Clinical Applications of Diffusion Imaging in the Spine

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Key points:

1) Diffusion imaging is a powerful technique in widespread use in whole body imaging that is a valuable adjunct to routine imaging protocols for the spine.
2) Diffusion imaging adds sensitivity and specificity in evaluating the osseous and soft tissue structures of the spine for neoplastic involvement.
3) Diffusion imaging adds sensitivity and specificity in evaluating the osseous and soft tissue structures of the spine in cases of suspected infection.
4) Protocol optimization and pending technical advances can and will provide critical improvements in image quality which should lead to routine use in the evaluation of diseases of the spine.

Disclosures: Speaker GE Healthcare

Synopsis:

There is a range of current and potential applications for DWI in the spine. As in the brain, the sensitivity of DWI to ischemic damage in the spinal cord may provide early identification of infarction. DWI has been exploited for its ability to detect and characterize lesions of the spinal marrow and potentially differentiate between benign and malignant vertebral compression fractures. While technical limitations persist to a varying degree, the applications for DWI in the spine have been extensively investigated. Despite challenges and lingering controversy over clinical utility for some applications, DWI is increasingly becoming part of the routine clinical spine MRI regimen. This presentation will review the basis for DWI for the evaluation of the spinal cord, osseous and soft tissues of the spine and review the imaging appearance of a variety of disease states.

Introduction:

The imaging assessment of the diffusion characteristics of water molecules on an intracellular and extracellular space level can herald powerful and information about normal and abnormal tissues and processes. Diffusion weighted imaging (DWI), a technique typically based on echo planar imaging (EPI), has been widely available for clinical purposes since the early 1990s. DWI rapidly achieved universal use for the evaluation of brain diseases, improving sensitivity and specificity of MR imaging (MRI) for a variety of disease states including infarction, infection, inflammation and hemorrhage. Of late DWI has achieved greater importance in evaluation of the abdomen, pelvis, prostate and breast **(1-3)** with increasingly routine use in day to day practice. Although DWI should be equally sensitive to diseases of the spine, it has been used far less frequently in this region. This is mainly because of the challenges placed by the spine's heterogeneous magnetic environment, the small size of the spinal cord, and motion in and around the spine.

There is, however, a range of current and potential applications for DWI in the spine. As in the brain, the sensitivity of DWI to ischemic damage in the spinal cord may provide early identification of infarction. DWI has been exploited for its ability to detect and characterize lesions of the spinal marrow and potentially differentiate between benign and malignant vertebral compression fractures. While technical limitations persist to a varying degree, the applications for DWI in the spine have been extensively investigated. Despite challenges and lingering controversy over clinical utility for some applications, DWI is increasingly becoming part of the routine clinical spine MRI regimen. This chapter will review the basis for DWI for the evaluation of the spinal cord, osseous and soft tissues of the spine and review the imaging appearance of a variety of disease states.

Diffusion weighted MRI (DWI)

Diffusion weighted imaging (DWI) is a powerful tool for tissue investigation with magnetic resonance (MRI). By sensitizing the MR image to perturbations of the random motion of water molecules in tissues, DWI provides unique insight into pathologic physiology **(4-6)**.

DWI revolutionized the evaluation of patients with suspected stroke by providing exquisite sensitivity to the presence of brain infarction, almost immediately after onset. DWI also provides the critical ability to differentiate chronic ischemic brain changes from those due to recent stroke in patients who present in the subacute stroke setting. Perhaps the most impactful role of cranial DWI is in characterization of brain lesions - the differentiation of stroke and abscess from tumor, and in the assessment and surveillance of demyelinating disease.). Of late DWI has become popular for imaging outside the brain and is now commonly used in the routine MR study of the breast, prostate, abdomen and pelvis, providing a boost in lesion detection. DWI also offers valuable characterization information useful in the differentiation of malignant from benign lesions as well as tumor from reactive and treatment related changes.

Technical considerations

Typically based on clinically available single shot EPI scanning techniques, DWI is rapidly acquired and motion resistant. While nearly ideal for imaging of the brain, EPI faces significant challenges in the spine. Bulk physiologic motion within the chest and abdomen or from swallowing, as well as motion from the spinal cord itself are sources of artifact. Susceptibility variation associated with the osseous structures and field variations adjacent to the cervicothoracic junction and the lungs may cause severe distortion. As a result, application of DWI to the vertebral column has been far less popular than elsewhere.

Alternative techniques based on single-shot and line scan fast spin echo have been investigated but as yet have failed to achieve clinical availability despite potential advantages over EPI **(7-8).** With minor modifications to current EPI based protocol parameters diagnostic quality studies of the spine can be obtained Reduced B values (400-500) and minimized frequency encoding each reduces echo times (TE) leading to improved SNR and reduced distortion **(LIST 1).**

LIST 1: Typical DW spine technique

TR, TE minimum

Frequency minimum (GE), 128 Siemens

Phase 192- 256

FOV 26

3-4 mm, skip 1

4 nex, acquisitions

B value:0, 4-500

Recent and continuing technical innovations impact greatly on EPI DWI of the spine. Applying the three diffusion gradients simultaneously instead of sequentially (3 in 1, GE Waukesha, WI) allows much shorter TE values which boosts SNR, reduces distortion and shortens scan times

(figure 1).

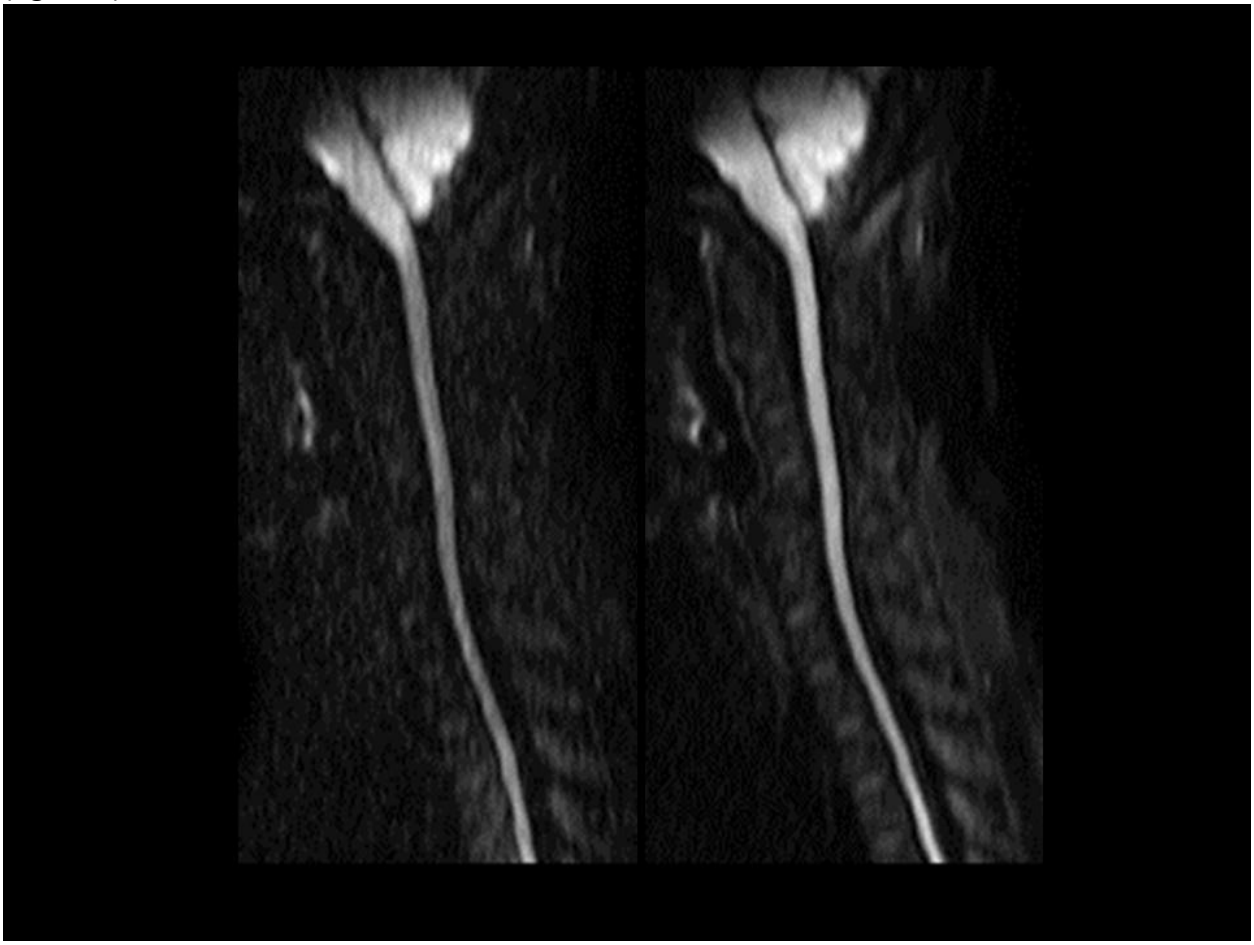

Figure 1: Enhancements to spine DWI. Note the improvement in speed, SNR and quality of depiction of the spinal cord when all 3 diffusion gradients are applied simultaneously (right, 3 in 1, scan time 0:38) when compared to the image obtained with traditional sequential (left, DTI 1:43) application . Both studies obtained at a PI factor of 2.

