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High-Resolution MR of the Spinal Cord in Humans and Rats

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Human and rat cervical spinal cords were imaged with high-resolution spin-echo and inversion-recovery pulse sequences in an experimental 1.9-T MR system. The gross morphology of the cord was easily discernible in fresh and fixed specimens, including the white and gray commissures, dorsal and ventral horns, and lateral and posterior funiculi. The T1, T2, and spin-density values for gray and white matter were determined from these images and were found to be 914 msec, 114 msec, and 71% for white matter other than the dorsal columns, and 946 msec, 87 msec, and 80% for gray matter in human spinal cords. These values are reduced considerably after formalin fixation: T1 to 56% (white matter) and 54% (gray matter) of prefixation values, T2 to 52% (white matter) and 70% (gray matter) of fresh values, and spin density to 90% (white matter) and 96% (gray matter) of prefixation values. Interestingly, the central gray matter demonstrates higher signal intensity than the white matter on both short and long TR/TE images. This intensity difference was observed for both human and rat spinal cords, before and after fixation, and can be explained by the relatively small T1 differences between gray matter and white matter and the gray matter–white matter spin-density ratios: 1.127 for fresh and 1.203 for fixed specimens.

MR imaging has been used extensively to document the gross morphology and pathology of the CNS [1–5]. The application of MR to studies of the brain in vivo has produced detailed images of its internal structures. The important physical parameters of T1, T2, and spin density for the gray and white matter of the brain have been evaluated by a number of investigators [6–9]. Hence, the MR contrast of gray matter versus white matter in the brain is thought to be well characterized for a given set of imaging parameters [10]. In vivo MR of the spinal cord has not progressed to the same extent as that of the brain; consequently, the MR properties of the spinal cord are not as well understood. However, as clinical image quality improves it is reasonable to expect that it will become possible to visualize the internal structure of the cord as well as its outline; for this reason it is desirable to have knowledge concerning the normal structure of the spinal cord. The goals of this study were (1) to demonstrate the gross morphology of the spinal cord with high spatial resolution; (2) to determine the MR parameters of T1, T2, and spin density for the gray and white matter within the spinal cord; and (3) to evaluate the effect of fixation upon MR parameters of the spinal cord to assess the degree to which fixed specimens can be used as accurate models of the spinal cord when freshly excised or in vivo.

Materials and Methods

Spinal cords were removed 24–36 hr postmortem from five unembalmed, refrigerated adult male cadavers. Typically, the cords were excised as a single piece (C1–T1) from the spinal column after the laminae were removed. The specimens were rinsed in saline, patted dry, and wrapped in plastic to prevent dehydration. In one case, the brain was also removed from the cadaver and imaged according to the same protocol so that a comparison of T1, T2, and

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spin density values for brain and spinal cord was possible. In one case, the entire spinal column was transected and the spinal cord was imaged in situ. The cadaver dissection and removal of the spinal cords required approximately 1 hr, and specimens were imaged immediately afterward, which took approximately 2½ hr. All specimens were allowed to warm as they were being removed and were imaged at ambient temperature.

Spinal cords (C1–L1) were also obtained from five adult male Sprague-Dawley rats. The cords were removed as a single piece by first transecting the spinal column and subsequently performing laminectomies for the length of the excised column. This dissection required approximately ½ hr and the MR study required 2½ hr to complete. The rat cords were imaged immediately after removal at room temperature. After imaging, all fresh cords, rat and human, were placed into 10% neutral buffered formalin and allowed to fix for at least 1 week before being imaged a second time.

