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in order to justify intervention to attempt repair. Our imperative should remain to better understand the pathologic behavior of TIAs, and importantly, to more strongly lead our clinical colleagues to the best care that can be offered to our collective patients.

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Diffusion-Weighted Imaging in the Distinction of Benign from Metastatic Vertebral Compression Fractures: Is This a Numbers Game?

As radiologists, one of the frequent problematic diagnostic dilemmas we face is trying to distinguish a benign from malignant fracture. Often I find myself feeling embarrassed when reflecting upon my response to a clinician when posed with the question, "Is this vertebral fracture benign or malignant?" On the surface, it seems not only a reasonable question, but with recent advances in MR imaging, a question one might assume to be answered quite easily. Unfortunately, to date, MR imaging has not increased our specificity to a point that a confident answer can be given on a routine basis.

Vertebral metastasis is common and can be seen in 10% of all patients with cancer. Benign osteoporotic compression fractures are also common, particularly in the elderly and in those patients receiving long-term steroid therapy. MR imaging is excellent in the assessment of the bone marrow. This is particularly true in images obtained in adults in which the high T1 signal intensity of normal fatty marrow provides an inherent contrast that allows for the easy depiction of marrow-replacement processes. Typically, malignant marrow lesions that have increased water will appear hypointense on T1-weighted images and hyperintense on conventional spin-echo images or fat-suppressed T2-weighted images such as short-TI inversion recovery and chemically fat-suppressed T2-weighted images. The basic problem, however, is that acute and subacute benign fracture with marrow edema results in a similar alteration of the marrow signal intensity. Therefore, the presence of signal intensity changes in the marrow on conventional images is not helpful in distinguishing acute to subacute fractures from malignant fractures.

Structural changes of the vertebral bodies and changes surrounding the vertebra have also been used to distinguish benign from malignant fractures. Adjuvant MR findings have been used to suggest that a malignant fracture may be present, such as complete replacement of the vertebral body marrow, involvement of the posterior elements, and an associated epidural or paraspinal mass. Unfortunately, these findings are not specific and can be seen with benign fractures. Conversely, lack of these associated findings does not exclude the presence of a malignant fracture. Benignity can be suggested if the vertebral signal abnormality only consists of a linear signal abnormality confined to the vertebral endplate. Contrast-enhanced MR imaging has not helped, because both benign and malignant vertebral fractures may enhance. The enhancement encountered in a benign fracture is presumably related to leakage of contrast agent through compromised vessels and the presence of granulation tissue.

In 1998, Baur et al (1) took a unique approach to this problem, studying 30 patients with 39 vertebral compression fractures. They used a time-reversed fast imaging sequence based on steady-state free precession (SSFP) to produce diffusion-weighted images. This SSFP sequence overcame many of the problems that prevent the performance of satisfactory echo-planar–based diffusion-weighted images in the spine but used a relatively low b value (165/mm^2) to achieve an adequate signal-to-noise ratio. In their study, all benign vertebral fractures were hypo- to isointense to adjacent normal bone marrow, and all malignancy-related fractures were hyperintense to normal bone marrow on diffusion-sensitized images. The explanation of their findings was as impressive as their results. Baur et al tested the hypothesis that the free mobility of water was different between acute benign fractures and pathologic fractures. The reduced mobility of water in pathologic fractures was the result of tumor cell accumulation and a subsequent reduction in the interstitial space. Increased mobility of water, on the other hand, was attributed to an increase in the interstitial space in relation to edema or hemorrhage in benign fractures. Although the results were promising, Baur et al indicated that bone marrow diffusion needed further investigation in a larger series of patients and that further study was necessary to clarify the changes of diffusion in the subacute and healing phase of fractures.

In an accompanying editorial, LeBihan (2) pointed out that further confirmation of these findings was necessary with proper quantitative analysis, which could not be performed with the SSFP technique employed by Baur et al. The basic problem was that

the T1 and T2 effects could not be separated from the diffusion effects, and therefore, one cannot imply that the signal changes they showed were solely related to diffusion. LeBihan also pointed out that the type and amount of tumor cells could have an effect on the abnormal diffusion.

