

# Cutting-Edge Imaging of the Spine

**Roland Bammer, Ph.D.**

Assistant Professor of Radiology  
Stanford University, Lucas Center  
1201 Welch Road, PS08  
Stanford, CA 94305-5488  
[rbammer@stanford.edu](mailto:rbammer@stanford.edu)

## 1. INTRODUCTION

Damage to the spinal cord may be caused by a wide range of pathologies and generally results in profound functional disability. Therefore, a reliable diagnostic workup of the spine is very important because even relatively small lesions in this part of the central nervous system can have a profound clinical impact. This is primarily due to the dense arrangement of long fiber tracts extending to and from the extremities within the spinal cord. Because of its inherent sensitivity to soft tissues and its capability of displaying long segments of the vertebral column in one examination, MRI has become the method of choice for the detection and diagnosis of many disorders in the spine [1]. MRI has revolutionized the assessment of patients who suffer from spinal cord symptoms because one can use it to rule out spinal cord compression or to determine abnormalities of the spinal cord itself. Despite the ultra-high resolution of MRI, its diagnostic specificity lags behind. Conventional MRI sequences of intramedullary lesions can frequently appear rather non-specific; consequently, it can be difficult to distinguish between inflammatory, neoplastic, or vascular changes without longitudinal information. Although conventional MRI sequences can delineate disorders of the intervertebral discs and of the osseous spine, distinguishing between degenerative changes of the vertebral bodies and inflammatory or neoplastic infiltration can be problematic, even with the application of contrast material. However, a variety of innovative MRI methods have been developed to improve spine imaging. These techniques include the development of better pulse sequences and new MR contrast parameters that offer a wider spectrum of biophysical parameters in deriving a diagnosis. This new “cutting-edge” technology profoundly impacts the ease and confidence of spinal disease interpretation and offers a more efficient diagnostic work-up of patients suffering from spinal disease.

## 2. CHALLENGES

While tremendous technical advances in brain MRI have been made during the past decade (e.g. DTI, BOLD, magnetization transfer MRI, etc.), these powerful methods are used much less frequently in spinal MRI because MRI of the spine is complicated by factors specific to the spine, such as the small size of the cord, truncation artifacts, physiological motion of the cord itself and nearby structures, and an inhomogeneous magnetic environment. Specifically, motion artifacts are potentially problematic in spinal cord imaging and can be due to a variety of reasons, such as CSF and blood pulsation, respiration, swallowing, and bulk motion. Depending on the pattern of motion, either random blurring or ghost artifacts will result. Here, CSF pulsation is especially bothersome in FLAIR imaging of spine since CSF which is not nulled can mask disease. In contrast to the brain, incomplete spinal CSF suppression is substantially more

problematic due to the difficulty of providing an effective inversion pulse for each slice. Moreover, spinal cord MRIs, in particular sagittal views, are often plagued by profound truncation artifacts (Gibbs ringing) which arise from the boundaries between the cord and CSF and manifest as parallel striations near sharp boundaries. To the untrained eye, these ringing artifacts might appear as pseudo-syrinx. Also, MRI of the spine is often challenged by magnetic susceptibility changes. These perturbations can emanate from the inhomogeneous susceptibility at the cervico-thoracic junction, the lungs, and parts of the vertebral bodies (e.g. osteophytes in spondylosis). Magnetic susceptibility changes can be also caused by hemorrhage (trauma patients) or surgical hardware (spine fixation). Consequently, the availability of new pulse sequences and reconstruction methods that adequately mitigate the aforementioned challenges are welcomed improvements for spinal cord MRI.