Imaging was performed on a 1.9-T, 31-cm bore, experimental system, and we used a special-purpose receiver coil (5-cm diameter, cylindrical, double saddle coil) [11]. The data acquisition matrix was 128 × 128, and we achieved a spatial resolution of either 300 μm or 150 μm. Spin-echo (SE) images, 3000/15, 20, 50, 100/1 (TR/TE/excitations) or 400/20/1, and inversion-recovery (IR) images, 3000/2000, 1200, 200, 50/15/1 (TR/TI/TE/excitations), were acquired. All pulse sequences were single-echo, single-slice, with a nonselective 180° refocusing pulse. T2 values were determined with a chi-squared minimization two-parameter fit, whereas T1 values were determined from these images by using a three-parameter fit [12]. Spin density was determined on one human cord, both fresh and fixed, and on one rat cord before fixation. For the spin-density calculation a phantom containing a 1 mM or 2 mM copper sulfate solution was included in the field of view. This was taken to represent 100% water content, and spin-density values were calculated by extrapolating signal intensities to TE = 0. We have measured T1 values of 980 msec and 528 msec for 1 mM and 2 mM copper sulfate solutions, respectively. Therefore, the density values for the solutions were calculated with a TR/T1 ratio of at least 3.

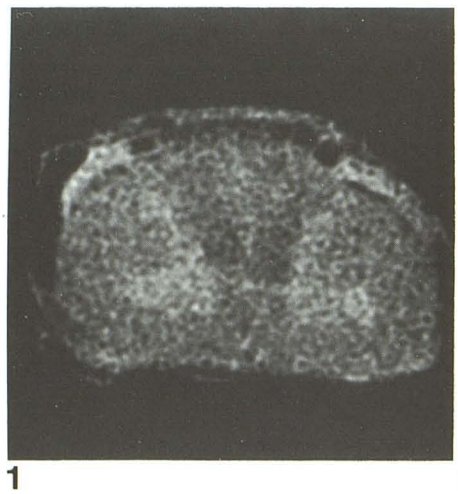
Results

The lateral and posterior funiculi, the dorsal and ventral horns, and the white and gray commissures of the fresh adult human spinal cord can be seen in the short TR/TE axial image (Fig. 1). In these short TR/TE images the white matter–gray matter contrast is the reverse of that seen in the brain, in that the gray matter of the cord appears more intense than does the white matter. In long TR/short and long TE axial images (3000/20, 50) (Fig. 2), the anatomic features of the spinal cord are very well delineated and gray matter continues to be more intense than white matter.

In one experiment the entire spinal column was imaged with the spinal cord left in situ. This procedure was performed to address the concern that the spinal cord may have been damaged in the process of removing it from the spinal column. The spinal cord when imaged inside the spinal column demonstrated the same white matter–gray matter contrast as the spinal cord when it was imaged alone (Fig. 3). Therefore, we believe that it is unlikely that dissection and specimen handling have produced profound alterations in the appearance of the images.

The values of T1, T2, and spin density as determined for gray and white matter in the fresh spinal cord are shown in Tables 1A (human) and 1B (rat). It is important to note that the observed value of T2 for gray matter is shorter than that of white matter. This observation runs contrary to reported T2 values in brain, where the gray matter T2 has often been found to be slightly longer than that of white matter [6]. Divided images—that is, calculated images in which one spin-echo image (3000/20) is divided by another with the same TR but a different TE (3000/100)—reflect only T2 values, as proton density and T1 effects are divided out [10]. These images represent a T2 map in which high pixel intensity corresponds to short T2 and can be used to corroborate the relative magnitude of the T2s measured for gray matter and white matter. The division image shown in Figure 4 shows that the gray matter T2 in the spinal cord is shorter than that of the white matter.

