BENHA MEDICAL JOURNAL bmj
Print ISSN 1110-208X.
Online ISSN 2357-0016

Role of Chemical Shift of MRI in Defining the Extent of Bone Tumors

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Received: 11 October 2023
Accepted: 25 November 2024

Abstract:

Background: Chemical shift imaging (CSI) is a valuable MRI technique that can aid in determining the extent of bone tumors by differentiating between tumor margins and surrounding red marrow or bone marrow edema. This study aimed to investigate whether chemical shift imaging is a useful addition to a tumor protocol for determining the extent of a skeletal tumor. **Methods:** This is a prospective study included 25 patients who have bone tumors and are candidates to MR imaging. The study was conducted at the radiology departments of the National Cancer Institute (NCI), Cairo University& Benha University hospital, Egypt. Patients underwent magnetic resonance imaging (MRI) with T1-weighted spin echo (T1SE), fluid-sensitive and CSI sequences. Tumor extent was recorded (in millimeters) on each sequence. Tumor extent on different sequences was compared. **Results:** The mean differences in the tumor extent between sequences were measured, there was good agreement between measurements of tumor extent on T1SE and CSI sequences in all cases (T1SE-CSI measurement difference range 0-1.4mm, $p>0.05$). Measurements from fluid sensitive sequences (T2WI and STIR) were significantly different from those of T1SE and CSI ($p<0.05$). **Conclusion:** Chemical-shift MRI is a potential additive technique to MRI imaging protocol of bone tumors. It is highly sensitive in identifying the exact area of tumor extent which is very important in surgical planning and it is a useful tool in differentiating marrow-replacing tumors from benign non-marrow replacing processes (red marrow and marrow edema).

Keywords: Chemical Shift; MRI; Bone Tumors.

Introduction

Over the past three decades, MRI has been proven as a valuable diagnostic tool in oncology. By providing high contrast resolution, MRI plays a central role in defining the intramedullary extent of a bone tumor, essential to surgical planning [(1)].

In particular, the signal intensity difference between normal bone marrow containing fatty marrow and a marrow-replacing intra-medullary tumor is best on a non-contrast T1-weighted spin echo (T1SE) sequence. Fluid-sensitive sequences as T2 weighting or short tau inversion recovery (STIR) have the potential to overestimate tumor extent due to the presence of perilesional bone marrow edema which may be similar in signal intensity to a tumor. With gadolinium administration, a tumor typically enhances on a T1 weighted sequence, although areas of non-tumoral tissue, such as perilesional inflammation, may also enhance, creating the potential for overestimating tumor extent on contrast enhanced T1 weighted imaging [(2)]**.**

An additional T1-weighted option for evaluating the bone marrow has been introduced with chemical shift imaging [CSI, in phase (IP) and opposed-phase (OP) gradient echo sequences] [(3)]**.**

CSI is a means of differentiating a marrow replacing tumor from abnormalities in the marrow that do not replace marrow fat. The latter include entities such as red marrow or bone marrow edema, commonly found around bone tumors. CSI is based on the principle that protons attached to water and fat process with slightly different frequencies; when a voxel contains fat and water, there is an additive effect on the signal in the IP image with at least a 20% loss of signal on the OP image. If the voxel contains a tumor replacing normal fatty marrow, there is only water within the voxel and there is no significant drop in signal (less than 20%) on the OP image compared with the IP image [(4)].

The purpose of this study was to investigate whether chemical shift imaging is a useful addition to a tumor protocol for determining the extent of a skeletal tumor.

Patients and methods

This prospective study was conducted at the Radiology Departments of the National Cancer Institute (NCI), Cairo University& Benha University hospital, Egypt, in the period between February 2022 & July 2023. Initially started with 35 patients, 10 of them were excluded as they showed lesions with a significant drop of signal in the out phase (>20%) when compared to the in phase (case 3) and 25 patients were subjected to the final analysis.

The study was approved by the Research Ethic Committee of Benha Faculty of Medicine (3.1.2022). Informed consents were taken from all participants or their parents before the start of the study.

