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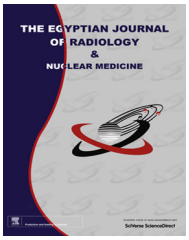

ORIGINAL ARTICLE

Value of diffusion weighted MRI in differentiating benign from malignant bony tumors and tumor like lesions

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KEYWORDS

Bone;
Tumors;
Tumor-like;
Diffusion;
Functioning MRI

Abstract *Aim of the work:* To assess the value of diffusion weighted MRI in the differentiation of benign and malignant bony tumors and tumor like lesions.
Patients and methods: This study included 100 patients (66 males and 34 females). Their ages ranged between 4 and 65 years and the mean age was 31.3 years. The patients were referred to MRI unit from orthopedic surgery and radiotherapy departments and oncology center in Mansoura University hospital. These patients were selected on clinical bases indicating or suggesting presence of bony tumors or tumor-like lesions as a primary diagnosis (e.g. swelling or signs of inflammation). The commonest clinical presentations were pain ($n = 71$) and swelling ($n = 61$). Other presentations included limitation of movement ($n = 20$), back pain ($n = 21$) and fever ($n = 20$). More than one symptom may be present in one patient. Patients included in our study were classified according to the pathological and radiological criteria into three groups: Benign bone tumors (14 patients); malignant bone tumors (51 patients); tumor-like lesions (35 patients).
Results: DWI with measurement of ADC values helped in the differentiation of benign and malignant bone tumors, as malignant bone tumors have mean ADC values less than (1.31×10^{-3}) mm^2/s; while benign bone tumors have mean ADC values 1.43×10^{-3} mm^2/s. Also, mean ADC values helped in differentiating malignant from inflammatory bony lesions as well as cystic from solid bony lesions.
Conclusion: DWI has been proven to be highly useful in the differentiation of benign, malignant bone tumors and tumor like bony lesions. Measurement of ADC values improves the accuracy

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of the diagnosis of bone tumors and tumor like lesions. Moreover, measurement of ADC values can be used in the follow up of tumors and their response to therapy.

1. Introduction

All imaging methods play a role in diagnosis of bone tumors. Plain radiography is the primary imaging modality to suggest the diagnosis and judge the nature of different bony lesions. CT is excellent for providing information about the anatomical extent of bony tumors (1).

MRI is the most sensitive imaging modality for detection of bony tumors and tumor like lesions. It is considered the gold standard for characterization of these lesions and can detect occult intra-medullary lesions with negative bone scan (2). Moreover, MRI is ideal for imaging bone marrow because of its superior ability to produce high resolution images with exquisite soft-tissue contrast (3).

Improvement of treatment and outcome of bone tumors require development of diagnostic tools that can help in differentiation between benign and malignant lesions in a non invasive and reliable manner (4). Diffusion-weighted magnetic resonance imaging (DWI) is a recent addition to the MR sequences conventionally employed. DWI provides qualitative and quantitative functional information concerning the microscopic movements of water at the cellular level (5).

The application of DW-MRI in bone marrow is today an established examination technique that provides a unique contrast and that can help in the detection of bone-marrow pathologies and the differentiation of benign and malignant bone-marrow lesions. It has been applied particularly successful in DWI studies of vertebral lesions and of vertebral compression fractures (6).

Literature has shown value of DWI for assessment of post-therapeutic response in primary bone tumors such as osteogenic and Ewing's sarcoma (5). Several studies have shown that there are significant differences in ADC values between patients who responded to treatment (and had higher ADC tumor values) and those who had no response (7,8). The clear value of the ability of DWI to highlight post-therapeutic responders versus non-responders is particularly pertinent as