### **3. ADVANCES IN MR HARDWARE**

In the last decade, spine MRI has benefited the most from the introduction of phase array coil technology [2] and high field systems. Both primarily increase the baseline signal-to-noise ratio (SNR) of a study which is a major factor for successful spine studies that are notoriously SNR deprived. With the recent advent of parallel imaging [3, 4], multi-element RF coils have been improved and have enhanced the SNR of high resolution MRI. This is significant because if the voxel size is very small, inadequate SNR will cause blurring which will be integrated by the eye of the observer and will negate any increases in image sharpness that might have been achieved. A recent development that leveraged upon the latest hardware developments and the popularity of contrast enhanced MRA is moving table MRI [5]. With the availability of combined head and spine arrays, the entire spine can be imaged without repositioning the patient and changing the coil. This is of great relevance because often the disease of a patient (e.g. MS) requires a total workup of the entire CNS. By either stepwise or continuously moving the patient table, the moving table approaches allow the seamless acquisition of an entire spine within one scan.

### **4. FAST SPIN ECHO**

T1-weighted and T2-weighted fast spin echo (FSE) or turbo spin echo (TSE) methods are definitely the working horses in spine MRI. Because of their robustness and minimal sensitivity to field inhomogeneities, these methods are very popular. In comparison to true spin echo methods, the contrast of FSE and TSE is slightly different and the speed and robustness against artifacts of FSE cannot be matched by true spin echo methods. Contrary to spin echo sequences, fat appears bright on FSE scans because of J-coupling cancellation [6]. Typically, spectrally selective fat saturation or short-tau inversion recovery (STIR) is used for fat suppression, but recently spectral-spatial excitation pulses have become increasingly popular. Shorter overall image acquisition times and increased SNR in T2-weighted FSE can be achieved by applying driven equilibrium pulses [7]. At the end of the FSE readout, the remaining transverse magnetization of long T2 species is realigned longitudinally by an echo reset pulse (i.e.  $-90^\circ$  pulse). This allows for significantly shorter repetition times in contrast to conventional T2-weighted FSE (T2w-FSE), which would suffer from an unacceptable loss of contrast. This method is especially attractive for 3D FSE where excellent contrast can be achieved with TR/TEs of approximately 200/60ms [8]. Because of its fast acquisition, 3D FRFSE is a good candidate for 3D myelographic imaging.

Certainly, parallel imaging methods, such as generalized autocalibrating partially parallel acquisitions (GRAPPA) [4] or sensitivity encoding for fast MRI (SENSE) [3], have also influenced spinal imaging. Parallel imaging utilizes complementary information from inhomogeneous RF reception profiles of the individual spine array coil elements for additional image encoding, thus reducing the number of phase encoding steps. The applications of parallel imaging to spine imaging are numerous. First, the overall scan time can be reduced by at least a factor of 2-3. Cutting down the examination time is very important because many patients with disease to the spine suffer from great pain when they are asked to lie down straight for a long period of time. Second, parallel imaging helps to reduce blurring in FSE sequences with long echo trains (e.g. T2w-FSE, single-shot FSE) [9]. Third, it has been shown that parallel imaging can help to reduce motion artifacts by simply increasing the number of signal averages in proportion to the parallel imaging reduction factor. Also, parallel imaging reduces geometric distortion and T2\* related image blurring in EPI-base sequences and is therefore of great value to fMRI [10] (see section 8) and DWI [11] (see section 9).

### **5. THREE-DIMENSIONAL MRI**

Using 3D sequences offers obvious advantages over 2D approaches, such as better through-plane resolution and shorter echo times. To achieve an adequate myelographic effect (i.e. hyperintense CSF relative to the cord), spoiled GRE sequences have been used with low flip angles and sufficiently long echo times to ensure adequate T2\* weighting. The requirement of a low flip angle limits the signal-to-noise ratio (SNR), an effect that can be offset to some extent by using narrow readout bandwidths. However, smaller bandwidths are predisposed to artifacts related to CSF pulsation, magnetic susceptibility, stronger water/fat shift, and motion. These factors can cause impaired conspicuity and errors in the assessment of potential foraminal compromise.

