

The Role of DWI in Differentiating Metastatic from Non-Metastatic Bone Lesions

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Abstract

Background: The bony skeleton is known to be a common site for metastasis which is the third most common site after the lung and liver. Prognosis for patients with metastatic osseous disease is generally poor and management options must be carefully weighted. It is, hence, critical to be able to pick up bone marrow lesions which require further investigations and intervention from benign lesions which can be conservatively managed.

Aim of Study: The purpose of this study is to investigate the potential application of DWI and quantitative ADC in differentiation of various bone marrow lesions raising the level of confidence in diagnosing metastatic from non-metastatic benign bone lesions.

Patients and Methods: Our study sample included 32 cases with different bone lesions, which were further classified into metastatic and non-metastatic lesions based on the standard of reference (6 months follow-up and histopathology if feasible). All lesions were subjected to evaluation using DWI-ADC assessment.

Results : The ADC value was able to correctly predict 90% (n=9/10) of metastatic lesions and 63.6% (n=14/22) of non-metastatic lesions with sensitivity 90.00% and specificity 63.6%, in predicting the malignant nature of metastatic lesions, a cut-off value of $1.26 \times 10^{-3} \text{ mm}^2/\text{s}$ was generated between the two groups according to the receiver operating characteristic curve (ROC) with *p*-value 0.012.

Conclusion: As a tool, diffusion weighted magnetic resonance imaging is a time efficient procedure that requires no extra patient preparations or contrast injection.

Quantitative assessment of DWI using the ADC maps could help in differentiation between benign and malignant nature of bone lesions especially when used in conjunction with conventional MRI sequences and qualitative DWI interpretation raising MRI ability to solve the diagnostic dilemma met while assessing bone lesions encountered in oncology patients.

Key Words: DWI – ADC = Bone metastasis – Benign bone lesions.

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Introduction

THE bony skeleton is known to be a common site for metastasis which is the third most common site after the lung and liver. Prognosis for patients with metastatic osseous disease is generally poor, and management options must be carefully weighted. It is, hence, critical to be able to pick up bone marrow lesions which require further investigations and intervention from benign lesions which can be conservatively managed, distinguishing metastasis from benign lesions such as focal red marrow reconversion, vertebral hemangioma, focal marrow edema and benign vertebral fractures can be difficult and challenging in everyday practice [1].

Magnetic resonance imaging (MRI) is the ideal imaging modality to monitor bone marrow changes in healthy and pathological states, thanks to its inherent rich soft-tissue contrast. Quantitative bone marrow MRI techniques have been also developed in order to quantify changes in bone marrow water-fat composition, cellularity and perfusion in different pathologies [2].

Diffusion-weighted imaging (DWI) is based on the Brownian motion of water in a tissue. In vivo random movement of water in the extracellular, intracellular, and intravascular compartment can be measured with DWI. There is an inverse relationship between the DWI signal and diffusivity [3].

Both qualitative and quantitative analysis are possible with DWI, ADC is one quantitative approach to DWI [3].

There are probably many factors influencing the diffusivity of water molecules in bone marrow, fat content probably plays a critical role. As a hydrophobic material, fat may act as a physical

barrier to the free diffusion of water molecules. Since fat is the major component of yellow marrow (~80%) and a significant component of red marrow ~ 40%), apart from adipose cells, bone trabeculae also act as a barrier to diffusion and probably contribute to the restricted diffusion of normal bone marrow [4]. Thus, any pathologies that displace normal fatty marrow or destroy bone trabeculae could encourage free water movement, resulting in higher ADC relative to normal background marrow [3].

Patients and Methods

Patients:

This is a cross sectional analytic study that included 32 patients with different bone lesions, which were further classified into metastatic and non-metastatic lesions based on the standard of reference (6 months follow up and histopathology if feasible). The study was conducted in National Cancer Institute, Cairo University, during the period from July 2021 to February 2022. This study was accepted by the ethics committee and all enrolled patients provided informed written consent.

Inclusion criteria:

Patients with history of known primary malignancy and bone marrow lesions on conventional MRI, CT or bone scan.

Cancer patients with newly developed or incidentally discovered bone lesion during follow-up.

Patients with suspicious bone lesions on CT or bone scan with the possibility of bone metastasis of unknown origin.

Exclusion criteria:

Patients who are claustrophobic or unable to undergo MRI examination owing to a pacemaker, critically positioned incompatible metallic foreign body or incompatible vascular implants.

Patients who are intolerant to contrast administration (especially patients with impaired renal functions or history of contrast allergies).

Technique of MRI:

All patients were examined with a 1.5-Tesla MRI system (Achieva Philips XR) closed magnet unit. The MRI protocol included the following pulse sequences:

- Multi planar MR imaging sequences without contrast including T1 (axial and coronal) and T2 WI (axial and sagittal) with fat-suppressed images utilizing 1.5 T scanner.