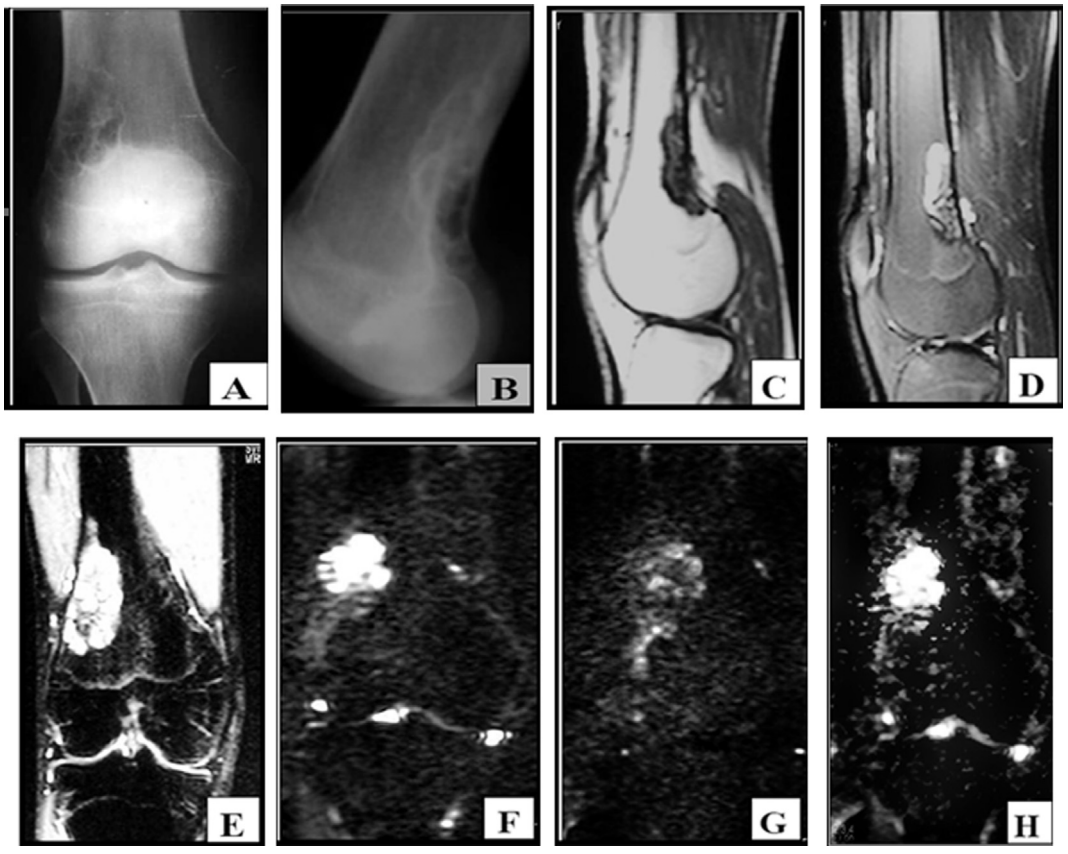

Fig. 1 Non ossifying fibroma: male patient, 22 years old complaining of right knee pain: (A and B) plain X-ray: AP and lateral views of the right distal femur showing irregular lobulated osteolytic lesion having sclerotic margins. (C) Sagittal T1WI showing the low SI of the lesion with surrounding signal void wall of sclerosis. (D and E): Sagittal T2 fat suppression and coronal STIR images showing the high SI of the lesion, its lobulated pattern and the signal void sclerotic wall. (F and G): diffusion-weighted images at different *b* values (0 and 1000): showing non restricted diffusion at *b* value 1000. (H) ADC map showing the mean ADC value about 1.27×10^{-3} mm^2/s.

Table 1 Showing different patterns of DWI in different cases of benign and malignant bone tumors and tumor like lesions.

Type of bony lesion	No.	DWI at $b = 1000$ s/mm^2	
		Restricted (high SI)	Unrestricted (low SI)
Benign	14	–	14
Malignant	51	26	25
Tumor-like	35	5	30
Total	100	31	69

From this table we have noticed that:
All benign lesions show free diffusion.
Malignant lesions may show free or restricted diffusion.
Most of tumors like lesions show free diffusion as benign lesions.

the tumor volumes were not shown to be significantly different between the two groups (9).

2. Patients and methods

2.1. Patient selection and clinical assessment

This study included 100 patients (66 males and 34 females). Their ages ranged between 4 and 65 years, mean age 31.3 years.

The patients were referred to MRI unit from orthopedic surgery and radiotherapy departments and oncology center in Mansoura University hospital. These patients were selected on clinical bases indicating or suggesting presence of bony tumors or tumor-like lesions as a primary diagnosis (e.g. swelling or signs of inflammation). The commonest clinical presentations were pain ($n = 71$) and swelling ($n = 61$). Other presentations included limitation of movement ($n = 20$), back pain ($n = 21$) and fever ($n = 20$). More than one symptom may be present in one patient.

Patients included in our study were classified according to the pathological and radiological criteria into three groups:

(a) Benign bone tumors (14 patients).
(b) Malignant bone tumors (51 patients).
(c) Tumor-like lesions (35 patients).

2.2. Radiological assessment

(A) *Plain X-ray:* it was the initial step, carried out for the suspected region in all patients. Routine antero-posterior and lateral views were done in addition to any special views if needed, such as oblique views.

(B) *Computed tomography (CT):* CT scans were carried out for 11 patients while 14 patients had their CT study performed before they were referred to us. CT was performed in the CT unit, in radiodiagnosis department of Mansoura University hospital; using Toshiba spiral CT machine (Asteion). Axial scans were done, from above to below the level of the lesion with 5–10 mm slice thickness. Thinner slices (3 mm) were needed to assess small lesions such as the detection of the nidus of osteoid osteoma or the sequestrum of osteomyelitis. Images were reviewed using both soft tissue and bone windows.

(C) *MR examination (MR):* done for all patients ($n = 100$), using the following protocol:

Conventional MRI ($n = 100$): suitable body or surface coil was used according to the site and extent of the lesion. Slice thickness (5–10 mm), interslice gap (1–2 mm), field of view (20–40 cm) and matrix (128×256). T1WI; short TR/TE:{TR/TE = 500/14 ms. NEX = 1–2}. T2WI long TR/TE: {TR/TE = 2000–4000/30–90 ms NEX = 3}. STIR, short tau inversion recovery: {TR/TE = 1420–1680/20–40 ms, Inversion (TI) = 150}. GRE, gradient echo: {TR/TE = 400–600/20–25 ms NEX = 2.4}. Flip angle = 20–25°.

Post contrast study: multiplanar T1 fat suppression was obtained ($n = 7$), immediately after intravenous administration of Magnivest (Gadoloinium DPTA) in a dose of 0.1 mmol/kg.