Inclusion criteria were patients known to have bone tumors and are candidates to MR imaging, patients undergo follow up (for metastatic workup) and patients who undergo other imaging modalities (e.g.: X-ray & CT) which reveal bone tumor.

Exclusion criteria were patients who have received chemo or radiotherapies, patients who are claustrophobic or unable to undergo MRI examination as owing to a pacemaker, critically positioned incompatible metallic foreign body or incompatible vascular implants, (contraindications to perform MRI) and patients who showed lesions with a significant drop of signal in the out phase when compared to the in phase (>20%).

All participants underwent the following assessments:

- Thorough clinical assessment and careful history taking.
- MR imaging: MRI was performed on high field system (1.5 Tesla) closed magnet unit.

Instructions & preparation of the patients:

Reassurance of the patients, simple explanation of the procedures after taking

written and verbal consents from the patient in adult cases or the patient's guardian if the patient is a minor or mentally unstable (e.g., comatose, mental retardation... etc.). All metallic objects were removed from the patient's body or clothes. Adult cooperative patients and teenagers were instructed to keep motionless & breathe calmly during the examination time. In young or uncooperative patients who cannot respond to instructions, they were subjected to thorough anesthesiology consultation and the candidates were exposed to sedation by an anesthesiology specialist and/or consultant.

MR protocol:

MRI was performed with a 1.5 tesla system using appropriate coil. Patients were submitted to the following MR sequences:

Multi planar MR imaging sequences including T1WI, T2WI and fat-suppressed images (STIR &/or PDWI fat sat).

Chemical shift imaging yielding in and out of phase images. The protocols were tailored according to the spatial orientation of each lesion including the used coil and imaging planes.

Imaging evaluation:

Regions of the tumor were defined as follows: any region of low signal intensity less than adjacent skeletal muscle on T1 SE imaging, any region with signal intensity greater than normal fat-suppressed fatty marrow on fluid-sensitive imaging and any region within the bone marrow with a drop in signal less than 20% on OP compared with IP gradient echo images. The extent of the tumor was measured in millimeters for every sequence.

For the chemical shift images, Loss of signal observed on OP compared with IP images can be appreciated visually, but more precisely expressed as a quantitative measure using region of interest (ROI) at the area of least signal drop in the OP image compared to the IP to calculate the relative signal intensity ratio (SIR) with the formula: SI (IP)/SI (OP), and can also be expressed as a percentage signal drop using: [(SI (IP)-SI (OP)) / (SI (IP)] x 100. Disler and co-workers showed that an SIR threshold of 0.8 also distinguished marrow-replacing tumors from benign non-marrow replacing processes (red marrow and marrow edema) in other parts of the body with sensitivities and specificities each of 95%. Processes that replace or displace marrow will contain no intravoxel fat, and will consequently have an SIR >0.8 (i.e., signal drop <20%) [(5)] **(Fig., 1).**

Conversely, >20% signal drop is required to confirm the absence of marrow replacement.

Statistical analysis

The collected data was revised, coded, and tabulated using the Statistical Package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Quantitative data were assessed for normality by the Shapiro-Wilk test and direct data visualization methods. Numerical data were summarized as means and standard deviations or medians and ranges. Categorical data were summarized as numbers and percentages. All statistical tests were two-sided. P values less than 0.05 were considered significant.

