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Added value of Dixon Technique in the assessment of bone marrow lesions.

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Abstract: Background: In clinical practice, acquisition of images with fat suppression is highly beneficial and can be accomplished via variable sequences. Dixon sequences are recognized as a dependable MRI method that can be applied to the evaluation of bone marrow lesions in order to solve problems. Dixon technique, in contrast to other fat suppression techniques, depend on the difference in resonance frequency between fat and water to obtain fat only, water only, in-phase, and out-of-phase images in a single acquisition. In addition, the Dixon technique permits the showing of maps illustrating the distribution of water and fat, which is not possible with conventional fat suppression techniques. Instead, the fat signal can be suppressed after postprocessing. Because of this, Dixon techniques have the exclusive capacity to measure the quantity of fat inside a bone lesion, enabling the differentiation between marrow replacing and non-marrow-replacing lesions. We would like to recommend adding Dixon sequences to the routine MRI protocol during the evaluation of bone marrow pathology as a problem-solving tool.

Keywords: Dixon, MRI, bone marrow lesions, fat suppression techniques.

Introduction

Many recent reviews examined the use of the Dixon sequence in the evaluation of musculoskeletal soft tissue disorders and bone marrow lesions [1, 2, 3]. The Dixon approach was initially created in 1984 and carries the name of its developer [4]. These days, almost all manufacturers offer chemical shift imaging (CSI) algorithms and Dixon-type pulse sequences as typical fat suppression methods, all under their own specific names. Siemens uses the generic name DIXON, Philips has multi-point or mDixon, and General Electric (GE) has its iterative decomposition of water and fat with echo asymmetry and least squares estimation (IDEAL) [5]. According to Maeder et al. [6], the Dixon approach can be applied to both gradient echo (GRE) and spin echo (SE) sequences. While GRE imaging of musculoskeletal tissues displays image contrast characteristics different from those of fast spin echo (FSE) pulse sequences, which are commonly used in the assessment of joints, there are differences between the GRE and SE MRI techniques, including an overall faster scanning time using GRE

[7]. Dixon approach provides maps of water and fat distribution and, in contrast to previous fat suppression features, permits the fat signal's contribution to be suppressed during post-processing instead of during capture [8]. Dixon technique application for quantitative assessment of fat fraction (FF), joint cartilage analysis, bone marrow studies, assessment of sacroiliitis, and reduction of magnetic susceptibility artifact in the presence of metallic implants has been demonstrated by several recent studies [2,9,10]. It is crucial to comprehend the technological basis of CSI to be able to interpret the four distinct imaging sets that were gathered using Dixon procedures. These sequences are: fat-only (FO), water-only (WO), out-of-phase (OP), and in-phase (IP). One conspicuous characteristic of OP imaging is the formation of a "black pen" around the organ and muscle compartments due to a chemical shift artifact at the fat–water interface [11].

Basic physical principles:

Understanding Dixon techniques requires knowing that fat and water are the primary constituents that generate the pictures viewed on MRI [12]. Water molecules' hydrogen nuclei resonance frequency is higher than that of fat molecules. The major peak of fat molecules and the peak of water molecules differs in frequency by 3.4 ppm in a homogeneous field. Since the equipment's field strength affects the absolute difference in frequency, it will vary from about 217.6 Hz at 1.5 T to about 435 Hz at 3.0 T. The transverse magnetization of water and fat in a gradient-echo (GRE) sequence begin in-phase right after the start of the excitation pulse; this phenomenon is referred to as in-phase imaging. These magnetizations will be in out of phase (180°), after 2.2 ms in a 1.5 T scanner or 1.15 ms in a 3.0 T scanner. When those echo times (TEs) are used to obtain the image, the signals from the fat and water are subtracted from one another and may cancel each other out if the amount of fat and water in each voxel is the same. The water and fat signals can be summed together during acquisition with higher TEs since they would be in phase [8,9]. Technically, obtaining images from an echo that nulling TE would not be practical. In order to generate the in-phase condition, an acquisition is carried out at twice the TE of the initial out-of-phase condition. This yields a signal that is the sum of the two contributions. This is the fundamental idea behind the two-point Dixon (2PD) technique, which is the process of acquiring images at two distinct TEs [4]. Water and fat separation is a stage in the post-processing of the in-phase and out-of-phase images, in which the in-phase and out-of-phase images are added to produce water-only image, and the in-phase image is subtracted from the out-of-phase image to produce fat-only image. Therefore, the fat water fraction in a region of interest can be measured using the Dixon technique with higher spatial resolution than what can be obtained using spectroscopy. The aforementioned concept can be used generally for the suppression or measurement of fat in different kinds of pulse sequences [12]. Initially, a few issues hindered the two-point Dixon (2PD) sequence's broad application. Firstly, there is not always a uniform magnetic field, particularly in locations that are large or have air-bone interfaces. In case of heterogenicity of the magnetic field, the sum and subtraction approach produces partial or incorrect separation of water and fat [8,9,13,14]. The Dixon approach has been improved to avoid the drawbacks of the 2PD sequence. A third echo or more echoes are added, along with the usage of multi-point Dixon—three- or six-point echoes. This leads to acquiring of "purer" fat and water images with optimal spatial resolution, in a faster acquisition time, and independent of any field heterogeneity [13,14,15].

