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Research Paper

Utility of opposed-phase magnetic resonance imaging in differentiating sarcoma from benign bone lesions

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ABSTRACT

Purpose: To investigate the utility of opposed-phase magnetic resonance imaging (OP MRI) in differentiating malignant from benign bone lesions.

Materials and methods: MRI scans of musculoskeletal lesions including opposed-phase imaging sequences were reviewed by both an experienced musculoskeletal attending radiologist, and a second year radiology resident. The change in signal from IP to OP images was measured. The reviewers' evaluation of the lesions based on T1 and T2-weighted images was compared to their evaluation with inclusion of the OP sequences.

Results: Twenty-seven lesions in bone were analyzed: 4 malignant primary bone lesions, 3 malignant soft tissue lesions to bone, 3 metastases from visceral malignancies, and 17 benign bone lesions. Benign lesions of bone dropped in signal on OP imaging by an average of 37.1%. Five of the benign lesions decreased in signal by less than 20%, and two increased. Malignant bone lesions dropped in signal by an average of 0.69% with one of the ten lesions showing a greater than 20% drop.

When OP sequences were included, concern for malignancy decreased in benign lesions and increased in malignant lesions, for both the resident and attending. Compared with standard MRI, inclusion of these sequences increased the overall confidence in diagnosis for both reviewers.

Conclusion: Opposed-phase imaging is helpful in differentiating benign from malignant lesions in bone. Confidence in diagnosis rose for both the attending and the resident as result of the inclusion of OP sequences.

1. Introduction

Magnetic resonance imaging (MRI) has great utility in evaluating musculoskeletal tumors. However, some lesions have an appearance on MRI that make it challenging to differentiate benign from malignant lesions. Even intravenous (IV) contrast sometimes does not allow differentiation of benign from malignant lesions: hemangiomas, Schmorl's nodes, and degenerative vertebral endplate changes all enhance with IV contrast. Opposed-phase MRI (also termed chemical shift imaging, or in-and-out of phase imaging) has shown value in this setting based on its ability to detect small amounts of fat, suggestive of a benign process. In these opposed-phase sequences, signal characteristics consistent with normal fat tissue are not found in malignant, marrow-replacing bone lesions [1,2].

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 precess 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 (see Fig. 1a–d). 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

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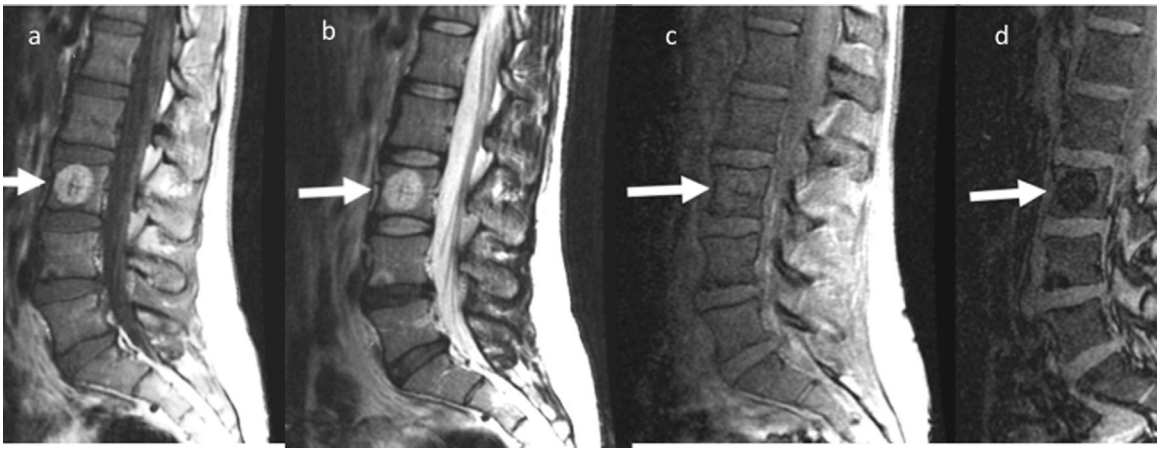

Fig. 1. a–d: 1a – Sagittal T1-weighted spin echo (SE); TR: 500 ms, TE: 9 ms. 1b – T2-weighted fast spin echo (FSE); TR: 4600 ms, TE: 88 ms. 1c – In-phase gradient-recalled echo (GRE): TR: 125 ms, TE: 4.6 ms, flip angle: 90°. 1d – coronal opposed-phase gradient-recalled echo (GRE): TR: 125 ms; TE: 2.3 ms, flip angle: 90°.

images is 2.3 ms. The images for both opposed and in-phase-imaging can be taken in about 20–30 s, or a single breath hold.