### **6. BALANCED STEADY STATE FREE PRECESSION IMAGING (SSFP)**

With the development of high performance gradients and more homogeneous magnets, balanced SSFP (bSSFP)[12] has reentered the arena of MRI sequences. The sequence has the advantage of providing high SNR and high tissue-to-CSF CNR. Specifically, the bSSFP signal is related to the ratio of T2 to T1. The data acquisition with bSSFP is also very fast and is ideally suited for 3D acquisitions. Here, the ultra-short repetition times used with bSSFP lead to a marked improvement in total imaging time when compared with conventional gradient echo imaging (~2.5 times faster) with no significant difference in resolution. With its fully balanced gradient waveform, bSSFP provides relative motion insensitivity and diminishes otherwise troublesome effects of CSF pulsation (see previous paragraph) compared to conventional gradient echo imaging. Generally, bSSFP allows for good visualization of the intradural cervical roots and might be useful for a more general evaluation of cervical degenerative disease if additional sequences are added that are better suited for evaluation of the foramina (e.g. axial FSE or 3D gradient echo imaging). Improved conspicuity of nerve roots can be achieved by combining bSSFP with fat suppression. Posttraumatic brachial plexus injuries can also be successfully imaged by bSSFP, which allows the definition of the avulsed roots through the axial native images and the display of the protrusion of the meninges through 3D MIP projections. Furthermore, it has been shown that 3D bSSFP provides better myelographic images than does a 3D spoiled gradient echo sequence and has considerable advantages in SNR and CNR. One current downside of bSSFP is its relatively poor GM/WM contrast and the occurrence of banding

artifacts. These banding artifacts occur in the presence of field inhomogeneities or imperfections in gradient refocusing. With increasing TR or poor shim, the frequency of “dark bands” increases.

## **7. MAGNETIZATION TRANSFER IMAGING (MT)**

Magnetic transfer (MT) imaging is based on the differences between "bound" water protons associated with macromolecules (proteins and cell membranes) and free or "bulk" water protons and their respective pool exchange [13]. An off-resonance RF pulse can saturate the bound water protons, leading to the transfer of some saturation from the bound water to the bulk water protons via dipole-dipole interactions and chemical exchanges. Hence, the addition of an MT pre-pulse to a sequence can generate a new contrast mechanism. If the same sequence is repeated with and without MT pulses, the MT effect in tissue can be mapped as an MT ratio (MTR). The MTR has to be carefully considered because it can be confounded by various parameters, such as the type of MT pulse, continuous *vs.* pulsed MT saturation, saturation efficacy, etc. Alternatively, the MT pulse can be applied to a routinely used sequence as an image contrast modifier. The addition of the MT pulse increases the sensitivity of the gradient echo images to intramedullary disease and is often used in MS patients. The intervertebral disk shows moderate MT suppression, so the addition of the MT pulse improves contrast between the disk and the adjacent CSF. An important additional advantage of the high-contrast MT gradient echo sequences is the high CSF signal preservation at much shorter TEs. This short TE reduces the magnetic susceptibility distortions that, for example, causes an exaggeration of foraminal stenoses and reduces artifacts from CSF pulsation and chemical shift. However, the improved contrast of the MT gradient echo images can be at the expense of decreased resolution, which is always of concern in cervical spine imaging. Another slight disadvantage of MT is the diminished ability to delineate the disk space on the axial images, which makes it slightly more difficult to define the exact anatomic level.

## **8. FUNCTIONAL MRI**

The application of fMRI [14] to the spinal cord appears to be a logical extension to its cephalad cousin, but in comparison has received relatively little attention thus far. Nevertheless, fMRI of the spinal cord has matured over the last years and now appears to be adequate as a research tool in clinical trials assessing spinal cord function. In addition to the usual challenges of obtaining high quality fMRI data, the relatively low number of publications appears to be a consequence of the considerable challenge of acquiring MRIs of the spinal cord. However, the urgent need for an fMRI method adapted for demonstrating function in the spinal cord arises from the fact that there is no other non-invasive, global method available that can measure cord function. Since the cord is contained within the vertebral column, it is relatively inaccessible without opening the spinal canal and risking injury to the cord by inserting electrodes or needles and inflicting pain that could confound the study. The only means of assessing the function of the cord relies on the patient being able to feel a stimulus or having the proper reflexes. However, this assumes that the sensory receptors, peripheral nerves, and relevant areas of the brain, are all functioning normally. Even with normal function of these areas, very little information can be garnered about the cord's function distal to the location of an injury and relevant physical and physiological information that may be needed for proper assessment of a patient's condition or the effectiveness of treatment is masked.

