without specific MR imaging patterns (Fig. 21).
Considering that the ADC values of viable tumor tissue and tumor necrosis are significantly different, DWI could be used to evaluate treatment response by analyzing changes in the cellularity of the tumor with time. Previous studies concluded that DWI is capable of providing earlier information about therapeutic results than those obtained from conventional MR imaging, considering that cellular changes usually precede reductions in tumor size. Previous reports concluded that DWI can be useful for evaluating the chemotherapeutic response of osteosarcomas and is considered to be a promising method for monitoring the therapeutic response of primary bone sarcomas.

**MONITORING TREATMENT RESPONSE**

The use of conventional MR imaging on follow-up of treated MSK soft tissue masses is traditionally based on anatomic approaches, such as measurements of tumor size and the degree of contrast enhancement. However, anatomic imaging for this purpose has significant limitations, including the presence of tumors that cannot be measured, poor measurement reproducibility, and mass lesions that persist after therapy. Because cellular death and vascular changes in response to treatment precede changes in lesion size, functional imaging such as DWI could provide earlier identification of patients with a poor treatment response or of those with tumor recurrence. Therefore, DWI could provide an opportunity to adjust individual treatment regimens more rapidly, sparing patients the unnecessary morbidity, expense, and delays in the initiation of effective treatment. Previous reports described an effective anticancer therapy that resulted in tumor lysis, loss of membrane integrity, increased extracellular space, and increase in water molecule diffusion. All these changes resulted in an increase in PIDC values.

Preclinical and clinical studies have reported on the usefulness of DWI as a sensitive biomarker capable of detecting early cellular changes in treated tumors that precede morphologic response. For instance, clinical studies
of gliomas, primary and metastatic liver cancers, and breast cancers have demonstrated an increase in ADC values in response to successful treatment.

In MSK tumors, several investigators have also demonstrated increasing ADC values with successful therapy (Fig. 22).

In the study by Oka and colleagues, which evaluated the chemotherapeutic response of osteosarcomas using the minimum ADC value in the solid components of tumors, a significant difference was demonstrated between patients with a good response to chemotherapy and those with a poor response.

In Fig. 20, evaluation of response to Ewing sarcoma treatment by using DWI in a 28-year-old man. (A) Axial T1 contrast-enhanced image. (B) Axial ADC map. A huge tumor in the scapular region with heterogeneous contrast enhancement (A), restricted diffusion on the ADC map (B, arrow), and PIDC = 0.61 × 10^{-3} \text{mm}^2/\text{s} in the pretreatment phase. (C) Axial T1 contrast-enhanced image. (D) Axial ADC map. The tumor got reduced after treatment (8 months later), with heterogeneous contrast enhancement (C), facilitated diffusion on the ADC map (D, arrow), and PIDC = 2.6 × 10^{-3} \text{mm}^2/\text{s}, suggesting good response to the treatment. The histopathologic analysis showed more than 90% of necrosis, which indicates a good response to treatment.

In Fig. 21, classic osteosarcoma in a 12-year-old boy. Evaluation of treatment response. (A, C, E) Sagittal T1-weighted fat suppression contrast-enhanced images. (B) Axial ADC map and (D, F) sagittal ADC map. Here there is a case of a huge osteosarcoma in the distal femur, with heterogeneous contrast enhancement before treatment (A) and areas of restricted diffusion in the ADC map (B) with PIDC = 0.89 × 10^{-3} \text{mm}^2/\text{s}. During the treatment, the tumor grew (C, E) and presented restricted diffusion in the ADC map (D, F) in the peripheral portion (F, short arrow) with PIDC = 0.87 × 10^{-3} \text{mm}^2/\text{s} and facilitated diffusion in the central part (F, long arrow) suggesting necrosis. There were no changes in the ADC map and in the PIDC value in the peripheral portion of the lesion, suggesting viable cells and consequently poor response to the treatment. The histopathologic analysis showed Huvos grade II necrosis (G, H&E, original magnification ×40).
DWI is also being used to assess the activity of residual disease after treatment and to detect early recurrence at a time when a salvage therapy might still be implemented (Fig. 23).37

Indeed, the differentiation of posttherapeutic soft tissue changes and residual or recurrent tumor is a common diagnostic problem because these abnormalities have the same appearance in morphologic imaging. Specifically, these pathologies are characterized by a high signal intensity on T2-weighted and short tau inversion recovery images and a low signal intensity on T1-weighted SE images.48

Baur and colleagues48 evaluated the signal characteristics of recurring solid soft tissue tumors and posttherapeutic soft tissue changes with DWI (Fig. 24).

The investigators demonstrated that posttherapeutic soft tissue changes showed a significantly higher diffusion than viable recurrent tumors. This is an expected finding because solid tumors demonstrate high cellularity and intact cell membranes, whereas as antineoplastic therapy progresses successfully the cellularity within the tumor decreases and cell membranes lose their integrity.17

Fig. 22. Non–Hodgkin lymphoma in the tibia in a 27-year-old man. Before treatment (A–D). (A) Sagittal STIR MR image shows a large heterogeneous hyperintense intraosseous tumor extending in to the soft tissues (arrows). (B) Axial T1-weighted fat-suppressed image after contrast injection shows solid enhancing mass extending to the soft tissues (arrows). (C) Axial DWI shows hyperintense mass (arrows). (D) ADC map shows restricted diffusion of the tumor (arrows) and PIDC = 0.62 × 10⁻³ mm²/s. Monitoring chemotherapy and radiotherapy 8 months later (E–H). (E) Sagittal T1-weighted fat-suppressed image after contrast injection shows heterogeneous enhancing intraosseous tumor that does not extend in to the soft tissues (arrows). (F) Axial T1-weighted fat-suppressed image after contrast injection shows heterogeneous enhancing intraosseous lesion (arrows). (G) Axial DWI shows hyperintense mass (T2 effect) (arrows). (H) ADC map shows facilitated diffusion of the tumor (arrows) and PIDC = 2.2 × 10⁻³ mm²/s, suggesting tumor necrosis and good response to treatment.
WHOLE BODY DW MR IMAGING

During the past decade, technological advances have led to the development of whole body MR imaging as well as whole body DW MR imaging. Now, within a single examination, it is possible to combine anatomic and functional information in whole body evaluation.49

Until recently, DWI performed with free breathing was considered to be impossible, because it was assumed that respiratory motion would lead to loss of DW image contrast.49 However, in 2004, Takahara and colleagues50 reported on the concept of DW whole body imaging with background body signal suppression (DWIBS). This technique intentionally uses free-breathing scanning rather than breath holding or respiratory triggering to visualize moving visceral organs and their lesions.51

DWIBS can be performed on most modern MR imaging scanners and is conducted in such a way as to suppress the signal of most tissues while highlighting potential malignancies or suspect lymph nodes in gray-scale inverted reformatted reconstructions.52 The technique is characterized by heavy diffusion weighting (b values of up to 1000–1500 s/mm² are applied) and the application of excellent fat suppression in order to optimize background body signal suppression and improve lesion conspicuity.49

Several clinical applications for DWIBS are emerging in the literature, especially for oncological imaging.53–55 Indeed, whole body DWI enables visualization of various primary and metastatic tumors exhibiting an impeded diffusion throughout the entire body.49 This modality may also be useful in the detection of relatively small...
lesions, for the identification and characterization of lymph nodes, and for monitoring response to cancer therapy.\textsuperscript{51} Chen and colleagues\textsuperscript{53} concluded that whole body DWI with ADC mapping can potentially be used for lesion detection. However, the true utility of whole body imaging requires further validation.

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