Parallel imaging capable spine coils, allow DWI at reduced TE values preserving SNR and reducing susceptibility effects. ***(FIGURE 2)***

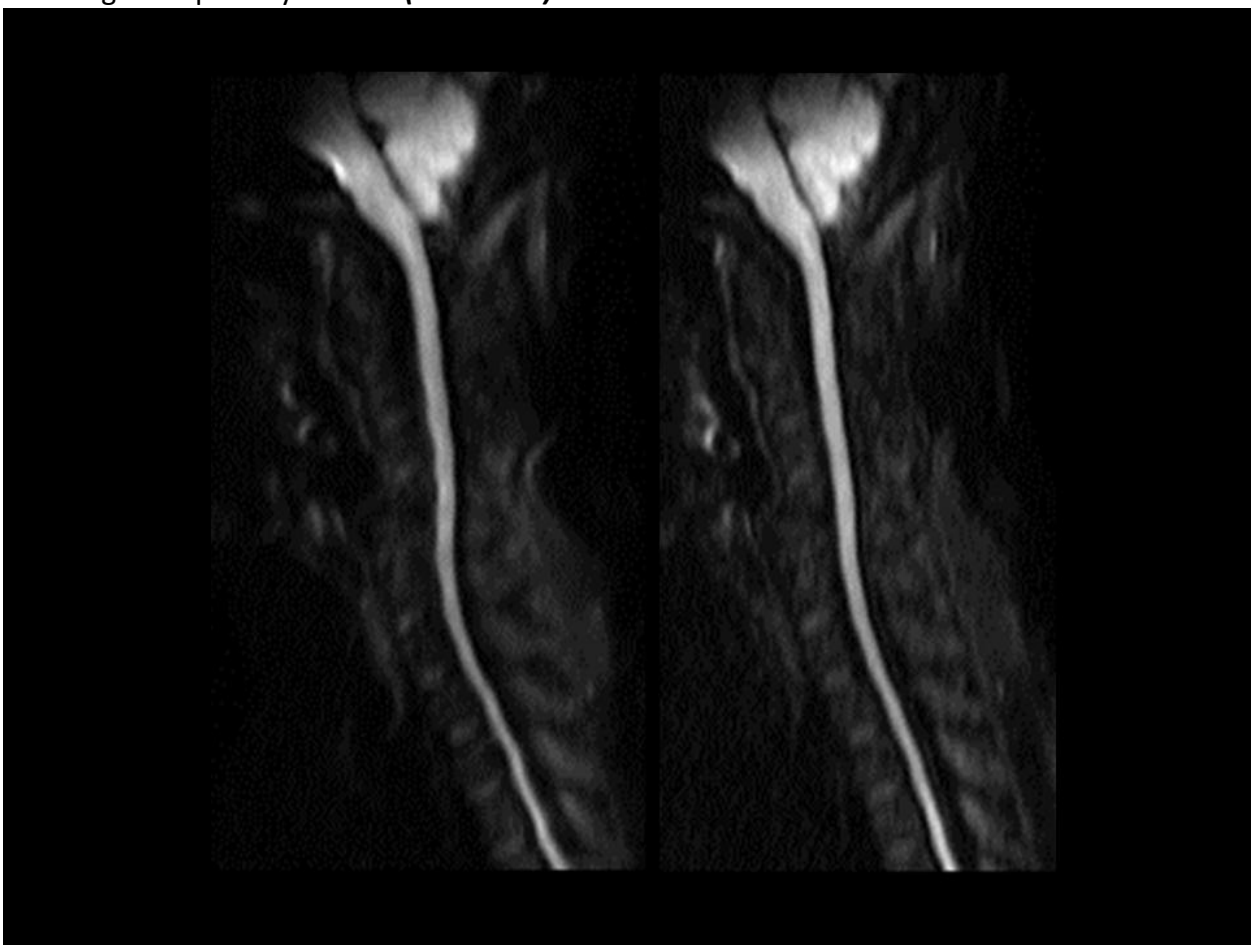

Figure 2: Parallel imaging (PI) in spine DWI. Note the improvement in accuracy of anatomical depiction of the spinal cord with reduced distortion using a PI factor of 2 (left) when compared to the image obtained without PI. Both images obtained with a 3 in 1 DWI technique.

More powerful gradient systems also allow shorter TE values at a given B value yielding either improved image quality or the use of higher B values. Recently available techniques such as

multi-shot EPI (***Siemens Erlangen, Germany***). **(FIGURE 3)**

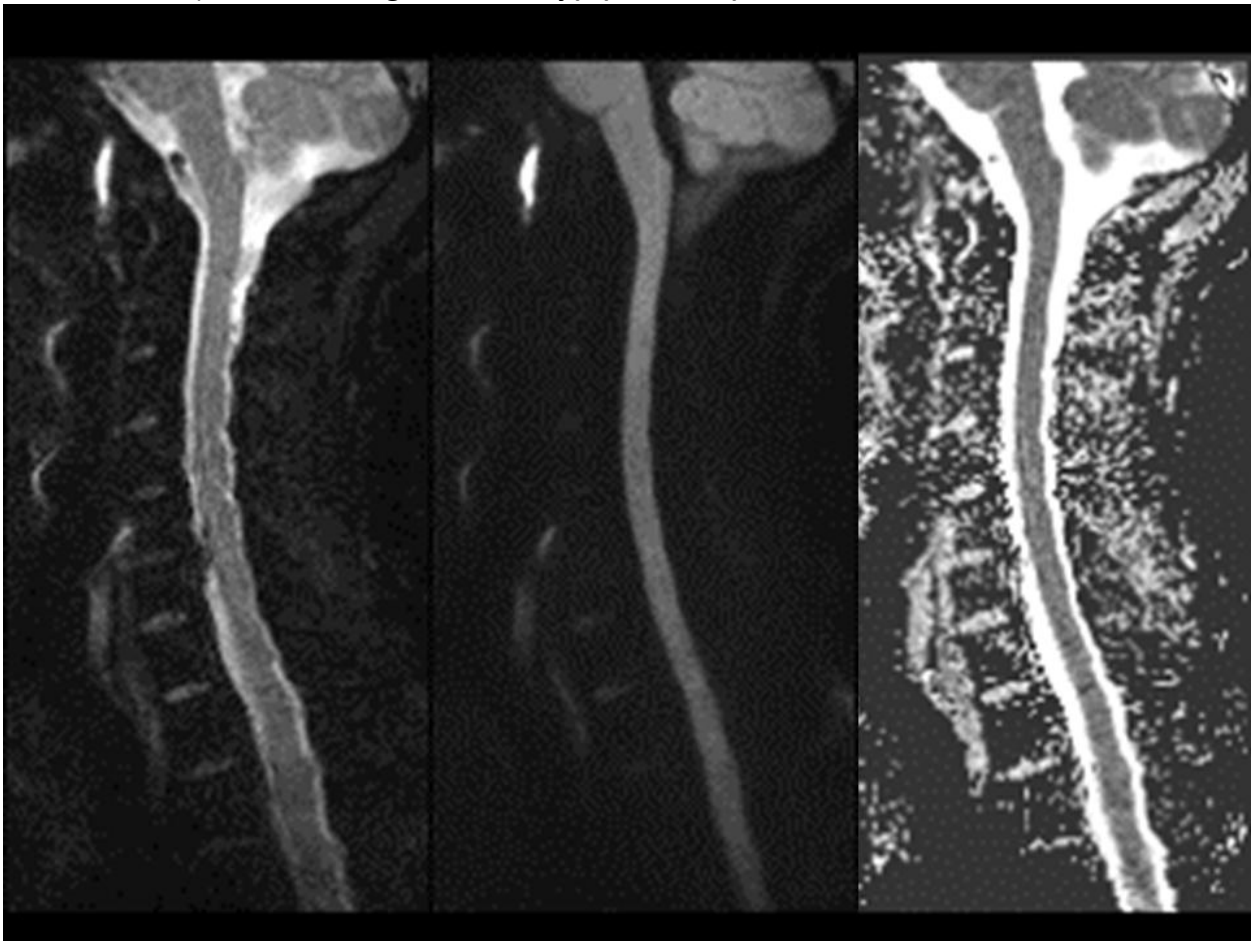

Figure 3: Multishot EPI DW image (RESOLVE) at 3T. Note the striking lack of distortion and high spatial resolution.

and restricted FOV DWI **(FIGURE 4)** are practical and artifact resistant, promising better suitability to applications in body and spine (**9-10).**

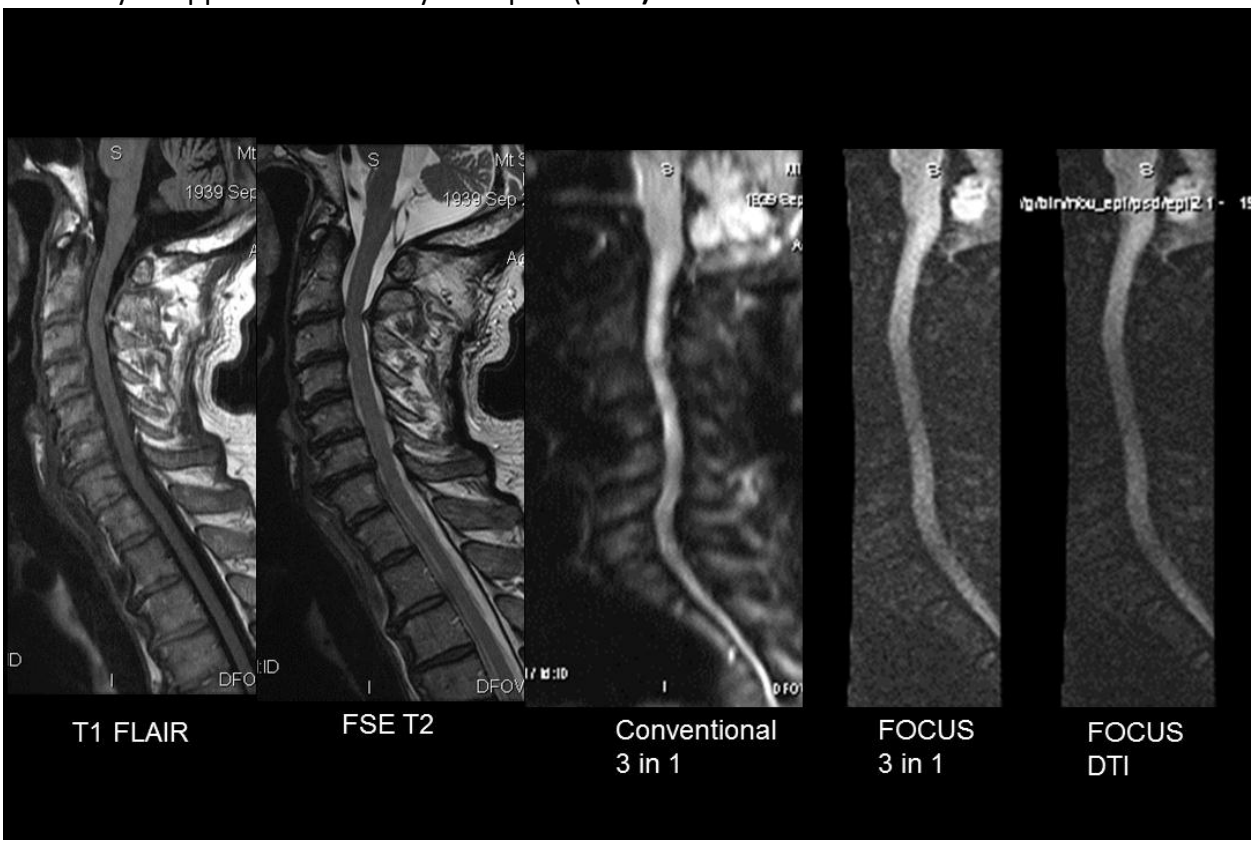

Figure 4: Restricted FOV EPI DWI (FOCUS). Note the striking reduction of distortion and high spatial resolution.