Many benign bone lesions contain variable amounts of fat, while malignant bone lesions replace or destroy the fatty bone marrow. A drop in signal on OP images indicates at least some fat content in the lesion, suggestive of a benign process (see Fig. 2a–d). Imaging software uses a region of interest (ROI) to measure the drop in signal, thus yielding a quantitative result. Previous studies have determined a drop in signal of 20% or more to be suggestive of a benign lesion [3]. A drop of 20% on OPI was found to capture all malignant lesions in the study, although this cut-off did allow for some benign lesions being included in the malignant category [3]. This 20% threshold seems to maximize the sensitivity and specificity of the test. A malignant lesion tends to contain little or no fat, resulting in little drop in signal from in-phase to out-of-phase sequences (see Fig. 3a–d). Previous research has shown that this correlates to the histology of the lesions [3]. The hypothesis of our study is that these sequences may play an important role in the imaging of musculoskeletal tumors, enhancing the ability to differentiate benign from malignant disease states and in some cases obviating the need for biopsy. Our goal is to investigate and quantify the extent of this capability, using data collected from blinded radiologists regarding their concern for malignancy, accuracy in diagnosis, and confidence in reading these imaging studies.

2. Materials and methods

Institutional review board approval was obtained for this study; informed consent was waived as this is a retrospective review. A keyword search of our institutional radiology information system was performed, querying for the phrases, “opposed phase” and “in and out of phase.” A senior musculoskeletal radiologist reviewed all MRIs to determine that the OP images were adequate for analysis. Twenty-seven lesions meeting these criteria were found.

Clinical records were examined to determine whether the lesions were benign or malignant. Inclusion criteria were either biopsy confirmation of lesions or at least 9 months of radiologic surveillance. In patients who underwent biopsy, tissue diagnosis was recorded; in those who did not undergo biopsy, documentation of clinical follow-up was utilized. Fifteen of the 27 patients had a biopsy-proven diagnosis of malignancy; only 10 of these exhibited bony involvement. Five of these were bone sarcoma and another five were soft tissue sarcoma or visceral carcinoma. One of the malignant lesions in bone represented direct, local invasion from a soft tissue mass. Of the 17 benign lesions, two were biopsy-proven (osteoid osteoma) and the other 15 were deemed benign based on lack of progression with follow-up imaging and examination of at least nine months. Duration of follow-up imaging ranged from nine to twenty-three months.

A senior musculoskeletal radiologist screened all cases and presented them to two other radiologists in a blinded fashion. These two radiologists were of different experience levels: one was a musculoskeletal radiologist with 5 years of experience and the other was a second-year radiology resident. The screening radiologist had access to the patient records and radiology reports. The two reviewers were blinded to the previous radiology reports as well as the clinical diagnoses.

All MR imaging was performed by using a 1.5 T unit (various vendors) and a phased-array surface coil. The following pulse