The values of T1, T2, and spin density for gray and white matter when fixed in 10% neutral buffered formalin are much less than the prefixation values, as shown in Tables 2A (human) and 2B (rat). Fixation resulted in reductions to 56% (white matter) and 54% (gray matter) of prefixation values for T1 and 52% (white matter) and 70% (gray matter) of prefixation values for T2 in human cords, and 36% (white matter) and 35% (gray matter) of prefixation values for T1 and 53% (white matter) and 78% (gray matter) of prefixation values for T2 in rat cords (see Table 3). The proton density was reduced after fixation for both gray matter and white matter. The ratio of gray matter to white matter spin density changed from



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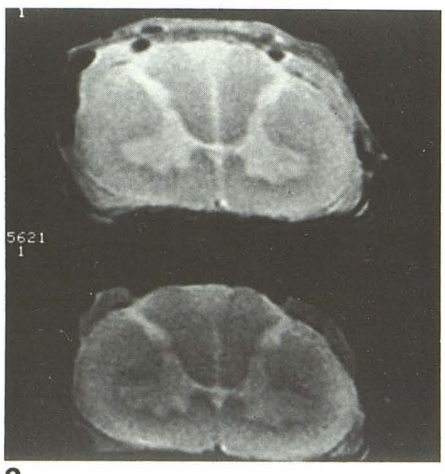

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Fig. 1.—MR image, 400/20, of fresh human cervical spinal cord. Although signal-to-noise ratio for this scan is low, gray matter has higher signal intensity than does white matter. In-plane resolution is 150 μm/pixel dimension.

Fig. 2.—MR images, 3000/20 (*top*) and 3000/50 (*bottom*), of fresh human cervical spinal cord. These images represent approximately the level of C5 and have an in-plane resolution of 150 μm/pixel dimension. Gray matter–white matter differentiation is clearly seen.

Fig. 3.—MR image, 3000/15, of fresh human spinal column. Spinal cord gray matter–white matter contrast is the same as in Fig. 2, and an in-plane resolution of 300 μm/pixel dimension was obtained. *Arrows* indicate image wrap-around (aliasing), which causes a portion of the vertebral body to be superimposed upon the spinous process. This foldover accounts for the high signal intensity in this region.

Fig. 4.—T2 map (division image) of fresh human spinal cord. This image is calculated by dividing one image (3000/20) by another image (3000/100). Since the effects of T1 and proton density appear in both the numerator and denominator images, the quotient (division image) is a T2 map in which high signal intensity corresponds to short T2.

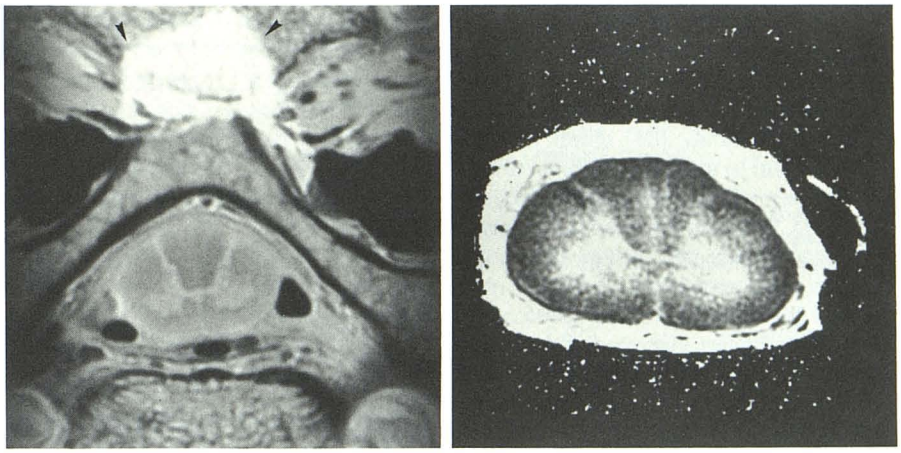

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TABLE 1A: T1, T2, and Spin Density in Spinal Cord: Fresh Human Specimens

Tissue	T1	T2	Spin Density (%)
Lateral white matter	914.5 (± 40.2 SD)	114.3 (± 13.6 SD)	71
Gray matter	945.5 (±76.5 SD)	87.0 (± 4.4 SD)	80
Dorsal columns	1047.3 (± 86.2 SD)	128 (±17.4 SD)	71

Note.—SD = standard deviation.