As the quality of the clinical diffusion image improves, DWI will gain even wider use in the routine diagnostic workup of spinal disorders.

Scientific study of diffusion imaging has focused on assessment and often quantitative measures of the apparent diffusion coefficient (ADC). Individual direction and trace weighted or combined direction DW images routinely manifest T2 effects which complicate assignment of diffusion imaging behavior. This has been cited as limiting the utility and scientific validity of early techniques that have been used in evaluating the spine (**11,12**). In routine practice, it can be more useful to interrogate routine, combined or trace diffusion images. These diffusion *weighted* images additively combine T2 effects with diffusion alterations to significantly boost conspicuity (if not specificity) of lesions which exhibit both diffusion restriction and T2 prolongation. As an example in the brain, while ADC values are lowest in the first few hours after stroke, it is only after T2 effects manifest that lesions are most conspicuous when on (trace weighted) DWI the combined signal contributions manifest the characteristic 'light bulb"

high signal appearance. In contrast, chronic strokes have high diffusion values which combine antagonistically with T2 prolongation to produce an isointense lesion. For clinical purposes, lower B values (e.g. 4-500 s/mm2) are typically used for spine imaging, allowing for significant T2 contribution to the trace weighted DWI. While in the interest of diffusion image 'purity' use of higher B values can effectively minimize T2 contribution, with clinically available techniques the proportional tradeoffs in increased distortion and reduced SNR are effectively limiting. On the other hand the synergistic contribution of combined T2 prolongation and diffusion restriction is likely responsible for some of the contribution made by DWI to the clinical MR imaging of spine disease discussed in this chapter.

Clinical Applications of DWI of the Spine

One of the most rewarding extracranial applications of DWI is for the evaluation of the spine. DWI provides diagnostic value similar to that provided in the brain when assessing diseases of the spinal cord. DWI also can contribute to the detection and characterization of intradural-extramedullary, and epidural lesions as well. Perhaps the most fruitful extracranial contribution of DWI is for the evaluation of marrow disease.

Metastatic disease and myeloma

DWI is a powerful adjunct to the routine imaging regimen used to detect and characterize extradural lesions. Studies have shown that diffusion is impaired within neoplastic tissue, and that a decrease in diffusion coefficient may indicate disease progression. Effective treatment may cause a transient decrease in diffusion, due to cytotoxic edema, but eventually diffusion increases significantly (**16).**

DWI adds sensitivity to the presence of osseous lesions of the spine. Added to the routine sequences employed for the assessment of suspected metastatic disease and myeloma, DWI improves the detectability and conspicuity of many lesions (**17**). In recently presented trials (**18,19**), approximately 50% of lesions, identified as part of an neoplastic MRI spine survey, were most conspicuous on trace weighted DWI compared to a combination of routine sequences including STIR, T1 pre and post contrast techniques. While approximately 20% of lesions were better seen on routine sequences, up to 10% of lesions were seen only on DWI or

were solely evident in retrospect with routine scanning techniques (***Figure 5***).

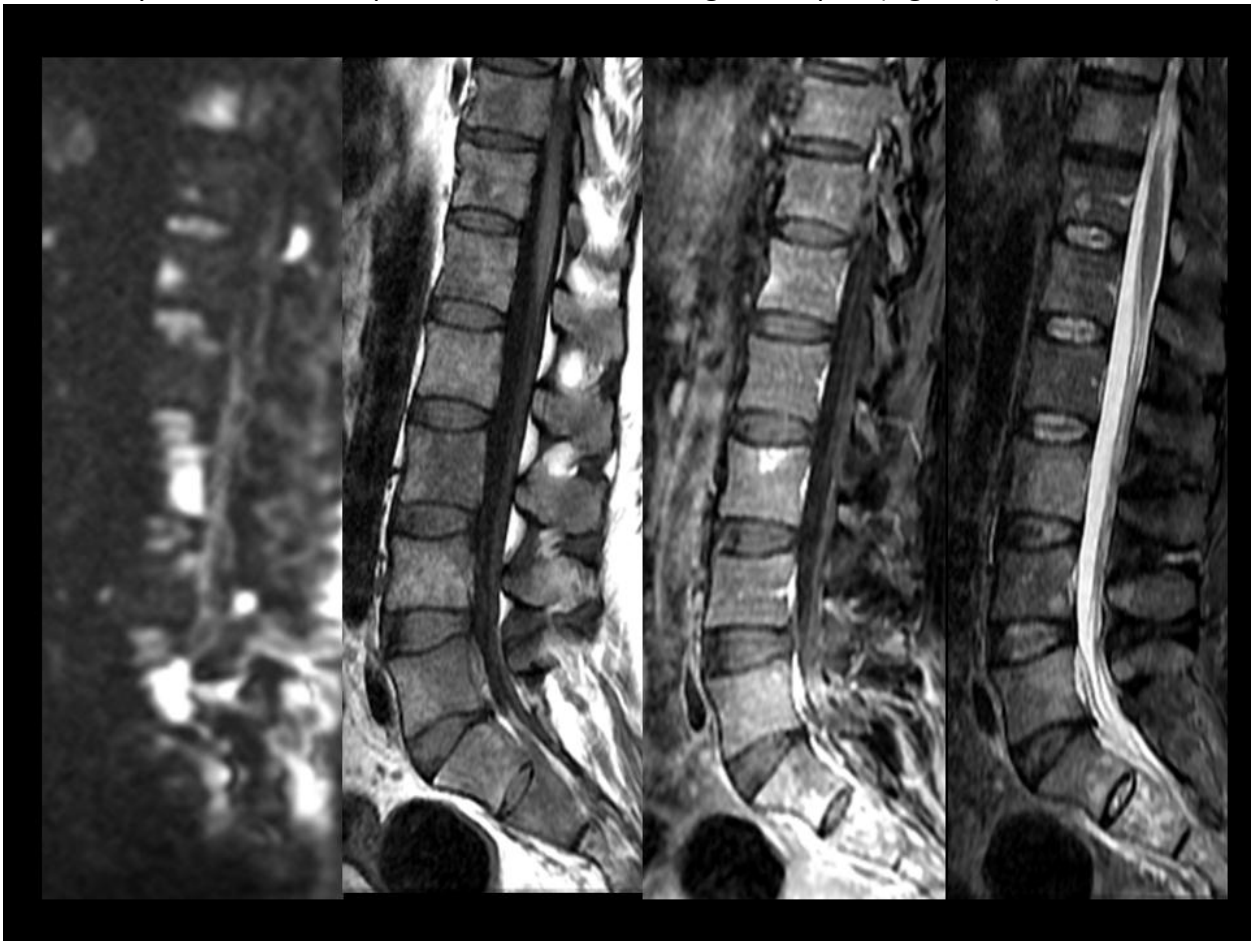

Figure 5: Metastatic disease. From left: DWI, T1 FLAIR, fat suppressed-contrast enhanced, T1 FLAIR, STIR. Note the superior conspicuity of many of the metastatic lesions with DWI.

DWI has gained wide use in whole body screening MRI due in part to the boost in sensitivity to bone lesions it provides. Rib and posterior spinal element lesions can be difficult to detect with routine screening techniques due to morphologic and orientation issues on survey studies. The high lesion to background ratios provided by DWI can be particularly helpful in these

circumstances (***FIGURE 6***).