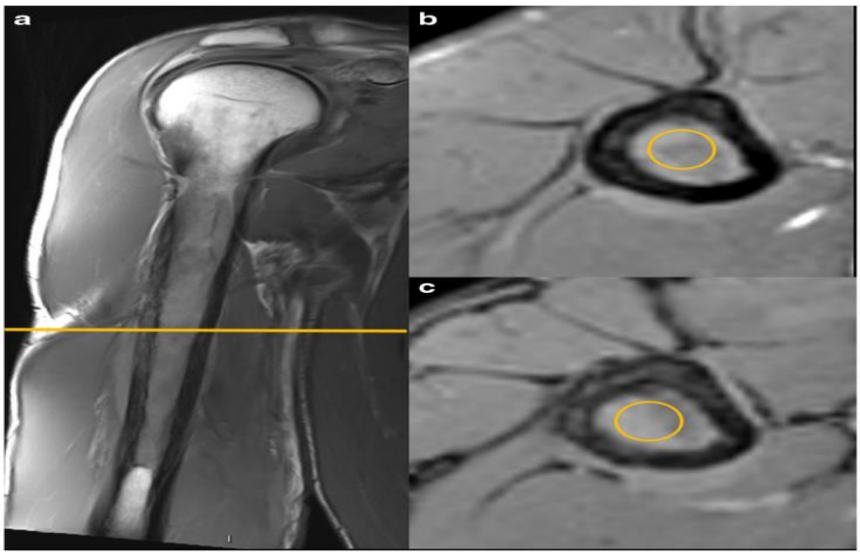

Fig.1 A 41-year-old man with lymphoma of the right humerus. Coronal T1-weighted image shows a marrow-replacing process in the diaphysis. Signal drop out on CSI is calculated using the qualitative method to measure the signal loss percentage (Q-ROI method). An ROI is drawn in a location of the least signal drop on the axial OP (Fig. 1c) compared with IP (Fig. 1b) based on qualitative/visual assessment. Then calculated using this formula: [(SI (IP)-SI (OP)) / (SI (IP)] x 100. The signal drop % was 4% compatible with marrow replacement [(6)]**.**

Results

The mean age of patients was 43 ±18.1 years and 15 patients (60%) were males, and 10 patients (40%) were females (**Table, 1).**

Tumors were found in long bones in 15 patients (60%) and 10 patients (40%) showed other bones tumors as vertebrae and clavicle (**Table, 2).**

The mean tumor length was measured in different sequences in **table 3** and the mean differences in the tumor extent between T1SE and other sequences were measured in **tables 4**. High significant measurement differences were found between T1SE and fluid sensitive sequences (p<0.001), and non-significant measurement differences between T1SE and CSI (p>0.05).

Also, measurement differences for the tumor extent between CSI and other sequences were measured in **tables 5**, and also showed high significant measurement differences between CSI and the fluid sensitive sequences (p<0.001), and non-significant measurement differences between CSI and T1SE (p>0.05).

Table 1: General characteristics.

Age (years)	Mean ±SD	43 ±18.1
Gender	Males n (%)	15 (60)
	Females n (%)	10 (40)

Table 2: Lesion location.

Location	long bones	15 (60%)
	other bones	10 (40%)
Total		25 (100%)

Table 3: The mean length of the tumors in different sequences.

Sequences	Mean length (mm)/range (mm)
T1SE	44.2 (25.6-87.7)
T2WI	48.4 (27.7-94.4)
STIR	51.6 (26.6-95)
CSI	42.7 (24.3-83.6)

Table 4: The mean differences in tumor extent between T1SE and other sequences.

Sequences	Mean difference (mm)/range (mm)	P value
T1SE-CSI (mm)	1.4 (0-4.1)	>0.05
T1SE-T2WI (mm)	4.1 (0-6.7)	<0.001
T1SE-STIR (mm)	7.4 (0-19.6)	<0.001

Table 5: The mean differences in tumor extent between CSI and other sequences.

Sequences	Mean difference (mm)/range (mm)	P value
CSI-T1SE (mm)	1.4 (0-4.1)	>0.05
CSI-T2WI (mm)	5.6 (0-11)	<0.001
CSI-STIR (mm)	8.9 (0-20)	<0.001

