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Most clinical MR evaluations of bone marrow are successfully performed with spin-echo methods, with T1-weighted images offering the best sensitivity to pathology. Poor specificity, however, prompts a search for alternative MR techniques that may yield more specific data. Chemical shift imaging methods may increase the accuracy of MR evaluations of marrow, particularly in the case of infiltrating diseases.

As techniques to assess marrow processes have evolved, magnetic resonance imaging has assumed an important role in evaluating the marrow space. This is particularly true with respect to neoplastic disease, infection and avascular necrosis.

Most clinical evaluations of bone and bone marrow are based on spin-echo imaging sequences. Multiplanar SE imaging provides high signal-to-noise images at reasonable scan times, with relative insensitivity to susceptibility effects and static field inhomogeneities. The T1-weighted SE image is a reliable screening technique for processes affecting the marrow space.

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Most pathology will be conspicuously depicted as an area of signal loss against a background of higher signal intensity normal marrow.

The temptation to substitute proton density-weighted or balanced images for true T1-weighted images should be resisted when evaluating the marrow space, even though the proton density images may be acquired at no time penalty using a variable echo acquisition when T2-weighted images are obtained. The proton density image provides optimal signal-to-noise (S/N), and thus the best depiction of anatomy. Marrow pathology may occasionally be missed on proton density images, however (Figure 1).

STIR TECHNIQUES

Conventional inversion recovery techniques generate heavily T1-weighted

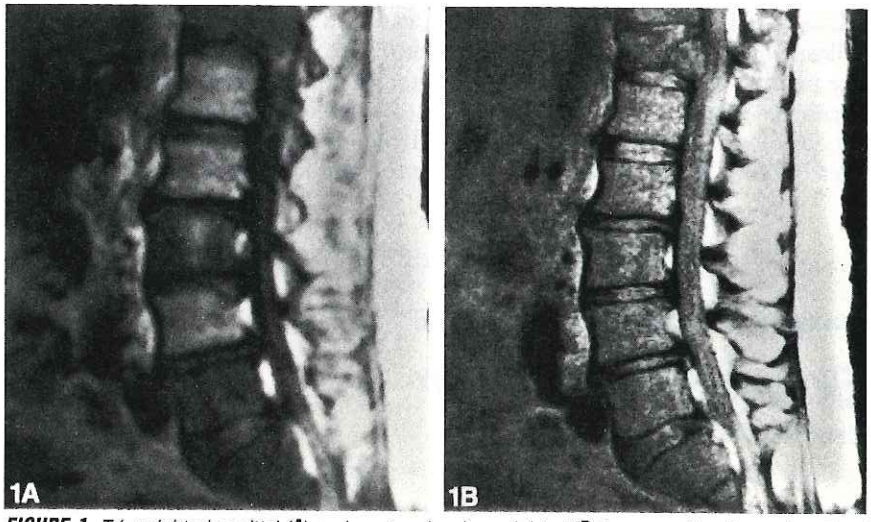


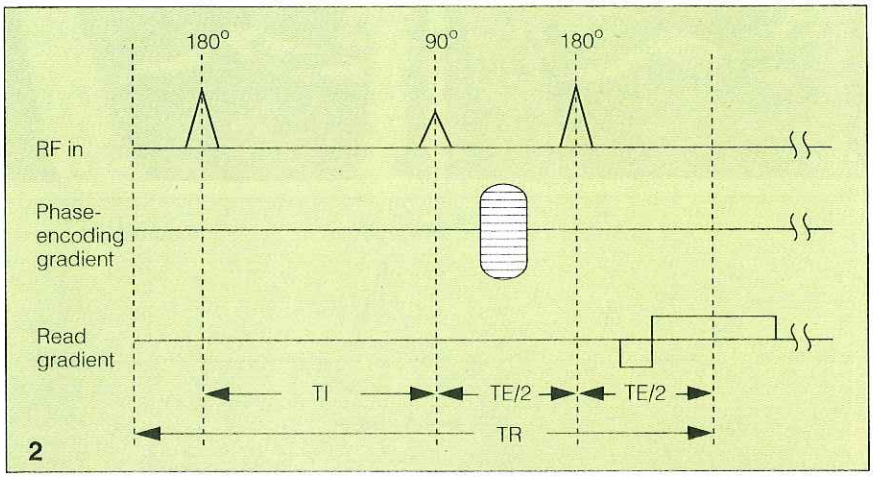
FIGURE 1. *T1-weighted sagittal (**A**) and proton density-weighted (**B**) images of lumbar spine. Focal marrow lesions involving multiple vertebral bodies evident on A are not apparent on B. (Courtesy of L. Solti-Bohman)*