- Gadolinium-enhanced T1-weighted sequences (post-contrast T1 fat sat Thrive).
- Diffusion-weighted sequence with multiple *b*-values (*b*-0, 50, 400 & 800). ADC maps were calculated from the diffusion-weighted images utilizing specific software at the workstation.
- The MRI protocols were tailored according to the site of the lesion including the used coil and imaging plans.

Image analysis:

I- Conventional and contrast enhanced MR analysis.

The lesion was identified on conventional MRI and the features of each lesion were recorded including:

- a- Site: Either appendicular or axial and subsequently the specific site in each entity was detected.
- b- Signal characteristics on T1, T2-weighted images and post contrast sequences:

1- On T1WIs lesions with a signal that is lower than, equal to or higher than that of muscle were considered as having low, intermediate, or high T1 signal respectively.

2- On the other hand, on T2WIs lesions having a signal lower than that of muscle were considered as having a low signal intensity; those with a signal that is equal to or higher than that of muscle but less than that of fat were identified as having an intermediate signal, while lesions with a signal higher than that of fat were considered as high-signal lesions.

3- Pattern of contrast uptake in the contrast-enhanced imaging; lesions were divided into non-enhancing, homogeneously or heterogeneously enhancing lesions. This aided in ROI placement while calculating the ADC value of each lesion such that the enhancing part of the lesion was selected.

- c- Intralesional changes: Intralesional changes were delineated including cystic changes, hemorrhage, or necrosis. Such changes were excluded during placement of the ROI while calculating the ADC values of the lesions.

II- Interpretation of diffusion weighted images and ADC calculation.

1- The lesion was determined on DWI and ADC map by using the conventional MR images as a guide. Signal intensity of the lesion on DWIs was recorded as being either hypointense or hyperintense.

2- Qualitative analysis of the DWI-ADC maps was done by correlating the signal intensity in DWI to the signal intensity in the ADC map, lesions with hyperintense signal in DWI and low signal in the ADC map were considered as having restricted diffusion, while those having low signal in DWI and bright signal in the ADC maps were considered as having facilitated diffusion.

3- Regarding the quantitative analysis of DWI, the ADC map was generated, and then the ROI was selected manually such that homogenous areas of the lesions guided by T2WI and contrast enhanced sequences were included, and the surrounding cortical bone was excluded to avoid contamination. The ADC value was automatically calculated to get mean, maximum and minimum ADC values.

4- The findings on MRI were analyzed and correlated with histopathological findings after needle biopsy or lesions' behavior upon 6 months follow-up.

Statistical analysis:

Mean ADC values were selected for statistical analysis and compared with the histopathological results or lesions' behavior upon 6 months follow-up.

ROC analysis (Receiver Operator Characteristic) was done to select the best cutoff point for the ADC value.

Standard diagnostic indices including sensitivity, specificity, positive-predictive value (PPV), negative-predictive value (NPV), and diagnostic accuracy were calculated.

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum, and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Kruskal-Wallis and Mann-Whitney tests (5). For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5 (6). ROC curve was constructed with area under curve analysis performed to detect best cutoff value of ADC for detection of metastasis. *p*-values less than 0.05 were considered as statistically significant.

Results

The study population included 32 patients with various bone lesions. The bone metastases and the benign lesions were identified by histological diagnosis if feasible or close radiological follow-up.

The total of 32 patients were examined of whom 15 were males (46.9%) and 17 (53.1%) were females with ages ranging from 4 to 72 years and with a mean age of 38.53 years.

This study included 32 bone lesions which were subjected to evaluation using conventional MRI sequences as well as DWI-ADC assessment.

The lesions were classified based on the standard of reference into two groups: metastatic (n=10) comprising 31.3% of lesions and benign non-metastatic (n=22) comprising 68.8% of lesions, the latter included wide range of benign bone lesions including degenerative, inflammatory, post-operative marrow changes, fibrous dysplasia and benign bone tumors, while the former included metastatic marrow lesions of different primary malignancies.

Regarding the site of the lesions, 20 (62.5%) lesions out of the 32 lesions occurred at the axial skeleton and 12 (37.5%) lesions occurred at the appendicular skeleton.

However, the site predilection of different lesions was as follows; 9 out of 10 (90%) metastatic lesions occurred in the axial skeleton and the remainder 1 out of 10 (10%) occurred in the appendicular skeleton, on the other hand, 11 out of 22 (50%) of benign lesions occurred at the axial skeleton and the rest occurred at the appendicular skeleton.

The lesions were assessed based on their T1WI and T2WI signals as well as their contrast enhancement pattern and intralesional changes as follows (Table 1).