Cases

Case 1: In this case, 8-year-old male with right femur intramedullary lesion. (A) Coronal T1WI shows hypointense lesion causing pathological fracture and bone deformity, the length of the lesion was measuring about 87.7mm. (B) Coronal STIR and Axial T2WI (C) images show hyperintensity of the lesion and the perilesional soft tissue edema, the length of the lesion in T2WI was measuring about 94.4mm and in STIR image was measuring about 95mm. D) In axial IP and OP images, after defining the lesion and the area of least signal drop in the OP image compared to the IP, the signal drop was 8% (less than 20%, confirming presence of a marrow replacing tumor), then the length of the lesion was measured (83.6), there was good agreement between measurements of tumor extent on T1SE and CSI sequences (T1SE-CSI measurement difference was 4.1 mm) and much more difference between measurements of the tumor extent between and CSI and fluid sensitive sequences (STIR-CSI measurement difference was 11.4 mm) ./ T2SE-CSI measurement difference was 10.8mm) (**Fig., 2).**

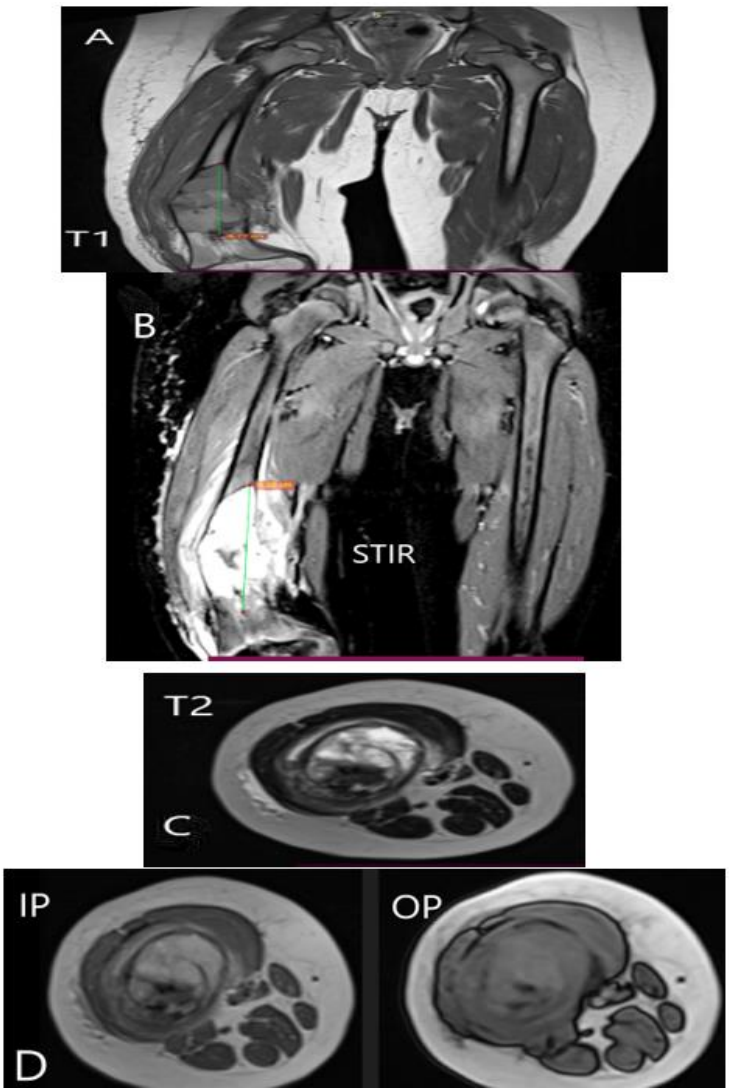

Fig.2: (A) Coronal T1WI image demonstrated a hypointense intramedullary lesion in right femur. (B) Coronal STIR showed hyperintensity of the lesion. (C) Axial T2WI displayed hyperintensity of the lesion. (D) Axial IP and OP images with non-significant drop of signal (8%).

