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Added values of diffusion weighted imaging, Dynamic contrast enhancement and opposed phase MRI in evaluation of bony lesions around the knee & ankle joints

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Abstract--Background: Magnetic resonance imaging (MRI) represents the most advanced imaging technique in diagnosis of bone tumors being more sensitive in assessing bone marrow changes and extent of tumors compared to CT and plain X-ray. The distinction between malignant and benign neoplasms is mandatory for appropriate therapeutic choices and planning. MRI has the upper hand in the assessment of such tumors due to its brilliant soft tissue discrimination. The use of multiparametric MRI techniques increase accuracy of discrimination between malignant and benign lesions. Results: This prospective study included 34 patients; 16 males and 18 females with musculoskeletal complaint around the knee & ankle joints. Their age ranged from 10 to 65 years (mean age was 26.65 ± 17.23 years). The cut off value of ADC for bony lesions (by ROC curve) was ≤ 1 to be considered malignant. At this cut off point; the sensitivity of ADC to detect malignant and to exclude benign lesions was 83.3 % and the specificity was 86.4 %. The cut off value for SIR for bony lesions (by ROC curve) was ≥ 0.89 to be considered

malignant. At this cut off point; the sensitivity of SIR to detect malignant and to exclude benign lesions was 91.7 % and the specificity was 90.9 %. The sensitivity of DCE in detection of malignant bony cases and exclusion of benign cases was 90.9 % with specificity measured 91.3 %. conclusions: Combination of DWI, ADC value, DCE & opposed phase – MRI to conventional MRI; completely noninvasive techniques with no radiation exposure and not time consuming, resulted in improvement of sensitivity, specificity and accuracy of MRI and thus increasing radiologist's confidence in image interpretation which will finally reflect on patients' outcome and prognosis.

Keyword---added values, diffusion weighted imaging, dynamic contrast enhancement, opposed phase MRI.

Background

Primary bone tumors are rare but account for a significant proportion of cancers occurring in childhood and adolescence. Malignant bone tumors need to be distinguished not only from their benign counterparts but also from tumor-like lesions, many of which are developmental or reactive in nature and are found commonly in the pediatric population [1]. Magnetic resonance imaging (MRI) represents the most advanced imaging technique in diagnosis of bone tumors being more sensitive in assessing bone marrow changes and extent of tumors compared to CT and plain X-ray, yet not that specific in differentiating benign from malignant lesion using conventional MRI imaging techniques [2].

Diffusion-weighted imaging (DWI) is the technique which allows measurement of the Brownian motion of water in the tissue micro-environment depending on the organization of the tissue, integrity of cell membranes and tortuosity of extracellular space. Apparent Diffusion Coefficient (ADC) is a numerical parameter which is calculated from DWI [3]. DW-MRI with ADC mapping is a rapidly, valuable, non-invasive and non-contrast tool for reliably differentiating between benign and malignant masses [4]. Opposed phase MRI imaging can differentiate between malignant and benign bone tumors as the signal changes between the in-phase and out of phase images differ between bone marrow tumors and non-neoplastic lesions [5].

Contrast enhanced -MRI (CE-MRI) differentiates hyperintense solid from fluid-containing lesions. The presence of homogeneous enhancement suggests a solid component mass. It also differentiates the tumor itself from peri-tumoral edema. CE-MRI is reserved for any lesions raising suspicion for malignancy and can be obtained with high spatial resolution using isotropic volumetric sequences [6]. Unlike conventional contrast-enhanced sequences, Dynamic contrast enhancement MRI (DCE-MRI) allows the evaluation of the temporal pattern of enhancement in the musculoskeletal system, perhaps best known for its use in oncologic applications (such as differentiating benign from malignant tumors, evaluating for treatment response after neoadjuvant chemotherapy, and differentiating postsurgical changes from residual tumor) [7].

Aim of the work

The aim of the study was to find cutoff value in ADC , DCE and SIR for differentiation between benign and malignant bony tumors and tumor – like lesions around the knee and ankle joints .

Methods

Study population

This cross-sectional retrospective study was performed in Diagnostic Radiology and Medical Imaging Department, referred from orthopedic and general surgery departments, at Tanta University Hospital during the period from October 2019 to October 2021. This study included 34 patients; 16 males and 18 females with age ranged between 10 to 65 years (mean of age was 26.65 ± 17.23 years). Those patients were selected on clinical bases suggesting presence of bony tumors or tumor – like lesions as a primary diagnosis. The clinical presentation included bony pain, swelling, fever and limitation of movement.

Inclusion criteria

Patients with masses suspected to be of bony origin discovered by conventional radiography.

Exclusion criteria

- Patients with claustrophobia, morbid obesity or MRI - non compatible cardiac pacemaker, clipped aneurysm or cochlear implant.
- Contraindication to intravenous contrast agents such as severe allergic reaction, renal impairment & heart failure.
- Patients who refused examination.

Methods

All patients in this study were subjected to the following:

- Written informed consents were obtained from all patients after full explanation of benefits and any expected risks during the course of this study were cleared to the participants and the ethical committee on time.
- Full history taking and clinical examination:
 - Personal history included age & sex.
 - History of the present illness: swelling; for distribution and time of occurrence – and other symptoms as pain, fever & limitation of movement.
 - Past history of trauma, systemic disease, the same pathology, known primary tumors, positive family history of musculoskeletal malignancy and past operative history.
 - Clinical examination included: general examination and local examination around the knee & ankle joints.

- Privacy of all patients' data was guaranteed and there was a code number for every patient's file that includes all investigations and data.
- Radiological examination:
 - Conventional MRI, DWI, opposed phase MRI & DCE-MRI.
 - MRI was performed using GE Signa Explorer 1.5-T closed magnet and Toshiba Vantage Titan 1.5-T scanner closed magnet at Diagnostic Radiology and Medical Imaging department, Tanta university hospital.

Patient preparation

The patients were asked about any contraindications for MR imaging examination as cardiac pacemaker, artificial valves or aneurysm clips. The patients were informed about the nature and duration of the examination (ranged from 20 to 45 minutes) and were instructed to remove any metallic objects and not to move during examination.