images (Figure 2). If the inversion time (T1) is made short, such that TR>2TI, a null point is created. The null point is the T1 value of a species of spins for which the net magnetization vector will be passing through the transverse plane at the inversion time (TI). These spins will have no net vector along the z-axis at the time of the 90° flip, and will thus be selectively suppressed. Short tau (inversion time) inversion recovery (STIR) is typically used to suppress signal from fat, and is an important technique for studying the marrow space, as well as for determining the soft tissue extent of primary bone lesions.[1,2] If TR is much larger than T1, as in most multiplanar acquisitions, the null point can be estimated as TI/ln2. For a typical T1 value of fat (250 msec at 1.5 tesla), the appropriate TI for marrow imaging would be 173 msec.

Despite poorer S/N as compared to SE imaging, STIR offers greater conspicuity of neoplasia (Figure 3).[3] Pathology is frequently characterized by concomitant increases in T1, T2 and proton density. For tissues with a T1> null point, prolonged T1 and T2 and increased proton density contribute additively to greater signal intensity.

In SE imaging, the contrast effects of prolonged T1 and T2 are opposed. In a sense then, STIR combines the contrast advantages of T1- and T2-weighted SE sequences. Conversely, with STIR, the effects of longer T1 are opposed by increases in T2 or proton density for tissues with a T1< null point. This feature of STIR is theoretical, as most pathology has a T1 greater than fat.

Disadvantages of the STIR technique include the nonspecificity of the abnormal findings. In fact, STIR is probably less specific than T2-weighted SE scans, which themselves are fairly nonspecific.[2] Slice coverage is also decreased with STIR as compared to SE. Thus, practically speaking, study times are longer.



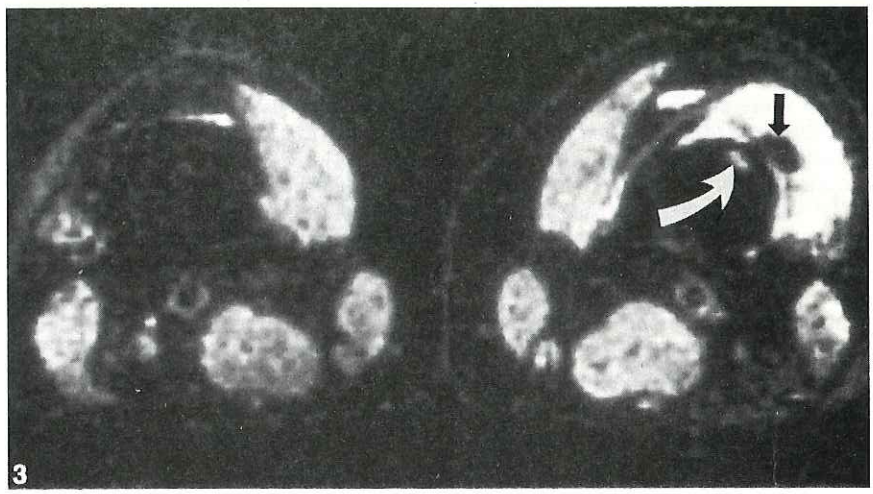
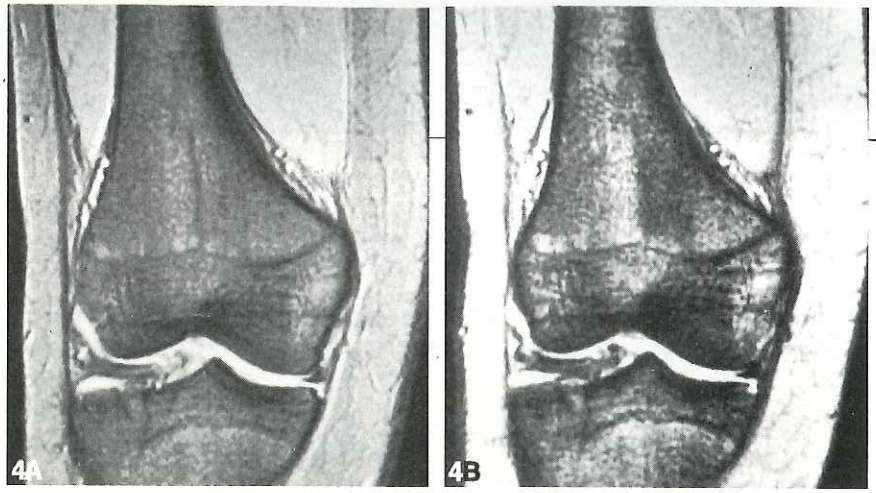