TABLE 1B: T1, T2, and Spin Density in Spinal Cord: Fresh Rat Specimens

Tissue	T1	T2	Spin Density (%)
Lateral white matter	697.5 (± 84.6 SD)	84.3 (± 2.6 SD)	53.2
Gray matter	719.3 (± 155.2 SD)	64.3 (± 5.9 SD)	77.9
Dorsal columns	721.3 (± 57.9 SD)	78.0 (± 10.9 SD)	51.9

Note.—SD = standard deviation.

TABLE 2A: T1, T2, and Spin Density in Spinal Cord: Fixed Human Specimens

Tissue	T1	T2	Spin Density (%)
Lateral white matter	508.5 (± 83.4 SD)	60.0 (± 3.9 SD)	64
Gray matter	511.3 (± 71.0 SD)	60.5 (±7.0 SD)	77
Dorsal columns	627.5 (±144.8 SD)	71.8 (±12.7 SD)	69.0 (± 3.1 SD)

SD = standard deviation.

TABLE 2B: T1, T2, and Spin Density in Spinal Cord: Fixed Rat Specimens

Tissue	T1	T2	Spin Density (%)
Lateral white matter	250.3 (± 89.3 SD)	44 (± 9.2 SD)	ND
Gray matter	253.3 (± 112.5 SD)	46 (± 9.3 SD)	ND
Dorsal columns	299.0 (± 98 SD)	55 (± 11.3 SD)	ND

Note.—SD = standard deviation; ND = not determined.

1.127 before fixation to 1.203 after fixation. In both fresh and fixed samples the gray matter–white matter contrast in short TR/TE images (400/20) and long TR/short and long TE images (3000/20, 50) is qualitatively the same, with gray matter showing higher signal than white matter (Figs. 5 and 6).

The brain from one of the cadavers was removed and imaged. In the short TR/TE images of the brain, white matter exhibited higher signal intensity than gray matter, as expected. Values of T1 and T2 calculated from the images show that white matter has shorter T1, shorter T2, and lower proton density than gray matter, see Table 4. The measured values for T1 of white and gray matter are in good agreement with values calculated for a field strength of 1.9 T using the expression of Bottomley et al. [7]. Similarly, there is good general agreement between the expected and observed values of T2. The division image of the brain (TR = 200, TE = 10 divided by TR = 3000, TE = 10) shown in Figure 7A represents a T1 map and demonstrates that, as expected, the T1 of the gray matter is longer than that of the white matter in brain. Also, the long TR/long TE image (3000/100) shown in Figure 7B demonstrates expected signal intensities for human brain tissue. That the images we have obtained and the T1, T2, and spin-density values we have calculated for these samples correspond closely to in vivo results lends credence to the use of ex vivo specimens to investigate the physical parameters of tissues in vivo.

We have assessed the impact that fixation has upon the MR parameters of the adult spinal cord. T1 and T2 values are reduced by fixation. In fixed human cord the white matter T1 average was 508.5 while the gray matter average was 511.3;

TABLE 3: T1, T2, and Spin Density in Human and Rat Spinal Cord: A Comparison of Fresh and Fixed Specimens

Tissue	T1			T2			Spin Density		
	Before Fixation	After Fixation	Percent of Original Value	Before Fixation	After Fixation	Percent of Original Value	Before Fixation	After Fixation	Percent of Original Value
Human lateral column white matter	914.5	508.5	56	114.3	60.0	52	71	64	90
Rat lateral column white matter	697.5	250.3	36	84.3	44	52	53		
Human gray matter	945.5	511.3	54	87.0	60.5	70	80	77	96
Rat gray matter	719.3	253.3	35	64.3	46	72	78		