Diffusion weighted MR imaging (DWI): DW images were obtained for all patients ($n = 100$). They were obtained using a multisection single shot spin echo-planar sequence (TR/TE/NEX: 2200/139MS/1) with diffusion sensitivities of b values = 0, 500 and 1000 s/mm^2. Diffusion gradients were applied sequentially in three orthogonal directions (X, Y and Z). Sections of 5 mm thickness, interslice gap of 1 mm, field of view 240–400 mm and 128×256 matrix were used for all images. Scanning time was about 120 s. The number of slices varied from patient to another, chosen in a manner that covered the entire tumor with an extra slice in each direction.

Post processing of DWI: four sets of DWIs for each section were obtained. The first 3 sets of images (trace images) corresponding to sequential application of the sensitization gradient in the X, Y and Z planes. The last set (ADC map)

Table 2 Showing different patterns of DWI and ADC values in different cases of benign tumors (14 cases).

Type of bony lesion	No.	Unrestricted (low SI) (on DWI at $b = 1000$ s/mm^2)	Solid component (Mean ADC value in mm^2/s)
Osteoid osteoma	1	1	1.36
Chondroblastoma	2	2	2.19
Osteochondroma	3	3	2.16
Enchondroma	1	1	2.11
Hemangioma	5	5	1.61
Non ossifying fibroma	1	1	1.27
Fibrous cortical defect	1	1	1.58
Total	14	14	

From this table we have concluded that:
The mean ADC value for benign chondroid tumors is about (2.15×10^{-3}) mm^2/s.
The mean ADC value for other benign tumors is about (1.43×10^{-3}) mm^2/s.