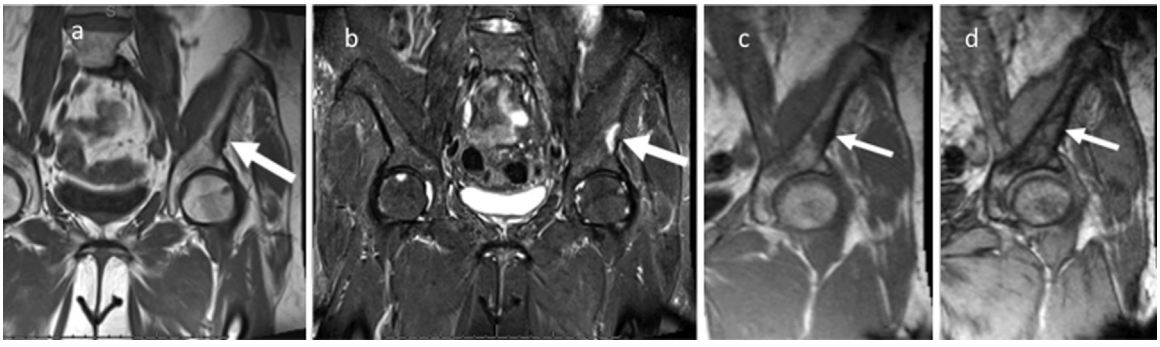

Fig. 2. a–d: 2a – Coronal T1-weighted SE; TR: 547 ms, TE: 12 ms. 2b – Coronal short tau inversion recovery (STIR); TR: 3830 ms, TE: 50 ms, inversion time (TI): 150 ms. 2c – Coronal in-phase GRE; TR: 206 ms, TE: 4.6 ms, flip angle: 70°. 2d – Coronal opposed phaseGRE; TR: 206 ms, TE: 2.3 ms, flip angle: 70°.

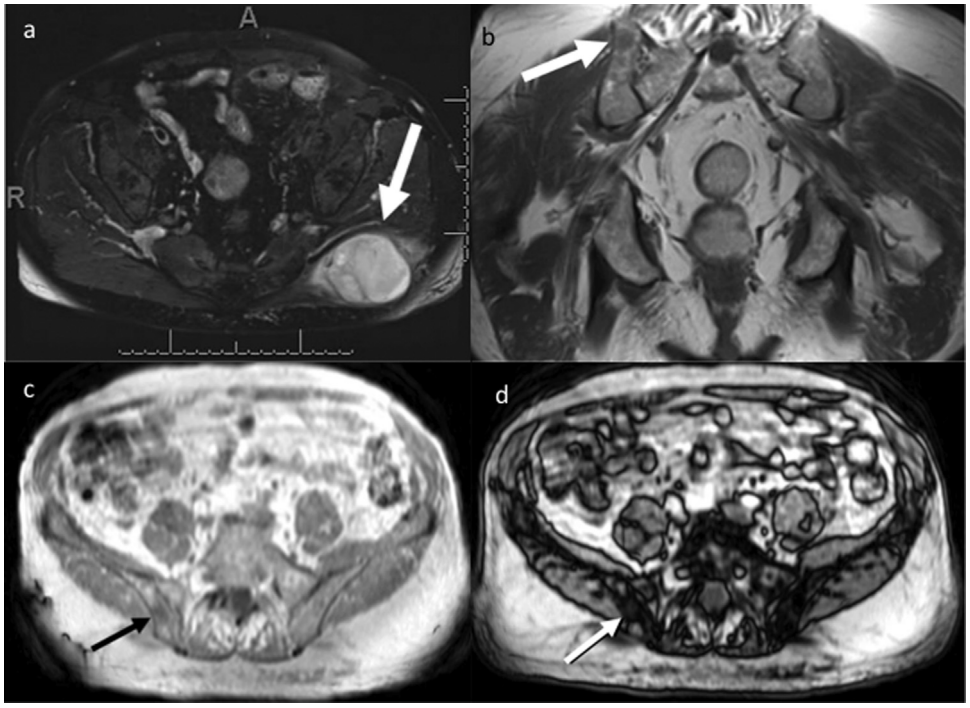

Fig. 3. a–d: 3a: Axial T2-weighted FSE with fat suppression showing large soft tissue mass; TR: 4551 ms, TE: 67 ms. 3b: Coronal T1-weighted SE of pelvic metastasis; TR: 684 ms, TE: 12ms. 3c: Axial in-phase GRE; TR: 213 ms, TE: 4.6 ms, flip angle: 80°. 3d: Axial opposed phaseGRE: TR: 206 ms, TE: 2.3 ms, flip angle: 70°.

sequences were used for all patients as part of our standard institutional protocol: T1-weighted spin-echo (400–700/8–16 [repetition time ms/echo time ms]) and fat-suppressed T2-weighted fast spin-echo (2000–5000/80–100, with an echo train length of 8) sequences, followed by in-phase (100–165/4.6; flip angle, 30°) and out-of-phase (100–165/2.3; flip angle, 30°) fast multiplanar spoiled gradient-echo sequences acquired using Dixon technique. Apart from TE, all other parameters were held constant for acquisition of in-phase and out-of-phase images. The field of view for exams varied depending on coverage required for the body area being scanned; the acquisition matrix was typically 256×192, and the section thickness and gap were typically 4.0 mm, with a skip of 1.0 mm.