MRI imaging protocol

Patients underwent conventional MRI first followed by DW-MRI, In-phase and out of phase imaging and finally DCE- MRI. The examination time ranged from 20-45 minutes.

- Conventional pre-contrast - MRI Protocol:
 - A scout 3 planes T1 weighted images (T1WI) were taken for localization of the subsequent slices.
 - Axial T1 and axial T2 weighted images with or without fat suppression.
 - Sagittal T2 STIR weighted images.
 - Coronal T1, T2 & STIR weighted images.
- DW – MRI protocol:
DW-MRI was acquired in the axial plane by using a single shot echo-planar imaging sequence with multiple b values (0, 500, 800, and 1000).
- Opposed phase – MRI
- Dynamic contrast-enhanced MRI protocol:
Post contrast gradient spin echo plane LAVA Flex images (on GE signa explorer 1.5 Tesla) was obtained immediately after manually injected gadolinium at a dose of 0.1 mmol/kg of body weight (maximum, 20 ml), this was followed by injection of 20 ml of normal saline flushing the tube. Images were obtained sequentially to be consumed about 120 seconds in about 5 phases. Finally, Axial, sagittal and coronal T1-weighted gradient-echo images were acquired as delayed images.

MR imaging analysis

All techniques were evaluated by two experienced consultant radiologists with more than 10 years of experience in musculoskeletal imaging

Conventional MR images

were analyzed for the following:

- Presence of bony lesion; its nature, size, extension and signal intensity in all

pulse sequences.

- Presence or absence of cortical destruction, periosteal reaction, marrow infiltration and soft tissue components.

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Interpretation of Diffusion Weighted Imaging

Qualitative analysis

Through observing the signal intensity of the lesion at DWI and corresponding ADC maps and comparison of both signals as follows:

- Lesions showing low signal intensity on DWI with high signal intensity at corresponding ADC maps were considered to have facilitated diffusion.
- Lesions showing high signal intensity on DWI with lowering of the signal in the corresponding ADC maps or heterogeneous signal at both diffusion and ADC maps were considered to have restricted diffusion.
- In lesions showing high signal intensity in both DWI and ADC maps, T2 shine through effect was considered.

Quantitative analysis

Following qualitative analysis, ADC color maps were automatically generated on the workstation with ROI (region of interest) placed over the solid portions of the examined lesion to calculate the ADC values (least ADC value / maximum restricted diffusion ($\times 10^{-3} \text{ mm}^2/\text{s}$)). A ROI was placed with a diameter not less than 0.5 cm and not exceeding 1.5 cm (i.e., with an average area of 1cm) and was placed at least 3 times, and then the mean ADC value for the lesion was calculated. ROI was placed at the most restricted areas of the solid component; to ensure that the same areas were measured, ROI - placed on the examined lesion at DWI - were cloned to all studies including ADC color maps. ROI were placed away from areas of necrosis to ensure accurate measurements. The ADC value was calculated for each mass lesion.

Interpretation of opposed phase-MRI

Qualitative analysis

This was done by comparing the morphological changes in signal intensity between the in and out of phase sequences, results were divided into lesions with signal drop and lesions showing no signal drop in opposed phase images compared to the in-phase images.

Quantitative analysis

through Signal intensity ratio (SIR): Quantitative assessment of signal intensity for each lesion was done by two different ROI, the first ROI was placed in the opposed phase images to limit the miscalculation via inclusion of the rim of chemical shift artifact found at the interface between fat and water containing tissues in the opposed phase images and the other ROI was placed at the in-phase images. Signal intensity of the minimum, maximum and average values was obtained for both in and opposed phase images and the average value was the mainstay for assessment. At least three measurements were acquired from

different locations for each sequence and the average value was taken into consideration to prevent bias. SIR was calculated by dividing the out-of-phase signal by the in-phase signal using the following formula (out phase signal / in phase signal).

Interpretation of DCE-MRI

Dynamic data analysis was done on the work station; the entire mass is included in the five phases of dynamic run acquisition at 120 second after gadolinium injection. ROI is manually placed over the most avidly enhancing mass, solid component, thick enhanced wall or septations of the lesion that can be helped by color map. Signal intensity (SI)–time curve was performed to assess the behavior of the lesion. The types of time intensity curves, Type I (no enhancement) and type II (faint gradual enhancement) with benign lesions and type IV (rapid rising curve and rapid wash out) with malignant lesions.

Statistical analysis of data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0(Armonk, NY: IBM Corp), Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level. The used tests were:

- Receiver operating characteristic curve (ROC)
It is generated by plotting sensitivity (TP) on Y axis versus 1- specificity (FP) on X axis at different cut off values. The area under the ROC curve denotes the diagnostic performance of the test. Area more than 50% gives acceptable performance and area about 100% is the best performance for the test. The ROC curve allows also a comparison of performance between two tests.
- Sensitivity
Positivity in diseased patients, expressed as percent = $TP / (TP+FN)$.
- Specificity
Negativity in non-diseased subjects, expressed as percent = $TN / (FP+TN)$.
- Positive Predictive value (PPV)
Percent of subjects with positive results who are diseased = $TP / (TP+FP)$.
- Negative Predictive value (NPV)
Percent of subjects with negative test results who are non-diseased
 $TN / (TN+FN)$.
- Accuracy
Rate of Agreement = $(\text{True positives} + \text{True negatives}) / \text{Total tested} \times 100$.

Results

Thirty-four patients were enrolled in this prospective study (16 males and 18 females) with male to female ratio: 47 % to 53 %. The age group of the study cohort ranged from 10 – 65 years, with a mean age of 26.65 ± 17.23 years. Those patients were divided into two groups according to clinical examination, plain x-ray, conventional and functional MRI results and histo-pathological results into:

- Benign bony tumors & tumor-like lesions (22 cases) namely: 3 cases of Non ossifying fibroma, 4 cases of osteochondroma, 2 cases of enchondroma, 1 case of chondromyxoid fibroma (Fig.1), 1 case of calcaneal lipoma, 2 cases of aneurysmal bone cysts at lower tibia & talus, 1 case of calcaneal cyst, 4 cases of osteomyelitis, 1 case of avascular necrosis, 1 case of bone infarction, 1 case of Charcot joint & 1 case of post-radiotherapy after sarcoma excision.
- Malignant bony tumors (12 cases) namely: 5 cases of osteosarcoma, 3 cases of Ewing sarcoma (Fig.2), 3 cases of metastatic deposits & 1 case of recurrent malignant giant cell tumor (Fig.3).