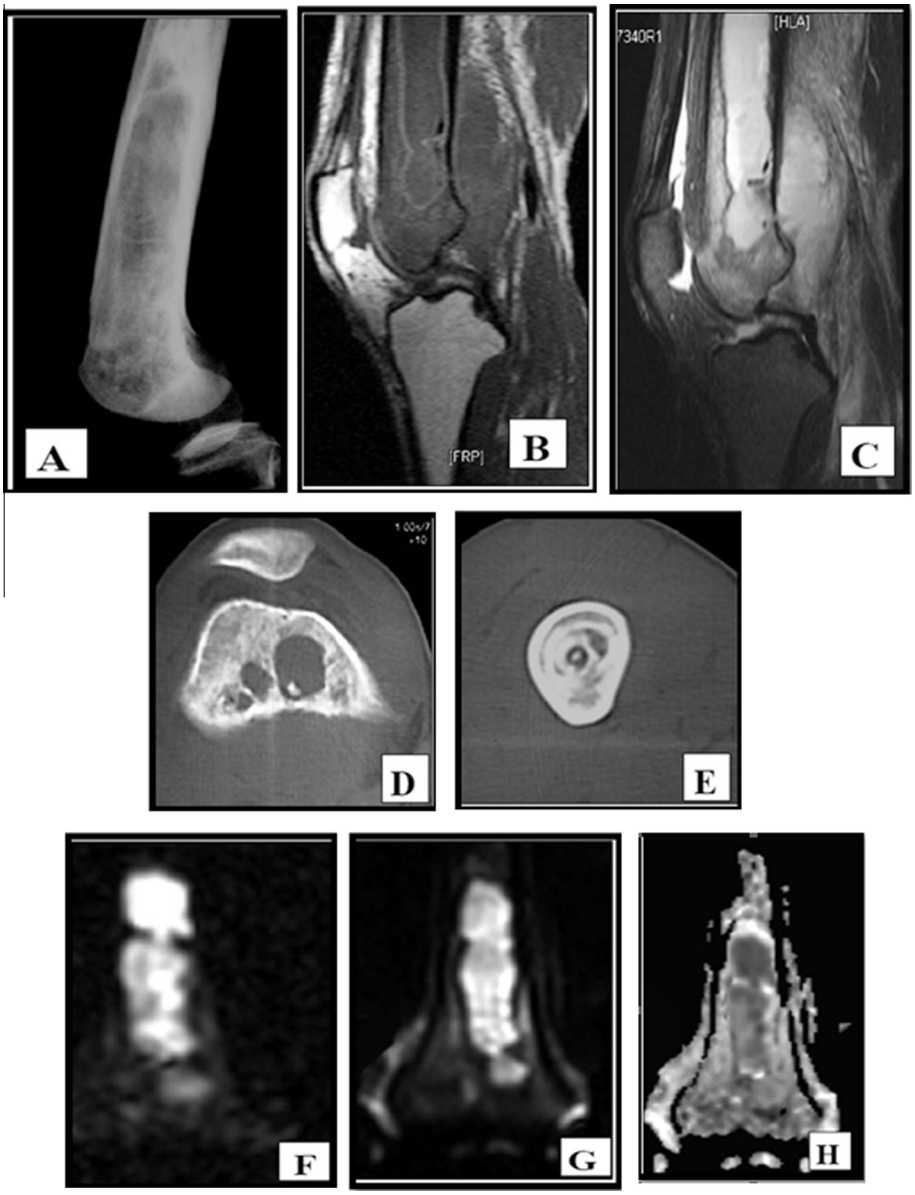

Fig. 2 Osteomyelitis: male patient aged 30 years old complaining of right lower thigh painful, swelling and fever: (A) Plain X-ray (lateral view) of the left distal femur showing an ill defined osteolytic lesion. (B) Sagittal T1WI showing the low SI of the lesion and the surrounding bone marrow. (C) Sagittal T2WI, with fat suppression showing the high SI of the lesion and the surrounding bone marrow. (D and E) Axial CT scan (bone window) showing small bony sequestra. (F and G) diffusion weighted images at *b* values (0 and 1000): showing non restricted diffusion I the peripheral parts (bone marrow edema) and high signal in the central part of the lesion (restricted diffusion). (H) ADC map showing the mean ADC value in the central part (0.9×10^{-3}) mm^2/s, while in the solid part (1.56×10^{-3}) mm^2/s.

corresponding to the average diffusion images where ADC measurement for any point or ROI can be measured. The trace images were obtained at different *b* values: 0, 500 and 1000.

Interpretation of diffusion weighted images:

1- The lesion was determined on DWI and ADC map by using the conventional MR images as a guide.
2- Signal intensity of the lesion on DWIs (b1000) is determined: either hypointense (free diffusion) or hyperintense (restricted diffusion).
3- Measurements of the apparent diffusion coefficient (ADC) were made using electronic cursor on the ADC map in different regions of interest (ROI) of the lesions and in comparable contralateral regions of normal tissue. The ADC values were expressed in $\times 10^{-3}$ mm^2/s.
4- The ROI for each lesion was placed at least 3 times, and then the mean ADC value for the lesion was calculated. Both solid parts and cystic parts (if present) of the tumors were assessed. ROI is placed the solid portion of the solid tumors and in the center of cystic lesions.

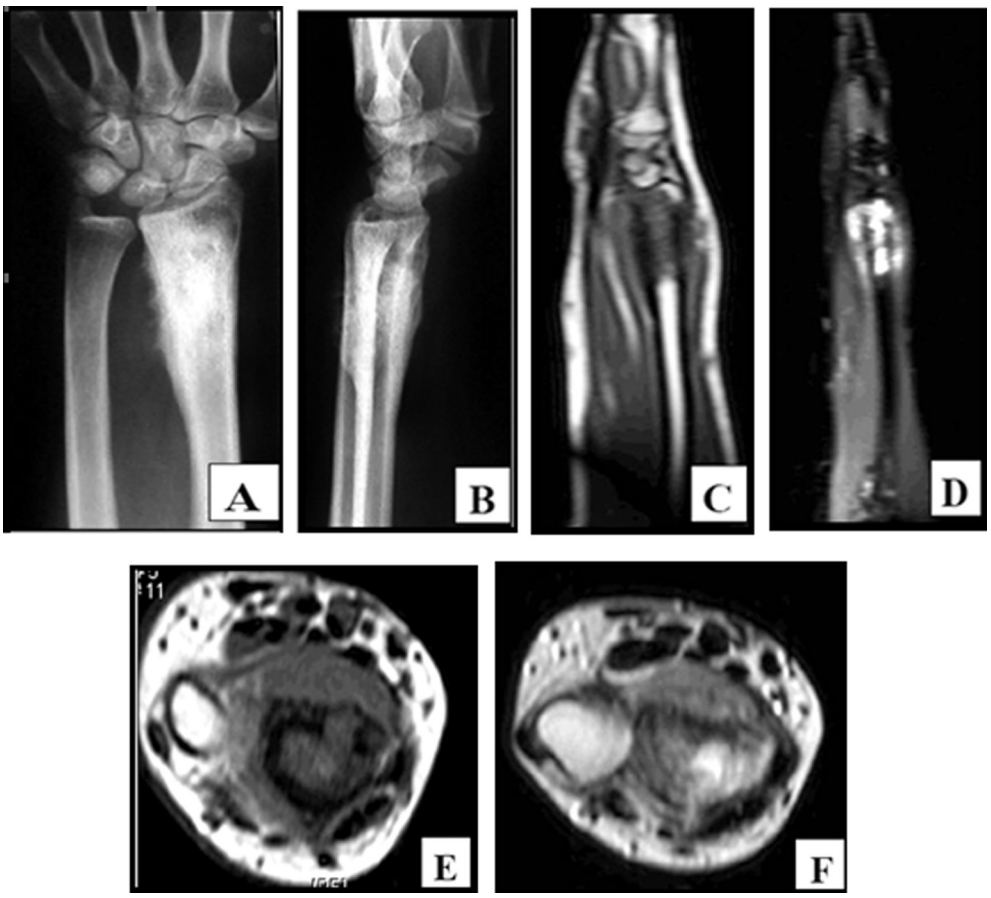

Fig. 3 Ewing's sarcoma: 21 year old female complaining of swelling and pain of the left radius: (A) Plain X-ray (AP and lateral views) of the left radius: showing diffuse sclerosis and periosteal reaction. (B and C) Sagittal and axial T1WIs showing lesion of intermediate SI and the cortical defect through which the lesion is passing outside the medullary cavity to form a soft tissue mass. (D and E) Sagittal STIR and axial T2WI showing high SI of the bony lesion and the associated soft tissue mass. (F and G): diffusion-weighted images at different *b* values (0 and 1000): showing high signal at *b* 1000 (restricted diffusion). (H) ADC map showing the mean ADC value about (0.7×10^{-3}) mm^2/s.