Most challenges of spinal cord fMRI arise from differences in the magnetic environment between the bone, cartilage, and tissues [15]. The net effect is subtle magnetic field variations within these materials and field gradients at their boundaries, which can cause distortion and loss of signal. Respiration is another confounder that causes the field distortions to fluctuate rhythmically. Likewise, pulsatile CSF motion around the cord, as well as the motion the CSF imparts to the spinal cord, is another challenge, and cardiac or peripheral gating is often necessary. Finally, the relatively small cross-section of the spinal cord and its long extent in the cephalo-caudal direction present another problem for MRI. This is because a trade-off is required between image resolution and the volume of tissue that can be imaged in a reasonable amount of time.

## **9. DIFFUSION WEIGHTED MRI**

Quantitative diffusion measurements in healthy volunteers confirmed the assumption that diffusion coefficients in the spinal cord are comparable to those of the brain and demonstrate diffusion anisotropy [16]. Anisotropic diffusion is characterized most accurately by diffusion tensor imaging (DTI) [17]. Similar to conventional MRI, the small size of the spinal cord and the adjacent CSF space sometimes make it difficult to quantify diffusion and to distinguish between gray and white matter. Often the acquisition matrix is lower than in conventional structural MRI and therefore a pseudo-syrinx is seen more frequently. Clinical applications of DWI include [18]:

*i) Spinal Cord Infarction:* With conventional MR sequences, it may take days to observe intramedullary signal changes following spinal cord ischemia. Even then, it is often hard to discriminate such changes from those caused by other etiologies such as myelitis. Such information, however, is necessary for trying more aggressive therapies such as rtPA treatment. Although the exact pathomechanism is still not fully clear, DWI has demonstrated high sensitivity to early ischemic changes in acute cerebral stroke. Recently, similar findings were also reported for the spinal cord, although the number of patients included was very small in each of these studies. This reflects existing difficulties in applying DWI to the spinal cord in the routine clinical setting.

*ii) Trauma:* Spinal cord trauma is the most frequent cause of acute para- or tetraplegia. In the U.S., approximately 20,000 patients per year will suffer from paralyzing spinal cord injury. Traumatic injury may result in cellular swelling and degeneration, the disruption of myelin membranes, or even more severe damage. In part, the initial cord injury and axonal transection cause the functional deficits that ultimately occur. Increased functional loss is also related to “secondary injury,” which is an immune response and can persist for several days, resulting in increased lesional size, swelling, and ultimately, the additional degeneration of axonal fiber tracts. The exact stage of traumatic injury is often difficult to characterize by conventional MRI because it tests for the functional integrity of the axons within the white matter tracts of the spinal cord. Similarly, conventional MRI can not detect possible therapeutic responses to neuroprotective drugs. In this context, Wallerian degeneration above and below the site of injury is known to be indicative of axonal loss. However, Wallerian degeneration as seen by conventional MRI occurs only with advanced progression of tissue damage and is not differentiable from edema. Diffusion-related parameters obtained from DWI might be better able to define the type and extent of spinal cord injury than conventional MRI, because different pathophysiologicals may affect diffusion properties differently. In experimental animal models of

spinal cord injury, the efficacy of DWI has been studied and a decrease of longitudinal ADC and an increase of transverse ADC were observed. A spinal trauma can be complicated further if syringomyelia develops. This is a cystic cavitation within the center of the spinal cord. In animal models, changes can be seen on ADC maps soon after 1 week, while conventional MRI is first positive only 4 weeks after the injury. The potential drawbacks for DWI in the presence of hemorrhagic components of traumatic tissue damage have been discussed earlier.