Regarding Conventional MRI

Suspicious aggressive features were found at 14 cases, 10 cases proved to be malignant, while benign non suspicious features were found at 20 cases; 18 cases proved to be benign. So, the sensitivity, specificity, PPV, NPV & accuracy of conventional MRI sequences in detection of malignant cases and exclusion of benign cases were 83.3 %, 81.8 %, 71.4 %, 90% & 82.3 % respectively.

Regarding DWI & ADC maps

- According to DWI: Restricted diffusion was found in 12 cases; 9 proved to be malignant, while facilitated diffusion was found in 22 cases; 19 proved to be benign, with the sensitivity, specificity, PPV, NPV & accuracy of DWI in differentiation between benign & malignant lesions were 75 %, 86.4 %, 75%, 86.4% & 82.3 % respectively.
- According to ADC values; ADC values of benign lesions ranged between $0.80 - 2.15 \times 10^{-3} \text{ mm}^2 / \text{sec}$, while ADC values of malignant lesions ranged between $0.59 - 1.05 \times 10^{-3} \text{ mm}^2 / \text{sec}$ with statistically significant difference between benign and malignant groups (P value = 0.020) as listed in table (1).

The cut off value of ADC for the bony lesions (by ROC curve) was ≤ 1 to be considered malignant ADC values ≤ 1 are seen at 13 cases; 10 cases proved to be malignant & ADC values > 1 are seen at 21 cases; 19 cases proved to be benign. At this cut off point; the sensitivity, specificity, PPV, NPV & accuracy of ADC to detect malignant and to exclude benign lesions were 83.3 %, 86.4 %, 76.9%, 90.5% & 85.3 %.

Regarding Opposed phase MRI

- Qualitative analysis: Drop of signal at out of phase related to in phase was seen at 21 cases (20 cases proved to be benign) with no drop of signal was seen at 13 cases (11 cases proved to be malignant).
- Quantitative analysis (according to SIR): SIR of benign lesions ranged between 0.2 – 1.1, while SIR of malignant lesions ranged between 0.8 – 1.8 with statistically significant difference between benign and malignant groups (P value 0.012) as listed in table (2).

The cut off value for SIR for bony lesions (by ROC curve) was ≥ 0.89 to be considered malignant. $SIR \geq 0.89$ are seen at 13 cases; 11 cases proved to be malignant & $SIR < 0.89$ are seen at 21 cases; 20 cases proved to be benign with the sensitivity, specificity, PPV, NPV & accuracy of SIR cut off point to detect malignant and to exclude benign lesions were 91.7 %, 90.9 %, 84.6%, 95.2% & 91.17 % respectively.

Regarding DCE-MRI

Type I curve (no enhancement) was found in 5 cases, all proved to be benign. Type II curve (slow gradual rising) was found in 18 cases; 16 cases proved to be benign & 2 cases proved to be malignant namely 1 case of osteosarcoma and 1 case of metastatic deposit. Type IV curve: (rapid early enhancement and rapid washout) was found in 11 cases; 10 cases proved to be malignant & 1 case proved to be benign namely 1 case of osteomyelitis. So, type I- and II-time intensity curves were more common at benign bony lesions and type IV time intensity curve was more common at malignant bony lesions with sensitivity, specificity, PPV, NPV & diagnostic accuracy of DCE in detection of malignant cases and exclusion of benign cases was 90.9 %, 91.3 %, 83.3%, 95.5 % & 91.17 % respectively

The added value of multiparametric MRI techniques in differentiation between benign and malignant bony lesions around the knee & ankle joints

- **By conventional MRI:** suspicious criteria were noted at 14 cases, 10 cases proved to be malignant and 4 cases proved to be benign namely 2 cases of osteomyelitis, the case of Charcot joint and the case of chondromyxoid fibroma, while non suspicious criteria were noted at 20 cases; 18 cases proved to be benign and 2 case proved to be malignant namely one case of osteosarcoma and one case of Ewing sarcoma, with sensitivity, specificity, PPV, NPV and accuracy measured 83.3 %, 81.8 %, 71.9 %, 90 % and 82.3 % respectively.
- **By adding DWI and ADC cut off value:** one case of osteomyelitis, the case of chondromyxoid fibroma (showed high ADC value) and the case of Ewing sarcoma (showed low ADC value) were excluded with sensitivity, specificity, PPV, NPV and accuracy measured 91.6 %, 90.9 %, 84.6 %, 95.2 % and 91.17 % respectively.
- **By adding opposed – phase MRI and DCE:** The case of Charcot joint was excluded (SIR value = 0.73) with type II curve, with sensitivity, specificity, PPV, NPV and accuracy measured 91.6 %, 95.4 %, 91.6 %, 95.4 % and 94.11 % respectively

So added values of MRI techniques showed higher diagnostic accuracy as compared to conventional MRI alone as shown at table (3).

Discussion

MR imaging has proven to be a valuable imaging tool as due to its ability to assess a wide range of anatomy and pathology. With its multiplanar capabilities and excellent soft-tissue contrast, MRI has established itself as one of the most

promising modalities for non-invasive evaluation of the musculoskeletal system [5]. Non-invasive techniques are required to obtain information about the function of the tissue of interest; Diffusion-weighted (DW) MRI and dynamic contrast studies are advanced techniques used in combination with MRI to improve its diagnostic accuracy [8]. This study included 34 patients, their age ranged from 10 to 65 years (median of age was 26.65 ± 17.23 years) that was near the study done by (Wang T., et al, 2014) [9], in which the median of age of the cases was 31.5 years.