FIGURE 2. *Pulsing diagram for STIR. If TR > 2TI, then TI can be selected to suppress fat. At 1.5 tesla, appropriate TI would be about 170 msec.* ***FIGURE 3.*** *Axial STIR image of parosteal osteogenic sarcoma of distal femur. Small intramedullary component of lesion is clearly depicted with this sequence (curved white arrow). Low signal within extraosseous mass represents tumor matrix ossification (straight arrow).*

GRADIENT-ECHO SCANS

Even relatively T1-weighted gradient-echo techniques depict bone marrow with characteristically low signal intensity. This low signal feature is a manifestation of intravoxel dephasing resulting from the discrepant diamagnetism of trabecular bone and other marrow elements,[4] a microscopic susceptibility effect. Indeed, the quantification of this susceptibility effect may serve as an alternate means of measuring trabecular bone density. Because signal intensity of marrow on gradient-echo (GE) scans is affected by trabecular bone, they will be less sensitive than SE scans for localizing hematopoietic marrow.[5]

Though one speaks of fat as a single, broad spectral peak, fat actually consists of multiple spectral components (e.g. vinyl, methylene protons). Thus, modulations in the fat signal might be expected on GE scans where chemical-shift-related dephas-



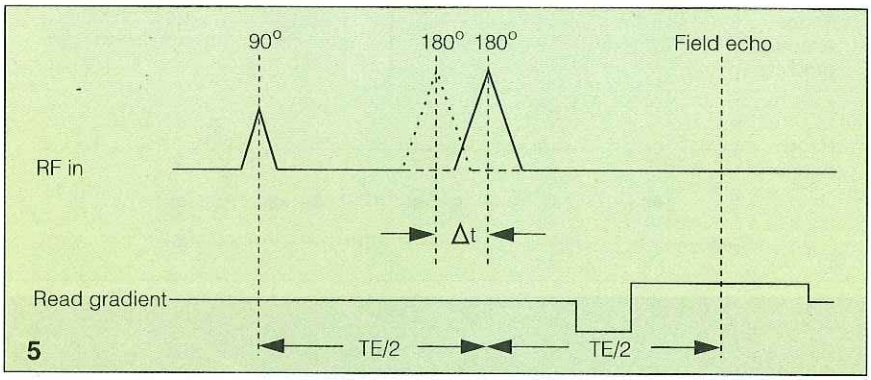


FIGURE 4. *Coronal GE scans of femur at TE = 20 msec (**A**) and 10 msec (**B**). Fat modulation is apparent in subcutaneous fat, but not in yellow marrow where signal characteristic is dominated by trabecular-induced dephasing. Thus, signal of marrow on A is 71% of that on B, while that of subcutaneous fat is actually greater—103% of that on B.* ***FIGURE 5.*** *Dixon phase contrast method. Offset 180° refocusing pulse used in opposed image acquisition is superimposed on same read-gradient structure as for in-phase acquisition. Field echo and resulting RF echo will then be out of phase. Δ(t) is set to equal one-quarter modulation between major fat and water spins.*

ing that occurs during the FID is not rephased at the echo. At 1.5 tesla, the major spectral components would be in phase at 20 msec, and out of phase at 10 msec (Figure 4). These modulations are evident in subcutaneous fat, but are overshadowed by susceptibility-related signal loss in the marrow space.[5]

A more familiar modulation exists for fat and water components. At 1.5 tesla, the periodicity of the fat-water modulation is approximately 4.6 msec, with fat and water being additive at TE = 9.1, 13.7, 18.3 and 22.9 msec. By alleviating intravoxel dephasing, scanning at the in-phase TEs will diminish—but not eliminate—the low signal boundary effects seen at tissue interfaces on GE scans.