Quantification methods:

Different methods have been employed to measure the quantity of fat present in a marrow lesion. The measurement of signal intensity (SI) drop on OP images compared with IP images is one of the most commonly used. On both IP and OP images, the same regions of interest (ROIs) are drawn in the bone, and the percentage decrease is calculated as the following ((SIP-SOP)/SIP) × 100 = SI %drop [16,17].

A SI decrease of more than 20% at 1.5 T is considered consistent with a benign fat-containing marrow lesion; on the other hand, a decrease of less than 20% is consistent with marrow fat being replaced due to a malignant process (Fig. 1) [16,17]. Additionally, at 3 T, Kumar et al. [18] conducted research on the ideal threshold and found that a 25% threshold SI drop resulted in at least 100% sensitivity and 86% specificity for the identification of marrow replacement.

SI (OP)/SI (IP) is the formula used to determine the relative signal intensity ratio, or SIR. Processes that replace marrow will therefore have a SIR cut-off value greater than 0.8. In contrast, non-marrow-replacing processes (Figs.1) will display a SIR <0.8 [19].

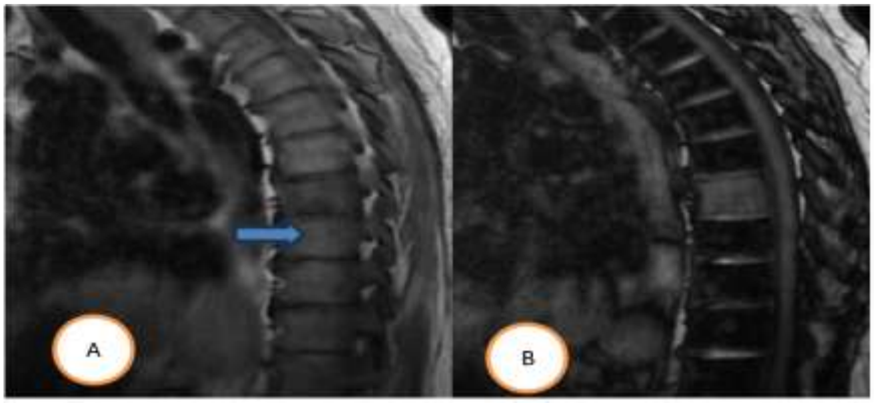

Figure (1): 59 year-old male with history of prostate cancer, presents focal hypointense lesion (blue arrow) within DV7. A) sagittal In-phase image B) Sagittal out-off- phase image of dorsal spine. The lesion show no drop of signal on OP images compared to IP images: % drop = 10.5% and SIR=89.5%. It is consistent with a marrow replacing process (metastasis).

Relative fat-fraction (rFF) maps can be computed from the fat- and water-only images, offering further information about the state of bone disease [20,21]. (Messiou et al., 2012, Bray et al., 2017). The SI on fat-only image divided by the sum of the SI on fat-only and SI on water-only images yielded the rFF maps. Malignant bone disease should have significantly lower rFF compared to normal fat-containing bone marrow since it typically does not contain fat (Fig.2) [22]. Kim et al, found the cut-off point of fat fraction to to discriminates between benign and malignant marrow lesions is ≤ 16.8%.