The total benign cases were 22 cases and malignant cases were 12 cases (64.7% and 35.3% respectively) and that was against the study done by (Geneidi EA., et al., 2016) [2], in which malignant cases were more common than benign cases representing (53.3 % and 46.7% respectively). The twenty two cases of proved benign bony tumors and tumor like lesions in this study showed facilitated diffusion in all cases except 3 cases that showed restricted diffusion representing 13.6 %, that was agreed by the study done by (Rao A., et al., 2019) [10], in which restricted diffusion was found in 20% of all benign cases. The study done by (Geneidi EA., et al., 2016) [2] reported that 93% of malignant cases showed restricted diffusion that was agreed by this study in which restricted diffusion seen at 75 % of malignant cases. While their comparative study between benign and malignant bony lesions according to DWI showed sensitivity, specificity and accuracy measured 94%, 50%, 73% respectively, this study showed sensitivity measured 75%, specificity 86.4%, PPV measured 75%, NPV 86.4% with accuracy measured 82.3.

In this study, the ADC values of benign cases ranged between $0.80 - 2.15 \times 10^{-3}$ mm² /sec (mean = 1.5 ± 0.43), while ADC values of malignant lesions ranged between $0.59 - 1.05 \times 10^{-3}$ mm² /sec (mean = 0.79 ± 0.17) with statistically significant results (P value measured 0.020). These results were supported by the finding of (Wang T., et al, 2014) [9] who revealed that the mean ADC value for benign bone tumors was ($1.17 \pm 0.36 \times 10^{-3}$ mm² /s) and malignant bone tumors was ($0.87 \pm 0.20 \times 10^{-3}$ mm² /s) with statistically significant results. By ROC curve, the cut off value for ADC in this study for better discrimination between benign and malignant bony lesions was 1, at that point the sensitivity was 83.3%, specificity 86.4%, PPV 76.9%, NPV 90.5% with accuracy measured 85.3%. Our results were agreed by (Rao A., et al., 2019) [10] who documented that ADC cut off point was 1.1 with sensitivity, specificity, PPV and NPV measured 89.7%,84.8%,82.5% and 95.3% respectively.

ADC cut off point that was recorded by (Peacenik Y., et al., 2013) [11] to discriminate between benign and malignant bony lesions was higher than this study (1.37) that is mostly due to presence of multiple cases of chondrosarcoma in his study which usually show higher ADC values than other malignancies. (Peacenik Y., et al., 2013) [11] mentioned that The highest ADC values were found in the cases of aneurysmal bone cysts and benign bone tumors that have chondroid matrix as enchondroma that agreed with this study in which the highest ADC values were found at 2 cases of enchondroma (2 and 2.1×10^{-3} mm²/sec) mostly due to cartilaginous content and 2 cases of aneurysmal bone cysts (2.1 and 2.15×10^{-3} mm²/sec) mostly due to high fluid content , however ADC value of osteosarcoma was (1.33×10^{-3} mm²/sec) that was different than

ADC value of osteosarcoma at this study ($0.59 \times 10^{-3} \text{ mm}^2/\text{sec}$) that showed the lowest ADC value.

Calcaneal lipoma case showed facilitated diffusion with low ADC value measured ($0.8 \times 10^{-3} \text{ mm}^2/\text{sec}$) that is below the cut off value and falsely overlapped with ADC values of malignant lesions mostly due to abundant amount of fat. Our results were in contrary with the study of (Rao A., et al., 2019) [10] who recorded that the ADC value of osteomyelitis was $0.5 \times 10^{-3} \text{ mm}^2/\text{sec}$, while in this study, the mean ADC value for osteomyelitis was $1.27 \times 10^{-3} \text{ mm}^2/\text{sec}$. Some benign lesions showed high signal at DWI and ADC maps indicating T2 shine through effect namely aneurysmal bone cysts of talus and tibia & cartilaginous cap of osteochondroma cases with high ADC values ranging between ($1.29 - 2.15 \times 10^{-3} \text{ mm}^2/\text{sec}$), this agreed with the study done by (Abdelhameed AM., et al., 2018) [12], in which aneurysmal bone cyst displayed high signal at DWI with high ADC value measured ($2 \times 10^{-3} \text{ mm}^2/\text{sec}$).

Cystic or necrotic areas seen within the malignant tumors had high ADC values than the solid parts, so it is misleading and measurement of ADC value by placing ROI on the solid enhancing areas is mandatory, this came in line with the study done by (Kotb SZ., et al., 2014) [13], in which ADC value of cystic regions was higher than solid regions. Therefore, in the current study, we concluded that ADC value was able to distinguish benign from malignant high signal intensity on DWI and this was in agreement with (Khoo MMY. et al., 2011) [14] who highlighted the necessity of correlating high b-value DW images with corresponding ADC values to prevent misinterpretation due to T2 shine-through effect. Regarding Dynamic contrast enhancement, in this study, visual assessment of the shape of the time intensity curve was the cornerstone as it was easy to perform considering the shape of the uptake and washout of contrast agent as agreed by (Lavini C., et al., 2009) [15].

Concerning time intensity curve, 5 cases of benign bony lesions showed type I curve, 16 benign cases and 2 malignant cases showed type II curve and type IV curve was found in 1 case of benign and 10 cases of malignant bony lesions, therefore, type I and II curves are highly suggestive of benign lesions and type IV curve is highly suggestive of malignancy, this came in line with (Abdelhameed AM., et al., 2018) [12], in which type II curve was more common with benign and type IV curve was more common at malignant lesions. DCE reflects lesion vascularity; however, sometimes there is an overlap between benign and malignant bone lesions, so it can't stand alone in discrimination between benign and malignant lesions. As in this study, type II curve was seen in 2 malignant cases and type IV curve was found in 1 benign case, and this agreed with (Geirnaerd MJA., et al., 2004) [16] who stated that in dynamic imaging, the first pass of the contrast agent serves to evaluate tissue vascularity and tumor perfusion. However, qualitative overlap sometimes occurs between the time intensity curves of highly vascular benign tumors and those of poorly vascularized malignant tumors.