CHEMICAL SHIFT IMAGING

Several techniques have been devised to create separate fat and water images by exploiting the resonant frequency offset of fat and water. At 1.5 tesla, this frequency difference is about 220 Hz (3.4 ppm). There are two major approaches to CSI: phase contrast and selective presaturation. Other, less familiar techniques will also be described.

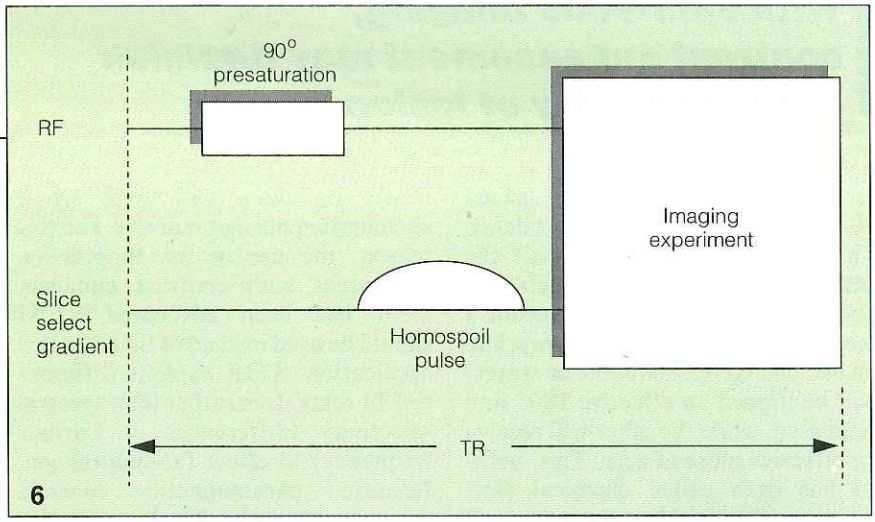
• *Phase contrast techniques.* The most familiar phase contrast technique is the Dixon method (Figure 5),[6] which incorporates two separate imaging sequences. The first is a conventional SE (in-phase image); the second is an identical SE sequence, with the same read-gradient structure, but with the 180° refocusing pulse applied a short time interval earlier. This interval is chosen to equal one-quarter of the period of modulation of the fat and water components, thus producing an out-of-phase or opposed echo. At 1.5 tesla, this interval is about 1.1 msec.

Adding the in-phase and opposed images yields an image of the major or predominant spectral component (per voxel), while subtracting the opposed image from the in-phase image yields an image of the minor component. Consequently, although signal intensity is based on spectral components, the Dixon method does not yield a fat or water image per se. In some areas of the image, such as muscle, the major component may be water; in others, such as subcutaneous tissue, it will be fat.

In addition to this limitation of phase "ambiguity," the Dixon method is also vulnerable to misregistration errors resulting from motion between the in-phase and opposed acquisitions. As with all phase contrast techniques, the Dixon method is also vulnerable to phase errors resulting from static field inhomogeneities or susceptibility effects. In general, the field variations in the area of interest must be less than the fat/water chemical shift (<3.4 ppm). In vivo susceptibility effects may exceed this, particularly over large fields-of-view.

To address the problems of phase ambiguity and phase errors encountered with the traditional Dixon method, modifications of this technique incorporating phase correction have been devised.[7,8] These methods are capable of producing true fat and water images. Phase-corrected images may be obtained without additional scan time by applying image processing techniques to the phase information in the opposed image.[8] These techniques are based on assumptions about the underlying phase structure of the image, however, and may be inadequate when the underlying phase structure of the image becomes complicated. A more analytic approach to phase correction is possible if a dual-echo acquisition is incorporated into a Dixon sequence.[7]

The Dixon method may also be enhanced by "chopper averaging," a process commonly used for combining data from multiple excitation aquisitions. Chopper averaging generates a true fat or water image, without postprocessing, while eliminating the risk of misregistration artifact between acquisitions. The phase ambiguity of the Dixon method is eliminat-