5- The quality of diffusion weighted images and ADC maps was evaluated, with the exclusion of non acceptable images that contained distortion or ghosting artifact.

2.3. Pathological assessment

MRI findings have been correlated with the pathological results obtained from either surgical excision or needle biopsy.

3. Results

DWI with measurement of ADC values helped in the differentiation of:

- *Benign and malignant bone tumors*, as malignant bone tumors usually have mean ADC values less than (1.31×10^{-3}) mm^2/s; while benign bone tumors have mean ADC values (1.43×10^{-3}) mm^2/s.
- *Malignant bone tumors and inflammatory bony lesions*: mean ADC values, more than (1.5×10^{-3}) mm^2/s. So, Ewing's sarcoma could be easily differentiated from osteomyelitis.
- *Cystic from solid lesions*(without the use of contrast media) as cystic lesions usually have mean ADC value more than (2×10^{-3}) mm^2/s.
- DWI by measuring ADC values can be used in the follow up of tumors and their *response to therapy* as tumor cell necrosis resulting from therapy makes diffusion more free with subsequent increased mean ADC values.
- *Chondroid tumors* usually have high ADC values (more than 2×10^{-3}) mm^2/s; with no significant differences between benign and malignant chondroid lesions.
- *Tumor like lesions:* inflammatory lesions are the commonest tumor like lesions (57%). They have high ADC values: more than $(1.5 \times 10^{-3}$ $mm^2/s)$ making it easily differentiated from Ewing's sarcoma. Cystic areas (abscesses) of untreated osteomyelitis show restricted diffusion with low ADC values due to the high viscosity of their content making water motion restricted. Cystic lesions like ABC and simple bone

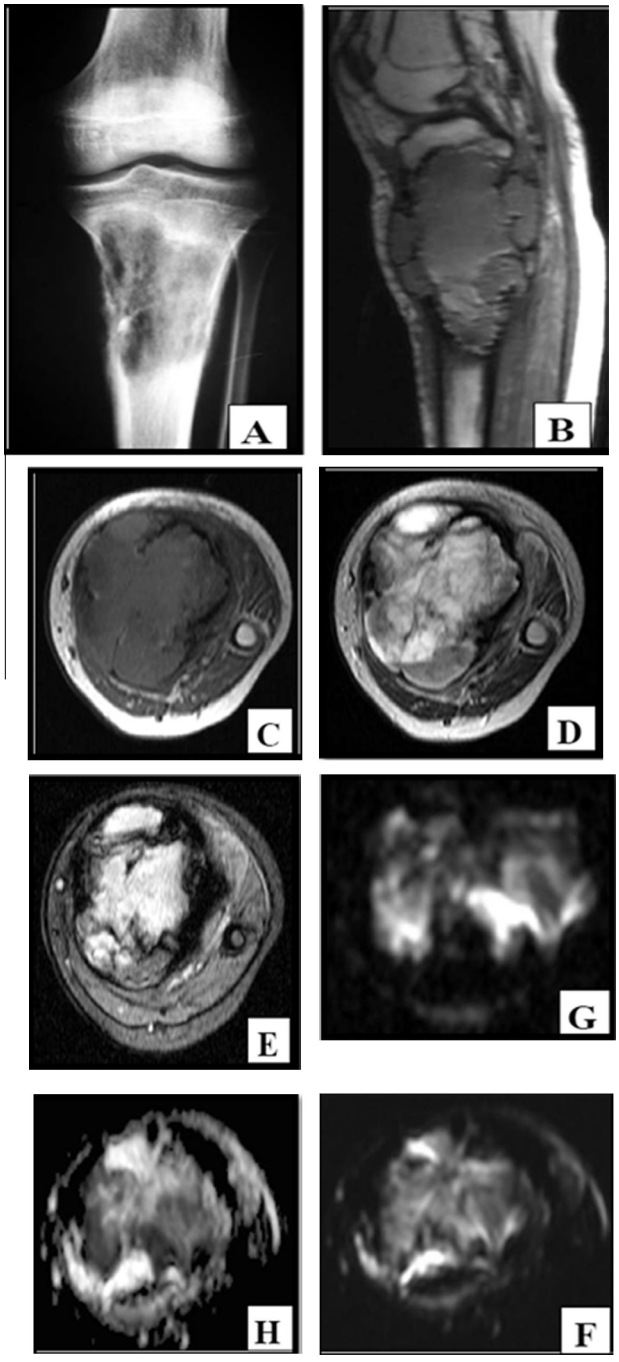

Fig. 4 Lymphoma: 17 year old male complaining of swelling and pain of the left knee: (A) Plain X-ray (AP view) of the left tibia: showing diffuse patchy sclerotic lesion mixed with osteolytic areas. (B and C) Sagittal and axial T1WIs intermediate SI of the lesion and the associated soft tissue component. (D and E) Axial T2WI and GRE images showing mixed high SI of the bony lesion and the associated soft tissue mass. (F and G): diffusion-weighted images at different *b* values (0 and 1000): showing high signal at *b* 1000 (restricted diffusion). (H) ADC map showing the mean ADC value about (1.2×10^{-3}) mm^2/s.

cysts can have high signal on DWI due to T2 shine through effect, but usually have high mean ADC values on ADC map (more than 2×10^{-3} mm^2/s).