Comparative statistical analysis between the results of dynamic contrast enhancement and the gold standard of cases in this study was done that revealed that the sensitivity of DCE to discriminate between benign and malignant bony

lesions was 90.9 %, specificity 91.3 %, PPV 83.3 %, NPV 95.3 % with diagnostic accuracy measured 91.17 % and this was in agreement with (Cao J., et al., 2017) [17] who assumed that the sensitivity, specificity and accuracy of DCE were 95.5 %, 87.7 % and 90.6 % respectively. Combination of DWI, ADC values and DCE showed more accurate results with higher sensitivity, specificity and accuracy measured 91.6 %, 95.4 % and 94.11%, that agreed with (Cao J., et al., 2017) [17] who stated that a combination of both DWI and DCE MRI is a promising method for differentiating malignant from benign bony lesions with sensitivity, specificity and accuracy measured 100 %, 85.7 % and 92.9 %,

As regard to opposed phase -MRI in the current study, SIR of benign cases ranged between 0.2 – 1.1 (mean = 0.72 ± 0.28), while SIR of malignant lesions ranged between 0.8 – 1.8 (mean = 1.2 ± 0.30) with statistically significant results (P value measured 0.012), these results were congruent with the study done by (Disler DG., et al., 2013) [18] who recorded that the mean SIR in benign lesions was 0.62 ± 0.13 and in malignant lesions was 1.03 ± 0.1 . By ROC curve, the cut off value for SIR in this study for discrimination between benign and malignant bony lesions was 0.89, at that point the sensitivity was 91.7 %, specificity 90.9 %, PPV 84.6 %, NPV 95.2 % with accuracy measured 91.17 %, this agreed with (Disler DG., et al., 2013) [18] who stated that cut off point for SIR was 0.81 with sensitivity and specificity measured equally 95 %.

The highest SIR value was found in 1 case of Ewing sarcoma (1.8) mostly due to high infiltration of the bone marrow by malignant cells, while the lowest SIR was found in the case of post radiotherapy bone marrow changes after sarcoma excision measured 0.2 , this disagreed with (Amin WM., et al., 2016) [19] , in which SIR of osteosarcoma was the highest value (1.2) and SIR of osteochondroma was the lowest value (0.2) , and agreed with (Disler DG., et al., 2013) [18] who found that SIR of bone marrow changes of the femur with radiotherapy after rectal cancer (hemopoietic tissue) was the lowest value measured 0.36. Combination of conventional MRI, DWI, ADC value and SIR showed higher sensitivity, specificity and accuracy compared with individual accuracy of each, this agreed with (Amin WM., et al., 2016) [19] who assumed that combination of DWI with SIR value gave better results as regards to sensitivity, specificity and accuracy.

Conclusions

Combination of DWI, ADC value, DCE & opposed phase – MRI to conventional MRI; completely noninvasive techniques with no radiation exposure and not time consuming, resulted in improvement of sensitivity, specificity and accuracy of MRI and thus increasing radiologist's confidence in image interpretation which will finally reflect on patients' outcome and prognosis.

List of abbreviation

Magnetic resonance imaging MRI
 Diffusion-weighted imaging DWI
 Apparent Diffusion Coefficient ADC
 Contrast enhanced -MRI CE-MRI

Dynamic contrast enhancement MRI ... DCE-MRI
 Region of interest ROI
 Signal intensity ratio SIR
 Receiver operating characteristic curve ... ROC curve
 Positive Predictive value PPV
 Negative Predictive value.... NPV
 TP true positive
 FP.... false positive
 TN True negative
 FN false negative

References

1. Abdelhameed AM., Ibrahim AM., Osman NM., et al. (2018) . The Role of Advanced Techniques of MRI in Evaluation of Pediatric Bone Tumors. *Egyption Journal of Hospital Medicine*. 71 : 3585 – 3590.
2. Amin WM. , Kotb HT. , Abdel-kerim AA. , et al. (2016) . Diffusion-weighted MRI and in-phase/opposed-phase sequences in the assessment of bone tumors. *Journal of Magnetic Resonance Imaging*. 44 : 565–572.
3. Cao J., Xiao L., He B., , et al. (2017) . Diagnostic value of combined diffusion-weighted imaging with dynamic contrast enhancement MRI in differentiating malignant from benign bone lesions. *Clinical Radiology*. 72: 793 - 799.
4. Disler DG., McCauley TR., Ratner LM., et al. (2013) . In-phase and out-of-phase MR imaging of bone marrow: prediction of neoplasia based on the detection of coexistent fat and water. *American Journal of Radiology* . 169: 1439–1447.
5. Drapé JL. (2013) . Advances in magnetic resonance imaging of musculoskeletal tumours. *Orthopaedics and Traumatology: Surgery and Research*. 99 : 115–123.
6. Geirnaerdt MJA., Van Rijswijk SP., Hogendoorn PCW., et al. (2004) . Soft-tissue tumors: value of static and dynamic gadopentetate dimeglumine-enhanced MR imaging in prediction of malignancy. *Radiology*. 233: 493–502.
7. Geneidi EA., Ali HI. and Dola EF. (2016). Role of DWI in characterization of bone tumors. *The Egyptian Journal of Radiology and Nuclear Medicine*. 47 : 919–927.
8. Hassanien OA., Younes RL. and Dawoud RM. (2018). Diffusion weighted MRI of soft tissue masses: Can measurement of ADC value help in the differentiation between benign and malignant lesions? *Egyption Journal of Radiology and Nuclear Medicine*. 49 : 681–688.
9. Jani, J. R., Bajamal, A. H., Utomo, S. A., Parenrengi, M. A., Fauzi, A. A., Utomo, B., & Dwihapsari, Y. (2021). Correlation between magnetic resonance imaging (MRI) and dynamic mechanical analysis (DMA) in assessing consistency of brain tumor. *International Journal of Health & Medical Sciences*, 4(2), 260-266. <https://doi.org/10.31295/ijhms.v4n2.1737>
10. Khoo MMY., Tyler PA., Saifuddin A., et al. (2011) . Diffusion-weighted imaging (DWI) in musculoskeletal MRI: a critical review. *Skeletal Radiology*. 40 : 665–681.
11. Kotb SZ., Sultan AA., Elhawary GM., et al. (2014) . Value of diffusion weighted MRI in differentiating benign from malignant bony tumors and tumor like lesions. *Egyption Journal of Radiology and Nuclear Medicine*. 45 :