By applying the same SSFP sequence in the imaging of the spine, Castillo et al (3) demonstrated that not all of the vertebral metastases they studied were hyperintense to normal marrow on diffusion-weighted images. In fact, three of five focal vertebral lesions were hypointense relative to marrow on diffusion-weighted images and seven of 10 patients with multiple lesions had hypointense or mixed hypointense and hyperintense lesions relative to marrow on diffusion-weighted images. They concluded that qualitative use of the diffusion-weighted SSFP sequence in the spine offered no advantage in the detection and characterization of vertebral metastases compared with that of non–contrast-enhanced T1-weighted imaging but was superior to T2-weighted imaging. Castillo et al, however, used conventional T2-weighted fast spin-echo sequences in which fat remains bright and may therefore obscure a metastatic marrow focus or make it appear hypointense relative to the fatty marrow. Because some metastatic foci were hypointense on the diffusion-weighted SSFP images and it is unclear whether the observed hyperintense signal on the diffusion-weighted SSFP image was T2 shine-through, many questions were raised about the utility of this sequence.

In this issue of the *AJNR*, Zhou et al (page 165) get to the heart of the matter by using a quantitative method to determine the apparent diffusion coefficient of vertebral compression fractures. Zhou et al report their findings in 27 patients with known cancer and suspected vertebral metastases. They present quantitative data of the apparent diffusion coefficient (ADC) values of 12 benign fractures and 15 metastases. Their data, which are primarily composed of mean ADC values obtained from histograms, support their hypothesis that quantitative data will improve the specificity of diffusion-weighted imaging of the spine. The mean ADC values were $1.9 \pm 0.3 \times 10^{-4}$ mm^2/s for metastatic vertebra and $3.2 \pm 0.5 \times 10^{-4}$ mm^2/s for benign fractures.

To determine the ADCs, the authors used a diffusion-weighted fast spin-echo sequence rather than the SSFP or EPI sequence. A single-shot mode addressed the issue of motion sensitivity and signal to noise was maximized with multiple averages with proper phase correction. Three b values (0, 150, and 250 mm^2/s) allowed for quantification. By using a commercial software package, regions of interest were placed on the diffusion-weighted images by obtaining coordinates of the lesions from conventional images. The ADC values were then plotted as histograms from which a statistical analysis was performed to yield the mean ADC value and the standard deviation.

The study by Zhou et al is important on many levels. First, they demonstrated that in the routine clinical setting ADC values could be calculated relatively easily in the marrow by using fast spin-echo diffusion-weighted imaging. Second, they convincingly demonstrated that qualitative evaluation of the diffusion-weighted images is problematic, because T2 shine-through effects can lead to a false-positive result (six of 12 benign fractures were hyperintense on diffusion-weighted images with an ADC of $2.8–3.3 \times 10^{-4}$ mm^2/s), and false-negative results were found on the diffusion-weighted images in four of the metastatic lesions (hypointense on diffusion-weighted images with an ADC of $1.6–1.9 \times 10^{-4}$ mm^2/s). The hypointensity observed in the metastatic lesions on diffusion-weighted images is conjectured to be the result of low cellularity and high water content. Third, they demonstrated a statistically significant separation between two distinct groups, namely benign and malignant fractures based on comparison of mean ADC values. Fourth, study of the histogram reveals that some overlap of ADC values exists in the two groups when one evaluates the distribution of ADC values between the benign and malignant compression fractures.

It is yet to be determined how benign lesions such as hemangiomas may affect the ADC of a compression fracture. The type of malignancy may also play a role in the alteration of the ADC. In addition, it is likely that the cellularity (or number of cells) can affect the ADC value. A larger patient group (or number of patients) needs to be studied with this technique. Improvement in signal-to-noise ratio with a multishot technique will likely improve the separation of the ADC between those with benign and those with malignant fractures. Although it is unclear how diffusion-weighted imaging of spinal marrow will take its place in everyday clinical practice, we can feel fairly confident that some form of quantification (or numbers), either by evaluation of the actual quantitative data or looking at ADC maps, will be necessary. At this point, diffusion-weighted imaging in the distinction of benign from metastatic vertebral compression fractures truly is a numbers game!

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