*iii) Spondylotic Myelopathy:* Degenerative spondylosis may cause significant narrowing of the spinal canal and ultimately can lead to compression of the spinal cord. Compromise of the spinal cord can also result from protruded or herniated discs, especially in the case of a narrow spinal canal. Clinically, such patients usually present with chronic progressive signs of myelopathy. In one of our studies, we found that spondylotic myelopathy presented with reduced ADC values, whereas the surrounding cord demonstrated elevated diffusivity. The former is presumably either due to cord compression or due to vascular compromise, while the latter is due to surrounding edema.

*iv) Neoplasms:* Current MR imaging sequences using contrast material are already quite effective for the correct diagnosis of different mass lesions. Because of the altered cellular matrix of neoplastic tissue which is picked up by DWI, this technique may add to the staging of tumors and could help to differentiate different types of mass lesions. Promising results have been shown for the brain, where researchers reported DWI's ability to differentiate between cerebral tumor types; similar results might be anticipated for the spine. For example, in one patient suffering from an astrocytoma in the cervical cord, we found that the lesion had a significantly elevated ADC. However, in high grade, heterogeneous tumors, such as glioblastoma multiforme or high grade astrocytomas, ADC values can vary over a large range and a general differentiation based on ADC can be difficult. Another approach is to use the orientational information obtained from DTI to perform fibertracking to determine whether a tumor invades or displaces fiber tracts. The latter might have consequences for the planning of surgical intervention.

*v) DWI in the osseous spine:* Because of its high vascularity, the osseous spine is a common target site for metastatic spread. Hence, painful vertebral metastases are frequently observed in patients with cancer (30%-70%) and may lead to various secondary problems, which range from fractures to the compression of the dural sac by epidural masses. MRI has evolved into one of the preferred methods for detecting vertebral metastasis, mainly because MRI rapidly detects when normal bone marrow is replaced by more hypercellular tissue or by other pathologies, which cause a higher water content. However, with conventional imaging, such as T1- and T2-weighted (fast) spin echo, or short tau inversion recovery sequences (STIR), it is often difficult to determine whether the cause of an acute vertebral compression fracture is osteoporosis or metastasis. Morphological signs, such as complete replacement of vertebral marrow, involvement of the posterior elements, and epidural or paraspinal masses, can be used to improve the diagnostic accuracy but may be equivocal. Results from recent studies have raised hope that DWI might be able to differentiate benign from malignant acute vertebral fractures. It has been reasoned that proton diffusivity is elevated in osteoporotic fractures because of bone marrow edema. Conversely, metastatic lesions might change diffusivity only moderately or even decrease it. It was postulated that a high cellularity of metastatic lesions, especially of actively growing tumors, would increase their intracellular volume fraction relative to the interstitial

space. Because the water diffusion coefficient is significantly lower in the intracellular space than in the extracellular space, ADC values of metastatic vertebral infiltration should be lower. Initial studies on DWI of the osseous spine to separate benign compression fractures from metastatic lesions were performed with a rather “exotic” diffusion-weighted SSFP sequence that is notoriously sensitive to confounders (e.g. relaxation times, B1 field, etc.) and that has an impressive discrimination capacity. However, subsequent studies using the more established Stejskal-Tanner based approach reported less enthusiastic and more mixed results. To date, the diagnostic utility of DWI to differentiate acute compression fractures is still controversial.

## 10. SUMMARY

“Cutting-Edge” technology often implies that the technology being developed is not readily available to every user or is still under investigation. Therefore, I hope this early overview stimulates the anticipation of, rather than frustration with, advances in imaging of the spine. The continuous progress of MR hardware and the development of new pulse sequences have led to a considerably improved diagnostic work-up of patients suffering from disease in their spines. This review is meant to serve as an introduction to the strengths and weaknesses of the most innovative and novel methods for imaging and their potential clinical applications.

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