- 467–476.
12. Lvini C., , Pikaart Bp., Schaap GR., et al. (2009) . Region of interest and pixel-by-pixel analysis of dynamic contrast enhanced magnetic resonance imaging parameters and time-intensity curve shapes: a comparison in chondroid tumors. *Magnetic Resonance Imaging*. 27: 62–68.
 13. Nassif MA., Rahim SA. and Hussien RZ. (2017) . The Role of Diffusion-Weighted MRI in the Characterization of Musculoskeletal Soft Tissue Tumors. *The Egyptian Journal of Hospital Medicine*. 69 : 1895 - 1899.
 14. Pekcevik Y., Kahya MO. and Kaya A. (2015). Characterization of soft tissue tumors by diffusion-weighted imaging. *Iranian Journal of Radiology*. 12 : 154 - 164.
 15. Pekcevik Y., Kahya MO., Kaya A., et al. (2013) . Diffusion-weighted Magnetic Resonance Imaging in the Diagnosis of Bone Tumors: Preliminary Results. *Journal of Clinical Imaging Science* : 63 - 75.
 16. Rao A., Sharma CH. and Parampalli R. (2019) . Role of diffusion-weighted MRI in differentiating benign from malignant bone tumors. *British Journal of Radiology*. 1 : 20-28.
 17. Sujlana P., Skrok J. and Fayad LM. (2018) . Review of dynamic contrast-enhanced MRI: Technical aspects and applications in the musculoskeletal system. *Journal of Magnetic Resonance Imaging*. 47: 875–890.
 18. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). Health and treatment of diabetes mellitus. *International Journal of Health Sciences*, 5(1), i-v. <https://doi.org/10.53730/ijhs.v5n1.2864>
 19. Vlychou M. and Athanasou NA. (2008). Radiological and pathological diagnosis of paediatric bone tumours and tumour-like lesions. *Pathology*. 40 : 196–216.
 20. Wang T., Wu X., Cui Y., et al. (2014). Role of apparent diffusion coefficients with diffusion-weighted magnetic resonance imaging in differentiating between benign and malignant bone tumors. *World Journal of Surgical Oncology*. 12 : 1–6.
 21. Zhao F., Ahlawat S., Farahani SJ., et al. (2014) . Can MR imaging be used to predict tumor grade in soft-tissue sarcoma?. *Radiology*. 272 : 192–201.

Figures titles and legends

Fig. (I): 17-year-old male patient presented by pain at the right thigh. (A, B, C) Sagittal T2, coronal STIR and axial T2 images: well defined abnormal signal intensity lesion at the postero-medial aspect of distal femoral meta-diaphyseal region associated with subtle cortical interruption, periosteal reaction, adjacent bone marrow edema and edematous changes at the nearby soft tissues. (D) Axial DWI : high signal intensity of the bony lesion, (E, F) Grey scale and colored ADC maps : high signal intensity of the lesion (T2 shine through effect) with ADC value ($1.6 \times 10^{-3} \text{ mm}^2 / \text{sec}$). (G, H) Coronal and Axial T1 with dynamic contrast study: mild heterogeneous enhancement. Post processing time intensity curve (I) showed type II curve (slow gradual rising curve). (J, K) Axial in phase and out of phase images : mild drop of signal of the bony lesion at out of phase image relative to in phase, SIR = 0.73. Pathological result was complicated chondromyxoid fibroma,

Fig. (II): 15-year-old female patient presented by heel pain for three months not responding to medical treatment. (A, B, C) Axial T2, axial STIR and sagittal STIR:

heterogeneous signal intensity lesion within the calcaneus with small necrotic areas, interrupted overlying cortex and adjacent soft tissue components. (D) Axial DWI: high signal intensity of the calcaneal mass (E, F): Grey scale and colored ADC maps: low signal of the solid component (white arrows) (restricted diffusion) with ADC value ($0.78 \times 10^{-3} \text{ mm}^2 / \text{sec}$) and high signal of the necrotic portion (T2 shine through effect) with ADC value ($2.3 \times 10^{-3} \text{ mm}^2 / \text{sec}$). (G, H) Sagittal and axial T1 FATSAT with dynamic contrast study: heterogeneous enhancement of the calcaneal lesion and the surrounding soft tissue component with post processing time intensity curve (I) showing type IV curve (rapid rise followed by rapid washout). (J, K) axial in phase and out of phase images: infiltration of the calcaneal bone with no drop of signal at out of phase relative to in phase, SIR = 1.8. Pathological result was calcaneal Ewing sarcoma

Fig. (III): 49-year-old female presented by swelling at the medial aspect of the upper leg for one month. (A, B, C) AxialT2, coronal T2 and coronal STIR sequences: bone cement at the upper tibia associated with thickened overlying cortex and soft tissue mass lesion at the medial aspect of the upper leg inseparable from the cortex. (D) Axial DWI: heterogeneous signal of the soft tissue mass, (E, F): Grey scale and colored ADC maps: low signal of the soft tissue mass with ADC value ($0.76 \times 10^{-3} \text{ mm}^2 / \text{sec}$). (G, H) Axial and coronal T1WI with dynamic contrast study: heterogeneous enhancement of the soft tissue mass with enhanced thickened upper tibial cortex and post processing time intensity curve (I) showing type IV curve (rapid rise followed by rapid washout). Pathological result was recurrent giant cell tumor with malignant transformation.

Tables titles and legends

- **Table (I):** ADC values of the benign and malignant bony tumors & tumor – like lesions around the knee & ankle joints.
- **Table (II):** SIR values of the benign and malignant bony tumors & tumor – like lesions around the knee & ankle joints.
- **Table (III):** Diagnostic accuracy of added values of MRI techniques in differentiation between benign and malignant bony lesions around the knee & ankle joints.