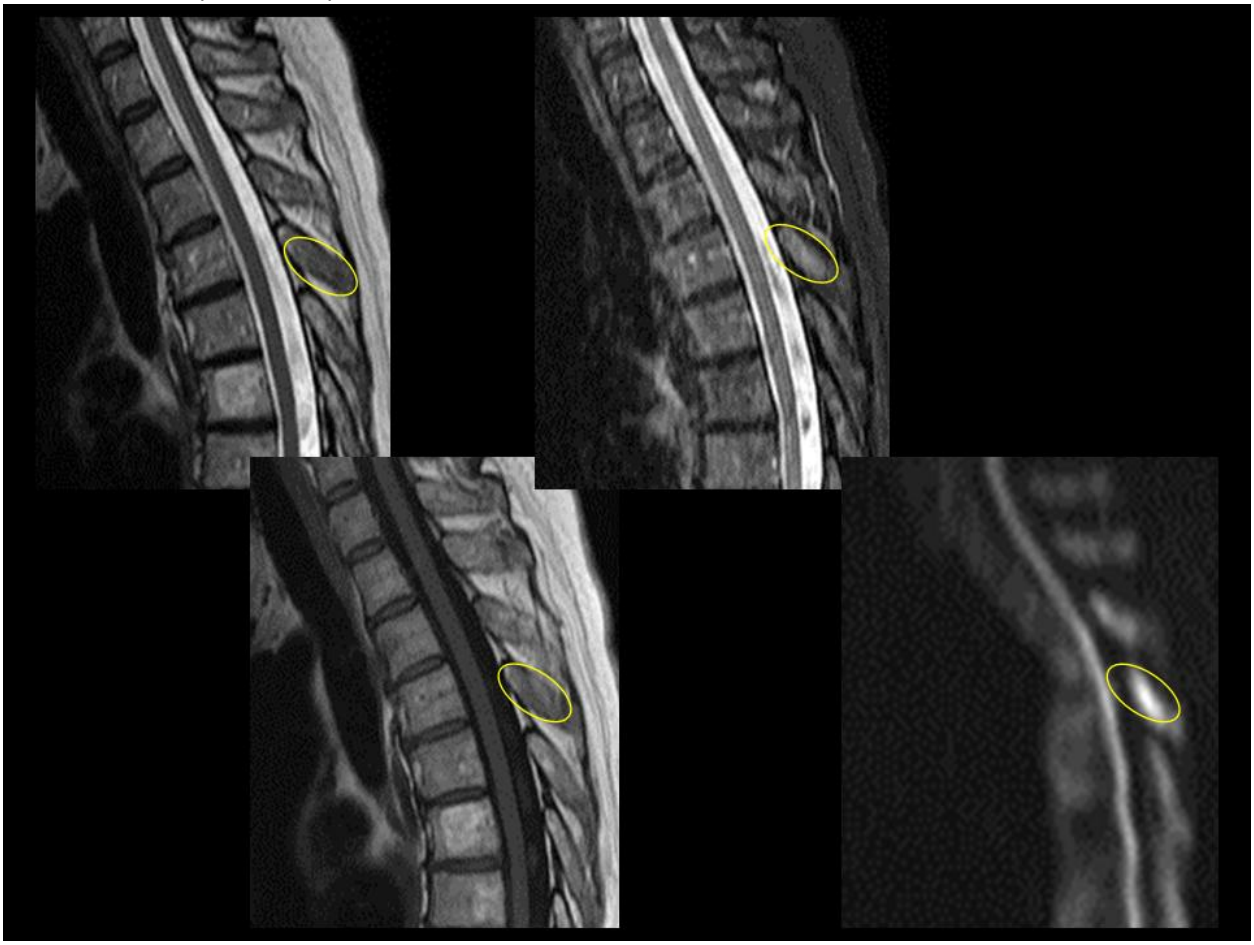

Figure 6: Metastatic myeloma. Clockwise from upper left: T2, STIR, DWI, T1 FLAIR. Note the highest conspicuity of the spinous process lesion (circle) with DWI.

Compression fractures

Acute vertebral fractures are a common clinical finding in elderly patients. Osteoporosis and tumor (primary and metastatic) the most common causes with the majority due to osteoporosis. In the United States, approximately 35% of women older than 65 years have osteoporosis. More than 700,000 new vertebral compression fractures occur every year in the United States alone. Ten percent of vertebral fractures detected in patients with osteoporosis however are of malignant rather than senescent origin. On the other hand, twenty five percent of the fractures in patients with a known malignancy are osteoporotic in origin. While MR is the most useful imaging technique for the evaluation and characterization of vertebral fractures in clinical practice, the differentiation of an osteoporotic or malignant fracture origin is challenging based on signal intensity criteria (**20,21**). Morphological criteria have been

proposed for differentiation, however these may not be sufficient to permit a definite diagnosis [**22,23**]. As DWI is quite sensitive to presence of neoplastic lesions of bone, there have been numerous investigations of its potential in the characterization of the etiology of acute compression fractures. Using a variety of prototype and clinically available techniques the efficacy remains controversial. Theory suggests that benign compression fractures would reveal manifestations of a rapid diffusion environment with water (edema) freely diffusing between the interstices of bone. Thus a senescent fracture would be expected to show diminished signal on DWI and elevated diffusion coefficients (**FIGURE 7).**

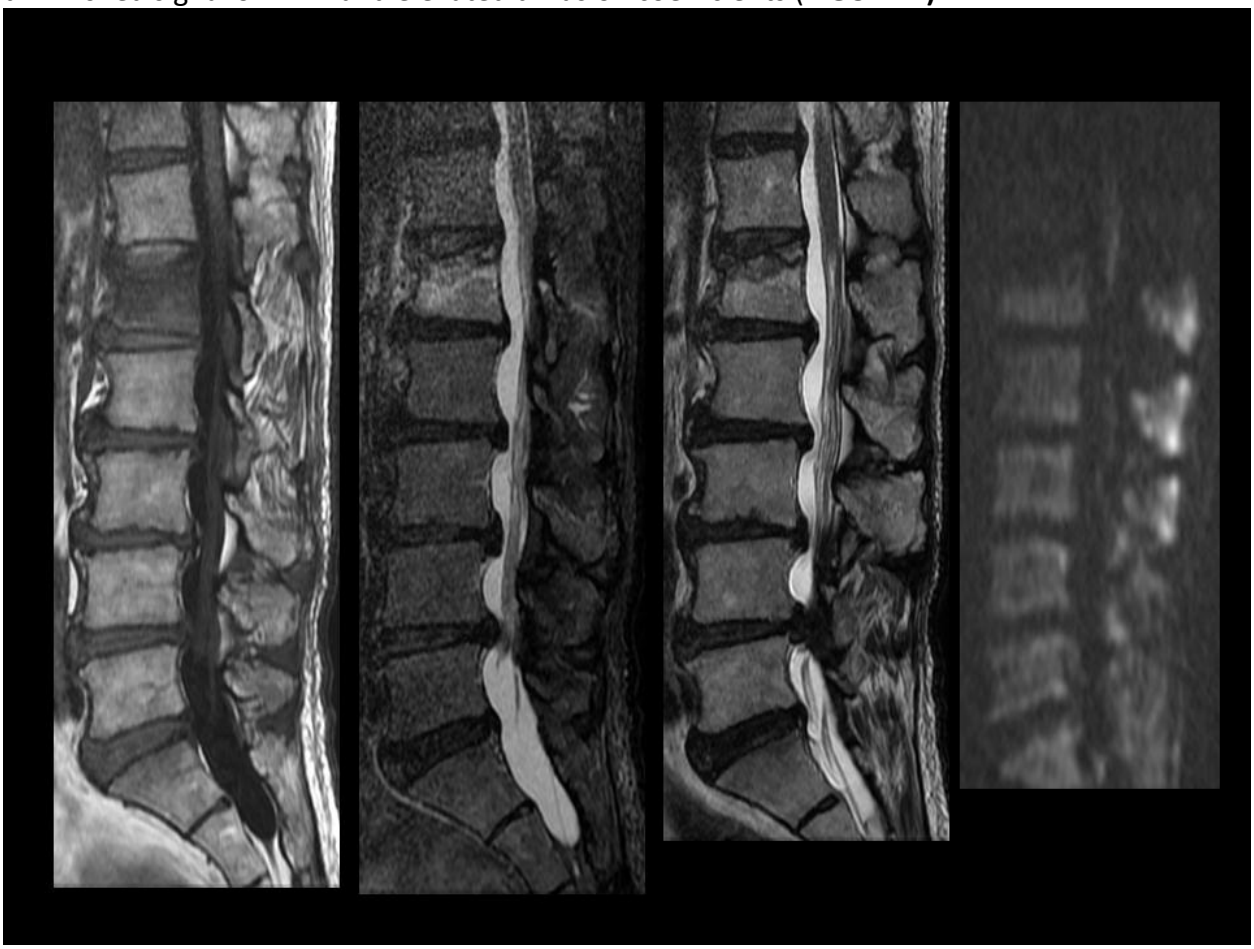

Figure 7: Senescent compression fracture. From left: T1 FLAIR, STIR, T2, DWI. Note the diminished signal on DWI associated with the recent compression fracture involving the superior end plate of L1.

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A malignant compression fracture, where tumor cells infiltrate bone, should show evidence of restricted diffusion compared to normal (and particularly edematous) marrow and show

increased signal on DWI and restricted diffusion (***FIGURE 8***).