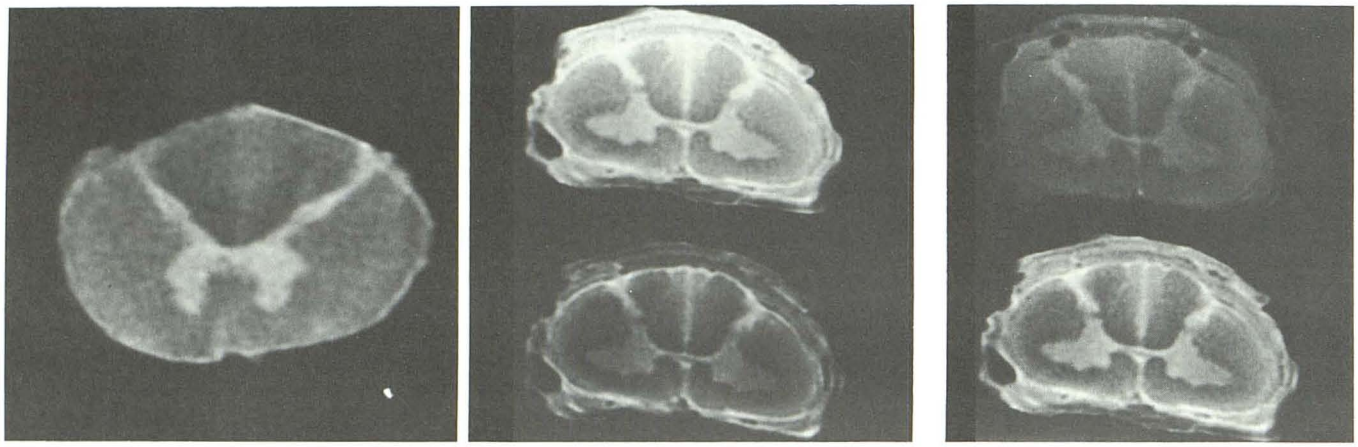

Fig. 5.—*A*, MR image, 400/20, of fixed human spinal cord.
***B*, MR images, 3000/20 (*top*) and 3000/50 (*bottom*), of fixed human spinal cord. Although level of spinal cord is slightly different in *A* and *B*, the in-plane resolution for both figures is the same: 150 μm/pixel dimension.**

Fig. 6.—MR image, 3000/20, of human spinal cord before (*top*) and after (*bottom*) fixation. Note that gray matter–white matter contrast remains qualitatively unchanged after fixation.

TABLE 4: T1, T2, and Spin Density in Brain

	T1 Calculated[a]	T1 Observed	T2 Calculated[a]	T2 Observed	Spin Density	
					In Vivo	Ex Vivo
White matter						
Corpus callosum	854	806	92	108	1.00[b]	1.00[c]
Gray matter						
Caudate nucleus	991	1015	101	117	1.296	1.286

[a] Derived from [7].
[b] Derived from Table 2, instrument A in [6]. Spin-density values are normalized to a white matter value of 1.00.
[c] Ex vivo spin density of white matter is normalized to 1.00 in order to compare relative gray matter and white matter spin densities ex vivo.

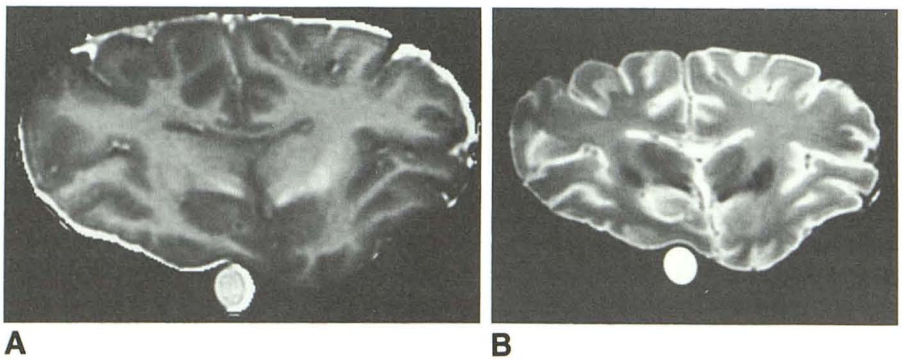

Fig. 7.—*A*, T1 map (division image) of fresh human brain. In this image [(200/10)/(3000/10)] high intensity is representative of short T1.
***B*, MR image, 3000/100, of fresh human brain taken at same location as *A*. Note contrast typical for gray matter–white matter on long TR/long TE images.**