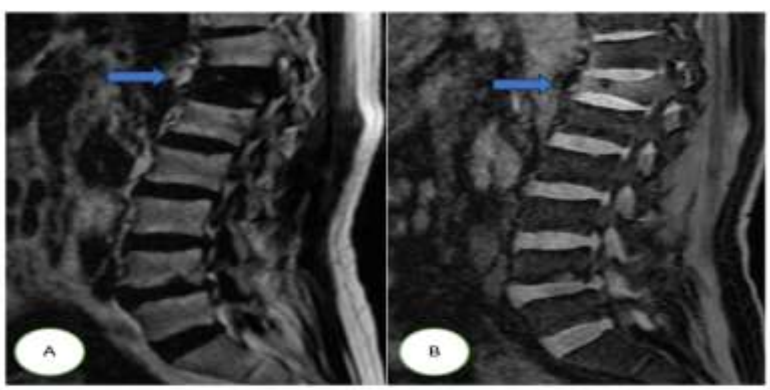

Figure (2): 63-year-old male with history of rectal cancer, presents focal hypointense lesion (blue arrows) within DV12 with loss of its height and anterior wedging. A) sagittal fat-only image B) Sagittal water-only image of dorsal spine. The lesion shows signal void on fat-only image: % fat It is consistent with a marrow replacing process (metastasis).

Clinical applications of Dixon techniques:

1-Dixon technique helps in diagnosis of most of the questionable benign bone marrow lesions detected on conventional MRI such as hematopoietic red marrow (Fig. 3), atypical hemangiomas and focal nodular marrow hyperplasia (FNMH). These lesions change the signal of normal fatty marrow and display low SI in comparison to normal marrow signal intensity. While, they are slight high SI in comparison to skeletal muscle. These lesions typically preserve enough of fat that allow a > 20% (1.5 T) or > 25% (3.0 T) signal loss on OP imaging (3,1723,24,25).

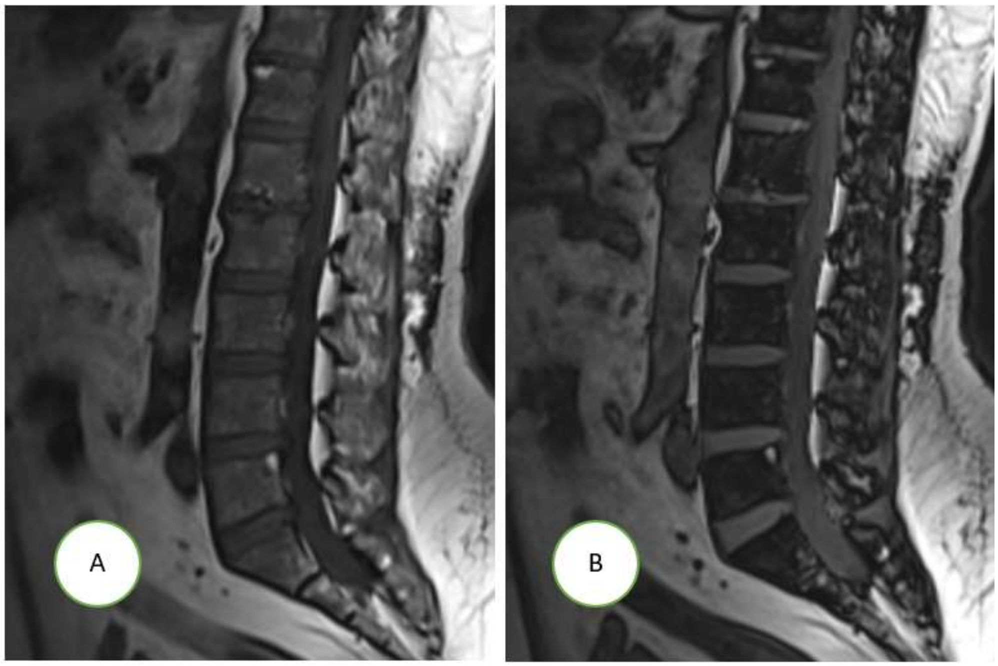

Fig. 3: Sagittal MRI of the lumbosacral spine of a 63-year-old man. A) IP Dixon image shows diffuse intermediate marrow SI due to hyperplastic red marrow B) OP image shows a profound reduction of marrow SI owing to its high fat content. % drop ranging from 65 to75% consistent with benign marrow process)

2-Differentiation of pathological from non- pathological vertebral fractures: A comparison of quantitative IP and OP chemical shift imaging (CSI) for benign vertebral compression fractures BVCFs (Fig. 4) and malignant ones showed statistically significant variations in SI (26,16). A reduction in SI of more than 35% on (1.0 T–1.5 T) OP images relative to IP images may be utilized as a threshold to distinguish osteoporotic from pathological spinal compression, according to research by Ragab al. (27). Further evidence that the fat fractions of acute BVCFs and malignant compression fractures obtained using the multipoint Dixon method are substantially different (lower fat fraction in malignant ones (Fig. 2) has also been demonstrated. This allows for even more differentiation between the two types of fractures (23,28).