Initially the standard T1 and T2-weighted images were reviewed. The reviewers evaluated the lesions for concern for malignancy on a scale of 0–5 (0=no concern, 1=minimal concern, 2=slight concern, 3=moderate concern, 4=substantial concern, and 5=major concern) and for confidence of benign vs. malignant nature (0=no confidence, 1=very unconfident, 2=mild confidence, 3=moderately confident, 4=very confident, and 5=complete confidence). This was followed by repeat review of the same patients with opposed-phase sequences included. The change in signal from IP to OP images was measured using region-of-interest (ROI) quantitative measurements. Lesions were categorized again using the scales above. Results were compared to biopsy results (when available) and follow-up imaging.

3. Results

Twenty-seven bone lesions were analyzed in 27 patients. Twelve of the patients were female and 15 were male. The mean age of the patients was 58 years with a range of 21–84 years. Ten lesions were determined to be malignant and 17 benign. Benign lesions of bone dropped in signal on out-of-phase imaging by an average of 37.1% (range 4–82.3%) when compared to in-phase-imaging. Five of the 17 benign lesions (29%) decreased in signal by less than 20%. Two benign lesions showed an increase in signal suggesting hemorrhage, consistent with osteoporotic compression fracture or edema. There were 10 malignant bone lesions, which dropped in signal by an average of 0.69% (range 2.9–49.8%). Six of these lesions demonstrated a rise in signal. Only one of the 10 malignant lesions showed a greater than 20% drop; this outlier represents bony extension of a soft tissue sarcoma, in a patient approximately 1 month postoperative from resection of her soft tissue mass. The abnormally large drop in signal may be explained by postoperative bony edema in the area of resection (see Table 1).

When evaluating standard MRI sequences (standard T1 and T2) concern for malignancy in benign lesions was 2.95 and 1.79 for resident and attending, respectively (see Table 2). This decreased to 2.11 and 1.47 with the addition of opposed-phase sequences. Concern for malignancy in malignant lesions was 3.78 and 4.11 for radiology resident and staff, respectively. This increased to 4.56 and 4.56 with the addition of opposed-phase sequences. Compared with standard MRI, overall confidence in diagnosis increased from 3.36 to 4.29 for the radiology resident with the addition of OP sequences and from 3.96 to 4.43 for the radiology attending.

4. Discussion

The merit of opposed-phase MRI imaging in characterizing and diagnosing bone lesions has been suggested in recent years [3–5]. The value of this technique has been shown in differentiating benign spine fractures from pathologic fractures [5]. It has also been used to identify lipid-containing adrenal adenomas and liver tumors [6,7]. The goal of our study was to investigate the enhancement of diagnostic capability in musculoskeletal oncology as result of this additional MRI sequence, as well as to explore any resultant difference in confidence in diagnosis for the radiologist. Our findings showed that this technique is a useful additional tool for differentiating between benign and malignant bone lesions, and utilization of this technique did significantly improve the

Table 1
Clinical information regarding lesions.