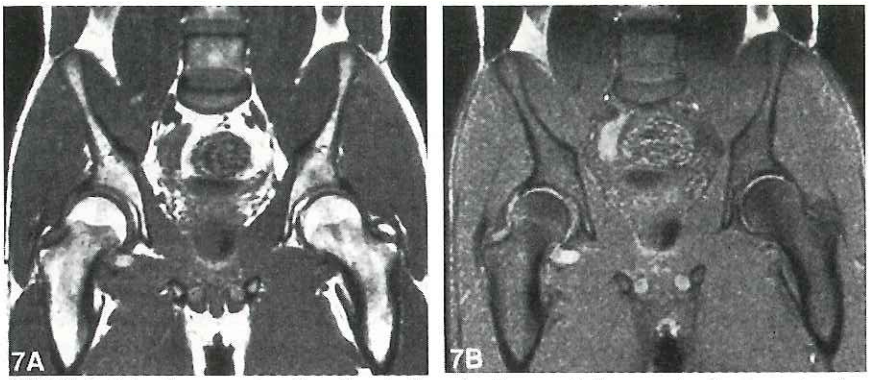


FIGURE 6. *Selective presaturation. Spectrally selective, spatially nonselective presaturation pulse is appended to normal imaging sequence. Excited spectral component is dephased by spoiling gradient prior to imaging experiment.* ***FIGURE 7.*** *Coronal spin-echo images of hips, without (**A**) and with (**B**) fat presaturation. Marrow signal in proximal femoral epiphysis is reduced by 78% on B. S/N for muscle on B is also reduced, but to lesser degree; 26% in this case.*

ed because the raw data from the opposed and in-phase acquisitions are combined prior to reconstruction, thus preserving phase information. Only a fat or water image is generated for each (2 NEX) acquisition. Limitations due to susceptibility effects will be the same as for other phase contrast techniques.

• *Selective presaturation.* A second major strategy for achieving CSI is the use of selective presaturation.[10,11] Chemical shift-selective techniques of this type may be referred to as CHESS. The technique appends to a standard imaging sequence a 90° pulse that is selective for either fat or water, followed by a spoiling gradient (Figure 6). The presaturated component does not contribute to the resulting image. The high degree of spectral selectivity required of the presaturation pulses may demand special pulsing schemes, such as so-called 1331 pulses.

CHESS techniques are attractive because they are easily adapted to various imaging schemes such as SE, GE, STEAM and multiplanar imaging.[12,13] Imaging times are not increased, but slice coverage is diminished, as it is with other presaturation techniques, (i.e., for flow suppression). The S/N in CHESS images is mildly reduced for nonsuppressed protons to a degree that is hardware-dependent. Like other CSI techniques, CHESS does not achieve ideal spectral selectivity in areas of field inhomogeneity. CHESS, unlike phase-sensitive methods such as the Dixon method, is not amenable to phase correction strategies. As in chopper averaging, only a fat or water image is available for each imaging experiment (Figure 7).

More effective spectral selectivity (fat suppression) may be achieved by combining two CSI techniques. A combination of chopper suppression and CHESS has been called hybrid CSI.[14] A hybrid method has the advantage of slightly improved fat suppression, but more importantly, it demonstrates decreased sensitivity to field inhomogeneities. As a result, more even fat suppression may be achieved over large fields of view.

• *Other CSI techniques.* The chemical shift between fat and water components is most commonly appreciated in the read-gradient direction, but similar shifts occur in the slice select direction. Slice-selective radiofrequency pulses excite overlapping but nonidentical slabs of fat and water protons. The magnitude of the offset between these slabs will be proportional to the slice select gradient strength. The result is a loss in axial resolution.

Chemical shift in the slice-selection direction can be exploited to achieve CSI.[15,16] By reversing the direction of the slice select gradient between the 90° and 180° pulses in a SE sequence, the chemical shift offset between slabs will occur in opposite directions. By altering the slice select gradient strength and/or changing the scan center frequency, the offset may be made large enough so the off-resonance slabs for the two excitations do not overlap. An image of only the on-resonance (nonshifted) component is thus obtained.

Gradient-reversal CSI has a less strict requirement for spectrally accurate RF pulses. If the scan center frequency has to be shifted too greatly to achieve effective suppression of the off-resonance component, however, gradient-reversal CSI will result in diminished S/N.