Case 2: 45-year-old male known of multiple myeloma with lower back pain. (A) Sagittal T1WI shows hypointense lesion at L4 lumbar vertebra, the length of the lesion was measuring about 25.6mm. (B) Sagittal T2WI shows hyperintensity of the lesion, the length of the lesion was measuring about 28.7mm. (C) Sagittal STIR image shows hyperintensity of the lesion, the length of the lesion was measuring about 29.7mm. (D) In sagittal IP and OP images, after defining the lesion and the area of least signal drop in the OP image compared to the IP, the signal drop was 7% (less than 20%, confirming presence of a marrow replacing tumor), then the average length of the lesion was measured (24.3), there was good agreement between measurements of tumor extent on T1SE and CSI sequences (T1SE-CSI measurement difference was 1.3mm) and much more difference between measurements of the tumor extent between and CSI and fluid sensitive sequences (STIR-CSI measurement difference was 5.4mm) ./ T2SE-CSI measurement difference was 4.4mm) **(Fig., 3).**

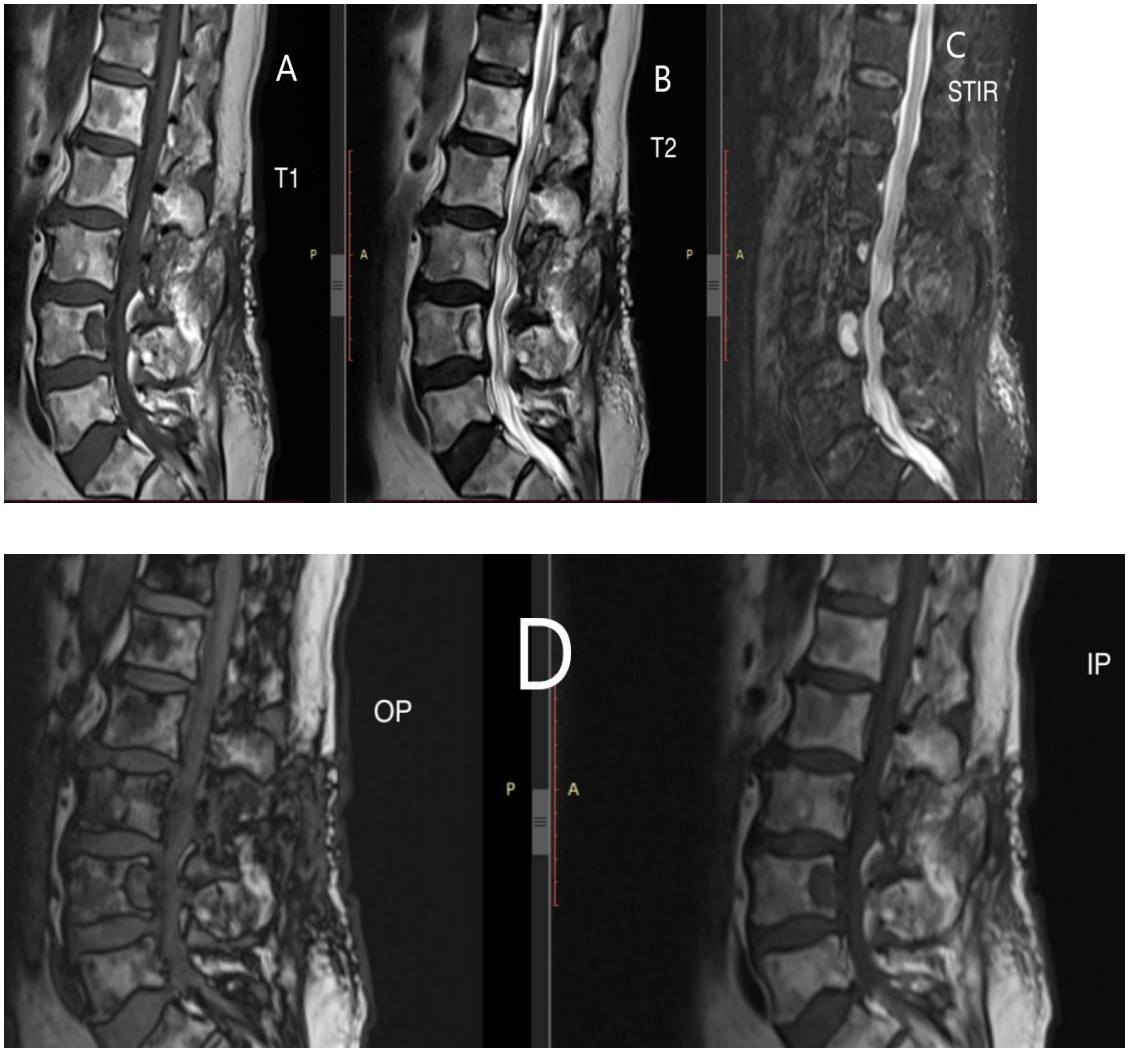