the white matter T2 average was 60.0 while the gray matter T2 average was 60.5 (Table 3). In the fixed rat tissue the T1 and T2 values of gray and white matter were shorter than the human values. However, as was the case with human tissue, after fixation the white matter T1 and T2 values were nearly identical to those of gray matter. However, proton density remains higher in gray matter than in white matter after fixation.

Discussion

High-resolution MR of both freshly excised and fixed spinal cords demonstrates excellent anatomic delineation of gray and white matter. With a spatial resolution of 150 μm per pixel the morphology of the central gray matter as shown by MR correlates well with gray matter anatomy. To date, we have not been successful in visualizing either tracts in the white matter or the laminar structure of the gray matter. A better understanding of the normal appearance of the structure of the spinal cord should help to increase the utility of MR in evaluating intrinsic abnormalities such as amyotrophic lateral sclerosis, posttraumatic or ischemic lesions, intramedullary cavities, and other diseases that result in alterations of the volume or configuration of gray or white matter.

The signal intensity for gray and white matter on short TR/TE images is dependent on the tissues' inherent biophysical parameters of T1, T2, and proton density. In the brain, white matter T1 is so much shorter than that of gray matter that white matter signal intensity exceeds gray matter intensity on short TR/short TE images in spite of the higher gray matter spin density. In the freshly excised spinal cord the gray matter–white matter contrast observed for short TR/TE images (gray matter with the higher signal intensity) is the reverse of that observed in the adult brain. In the spinal cord the T1 of gray matter is only slightly shorter than dorsal column white matter and very slightly longer than lateral column white matter. Therefore, there is very little T1 contrast to be observed and the gray matter–white matter contrast is dominated by the gray matter's higher spin density. Fixed spinal cords reveal this same pattern of gray matter–white matter contrast, which is also caused by the difference in spin density, since there is virtually no T1 or T2 difference between gray matter and lateral column white matter (Table 3).

We have observed a close correspondence between the spin-density ratio of brain gray matter/white matter (caudate nucleus/corpus callosum) ex vivo and in vivo. Breger et al. [6] report spin-density ratios in vivo of 1.165 to 1.296, having obtained the higher ratio with techniques that they believe to be more reliable, while we have measured a spin-density ratio ex vivo of 1.286. This similarity suggests there were no extreme postmortem changes in the tissue we examined that would distort our measurements, and that our values are consistent with the range of values reported by other groups.

That the T2 values of the gray matter in the fresh spinal cord specimens were found to be shorter than those of the white matter stands in contradistinction to the commonly reported results in adult brain. Whether this observation truly represents the relationship that exists in the cord in vivo or is an artifact due to posthumous changes must be considered. In a study of the changes in the MR characteristics of liver and spleen as a function of time elapsed from death to data acquisition it was found that the T1 did not change for 6 hr and the T2 for 48 hr after death [13]. Similarly, relaxation times of the cerebral cortex and white matter of rat brain have been found not to change in the first 24 hr after biopsy [14]. In fresh ex vivo brain we observed gray matter T1 and T2 to exceed those values for white matter, the same relationship as has been reported in vivo [6–9]. In the one case in which the brain and spinal cord of the same cadaver were studied, the spinal cord T1, T2, and spin-density relationships were typical of those of the other spinal cords, while the brain results were consistent with reported values for in vivo brain. This supports our belief that the relaxation times and spin-density ratios we have measured for fresh human and rat spinal cords reflect in vivo values rather than postmortem artifact.

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