The gradient-reversal technique can also be applied to conventional imaging to correct for chemical shift-related inaccuracies in the slice profile. When equal offsets for both fat and water are created by using an intermediate scan center frequency, gradient reversal effectively images an overlap region, creating spatial coherence of the fat and water components. In this way, axial resolution is improved, but S/N is diminished.

CSI can also be achieved by a different modification of the SE sequence. The 180° refocusing pulse

With spin-echo imaging, contrast enhancement may diminish the conspicuity of lesions

can be replaced by two closely spaced 90° pulses, separated by a short delay. This delay is set to equal half the period of the fat/water modulation: about 2.2 msec at 1.5 tesla. By using a second 90° pulse of the appropriate phase, one component (fat or water) will be flipped an effective 180° and refocused, while the other will receive an effective pulse of zero. This method has been called chemical shift imaging with double pulse refocused echoes, or CIDRE.[17]

The spectral component that has been suppressed on the first echo can be reimaged at a longer TE using a later, conventional 180° pulse. In this delayed echo, the spectral component imaged in the first echo will be suppressed. Separate fat and water images may thus be obtained in the same multiecho acquisition, at different TE values.

This technique shares the same sensitivity to field inhomogeneities as other phase-sensitive techniques. Deviation of the paired 90° pulses will not degrade the spectral selectivity of the first echo, but will compromise S/N. This method requires no postprocessing, is compatible with multiplanar acquisition schemes, and can be done with one acquisition.

A similar modification of the SE sequence uses a prolonged 180° refocusing pulse (about 10 times the duration of a conventional RF pulse) with a narrow frequency spectrum (relative to the fat/water chemical shift) to achieve chemical selectivity.[18] This technique is robust with respect to flip angle variations. Because the 180° refocusing pulse is not spatially selective, however, multiplanar acquisition is not possible, which limits the utility of this technique.

CONTRAST ENHANCEMENT

The utility of paramagnetic contrast enhancement (gadolinium-DTPA or DOTA) in the evaluation of marrow processes has been limited, particularly with respect to infiltrative or diffuse disease. With SE imaging, contrast enhancement may diminish the conspicuity of lesions in the marrow space, rendering them more nearly isointense with high signal surrounding normal marrow. For this reason, the use of fat suppression techniques with contrast enhancement has been advocated.[19] CSI should be used instead of STIR in this application. STIR exploits differential T1 relaxation rather than spectral selectivity (differences in Larmor frequency) to effect fat suppression. Because paramagnetic contrast causes preferential T1 shortening in areas of pathology, the conspicuity of lesions on STIR may potentially be diminished after enhancement.

Alternatively, image subtraction may be used to improve visualization of enhancing areas.[20] This is a feasible technique since precontrast T1-weighted images are almost always obtained. As with other techniques employing image arithmetic, this approach is vulnerable to misregistration artifacts secondary to motion or flow.

Quantitative methods applied to the enhanced study may offer more specific diagnostic information. Dynamic enhanced FLASH of focal bony lesions, for instance, has been studied in the discrimination of benign versus malignant disease, or recurrent and inflammatory change.[21]

POTENTIAL AND LIMITS

MRI has emerged as an effective means of detecting pathology in the marrow space. Most clinical MR evaluations can be successfully performed with SE techniques. T1-weighted SE images offer great sensitivity for marrow pathology. The poor specificity of the MR findings, however, prompts a search for alternative MR techniques that may yield more specific data. For instance, the differentiation between marrow pathology—myelofibrosis, for example—and normal hematopoietic marrow may be difficult on routine SE images.[22,23] At this time, STIR and conventional GE techniques do not appear to improve the specificity of the MR evaluation of marrow disease. Dynamic contrast-enhanced MRI may provide more specific information regarding benignancy versus malignancy, but can be unwieldy to perform reliably.

CSI methods may increase the accuracy of MR evaluations of marrow, particularly in the case of infiltrating diseases. The subject of CSI is confusing because of the large number of available techniques that may produce spectral selectivity. In addition to enhancing the conspicuity of disease in some cases,[24] CSI methods may also facilitate new assessments lending further specificity. ■

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