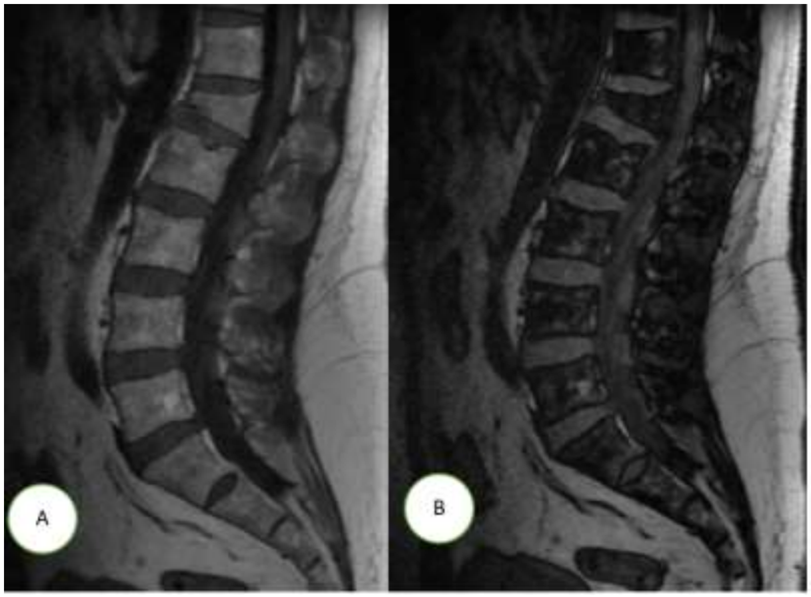

Fig. 4: Sagittal MRI of the lumbosacral spine of a 71-year-old man. A) IP Dixon image shows partial loss of height of DV1 with anterior wedging B) OP image shows a reduction of marrow SI owing to its high fat content. % drop = 79% consistent with benign osteoporotic fracture).

3-Assessment of malignant bone marrow lesions like multiple myeloma, primary and metastatic bone marrow lesions as well as post treatment response: It has long been known that MRI is an extremely specific and sensitive method of detecting skeletal metastases [(29)]. More recently, the detection of skeletal metastases by Dixon sequences has been assessed. It was also found that the FO sequence significantly improved lesion conspicuity when compared to T1W SE images. Healed myeloma and healed skeletal metastases can show changes in bone marrow fat to water ratio [(30)].

Better bone marrow metastasis identification is not the sole benefit; quantitative evaluation of the % drop and % fat can also be useful. In recent times, the effectiveness of whole-body Dixon techniques has been reported [(12)]. Therapy Monitoring is another use for it. Diffusion-weighted imaging in conjunction with Dixon sequences improves metastasis identification and aids in recognizing the detailed alterations that occur inside the bone marrow as a result of treatment. Furthermore, Dixon sequences provide quantitative data on the fat and water levels in red bone marrow during therapy which are useful as biomarkers for treatment monitoring (Fig. 5) [(19)].