Statistical analysis for the mean ADC values measured in the solid part of the bone tumor, revealed the following:

- There was a significant statistical difference between malignant and non malignant lesions (benign and tumor like lesions) ($P = 0.001$).
- There was no significant statistical difference between benign and tumor like lesions.
- There was significant statistical difference between malignant and tumor like lesions ($P = 0.007$).
- There was no significant statistical difference between benign and malignant lesions.
- However, after the exclusion of chondrosarcomas from malignant lesions, there was significant statistical difference between benign and malignant lesions ($P = 0.00$).

4. Discussion

The advantages of MRI permit the precise evaluation of the aggressiveness of different lesions through detection of their extent and muscle infiltration (as in malignant tumors and inflammatory lesions). So, we are in agreement with Harms and Greenway, 1992 (10); who stated that MRI is helpful in the evaluation of the aggressiveness of different lesions.

In our study we have found that, after exclusion of chondroid tumors, the ADC values of benign bony tumors ($n = 8$) ranged from 1.26 to 1.58×10^{-3} mm^2/s (Fig. 1); with the mean ADC value about (1.43×10^{-3}) mm^2/s. (Table 2). Chondroid tumors should be excluded because they have a special character where the lesions show no significant difference between ADC values calculated in benign and malignant lesions (Table 5) due to the characteristic nature of the chondroid matrix which has a high fluid content; as explained by Hayashida et al., 2006 (9,11) (Fig. 2).

Five cases of osseous hemangiomas (Fig. 5) were included in our study and they had ADC value of about 1.6×10^{-3} mm^2/s but this differs from that stated by Einarsdottir et al., 2004 (12) who found that ADC value of hemangioma was 1.10×10^{-3} mm^2/s. These results are considered relatively low for a highly vascular benign tumor, but Kim et al., 1998 (13) attributed the low ADC values in some hemangiomas to the fact that hemangioma sometimes contains fibrous tissue and thrombosis in its vascular spaces which causes reduction in its ADC values.

Inflammatory lesions (Fig. 2) are the commonest tumor-like lesions (57%) (Fig. 6). They have high ADC values $(1.5 \times 10^{-3}$ $mm^2/s)$ making it easily differentiated from Ewing's sarcoma. Cystic area (abscesses) of untreated osteomyelitis shows restricted diffusion with low ADC value due to high viscosity of its content making water motion restricted (Table 4). This is in agreement with Wong et al., 2004 (14) who stated that abscess has restricted diffusion with low ADC value due to high viscosity of its content caused by pus, inflammatory cells and granulation tissue.

In this study, ADC values of solid malignant tumors ($n = 51$) ranged from 0.6 to 2.05×10^{-3} mm^2/s with mean ADC $(1.39 \times 10^{-3}$ $mm^2/s)$ (Fig. 3). After exclusion of chondrosarcoma, all other malignant tumors will be ranged from 0.6 to 1.8×10^{-3} mm^2/s with mean ADC ($n = 48$) $(1.39 \times 10^{-3}$ $mm^2/s)$ (Table 3). This was nearly in agreement