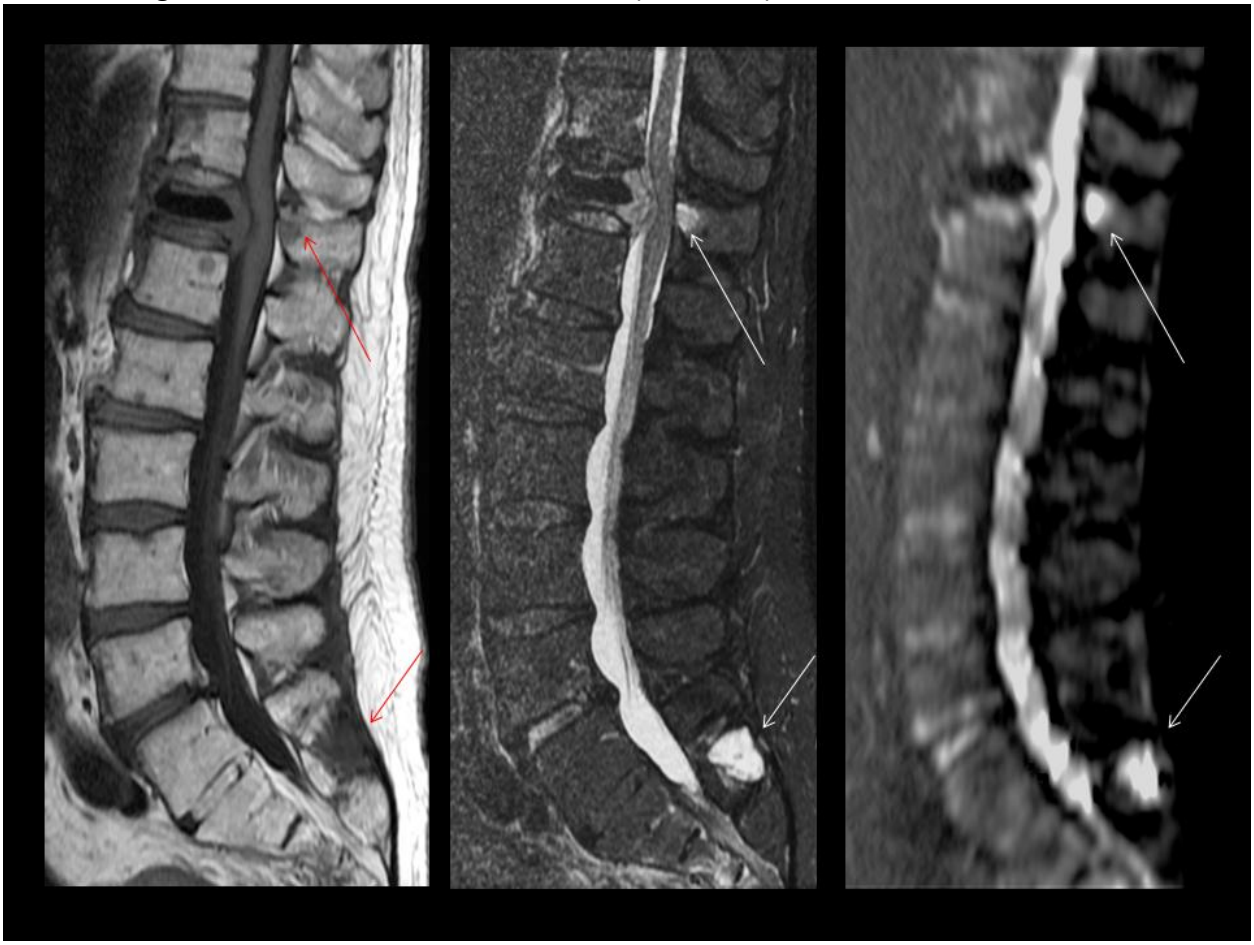

Figure 8: Metastatic myeloma. From left: T1 FLAIR, STIR, DWI. Note the striking conspicuity of the tumor (arrows) within the compressed, T11 vertebral body, post-vertebroplasty. Note also the posterior element tumor at L5.

To date consensus has not shown DWI to be a definitive tool for the challenging differentiation of benign senescent compression fractures from pathologic fractures (***Figure 9***). While some have reported excellent and characteristic results, others have described a wide spectrum of

signal changes in pathologic fractures (**24-26**).

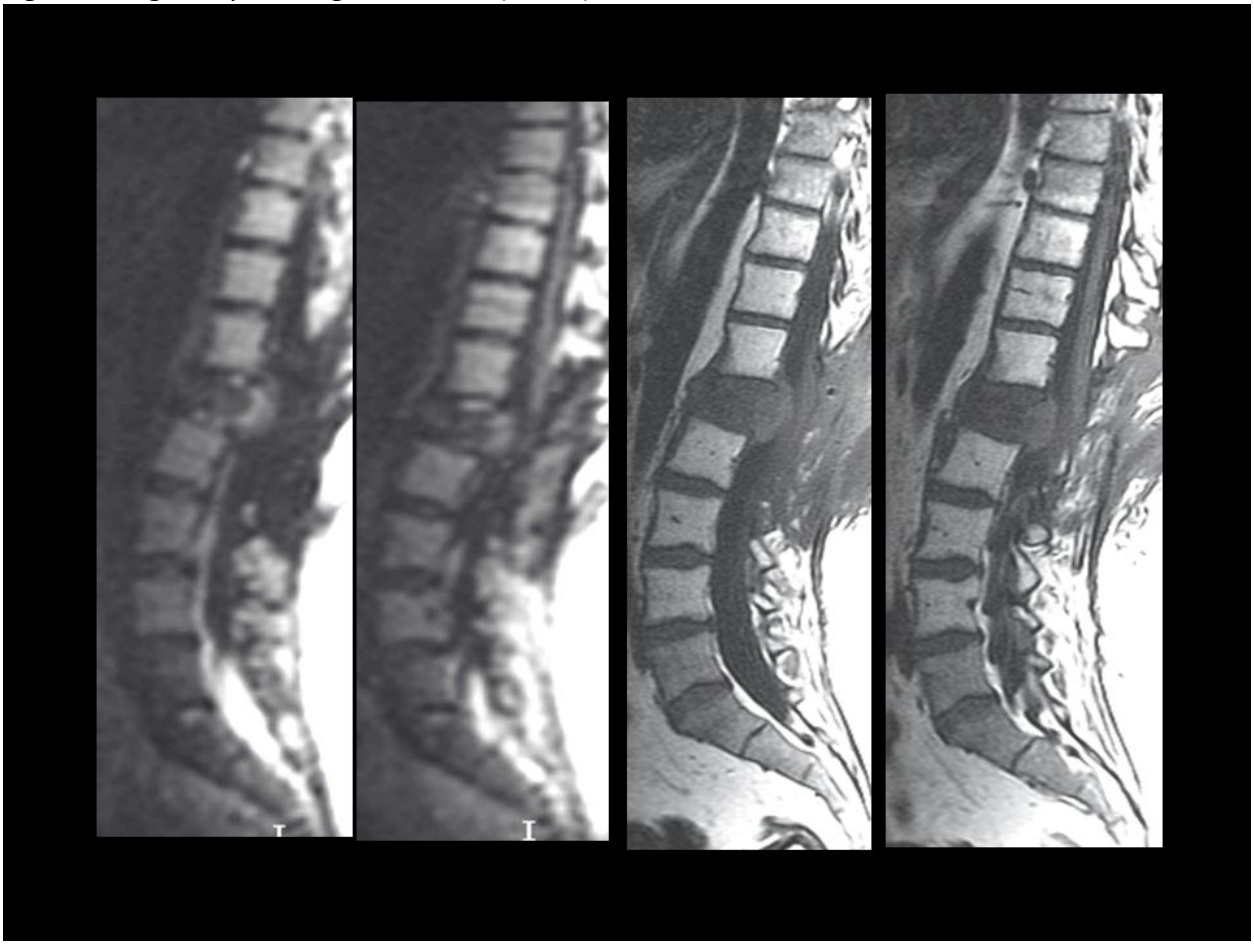

Figure 9: Pathologic compression fracture, post decompression. From left: ssFSE DWI and T1 SE. Note the residual tumor at L1 shows atypical isointensity and hypointensity rather than predicted diffusion restriction.

This may be due to the complexity and overlap of edema, hemorrhage, and bone fragmentation in both conditions and the varied expected associated appearance on DWI.

Infectious disease

As in the brain, DWI can be helpful in the evaluation and detection of infectious disease (***Figure 10***).

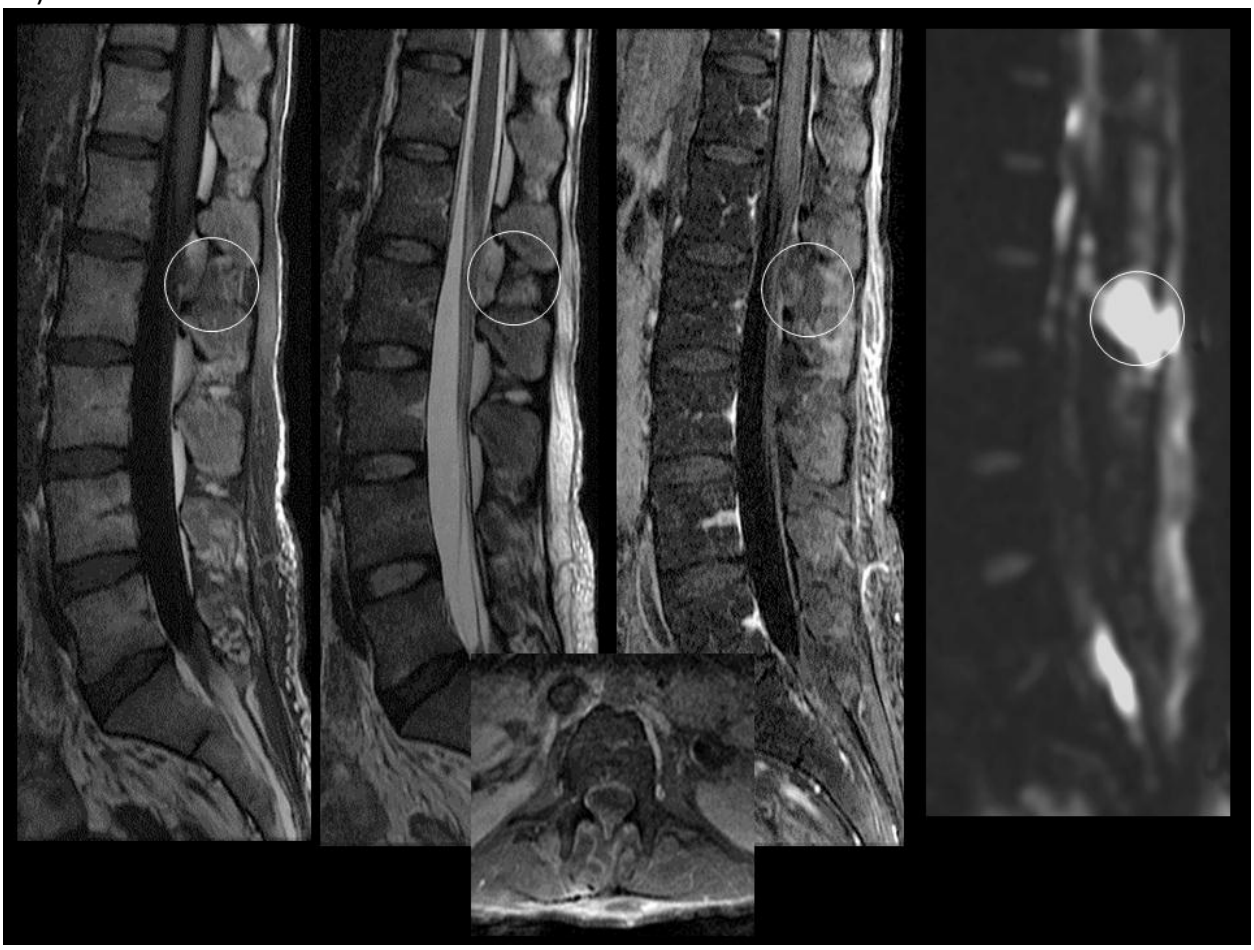

Figure 10: Epidural abscess. From left: T1 FLAIR, T2, fat suppressed-contrast enhanced T1 FLAIR, DWI. Inset: axial fat suppressed, contrast enhanced T1. Note the characteristic striking diffusion hyperintensity involving the posterior epidural region at L1-2 (circles).