Fig.3: (A) Sagittal T1WI image demonstrated a hypointense lesion in L4 vertebra. (B) Sagittal T2WI showed hyperintensity of the lesion. (C) Sagittal STIR displayed hyperintensity of the lesion. (D) Sagittal IP and OP images with non-significant drop of signal (7%).

Case 3: 37-year-old male with left arm pain and edema. (A) Coronal T1WI shows left mid humeral shaft hypointense lesion with no extension to surrounding soft tissue; the length of the lesion was measuring about 25.7mm., (B) Coronal T2WI shows hyperintensity of the lesion, the length of the lesion was measuring about 27.7mm, (C) Coronal STIR image shows hyperintensity of the lesion, the length of the lesion was measuring about 26.6mm, (D) In axial IP and OP images the whole lesion shows a significant drop in signal in the OP image compared with the IP image (more than 20%), which means that the lesion is containing fat (not a marrow replacing tumor), in this case, atypical hemangioma is highly suggestive as it is (low signal in T1 and high signal in T2 and STIR) unlike the typical hemangioma that is (high signal in T1 as it is rich in fat, also high signal in T2 and STIR), the length of the lesion was measuring about 24.8mm, So CSI can help in differentiating marrow replacing tumors from benign non-marrow replacing lesions like atypical hemangioma **(Fig., 4).**