Variable T1WI and T2WI signal intensities were retrieved from both comparison groups as described in (Table 1).

Regarding the pattern of contrast enhancement, 60% (n=6) of metastatic lesions showed heterogeneous contrast enhancement, 30% (n=3) had homogenous enhancement pattern and the rest 10% (n=1) were non enhancing.

On the other hand, about 40.9% (n=9) of benign non metastatic lesions were homogeneously

enhancing, 40.9% (n=9) were heterogeneously enhancing and the rest 18% (n=4) were non enhancing (Table 1).

Contrast enhancement had no significant correlation to the ADC value of different lesions (p -value=0.072). Most of the metastatic and non-metastatic osseous lesions whether having low or high ADC values showed post-contrast enhancement this could be explained by the nature of the lesions; either benign lesions including inflammatory conditions and benign osseous tumors like osseous hemangioma which had relatively high ADC values or metastatic lesions mostly possessing low ADC values all showed post contrast enhancement of varying pattern.

Regarding the various intralesional changes, 20% (n=2) of metastatic lesions showed internal necrosis and 20% (n=2) showed intralesional hemorrhage, while 27.3% (n=6) of non metastatic benign lesions showed cystic changes, 4.5% (n=1) showed internal necrosis and 13.6% (n=3) showed intralesional hemorrhage (Table 1).

Table (1): Displays the T1WI, T2WI signals of the lesions as well as their contrast enhancement pattern and intralesional changes.

	Group			
	Metastatic		Non-metastatic	
	Count	%	Count	%
<i>T1 WI signal:</i>				
Low	6	60.0	6	27.3
Isointense	2	20.0	10	45.5
High	2	20.0	6	27.3
<i>T2WI signal:</i>				
Low	2	20.0	4	18.2
Isointense	6	60.0	5	22.7
High	2	20.0	13	59.1
<i>Contrast enhancement:</i>				
Non-enhancing	1	10.0	4	18.2
Homogeneously enhancing	3	30.0	9	40.9
Heterogeneously enhancing	6	60.0	9	40.9
<i>Intralesional changes:</i>				
Cystic changes	0	0.0	6	27.3
Hemorrhage	2	20.0	3	13.6
Necrosis	2	20.0	1	4.5

Qualitative analysis of the diffusion-weighted magnetic resonance imaging (DWI) signal intensity of the lesions in correlation to the corresponding ADC image was performed for all lesions, this could correctly predict 70% of metastatic lesions (n=7/10) and 68.2% of non-metastatic lesion (n=15/22) with sensitivity of 70% and specificity of 68.2% in predicting the malignant nature of the lesions (Table 2).

Table (2): Qualitative analysis of DWI-ADC map.

	Group			
	Metastatic		Non-metastatic	
	Count	%	Count	%
<i>Qualitative analysis of DWI ADC map:</i>				
Restricted diffusion	7	70.0	7	31.8
Facilitated diffusion	3	30.0	15	68.2

Quantitative analysis of diffusion-weighted magnetic resonance imaging-apparent diffusion coefficient value:

Calculation of the mean, maximum and minimum apparent diffusion coefficient values of the lesions was found to be efficient in differentiating metastatic from non-metastatic bone lesions (p -value 0.012), such that the mean ADC value of metastatic lesions was found to be $0.86 \times 10^{-3} \text{ mm}^2/\text{s}$ and that of non-metastatic lesions was $1.4 \times 10^{-3} \text{ mm}^2/\text{s}$ with a cut-off value of $1.26 \times 10^{-3} \text{ mm}^2/\text{s}$ between the two groups that was generated according to the receiver operating characteristic curve (ROC) (Fig. 1 & Table 3) and (Fig. 2 & Table 4).