Tables

Table I

ADC values of the benign and malignant bony tumors & tumor – like lesions around the knee & ankle joints

Diagnosis	N.	Mean	Std. Deviation	Minimum	Maximum
<i>Non-ossifying fibroma</i>	3	1.17	0.045	1.02	1.32
<i>Osteochondroma</i>	4	1.80	0.091	1.70	1.90
<i>Enchondroma</i>	2	2.05	0.070	2.00	2.10
<i>Chondromyxoid Fibroma</i>	1	1.60	.	1.60	1.60
<i>Calcaneal lipoma</i>	1	0.80	.	0.80	0.80

<i>Aneurysmal bone cyst</i>	2	2.12	0.035	2.10	2.15
<i>Calcaneal cyst</i>	1	1.98	.	1.98	1.98
<i>Osteomyelitis</i>	4	1.28	0.31	0.82	1.51
<i>Avascular necrosis</i>	1	1.05	.	1.05	1.05
<i>Bone infarction</i>	1	0.85	.	0.85	0.85
<i>Charcot joint</i>	1	0.86	.	0.86	0.86
<i>Post – radiotherapy</i>	1	1.54	.	1.54	1.54
<i>Osteosarcoma</i>	5	0.78	0.21	0.59	1.05
<i>Metastatic deposits</i>	3	0.76	0.14	0.62	0.91
<i>Ewing sarcoma</i>	3	0.80	0.21	0.65	1.05
<i>Recurrent malignant GCT</i>	1	0.87	.	0.87	0.87

Table II
SIR values of the benign and malignant bony tumors & tumor – like lesions
around the knee & ankle joints

Diagnosis	N.	Mean	Std. Deviation	Minimum	Maximum
<i>Non-ossifying fibroma</i>	3	0.72	0.0113	0.65	0.80
<i>Osteochondroma</i>	4	0.71	0.057	0.65	0.79
<i>Enchondroma</i>	2	0.64	0.063	0.60	0.69
<i>Chondromyxoid Fibroma</i>	1	0.73	.	0.73	0.73
<i>Calcaneal lipoma</i>	1	0.56	.	0.56	0.56
<i>Aneurysmal bone cyst</i>	2	0.80	0.00	0.80	0.80
<i>Calcaneal cyst</i>	1	0.54	.	0.54	0.54
<i>Osteomyelitis</i>	4	0.90	0.190	0.69	1.1
<i>Avascular necrosis</i>	1	0.52	.	0.52	0.52
<i>Bone infarction</i>	1	0.71	.	0.71	0.71
<i>Charcot joint</i>	1	0.73	.	0.73	0.73
<i>Post – radiotherapy</i>	1	0.2	.	0.2	0.2
<i>Osteosarcoma</i>	5	1.11	0.25	0.8	1.50
<i>Ewing sarcoma</i>	3	1.33	0.420	0.99	1.8
<i>Metastatic deposits</i>	3	1.3	0.34	1.05	1.7
<i>Recurrent malignant GCT</i>	1	1.01	.	1.01	1.01

Table III
Diagnostic accuracy of added values of MRI techniques in differentiation between
benign and malignant bony lesions around the knee & ankle joints

Bony Lesions around knee & ankle joints					
	Sensitivity	Specificity	PPV	NPV	Accuracy
<i>Conventional MRI</i>	83.3 %	81.8 %	71.4 %	90 %	82.3 %
<i>Conventional MRI + DWI + ADC cut off value</i>	91.6 %	90.9 %	84.6 %	95.2 %	91.17 %
<i>Conventional MRI + DWI + ADC cut off value + Opposed phase MRI + DCE</i>	91.6 %	95.4 %	91.6 %	95.4 %	94.11 %

Figures

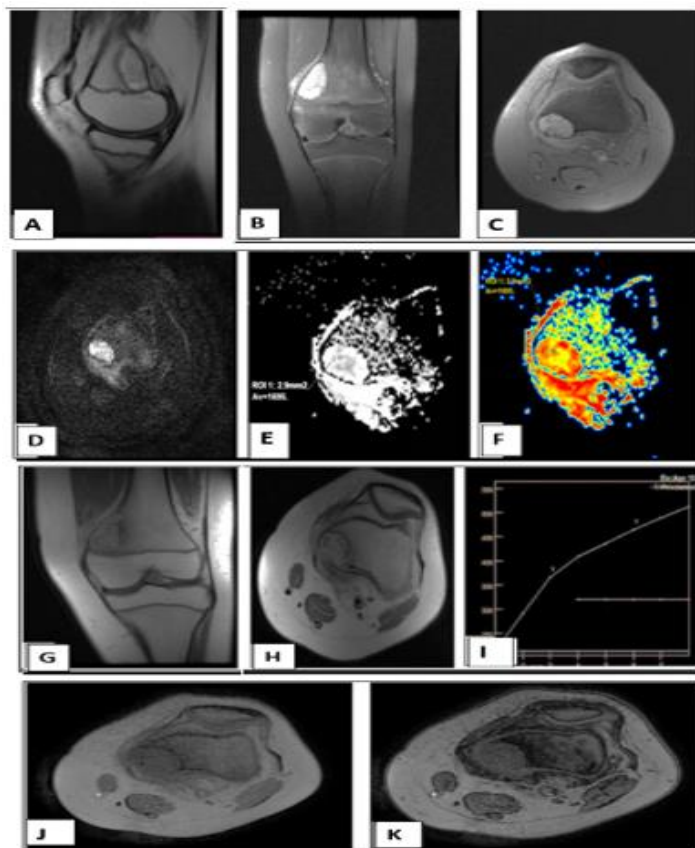


Figure I. 17-year-old male patient presented by pain at the right thigh. (A, B, C)

Sagittal T2, coronal STIR and axial T2 images: well defined abnormal signal intensity lesion at the postero-medial aspect of distal femoral meta-diaphyseal region associated with subtle cortical interruption, periosteal reaction, adjacent bone marrow edema and edematous changes at the nearby soft tissues. (D) Axial DWI : high signal intensity of the bony lesion, (E, F) Grey scale and colored ADC