Osteomyelitis, discitis and abscess reveal characteristic hyperintensity which can be critical to diagnosis (***Figure 11***) (**27**).

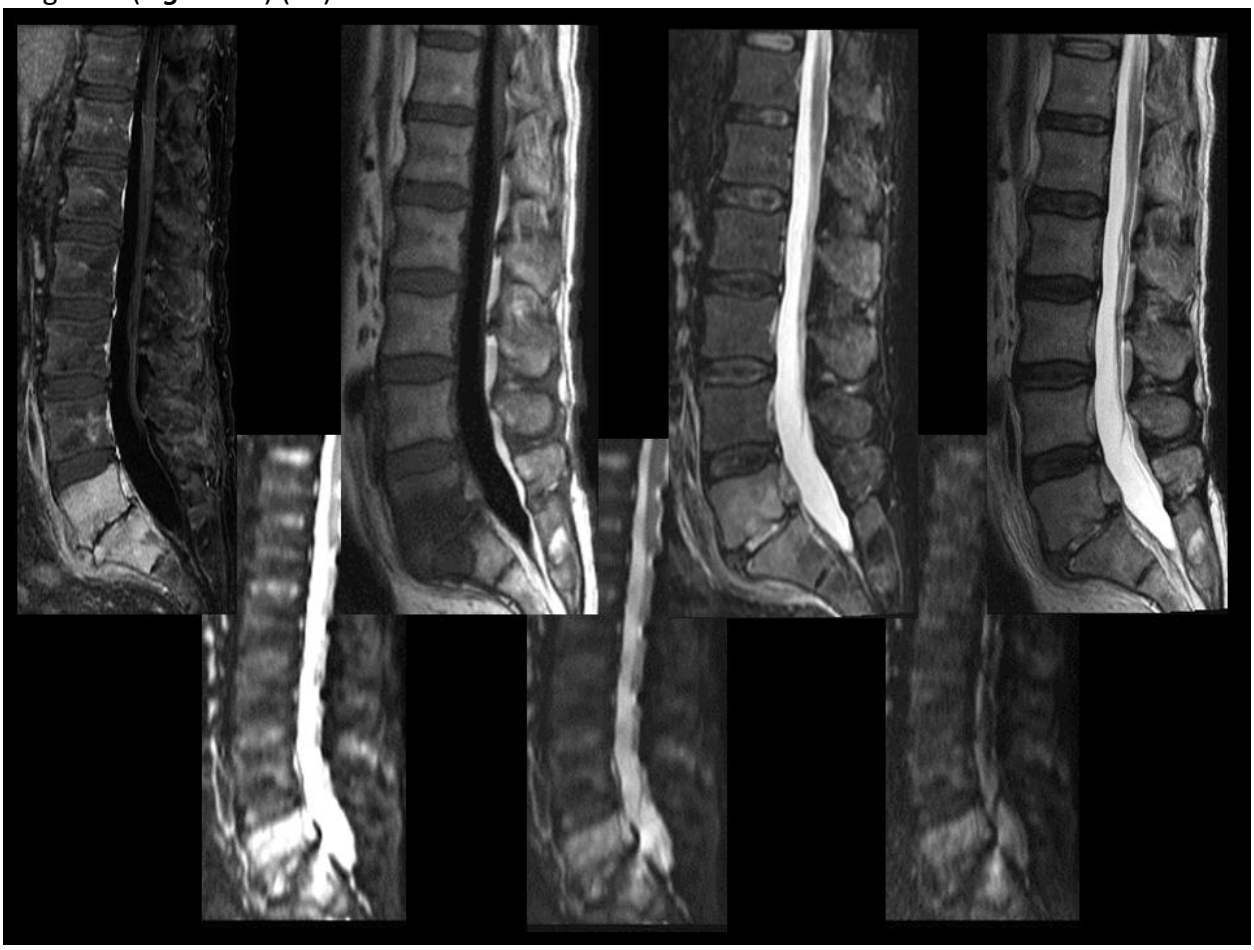

Figure 11: Osteomyelitis and discitis. Clockwise from upper left: Fat suppressed-contrast enhanced T1 FLAIR, T1 FLAIR, STIR, T2, DWI B=500,150,0. Note the diffuse increase in signal within the L5 and S1 vertebral bodies on DWI. The signal changes and enhancement on routine imaging sequence are characteristic of infection.

Diffusion can be useful in following the course of treatment, and may outperform routine scanning sequences in detecting response and recurrence (***Figure 12***).

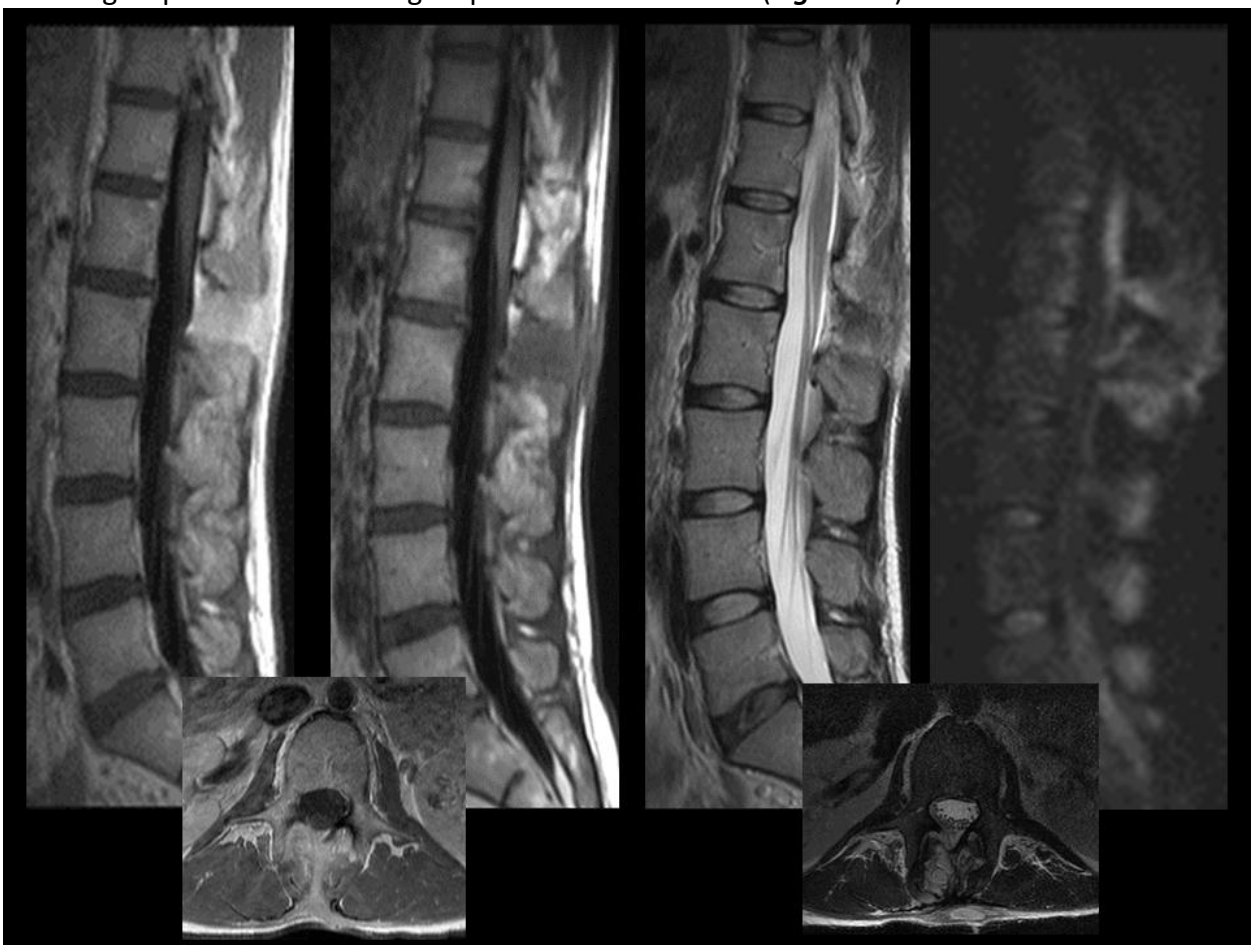

Figure 12: Treated osteomyelitis. From left: T1 FLAIR, contrast enhanced T1 FLAIR, T2, DWI. Inset: Axial T1 post contrast (left) and T2. Same case as previous figure. Note the absence of continued diffusion restricted after surgical and antibiotic therapy.

Degenerative disc and joint disease

Degenerative disease of the spine has a spectrum of characteristic appearances on DWI which correlate with those described by Modic et.al. (**28).** To avoid ghosting due to the precession frequency differences between fat and water all EPI images are fat suppressed. This leads to a characteristic widened disc space appearance in patients who manifest type II fatty changes in

marrow adjacent to the endplates (***Figure 13***).