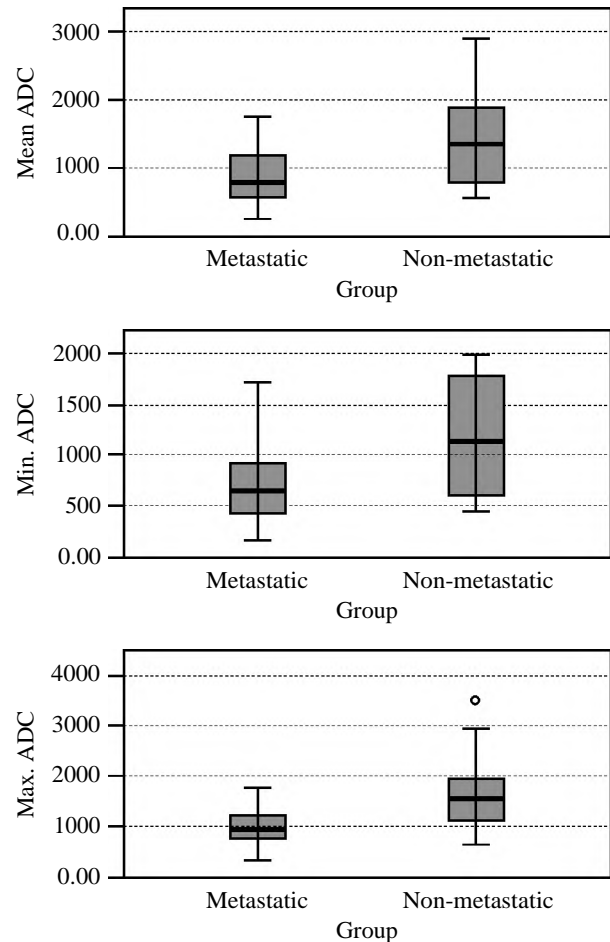


Fig. (1): Mean, maximum and minimum ADC values in both groups.

Table (3): Showing the mean, maximum and minimum apparent diffusion coefficient values of the lesions of both groups.

	Group										p-value
	Metastatic					Non-metastatic					
	Mean	SD	Median	Mini	Max.	Mean	SD	Median	Mini	Max.	
Mean ₃ ADC (x10 ⁻³ mm ² /s)	0.86	0.45	0.79	0.25	0.17	1.4	0.61	1.35	0.56	2.9	0.012
Max. ₃ ADC (x10 ⁻³ mm ² /s)	0.1	0.48	0.93	0.32	1.78	1.66	0.71	1.55	0.64	0.34	0.012
Min. ₃ ADC (x10 ⁻³ mm ² /s)	0.72	0.46	0.64	1.40	1.70	1.17	0.52	1.14	0.45	1.99	0.028

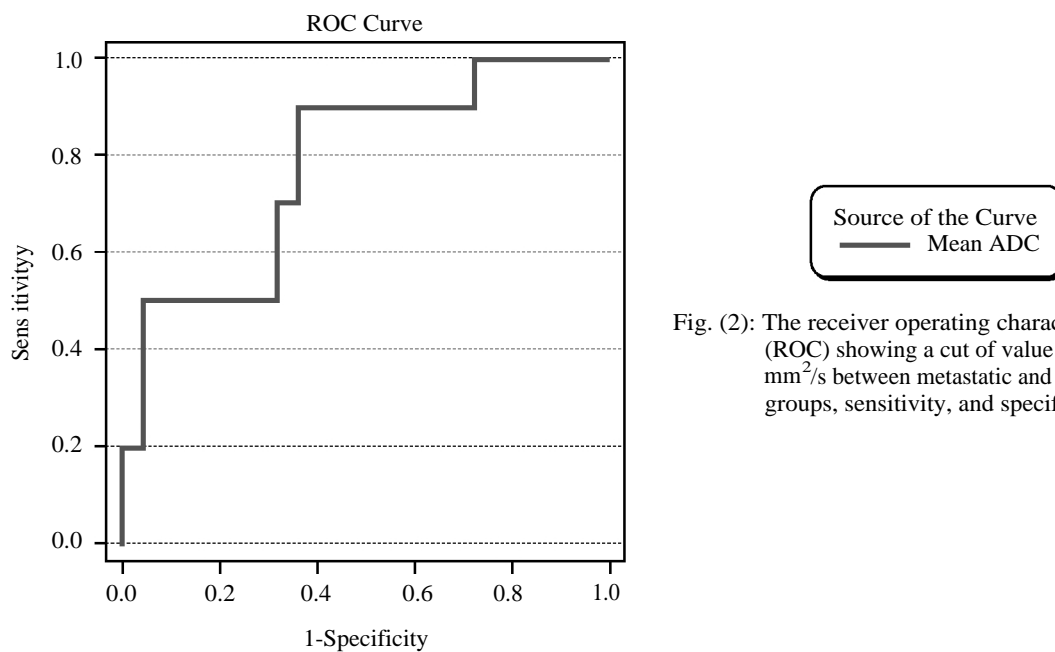


Fig. (2): The receiver operating characteristic curve₃ (ROC) showing a cut of value of 1.26 x 10⁻³ mm²/s between metastatic and non-metastatic groups, sensitivity, and specificity.

Table (4) Receiver operating characteristic curve analysis.

Area under the curve	p-value	95% Confidence interval		Cut-off	Sensitivity %	Specificity %
		Lower bound	Upper bound			
0.777	0.002	0.603	0.951	1.26x 10 ⁻³ mm ² /s	90	63.6

Calculating the ADC value of the lesions was able to correctly predict 90% (n=9/10) of metastatic lesions and 63.6% (n=14/22) of non-metastatic lesions with sensitivity 90% and specificity 63.6%, meaning that ADC measurement had better sensitivity in detecting the malignant nature of the metastatic lesions than qualitative analysis of DWI (Table 5).