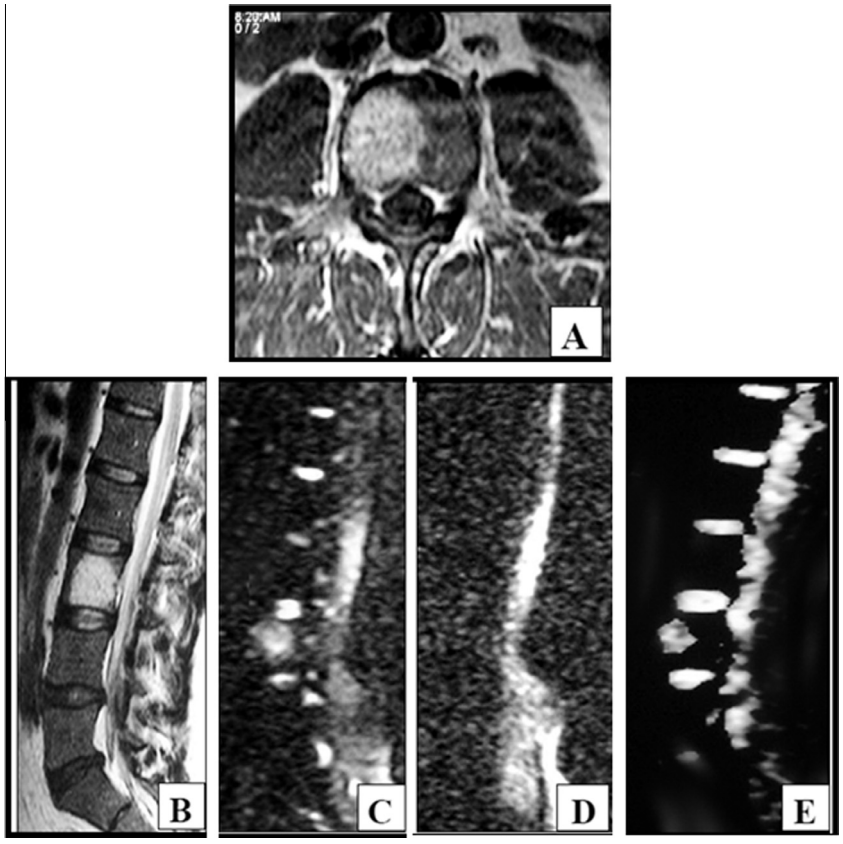

Fig. 5 Hemangioma: 17 year old male complaining of swelling and pain of the left knee: (A) Axial T1 and T2WI showing high SI of the lesion on both pulse sequences. (B and C): diffusion-weighted images at different *b* values (0 and 1000): showing complete absence of the lesion at *b* 1000 image (non restricted diffusion). (D) ADC map showing the mean ADC value about (1.4×10^{-3}) mm^2/s.

Table 3 Showing different patterns of DWI and ADC values in different cases of malignant tumors (51 cases).

Type of bony lesion	No.	Appearance on DWI at $b = 1000$ s/mm^2		Mean ADC value $\times 10^{-3}$ mm^2/s	
		Restricted (high SI)	Unrestricted (low SI)	Solid component	Cystic component
Osteosarcoma	13	5	8	1.39	–
Chondrosarcoma	3	1	2	2.05	–
Lymphoma	9	4	5	1.7	–
Ewing's sarcoma	8	4	4	1.18	2.3
Plasmacytoma	2	1	1	1.1	–
Leukemia	1	1	–	0.9	–
Multiple myeloma	1	–	1	1.44	–
Ameloblastoma	1	1	–	1.53	
Metastatic	13	9	4	1.21	
Total	51	26	25		

From this table we have concluded that:
The mean ADC value for malignant chondroid tumors is about (2.05×10^{-3}) mm^2/s.
The mean ADC value for other malignant tumors is about (1.31×10^{-3}) mm^2/s.

with Nagata et al., 2005 (15) who recommended the separation of cartilaginous tumors from other malignant tumors due to their high shooting values on ADC maps (Table 6).

In the present study, we had 9 cases of lymphoma, 4 out of them showed restricted diffusion while the remaining 5 cases showed free diffusion (Fig. 4). The mean ADC value was about 1.7×10^{-3} mm^2/s; ranging from 1.02 to 1.9×10^{-3} mm^2/s. This was not in agreement with Barboriak, 2003 (16) who reported strongly reduced ADC $(0.64 \times 10^{-3}$ $mm^2/s)$ and Guo et al., 2002 (17) who stated that lymphoma in brain had lower ADC values compared to other tumors. This high ADC and non restricted diffusion in our cases of lymphoma may be cleared out by what was mentioned by Holscher et al., 1996 (18) who stated that the two most