Patient	Age	Gender	Lesion location	Diagnosis	Change in signal
Malignant lesions in bone					
1	83	F	Right acetabulum	Pelvic chondrosarcoma	17.8% Rise
2	84	F	T8	Metastatic carcinoma	5.1% Rise
3	66	M	T12	Metastatic epithelioid malignancy	2.9% Drop
4	62	F	Left ilium	Metastatic carcinoma	14.1% Rise
5	57	F	Right acetabulum	Lymphoma	8.9% Rise
6	74	M	Left posterior ilium	Large B-cell lymphoma	14.2% Drop
7	65	F	Right iliac crest	Multiple myeloma	10% Rise
8	35	F	Left femoral neck	Leiomyosarcoma of great vessels	11.1% Rise
9	51	F	Proximal humerus	Extension of soft tissue sarcoma	49.8% Drop
10	83	M	R proximal femur	Metastatic high-grade soft tissue sarcoma with myxoid change	7% Drop
				Average	0.69% Drop
Benign lesions in bone					
11	65	M	Distal femur	Normal marrow adjacent to myxoid liposarcoma[a]	33% Drop
12	83	F	T12	Hemangioma with history of metastatic carcinoma[a]	58% Drop
13	64	F	Right proximal femur	Metastatic sarcoma[a]	68.9% Drop
14	53	M	Femoral shaft	Normal marrow, with adjacent metastatic leiomyosarcoma[a]	40.3% Drop
15	52	M	Iliac crest	Post-op bone marrow changes, adjacent chondrosarcoma[a]	46% Drop
16	21	M	Sacrum	Osteoid osteoma	4.2% Rise
17	60	M	T9	Compression fracture, benign[a]	28.7% Rise
18	62	M	L2	Osteoid osteoma	46.5% Drop
19	75	M	L2	Fracture[a]	64.4% Drop
20	47	M	L5	Presumed atypical hemangioma[a]	4.1% Drop
21	54	M	T1	Presumed hemangioma[a]	9.4% Drop
22	34	M	T–L junction	Presumed atypical hemangioma[a]	68.1% Drop
23	58	F	L4	Presumed hemangioma[a]	51.1% Drop
24	58	F	L5	Presumed hemangioma[a]	4% Drop
25	44	M	Diffuse marrow	Presumed marrow heterogeneity[a]	71.3% Drop
26	46	F	Posterior ilium	Presumed marrow abnormality[a]	15.6% Drop
27	30	M	Diffuse marrow	Presumed marrow abnormality, no discrete lesions[a]	82.3% Drop
				Average	37.1% Drop

This table demonstrates the clinical information regarding the 27 patients, including the change in signal of the lesion on opposed-phase imaging. The average for the signal changes of malignant and benign groups is shown.

[a] These diagnoses were made based on history, physical exam, and imaging characteristics and were followed by sequential MRI scans; biopsy was not performed. The remaining lesions without [a] were diagnosed with biopsy.

Table 2
Impact of OP MRI on radiologist interpretation.

	Concern in benign cases	Concern in malignant cases	Confidence in diagnosis
T1/T2 only			
Resident	2.95	3.78	3.36
Attending	1.79	4.11	3.96
Addition of opposed phase			
Resident	2.11	4.56	4.29
Attending	1.47	4.56	4.43

This table demonstrates the effect that the addition of opposed phase imaging sequences has on radiologists' ability to correctly interpret MRI scans of the lesions in question. As illustrated, their accuracy in diagnosing malignant lesions, as well as their confidence in this diagnosis, improved with the addition of opposed phase sequences.

radiologists' confidence levels in terms of diagnosis. Both the clinical and financial value of this technique is important to consider, as the ability to confidently identify benign lesions from malignant ones can obviate the need for unnecessary biopsies and surgical procedures (see Fig. 4a–d).

One of the benign lesions in our study, an acute compression fracture, showed a considerable increase in signal on OP imaging. This was due to hemorrhage and illuminates an important caveat when using this technique: in the acute phase, blood products can result in an increase in signal intensity on OP imaging. The STIR and T2 sequences are critical in elucidating this nuance, and it is important for the clinician to realize that opposed-phase imaging should be used with caution in evaluating lesions that are prone to hemorrhage. One osteoid osteoma also demonstrated an increase in signal, which could be explained by the intense edema surrounding the nidus. Soft tissue sarcoma metastasis to bone occurred in one patient who demonstrated a high magnitude of drop in signal on OP sequences, likely due to her postoperative state and resultant bony edema. This represents one of the limitations of this imaging technique: while it is a fairly reliable predictor of bone malignancy, the threshold of a 20% drop in signal is not completely generalizable to malignancy in bone.

The impact of opposed phase imaging on radiologist confidence was an interesting finding of this study. In terms of confidence in their diagnosis of a benign versus malignant lesion, the presence of opposed phase images for review certainly improved the reader's confidence. However, inappropriate confidence could lead to inaccurate diagnoses and devastating clinical consequences. In the case of acute hemorrhage, for example, there are nuances of these MRI techniques that must be understood to ensure accurate and appropriate interpretation of their results. It is also important to note that opposed-phase imaging is not a stand-alone technique. Ideally these sequences would be incorporated into a holistic review of all T1, T2, and TE MRI sequences, with contrast enhancement when appropriate, which have better resolution due to better spatial orientation and lower signal-to-noise ratio.