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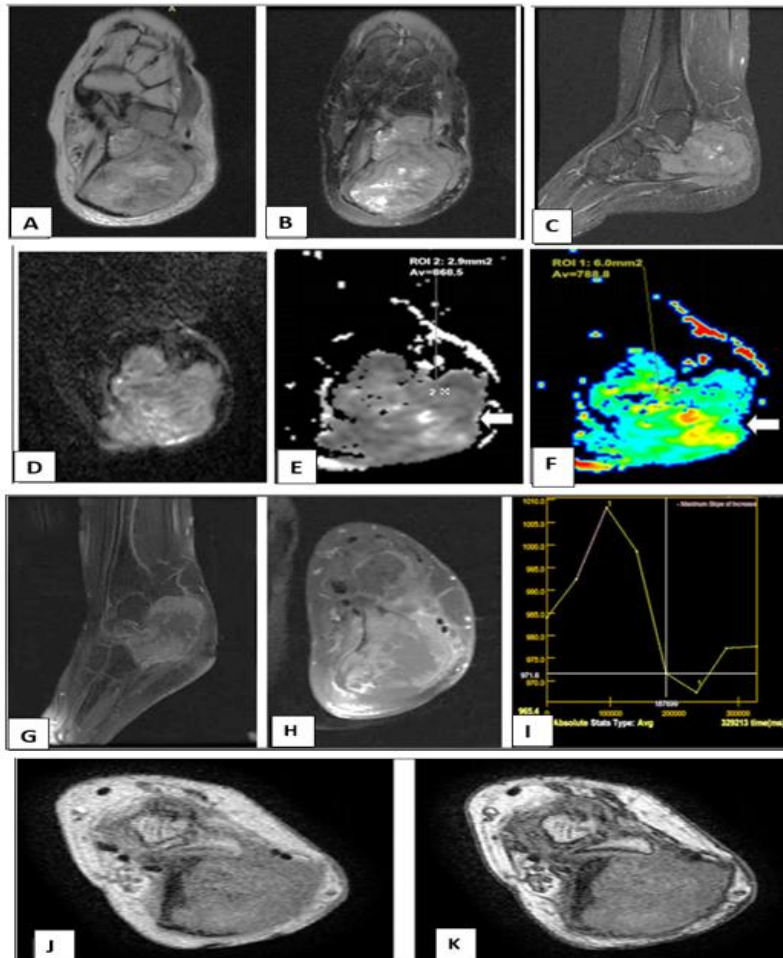


Figure II. 15-year-old female patient presented by heel pain for three months not responding to medical treatment. (A, B, C) Axial T2, axial STIR and sagittal STIR: heterogeneous signal intensity lesion within the calcaneus with small necrotic areas, interrupted overlying cortex and adjacent soft tissue components. (D) Axial DWI: high signal intensity of the calcaneal mass (E, F): Grey scale and colored ADC maps: low signal of the solid component (white arrows) (restricted diffusion) with ADC value ($0.78 \times 10^{-3} \text{ mm}^2/\text{sec}$) and high signal of the necrotic portion (T2 shine through effect) with ADC value ($2.3 \times 10^{-3} \text{ mm}^2/\text{sec}$). (G, H) Sagittal and axial T1 FATSAT with dynamic contrast study: heterogeneous enhancement of the calcaneal lesion and the surrounding soft tissue component with post processing time intensity curve (I) showing type IV curve (rapid rise followed by rapid washout). (J, K) axial in phase and out of phase images: infiltration of the

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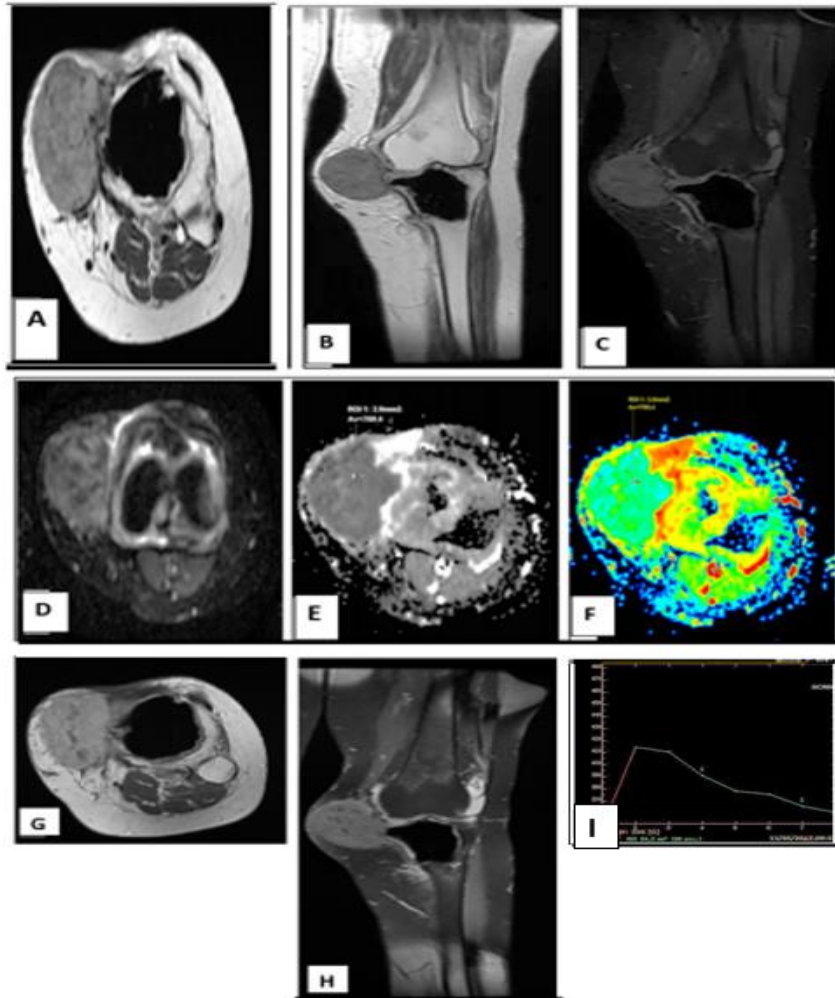


Figure III. 49-year-old female presented by swelling at the medial aspect of the upper leg for one month. (A, B, C) Axial T2, coronal T2 and coronal STIR sequences: bone cement at the upper tibia associated with thickened overlying cortex and soft tissue mass lesion at the medial aspect of the upper leg inseparable from the cortex. (D) Axial DWI: heterogeneous signal of the soft tissue mass, (E, F): Grey scale and colored ADC maps: low signal of the soft tissue mass with ADC value ($0.76 \times 10^{-3} \text{ mm}^2/\text{sec}$). (G, H) Axial and coronal T1WI with dynamic contrast study: heterogeneous enhancement of the soft tissue mass with enhanced thickened upper tibial cortex and post processing time intensity curve (I) showing type IV curve (rapid rise followed by rapid washout). Pathological result was recurrent giant cell tumor with malignant transformation