Table (5): Quantitative analysis using the ADC values of different lesions.

	Group			
	Metastatic		Non-metastatic	
	Count	%	Count	%
Mean ADC ₃ : <1.26x10 ⁻³ mm ² /s	9	90.0	8	36.4
>1.26x10 ⁻³ mm ² /s	1	10.0	14	63.6

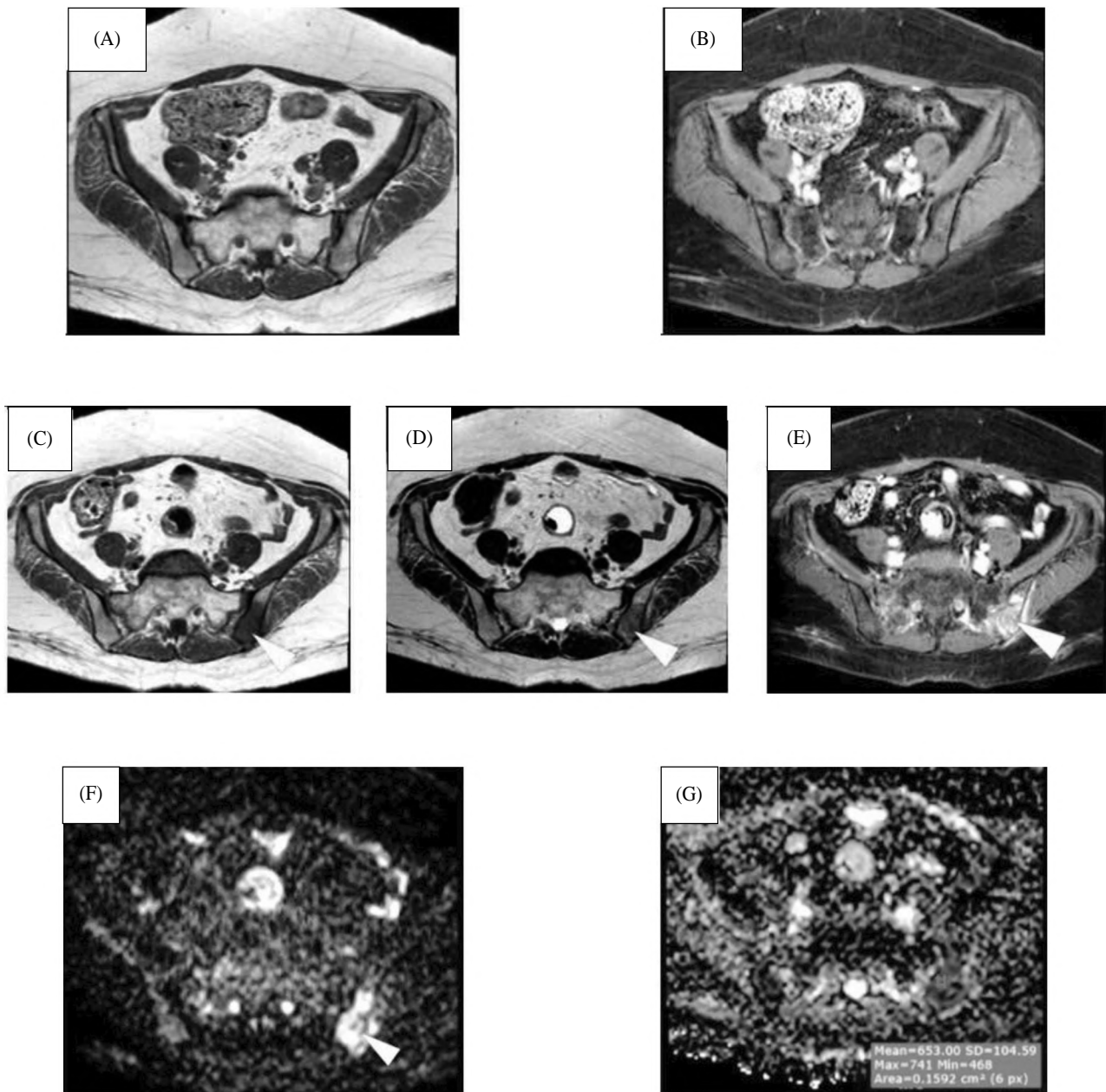


Fig. (3): (Case 1): 46 years old female patient with pathologically proven rectal adenocarcinoma post-surgical excision, upon follow up the pelvic MRI showed a newly developed metastatic bone marrow lesion. (A and B): Axial T1WI and T1 fat sat post-contrast five months earlier showing rather normal marrow signal of the pelvic bones with no definite focal lesions. (C, D and E): Latest MRI examination of the pelvis showing a newly developed left iliac bone marrow lesion eliciting low T1, intermediate T2 signal and heterogeneous postcontrast enhancement (arrowheads). (F and G): The forementioned lesion displayed bright signal in DWI and mean ADC value of $0.65 \times 10^{-3} \text{ mm}^2/\text{s}$. Diffusion restriction and ADC value ($<1.26 \times 10^{-3} \text{ mm}^2/\text{s}$) agreeing with a newly developed metastatic bone marrow lesion discovered upon regular follow-up.