There are several limitations to our study. The sample size is low, partly due the relative rarity of sarcoma and also to the rarity of the chemical shift imaging sequences being performed in our study subjects. As a retrospective review, the authors were limited to the patients' images available, performed at a prior date. Some

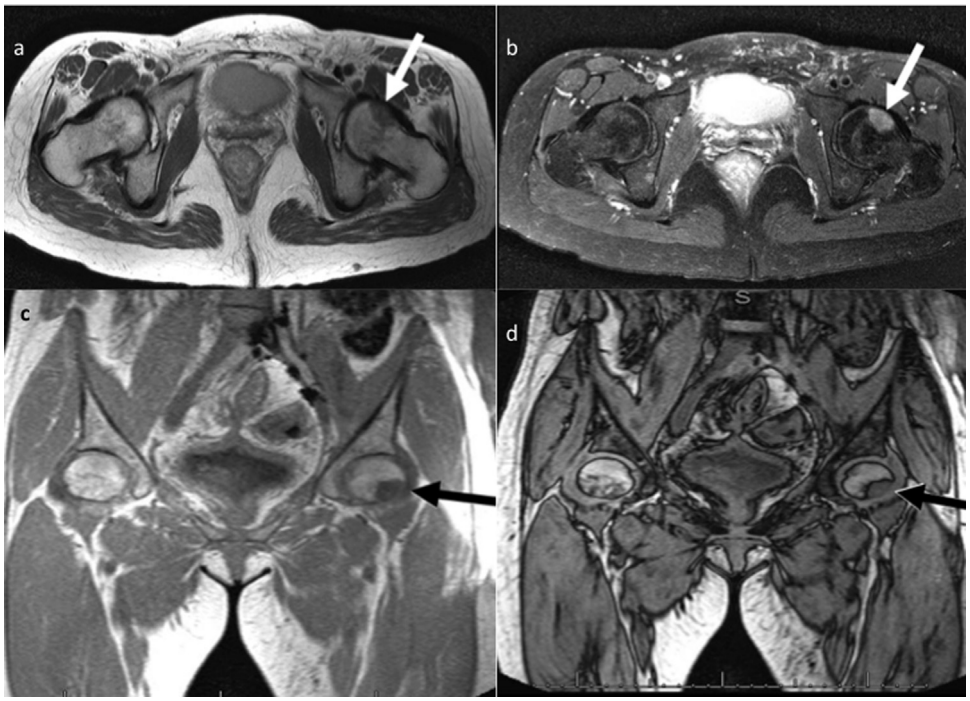

Fig. 4. a–d: 4a: Axial proton-density weighted; TR: 2173 ms, TE: 40 ms. 4b: Axial T2 fat-suppressed FSE; TR: 2518 ms, TE: 70 ms. 4c: Coronal in-phase GRE: TR: 234 ms, TE: 4.6 ms, flip angle: 80°. 4c: Coronal opposed-phase GRE: TR: 234 ms, TE: 2.3 ms, flip angle: 80°.

of the images in our study were imported from outside facilities, so there was variability in equipment and imaging parameters. However all images were reviewed for adequacy by an experienced musculoskeletal radiologist who was not a reviewing radiologist in the study. Another weakness of any retrospective review is the possibility of selection bias, as the study sample may be an inappropriate representation of the overall population. Future research could be directed towards investigating the comparative efficacy of opposed phase MRI to that of contrast-enhanced MRI, which is currently a highly-utilized technique for imaging musculoskeletal tumors, as this was not specifically explored in this study.

5. Conclusion

It is the authors' belief that opposed-phase imaging is useful additional tool in evaluating bone tumors. It improves diagnostic accuracy and this results in higher confidence level on the part of radiologists attempting to diagnose these lesions and convey an appropriate sense of concern for malignancy. Further study is needed on the accuracy and reliability of this technique in a larger heterogeneous group of patients with bone lesions, to more effectively quantify the tests' true accuracy, precision, negative predictive value, and positive predictive value. However, we urge all orthopaedic surgeons ordering MRI scans on bone lesions to consider this additional sequence to help guide their diagnosis and management of patients.

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