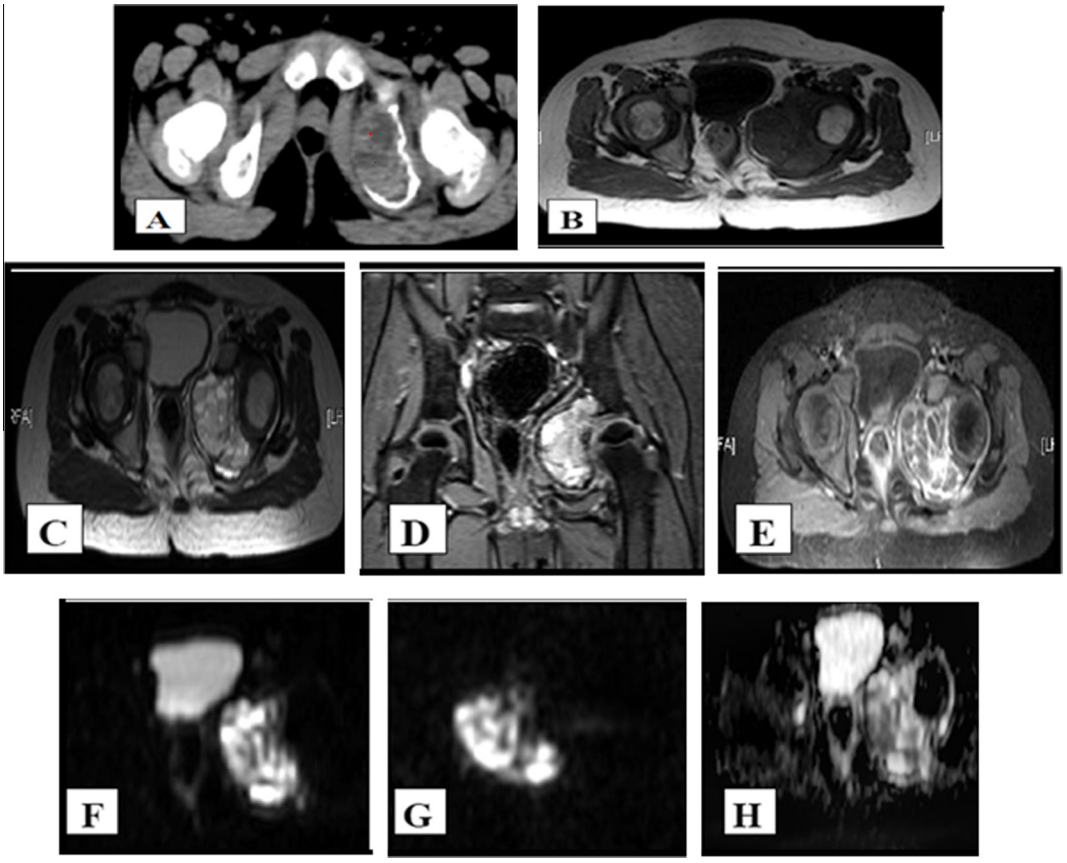

Fig. 6 Aneurysmal bone cyst (ABC): 15 year old male complaining of pain of the left hip: CT scan of the pelvic bones: showing an expansile bony lesion affecting the left acetabulum. Axial T1WI showing intermediate SI of the lesion which has intra-pelvic extension, with mild compression of the urinary bladder and rectum. (C and D) Axial T2WI and coronal T2 fat suppressed image: showing mixed high SI of the bony lesion with the presence of fluid-fluid levels. (E) Post contrast axial T1WI with fat suppression showing the enhancing septae of the lesion. (F) diffusion-weighted images at different *b* values (0 and 1000): showing high signal at *b* 1000 diffusion weighted image. (H) ADC map showing the mean ADC value about (2.1×10^{-3}) mm^2/s.

Table 4 Showing different patterns of DWI and ADC values in different cases of tumor-like lesions (35 cases).

Type of bony lesion	No.	Appearance on DWI at $b = 1000$ s/mm^2		Mean ADC value $\times 10^{-3}$ mm^2/s	
		Restricted (high SI)	Unrestricted (low SI)	Solid component	Cystic component
Inflammatory	20	3	16	1.58	2.13
ABC	6	1	6	–	2.48
Simple bone cyst	2	1	1	–	2.6
Fibrous dysplasia	4	–	4	0.97	2.04
Bone marrow edema	3	–	3	1.63	–
Total	35	5	30		

From this table we have concluded that:
The mean ADC value for solid tumor-like lesions is about (1.39×10^{-3}) mm^2/s.
The mean ADC value for cystic tumor-like lesions is about (1.31×10^{-3}) mm^2/s.

important components of signal attenuation on DWIs are water molecules in the extra cellular space and perfusion. Accordingly, Van Rijswijk et al., 2002 (19) explained the overlapped ADC values by the contribution of perfusion to the ADC values. The perfusion fraction of malignant tumor tends to be higher due to increased tumor cell packing than that of benign masses.

Thirteen cases of metastasis were included in this study, their ADCs values ranged from 0.42 to 1.4×10^{-3} mm^2/s. The lowest value was of the undifferentiated carcinoma while the highest one was of differentiated hepatocellular carcinoma indicating that the more differentiation of a tumor (less packed cells), the more the diffusion and the higher ADC values. In this study the ADC of metastatic hepatocellular carcinoma

Table 5 Showing different patterns of DWI and ADC values in different pathologies (100 cases).

Type of bony lesion	No.	Mean ADC value $\times 10^{-3}$ mm^2/s	
		Solid component	Cystic component
Benign	14	2.15 (chondroid) 1.43 (others)	-
Malignant	51	2.05 (chondroid) 1.31 (others)	2.3
Tumor like	35	1.39	2.31
Total	100		

From this table we have concluded that:
Chondroid tumors (benign and malignant) have ADC value more than (2×10^{-3}) mm^2/s.
There is significant difference between ADC values of benign and malignant solid tumors (after exclusion of chondroid tumors).

Table 6 Statistical significance on comparing ADC values (measured in the solid parts) of benign versus malignant bony lesions.

	P value
Malignant and non malignant lesions (benign and tumor like lesions)	0.001
Benign and tumor like lesions.	852
Malignant and tumor like lesions	0.007
Benign and malignant lesions.	039
Benign and malignant lesions (after the exclusion of chondrosarcomas)	0.001

P value is significant if < 0.05.

$(1.40 \times 10^{-3}$ mm^2/s) is nearly similar to that of Taouli et al., 2002 (20) who reported that mean ADC of HCC is 1.33×10^{-3} mm^2/s. Furthermore, they suggested that the threshold ADC for the distinction between benign and malignant liver masses is 1.5×10^{-3} mm^2/s.

Similar to Lang et al., 1998 (21), we found low signal intensity in necrotic tumors on DWIs, indicating rapid diffusion of water molecules as a result of loss of membrane integrity. This was demonstrated in two cases of osteosarcoma for which we did follow up DWIs to monitor tumor response to therapy. The signal intensity of the lesion decreased on DWIs (at $b = 1000$ s/mm^2) indicating more free water diffusion caused by cell necrosis. Similarly ADC values significantly increased. These findings are similar to those observed by Einarsdottir et al., 2004 (12) and Hayashida et al., 2006 (9,11).

5. Conclusion

DWI has been proven to be highly useful in the differentiation of benign, malignant bone tumors and tumor like bony lesions (Table 1). When combined as a complementary sequence with conventional MRI with the measurement of ADC values, the accuracy of the diagnosis of bone tumors and tumor like lesions will be improved. Moreover, measurement of ADC values can be used in the follow up of tumors and their response to therapy.

Conflict of interest

None.

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