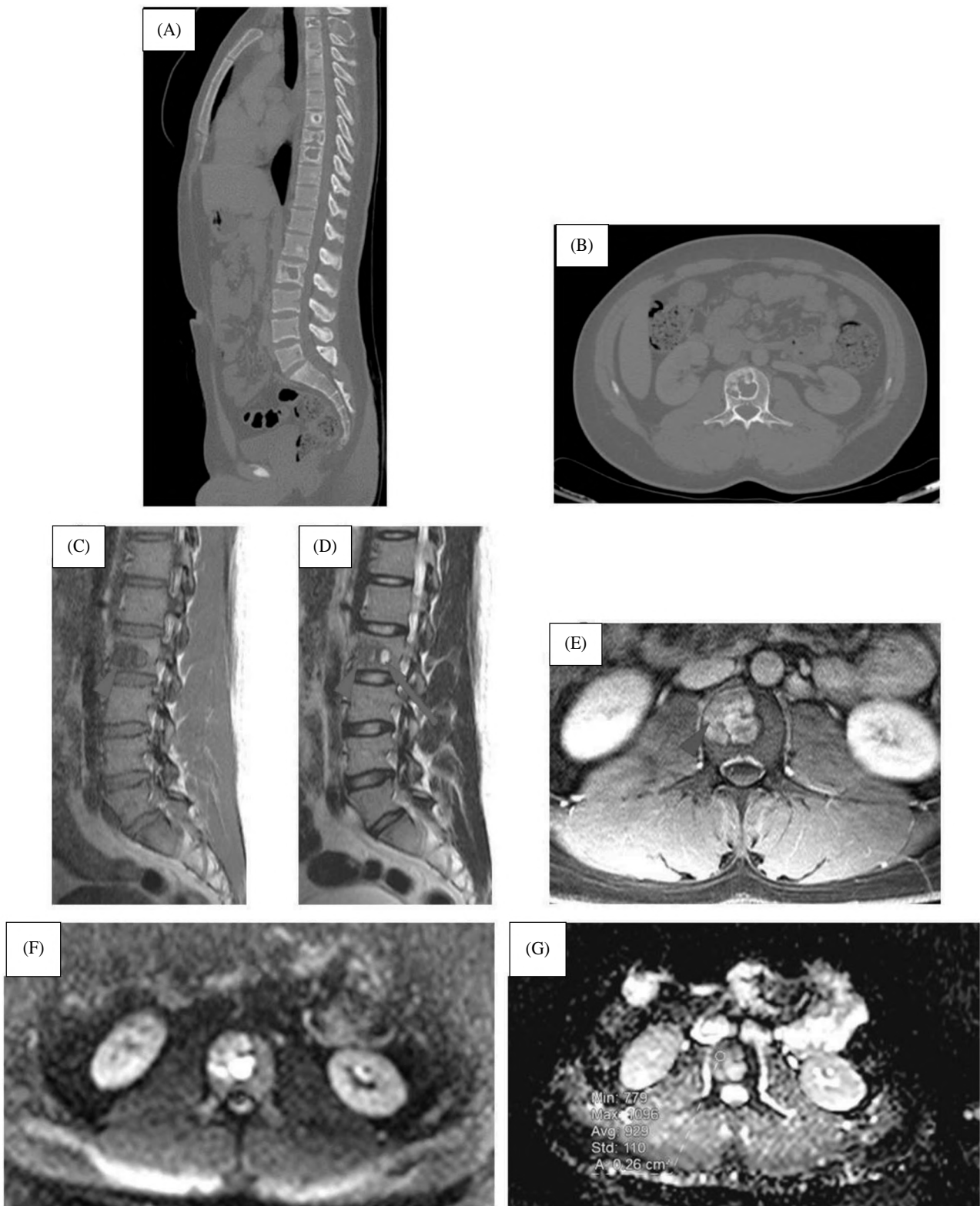


Fig. (4): (Case 2): 23 years old male patient presented to the clinic with bone scan reported widespread hypermetabolic osseous lesions and preliminarily diagnosed as widespread bone metastasis of unknown origin. (A and B): Sagittal and axial CT scan of the spine (bone window) showing multi-level vertebral body/spinous process lytic lesions with sclerotic margins and ground glass/cystic matrix, some of them are associated with mild cortical expansion. (C, D and E): Sagittal T1WI, T2WI and axial T1 fat sat post-contrast focusing on the lumbar vertebrae showing L2 vertebral body lesion displaying low T1 and T2 signal and heterogeneous post contrast enhancement (arrowheads) corresponding to the ground glass part of the lesion shown in the CT. The cystic part of the lesion is well demonstrated in T2WI as well (arrow). (F and G): The forementioned lesion displayed bright signal in DWI and mean ADC value of $0.9 \times 10^{-3} \text{ mm}^2/\text{s}$. Pathology: Fibrous dysplasia. The multiplicity of the lesions, metabolic activity on bone scan, morphological appearance in conventional MRI sequences and the restricted diffusion / low ADC value in such lesions were all strong suggestive factors of metastatic lesions, this came in contradiction with the benign pathology of the lesions.

Discussion

Diffusion-weighted imaging (DWI) and ADC maps were recently employed in many researches to assess its efficiency in detecting the nature of different bone lesions and differentiating metastatic from non-metastatic benign bone lesions [3,7]. This was also our study's target so that we increase the level of confidence in differentiating various lesions, thus, solving this diagnostic mystery particularly in patients with known primary malignancy.

The sample size for this study included 32 patients, 15 were males and 17 were females with ages ranging from 4 to 72 years and with mean age of 38.53 years.

This study included 32 bone lesions which were subjected to evaluation using conventional MRI sequences as well as DWI-ADC assessment. We categorized the 32 lesions into two groups being either metastatic (n=10) or non-metastatic benign bone lesions (n=22).

In our study, most non-metastatic benign lesions (n=18) (81.8%) showed isointense to high T2 signal intensity, while the minority of lesions (n=4) showed low T2 signal intensity which were as follows, 2 lesions were fibrous dysplasia and 2 lesions were giant cell tumors, agreeing with Wang et al. [8] who studied 198 bone lesions and described their signal characteristics, 18 lesions of which were fibrous dysplasia and 39 were metastatic lesions and agreeing with Purohit et al. [9] who reviewed the features of giant cell tumors in different imaging modalities including MRI.