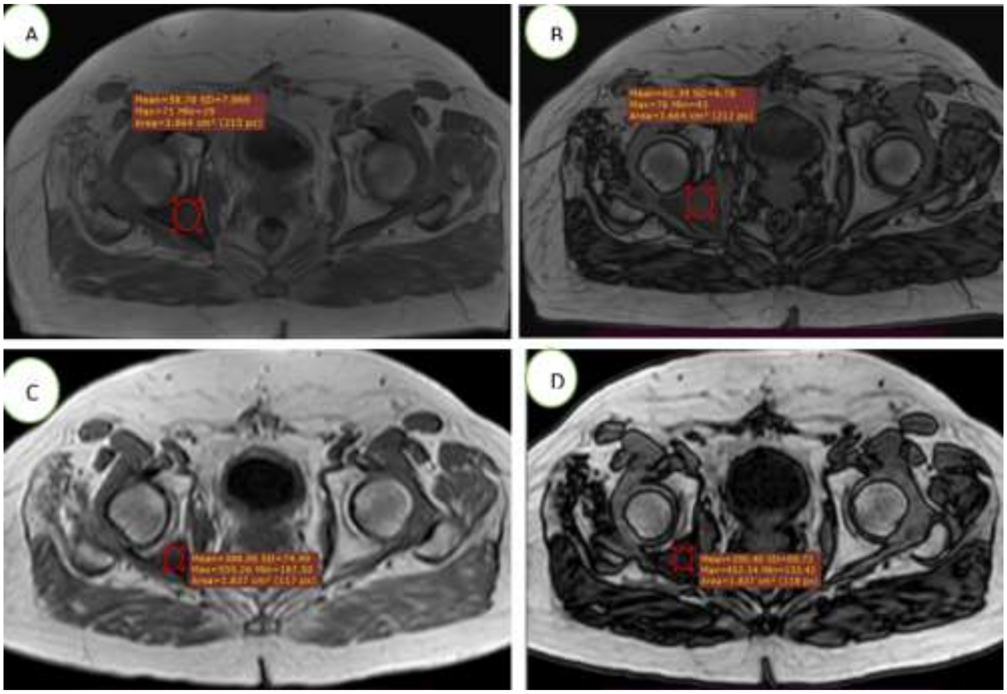

Fig. 5: Axial images of 46-year-old man with prostatic cancer. A) axial IP Dixon image before therapy B) OP image before therapy, C) axial IP Dixon image after radiotherapy follow up after 4 months D) axial OP Dixon image after radiotherapy % drop in 1st study= -7.9% (consistent with malignant bone marrow replacing lesion… metastasis) and in 2nd study= 25.2% denoting good response to treatment confirmed by PET CT.

Limitations and pitfalls of the Dixon technique:

There are restrictions with Dixon's methods as well. They don't entirely address the problems with artifacts in extremely heterogenous locations, including the vicinity of remaining metallic devices, which might make the assessment difficult. In certain instances, STIR sequences continue to be more dependable for suppressing fat around large metallic prostheses [(8)].

"Fat–Water Swapping Artefact" arises from an inaccurate determination of voxel contents due to a computational error in areas of field heterogeneity. When a fat-only image is wanted, it converges to the incorrect substance in this manner, resulting in a water-only image. This issue could be resolved by adding a third echo to account for field heterogeneity, which would lengthen the scan time but increase the technique's robustness [(31)].

The final signal obtained is affected by field strength, TE, and flip angle. So, when the fat fraction measured and during the characterization of bony lesion, we should put in mind that they are sensitive to small variations in scanning parameters. Generating of accurate and dependable readings requires a deep comprehension of the MRI technique [(28)].

Atypical hemangiomas, myelofibrosis (Fig.6), and compacted bone after healing fractures are examples of sclerotic fat containing marrow lesions. and Paget's disease can also result in an inadequate drop in SI on OP images, making it difficult to distinguish them from lesions that have infiltrated the marrow. Swartz and Roberts, who described a case of a pelvic lesion that was mistakenly positive and had imaging characteristics that pointed to marrow fibrosis. CT must be done to go over such an obstacle [(32)].

Fig. 6: Coronal MRI of the lumbar spine of a 55-year-old man. A) IP Dixon image shows diffuse intermediate SI of the examined bone marrow B) OP image shows no reduction of marrow SI due to diffuse bone fibrosis confirmed by biopsy (1ry myelofibrosis). C) sagittal CT bone window of vertebral column shows diffuse sclerosis. % drop =12 % consistent with marrow replacing process (one of the pitfalls).

False-positive errors include benign tumors replacing normal bone marrow, hematoma at fracture sites, benign cysts or geodes replacing bone marrow (Swartz et al., 2009), and second stage osteomyelitis. CSI sequences' signal alterations in the context of osteomyelitis vary based on stages of evolution. Only mild edema without fat marrow replacement is present in early osteomyelitis, indicating a percentage of signal reduction greater than 20%. However, if the condition develops, pus or an abscess may form in the medullary canal, which would prevent a signal drop between IP and OP images. Then, dense inflammatory cells and purulent material (% drop <20%) may serve as a marrow-replacing process caused by osteomyelitis [19].

False-negative pitfalls include renal cell carcinoma metastases containing fat and previous chemotherapy or radiotherapy may induce the appearance of intralesional fat, which could lead to false-negative results. This pitfall must be kept in mind when bone marrow imaging results are being reported [32].

Conclusion:

Dixon technique is recognized as a dependable MRI technique that can be used to solve the problems during the evaluation of bone marrow lesions. It is a useful technique for characterizing bone lesions by quantifying the amount of microscopic intracellular fat. It provides more strong fat suppression than other sequences and can be used in combination with multiple different sequences (gradient and spin echo) and using different weightings (T1, T2, or proton density).

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