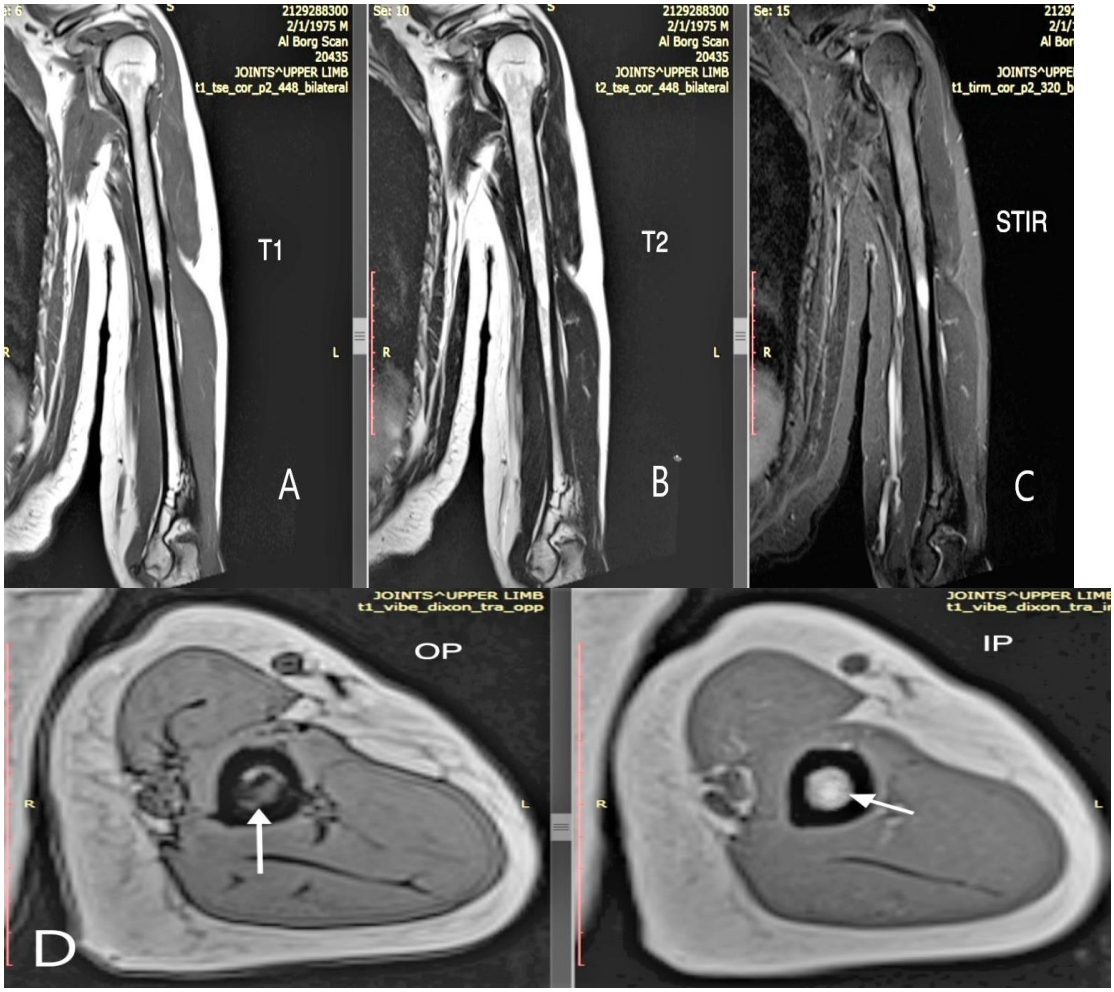

Fig.4: (A) Coronal T1WI image demonstrated a hypointense intramedullary lesion in left mid humeral shaft. (B) Coronal T2WI showed hyperintensity of the lesion. (C) Coronal STIR displayed hyperintensity of the lesion. (D) Axial IP and OP images with significant drop of signal (>20%).

Discussion

Because of its high resolution, tissue contrast, and multi-planar capabilities, magnetic resonance imaging (MRI) is an important imaging modality for the preoperative staging and post treatment evaluation of musculoskeletal tumors. Although radiography, ultrasonography, and computed tomography (CT) are useful for tumor evaluation, MRI is the modality of choice to determine the extent of the lesion before intervention [(7)].

MRI can extend the diagnostic evaluation by demonstrating several tissue components. Also, it is very helpful in local staging and surgical planning by assessing the degree of extension and invasion of the adjacent physeal plates, joints, muscle compartments and neurovascular bundles. It can be used in assessing response to neoadjuvant therapy and further restaging [(8)].

MRI is the gold standard for determining the extent of primary bone tumors due to the high contrast resolution it provides. While there are a variety of MR pulse sequences available for evaluating tumors, including those that provide anatomical information (T1-W, T2-W, static post contrast imaging), those that provide functional information (diffusion-weighted imaging, dynamic contrast-enhanced MRI)

and those that provide metabolic information (MR spectroscopy), an anatomical non-contrast T1-weighted sequence is often adequate for determining the intramedullary extent of a bone tumor [9].

With T1SE, bone tumors have significantly different signal characteristics compared with native fatty marrow and classically exhibit well-defined morphology against the surrounding normal marrow [2].

Fluid sensitive sequences (T2WI and STIR) tend to overestimate the tumor extent, mainly due to perilesional edema that can sometimes be challenging to distinguish from the tumor [10].

A chemical shift sequence with in-phase and OP gradient echo imaging has emerged as an important technique for differentiating a marrow-replacing tumor from non-neoplastic marrow abnormalities, such as bone marrow edema or red marrow [11].

This imaging technique exploits the difference in signal seen on in-phase (IP) and out-of-phase (OP) sequences: this difference is based on the phenomenon that hydrogen atoms attached to water and lipid process at different frequencies. On the in-phase imaging, fat and water signals are additive when these tissues are in the same voxel. On OP images, the two vectors are opposite, resulting in the two signals canceling. When lipid and water exist simultaneously in a benign lesion, the result is a drop in signal on OP images when compared to IP images of the same lesion [12].