As for metastatic lesions the majority (n=8) (80%) showed intermediate to high T2 signal intensity while 2 lesions (20%) showed low T2 signal intensity, such results agree with the description of Wang et al. [8].

Regarding the pattern of contrast enhancement, about 40.9% (n=9) of benign non-metastatic lesions were homogeneously enhancing, 40.9% (n=9) were heterogeneously enhancing and the rest 18% (n=4) were non enhancing.

On the other hand, 60% (n=6) of metastatic lesions showed heterogeneous contrast enhancement, 30% (n=3) had homogenous enhancement pattern and the rest 10% (n=1) were non enhancing.

Most of the lesions whether metastatic or non-metastatic osseous lesions showed post-contrast enhancement this could be explained by the nature of the lesions; either benign lesions including inflammatory conditions, benign osseous tumors

like osseous hemangioma and tumor-like conditions or metastatic lesions all showed post contrast enhancement of varying pattern, and this was consonant to the review done by Fukuda et al. [3] who reviewed the role of different quantitative MRI techniques in assessment of different bone lesions and described different contrast enhancement patterns of the lesions.

The qualitative analysis of DWI-ADC signals was performed, the lesions were classified into lesions possessing facilitated diffusion and lesions with restricted diffusion. 70% (n=7) of metastatic lesions had restricted diffusion, while the rest 30% (n=3) had facilitated diffusion, this could be explained by intralesional necrosis found in these lesions, this was congruent with the review done by Fukuda et al. [3] who observed that intralesional liquified necrosis in bone tumors could possess high ADC values up to $2.29 \times 10^{-3} \text{ mm}^2/\text{s}$. On the other hand, 68.2% of non-metastatic benign lesions (n=15) had facilitated diffusion and the rest 31.8% (n=7) had restricted diffusion this could be due to the complexity of these benign lesions in terms of bone fragmentation, cellular composition, and hemorrhagic components, this agreed with the description of Fukuda et al., as well [3].

On the other hand, the quantitative assessment of the DWI was done by measuring the ADC values as done by many authors.

Kaur et al. [10] proposed ROC analysis of mean ADC for 65 benign and 35 malignant lesions most of which were metastatic lesions (n=24), this yielded threshold cut off value of $1.21 \times 10^{-3} \text{ mm}^2/\text{s}$ (p value <0.05) where malignant lesions were defined to be more than $1.21 \times 10^{-3} \text{ mm}^2/\text{s}$ and benign lesions were defined to be less than $1.21 \times 10^{-3} \text{ mm}^2/\text{s}$ with sensitivity and specificity of 100% and 92.3% for differentiating benign and malignant nature of the lesions. The standard of reference was histopathological assessment, characteristic CT appearance or lesions' behavior upon 6 months follow-up.