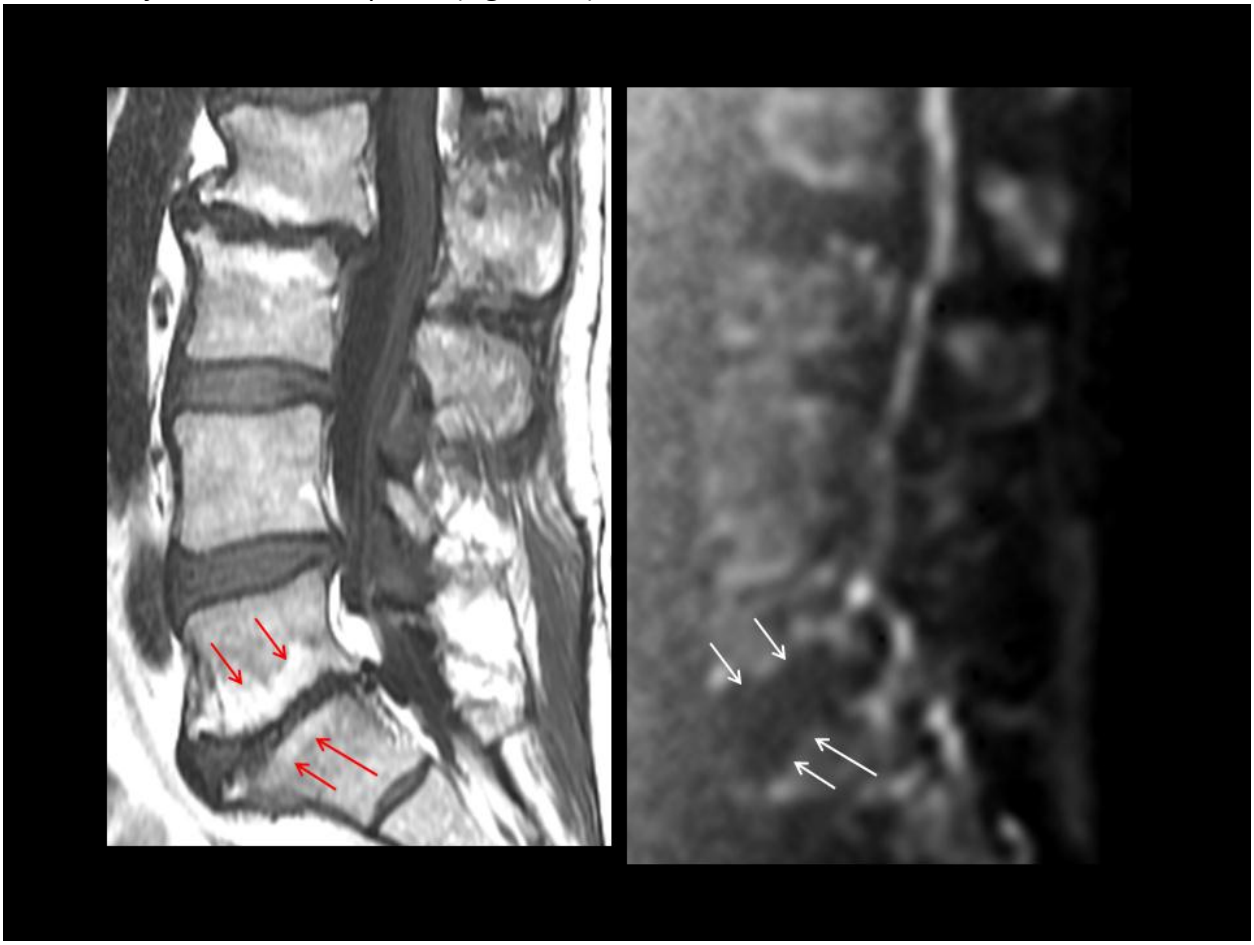

Figure 13: Type II Modic changes. T1 FLAIR (left) and DWI. Note the characteristic fatty changes on T1WI that manifest as diminished signal on the (routinely) fat suppressed DWI creating the appearance of a widened disc space.

The endplate sclerosis of the type III pattern will manifest as diminished signal on conventional and DW sequences. Despite the broad clinical utility of MRI in the spine, definitive differentiation between degenerative changes of the vertebral bodies and inflammatory disease may be problematic with conventional unenhanced and contrast enhanced MRI sequences (**29**). The appearance of type I degenerative signal changes in the spine can, not uncommonly, overlap with and raise the concern for osteomyelitis and discitis using routine imaging sequences. The granulation tissue and edema about the vertebral endplates in patients with, often symptomatic, type I changes are associated with a “claw” of increased signal and

diffusion restriction at the advancing border of the proliferative process (***Figure 14***).

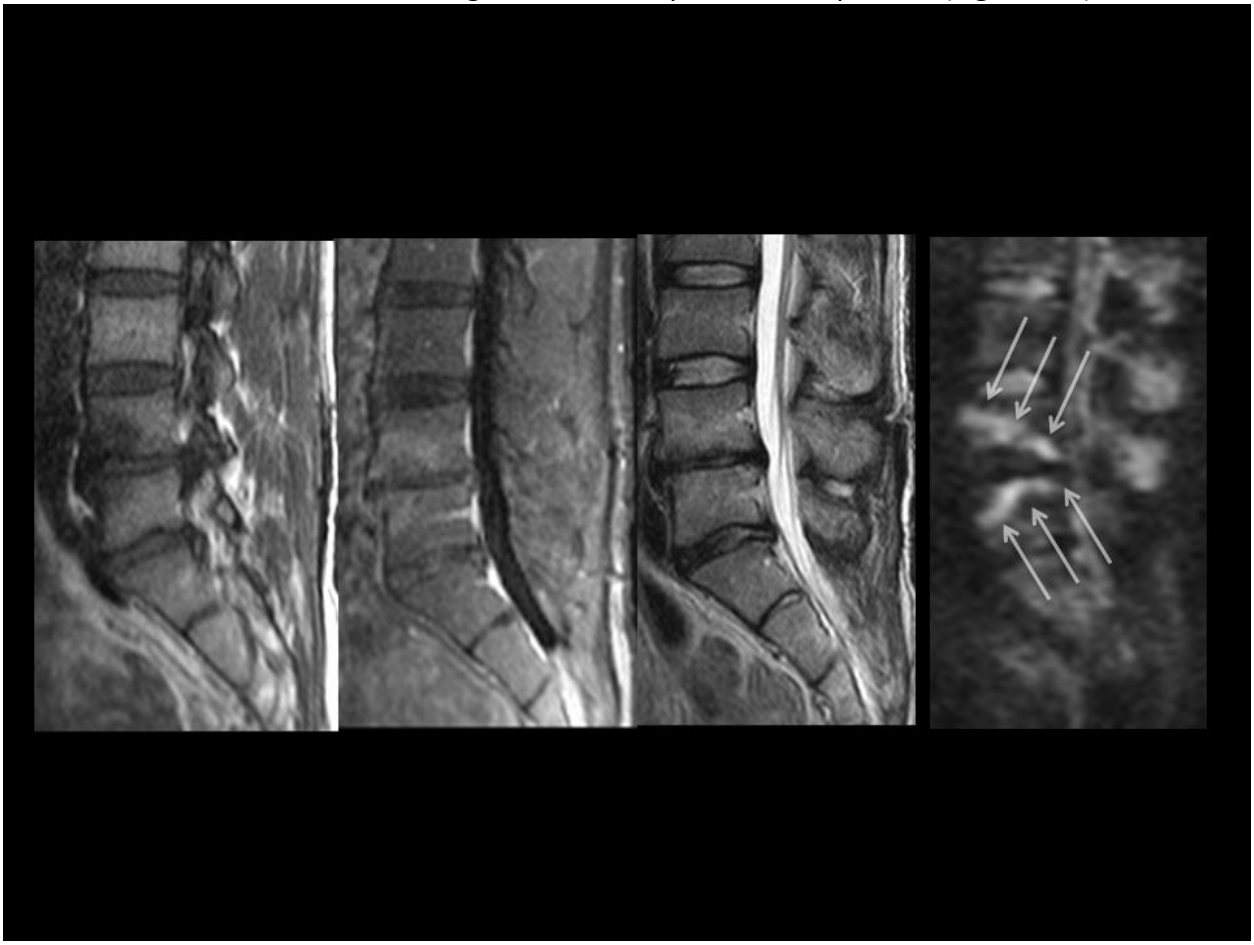

Figure 14: “Claw –sign” Modic I changes. From left: T1 FLAIR, contrast enhanced-fat suppressed T1 FLAIR, T2, DWI. Note the non-specific signal changes about the L4-5 disc space on routine imaging sequences. The DWI reveals paired well defined linear regions of increased signal at the border zone between the abnormal and normal marrow mitigating against the likelihood of infection.