IP and OP sequences are easily acquired during a standard musculoskeletal protocol, using a dual gradient-echo technique with T1 weighting. Protocol for IP and OP MRI differs depending on the strength of the magnetic field: with a 1.5 T magnet, the interval on TE (time to echo) between IP and OP images is 2.3ms. The images for both opposed and in-phase-imaging can be taken in about 20–30 s, or a single breath hold [13].

Our study investigated chemical shift imaging (CSI) with in-phase (IP) and opposed-phase (OP) gradient-echo sequences as a good addition to the MRI protocol in imaging and defining the extent of bone tumors. The study included 25 patients, the mean age was 43 ±18.1 years, 15 patients were males, and 10 patients were females. Tumors were found in long bones in 15 patients (60%) and 10 patients (40%) had bones tumors in another sites like vertebrae and clavicle.

In Del Grande and his colleges investigated chemical shift imaging (CSI) with in-phase (IP) and opposed-phase (OP) gradient-echo sequences as an alternative sequence to spin-echo T1 imaging for defining skeletal tumor extent. The study involved 23 patients; the mean age was 31.12 (range, 7-79) years old. and 14 patients were males, and 9 patients were females and the tumors involved 7 femurs, 4 tibias, 2 fibulas, 4 humeri, 5 iliac bones, 3 ischial bones, 2 pubic bones, one sacral bone, one scapula, and one rib [2]. The results of the previous study were in line with our study.

Another study [14] agreed with our results on comparing between of T1SE and out-of-phase sequence in the assessment of length of appendicular bone tumors in 90 patients, they stated that male patients were more than females (53 males and 37 females) with a mean age and range of 36.4 years and range 2-77 years respectively.

Our study showed good agreement between measurements of tumor extent on T1SE and CSI sequences in all cases (T1SE-CSI measurement difference range 0-1.4mm). Measurements from fluid sensitive sequences (T2WI and STIR) were significantly different from those of CSI.

Also, Del Grande et al., in their study showed a good agreement between measurements of tumor extent on T1SE and CSI sequences in all cases (T1SE-CSI measurement difference range 0-13.2 mm, $p>0.05$). Measurements from other

sequences were significantly different from those of T1SE (p<0.05). They concluded that chemical shift imaging is a useful adjunct MR technique to define the extent of bone tumors with more accuracy than fluid sensitive sequences [(2)].

Similarly, Saifuddin et al., in their study affirmed a very good agreement on both sequences the T1SE and OP sequences correlating for tumor length (ICC = 0.94-0.98). They concluded that the OP sequence is comparable to T1SE for assessment of the length of appendicular bone tumors, and more accurate in the presence of extensive reactive marrow edema [(14)]. They also, showed that CSI with IP and OP sequences can differentiate a surrounding bone marrow edema from a fat replacing tumors.

So, we can say that chemical shift imaging is a useful adjunct MR technique for defining the exact area of tumor extent on routine non-contrast imaging, with much more accuracy than fluid sensitive sequences (T2WI and STIR) that overestimate the tumor extent which is very important in surgical planning and also can differentiate marrow-replacing tumors from benign non-marrow replacing processes (red marrow and marrow edema).

Conclusion

Chemical-shift MRI is a potential additive technique to MRI imaging protocol which is useful for the evaluation of the extent of bone tumor. It is highly sensitive in identifying the exact area of tumor extent which is very important in surgical planning and helps in differentiating marrow replacing tumors from benign non-marrow replacing processes (red marrow, marrow edema and benign lesions as hemangioma).

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution

Authors contributed equally in the study.

Conflicts of interest

No conflicts of interest.

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To cite this article: Sally M. Abd El-Lateef a, Mahmoud I. Kandil b, Amr A. Sakr. Role of Chemical Shift of MRI in Defining the Extent of Bone Tumors. BMFJ 2025;42(1):12-22