We followed the research model proposed by Kaur et al. [10] however, we reached a cut-off value of $1.26 \times 10^{-3} \text{ mm}^2/\text{s}$ (p-value 0.012), above which a lesion is considered of benign nature and below which the lesion is regarded as metastatic malignant lesion. The sensitivity and specificity of this cut off were estimated to be 90% and 63.6% and these were lower than the values reported by Kaur et al. [10] secondary to the diversity of lesions included in our study that resulted in an overlap in ADC values between metastatic and non-metastatic groups.

In our study the mean ADC value for metastatic lesions ($0.86 \times 10^{-3} \text{ mm}^2/\text{s}$) was slightly higher than the value described by Kaur et al. [10], this is thought to be due to the diversity of the primary malignancies and technical differences used during ROI placement while assessing the lesions. On the other hand, the mean ADC value for non-metastatic lesions was about ($1.4 \times 10^{-3} \text{ mm}^2/\text{s}$) slightly lower than the value described by Kaur et al. [10] this can be explained by inclusion of a wide range of non-metastatic benign lesions in our study possessing tissue compositions that favor slight diffusion restriction as described by Pekcevik et al. [1] who studied the role of DWI in diagnosis of different bone tumors and fibrous dysplasia owing to the presence of dense fibrous stroma restricting water diffusion.

Hajalioghli et al. [11] used the mean ADC value of 10 atypical vertebral hemangiomas and 13 vertebral metastatic lesions to reach a cut-off ADC value of $0.95 \times 10^{-3} \text{ mm}^2/\text{s}$ (p -value 0.01) between the two study groups with mean ADC of ($1.8 \times 10^{-3} \text{ mm}^2/\text{s}$) for benign lesions and mean ADC ($1 \times 10^{-3} \text{ mm}^2/\text{s}$) for metastatic lesions.

Similarly, Cao et al. [12] utilized the mean ADC value to differentiate between 32 benign lesions specifically atypical vertebral hemangiomas and 52 metastatic vertebral lesions, this showed sensitivity and specificity of 87.5% and 88.5% in detecting the nature of the lesions (AUC=0.911, 95% CI: 0.829-0.993, p -value <0.01), they used similar standard of reference which was histopathological assessment or lesions' behavior upon 6 months follow-up.

Our study had some limitations such as the small sample size which might not reflect the entire population raising the importance of future more expanded research. Manual ROI placement while performing quantitative analysis of the lesions is one pitfall that might allow the analysis to get biased.

Conclusion:

As a tool, diffusion weighted magnetic resonance imaging is a time efficient procedure that requires no extra patient preparations or contrast injection.

Quantitative assessment of DWI using the ADC maps could help in differentiation between benign and malignant nature of bone lesions especially

when used in conjunction with conventional MRI sequences and qualitative DWI interpretation raising MRI ability to solve the diagnostic dilemma met while assessing bone lesions encountered in oncology patients.

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دور الرنين المغناطيسي الإنتشاري فى التفريق بين ثانويات العظام وآفات العظام الحميدة

إن التفرقة بين ثانويات العظام ومختلف آفات العظام الحميدة أحياناً ما تكون ممكنة وصعبة وبالأخص فى مجموعة حرجة من المرضى كمرضى الأورام الخبيثة بمختلف أنواعها. لذلك توجهنا إلى بحث قيمة الرنين المغناطيسى الإنتشاري ومعامل الإنتشار الظاهر فى التفريق بين ثانويات العظام وآفات العظام الحميدة تم فحص ٣٢ بؤرة عظمية بإستخدام الرنين المغناطيسى الإنتشاري وقياس قيم معامل الإنتشار الظاهر لكل منهم ثم تم تصنيف البؤر المختلفة إلى مجموعتين بناءً على طبيعتهم المتوقعة عن طريق متابعتهم خلال فترة ٦ أشهر على الأقل أو الفحص المجهري لهذه البؤر وهم إما ثانويات أم لا ثانويات نجح معامل الإنتشار الظاهر فى توقع ٩٠٪ (٩/١٠) من الثانويات بشكل صحيح، و ٦٣.٦٪ (١٤/٢٢) من اللانويات بحساسية ٩٠٪ ونوعية ٦٣٪.

تم تحديد نقطة فاصلة إحصائية ما بين قيم الثانويات واللانويات وهى ١٢٦٠ مم مربع / ثانية بناءً على ما سبق فإنه من الممكن إستخدام معامل الإنتشار الظاهر كعنصر مساعد قوى للتفريق بين ثانويات العظام وآفات العظام الحميدة، مما يتحدد عليه مرحلة الأورام الخبيثة المختلفة وما يترتب عليه من خطط علاجية.