When present, the presence of the ‘claw’ mitigates against the likelihood of infection. In a recently presented trial including cases of known infection, cases where infection was suggested based on routine MR imaging and cases with routine symptomatic type I findings the ‘claw’ sign had a very high positive and negative predictive value with respect to the possibility of infection and was much more useful than the presence or absence of contrast enhancement

and/or high T2 disc signal **(30)** IMAGES of infection and the claw ***(Figure 15).***

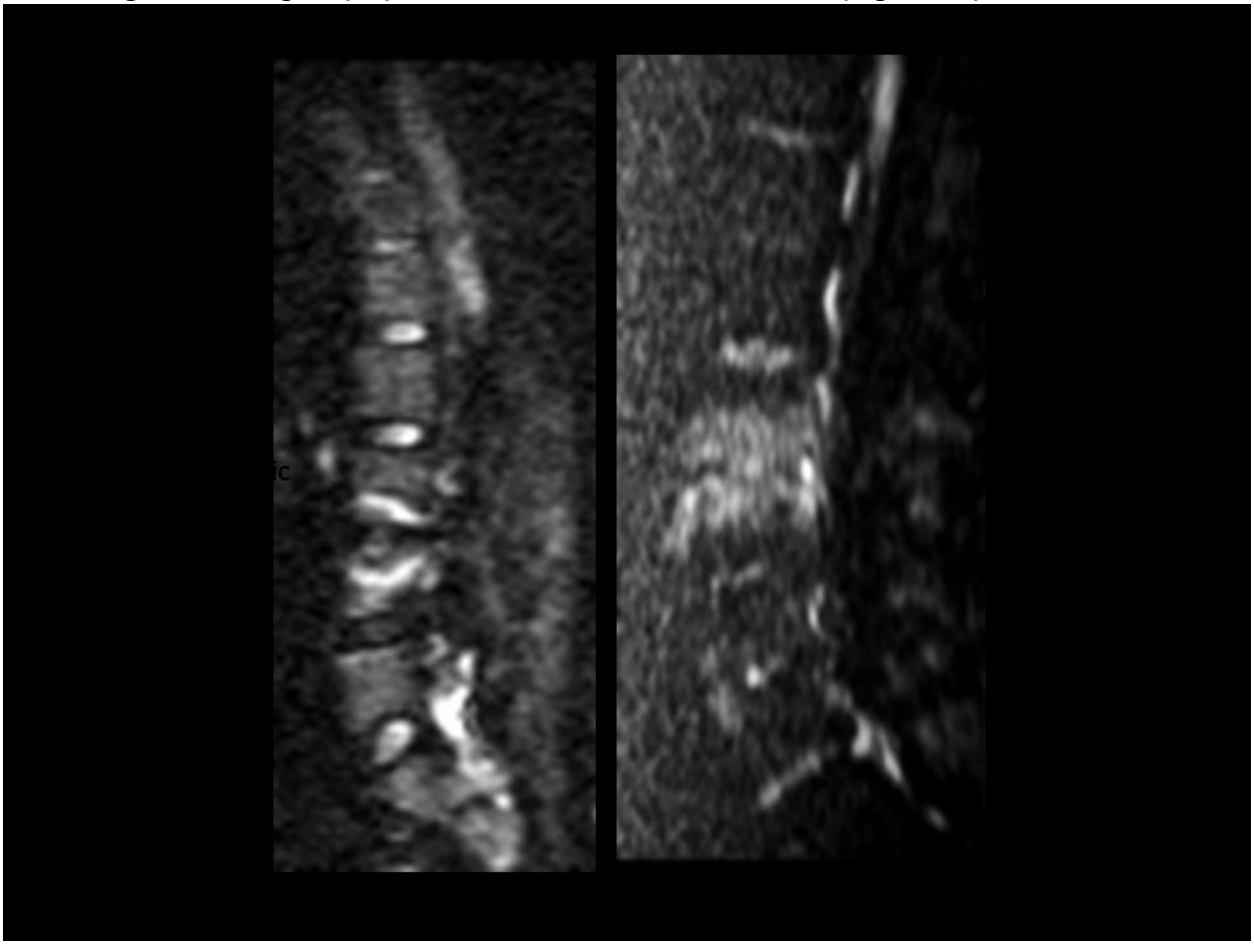

Figure 15: Modic I degenerative changes and osteomyelitis. DW images show a well-defined high signal “claw” (left) consistent with degenerative disease and amorphous increased signal (right) in a case of proven osteomyelitis.

Summary

Diffusion weighted imaging is one of the most powerful tools used in clinical magnetic resonance imaging. This universally available technique is a valuable complement to the array of routine spine MR imaging and offers a valuable boost in sensitivity as well as improved lesion characterization.

References

1. Koh D-M and Collins DJ. Diffusion-Weighted MRI in the Body: Applications and Challenges in Oncology. AJR June 2007 vol. 188 no. 6 1622-163.
2. Shimofusa R, Fujimoto H, Akamata H, et al.. Diffusion-weighted imaging of prostate cancer. J Comput Assist Tomogr. 2005 Mar-Apr;29(2):149-53.
3. Park MJ, Cha ES, Kang BJ et al. The Role of Diffusion-Weighted Imaging and the Apparent Diffusion Coefficient (ADC) Values for Breast Tumors Korean J Radiol. 2007 Sep-Oct; 8(5): 390–396.
4. Le Bihan D Molecular diffusion nuclear magnetic resonance imaging. Magnetic resonance quarterly 1991, 7(1):1-30
5. Thomsen C, Henriksen O and Ring P. In Vivo Measurement of Water Self Diffusion in the Human Brain by Magnetic Resonance Imaging. Acta Radiologica 1987, Vol. 28, No. 3 , Pages 353-361
6. Mulkern RV, Spencer RGS, Diffusion imaging with paired CPMG sequences, Magnetic Resonance Imaging, Volume 6, Issue 6, November–December 1988, Pages 623-631
7. Gudbjartsson H, Maier SE, Mulkern RV, et al. Line scan diffusion imaging. Magnetic Resonance in Medicine. Volume 36, Issue 4, pages 509–519, October 1996
8. Xu D, Henry RG, Mukherjee P, et. al. Single-shot fast spin-echo diffusion tensor imaging of the brain and spine with head and phased array coils at 1.5 T and 3.0 T. Magn Reson Imaging. 2004 Jul;22(6):751-9.
9. Saritas EU, Cunningham CH., Lee JH, et.al. DWI of the Spinal Cord with Reduced FOV Single-Shot EPI Magn Reson Med 60:468–473, 2008
10. Atkinson D, Counsell SJ, Larkman DJ, et.al. Navigated Multi-Shot EPI Diffusion Imaging of the Spine. Proceedings ISMRM 2006, Seattle. Abstract 1038
11. Castillo M, Arbelaez A, Smith JK, et.al.. Diffusion-weighted MR imaging offers no advantage over routine noncontrast MR imaging in the detection of vertebral metastases. AJNR Am J Neuroradiol. 2000 May;21(5):948-53
12. Castillo M. Diffusion-weighted imaging of the spine: is it reliable? AJNR Am J Neuroradiol. 2003 Jun-Jul;24(6):1251-33
13. Le Bihan D, Mangin JF, Poupon C, et.al. Diffusion tensor imaging: concepts and applications. J Magn Reson Imaging [2001]
14. Hesseltine SM, Ge Y, Law M. Applications of diffusion tensor imaging and fiber tractography. Applied Radiology Volume 36, Number 5, May 2007
15. Clark CA, Werring DJ. Diffusion tensor imaging in spinal cord: methods and applications – a review. NMR in Biomedicine Special Issue: Diffusion tensor imaging and axonal mapping - state of the art . Volume 15, Issue 7-8, pages 578–586, November - December 2002
16. Herneth AM, Friedrich K, Weidekamm C et al., “Diffusion weighted imaging of bone marrow pathologies,” European Journal of Radiology, vol. 55, no. 1, pp. 74–83, 2005.
17. Luboldt W, Küfer R, Blumstein N et.al. Prostate Carcinoma: Diffusion-weighted Imaging as Potential Alternative to Conventional MR and C-Choline PET/CT for Detection of Bone Metastases. December 2008 Radiology, 249, 1017-1025.

18. Parag Y, Delman B, Pawha P, Tanenbaum L. Diffusion weighted imaging facilitates detection of spinal metastases and assists in the diagnosis of equivocal lesions. Proceedings American Society of Spine Radiology Annual Meeting 2010, American Society of Neuroradiology Annual Meeting 2010, European College of Radiology Annual Meeting 2010.
19. Kessler J, Pawha P, Shpilberg K, Tanenbaum L. Diffusion weighted imaging facilitates detection of spinal multiple myeloma and assists in diagnosing equivocal lesions. Proceedings American Society of Spine Radiology Annual Meeting 2011, American Society of Neuroradiology Annual Meeting 2011, European College of Radiology Annual Meeting 2011.
20. Frager D, Elkin C, Swerdlow M et.al. Subacute osteoporotic compression fracture: misleading magnetic resonance appearance. Skeletal Radiol, 17(2):123–126,1988.
21. Rupp RE, Ebraheim NA, Coombs RJ. Magnetic resonance imaging differentiation of compression spine fractures or vertebral lesions caused by osteoporosis or tumor. Spine (Phila Pa 1976), 20(23):2499–503; discussion 2504, 1995.
22. Yuh WT, Zachar CK, Barloon TJ, et.al. Vertebral compression fractures: distinction between benign and malignant causes with MR imaging. Radiology, 172(1):215–218, 1989.
23. Baker LL, Goodman SB, Perkash I et.al. Benign versus pathologic compression fractures of vertebral bodies: assessment with conventional spin-echo, chemical-shift, and STIR MR imaging. Radiology, 174(2):495–502, Feb 1990.
24. Dietrich O, Biffar A, Reiser MF et.al. Diffusion-weighted imaging of bone marrow. Semin Musculoskelet Radiol. 2009 Jun;13(2):134-44
25. Karchevsky M, Babb JS, Schweitzer ME. Can diffusion-weighted imaging be used to differentiate benign from pathologic fractures? A meta-analysis. Skeletal Radiol. 2008 Sep;37(9):791-5
26. Park SW, Lee JH, Ehara S et.al. Single shot fast spin echo diffusion-weighted MR imaging of the spine; Is it useful in differentiating malignant metastatic tumor infiltration from benign fracture edema? Clin Imaging. 2004 Mar-Apr;28(2):102-8.
27. Dunbar JA, Sandoe JA, Rao AS et.al. The MRI appearances of early vertebral osteomyelitis and discitis. Clin Radiol. 2010 Dec;65(12):974-81.
28. MT Modic, PM Steinberg, JS Ross et.al. Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. January 1988 Radiology, 166, 193-199.
29. Eguchi Y, Ohtori S, Yamashita M et.al. Diffusion magnetic resonance imaging to differentiate degenerative from infectious endplate abnormalities in the lumbar spine. Spine (Phila Pa 1976). 2011 Feb 1;36(3):E198-202.
30. Poplawski MM, Pawha P, Naidich TP, Tanenbaum LN. Diffusion-weighted MRI (DWI) "claw sign" is useful in differentiation of infectious from degenerative Modic I signal changes of the spine. Proceedings of the American Society of Neuroradiology. 50th Annual Meeting. April 2012. New York, NY.