Ultrahigh-resolution quantitative spinal cord MRI at 9.4T

Ole Geldschläger1 | Dario Bosch1,2 | Nikolai I. Avdievich1 | Anke Henning1,3

1High-Field Magnetic Resonance Center, Max Planck Institute for Biological Cybernetics, Tübingen, Germany
2Biomedical Magnetic Resonance, University Hospital Tübingen, Tübingen, Germany
3Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, USA

Purpose: To present the results of the first human spinal cord in vivo MRI scans at 9.4T.

Methods: A human brain coil was used to image the human spinal cord at 9.4T. All anatomical images were acquired with a $T_2^*$-weighted gradient-echo sequence. A comparison of the influence of four different $B_0$ shimming routines on the image quality was performed. Intrinsic signal-to-noise-ratio maps were determined using a pseudo-multiple replica approach. Measurements with different echo times were compared and processed to one multiecho data image combination image. Based on the multiecho acquisitions, $T_2^*$-relaxation time maps were calculated. Algorithmic spinal cord detection and gray matter/white matter segmentation were tested.

Results: An echo time between 9 and 13.8 ms compromised best between gray matter/white matter contrast and image quality. A maximum in-plane resolution of $0.15 \times 0.15 \, \text{mm}^2$ was achieved for anatomical images. These images offered excellent image quality and made small structures of the spinal cord visible. The scanner vendor implemented $B_0$ shimming routine performed best during this work. Intrinsic signal-to-noise-ratio values of between 6600 and 8060 at the upper cervical spinal cord were achieved. Detection and segmentation worked reliably. An average $T_2^*$-time of $24.88 \, \text{ms} \pm 6.68 \, \text{ms}$ for gray matter and $19.37 \, \text{ms} \pm 8.66 \, \text{ms}$ for white matter was calculated.

Conclusion: The proposed human brain coil can be used to image the spinal cord. The maximum in-plane resolution in this work was higher compared with the 7T results from the literature. The 9.4T acquisitions made the small structures of the spinal cord clearly visible.

Keywords
9.4 Tesla, high-field magnetic resonance imaging, relaxometry mapping, segmentation, spinal cord magnetic resonance imaging
1 | INTRODUCTION

Today MRI is an indispensable method for clinical diagnostic and research investigations of the human spinal cord (SC). For SC-related diseases such as multiple sclerosis,1–3 amyotrophic lateral sclerosis,4 spondylosis,5 or SC injury6 MRI is the technique of choice for primary diagnostics, patient stratification, and therapy monitoring. Furthermore, it has been reported that in patients with multiple sclerosis, gray matter (GM) lesions in the SC may be detectable more readily than GM lesions in the brain, which illustrates the importance of SC imaging investigations in general.7

Small structures within the SC are inherently challenging to image at lower B0 field strengths; hence, field strength is of important relevance for SC measurements. Utilizing higher field strengths provides a higher signal-to-noise-ratio (SNR), facilitates higher spatial resolutions, and potentially improves diagnostic power. For example, it has been shown that the detection of small lesions in patients with multiple sclerosis at 3T MRI is improved versus 1.5T MRI.8,9 Sigmund et al10 and Zhao et al11 have published comparisons of anatomical SC images, which display excellent improvement of the image quality at 7T versus 3T. Additionally, it has been shown that in patients with multiple sclerosis, on average 4.7 white matter (WM) lesions can be detected at 7T in the SC, whereas at 3T only 3.1 WM lesions can be found. This increase of 52% emphasizes the advantages of higher field strengths for SC MRI.12

Barry et al13 gave an excellent review on the current state of “Spinal Cord MRI at 7T” included also the advantages of ultrahigh-field strength for different imaging modalities beyond anatomical MRI. To take it a step further, this study presents in vivo MR measurements of the SC at a field strength of 9.4T, which could theoretically offer about twice the SNR compared with MRI at 7T with similar radiofrequency (RF) coils and sequences.14,15 To our knowledge, with the exception of our own preliminary work published in a conference abstract,16 these are the first human in vivo SC MRI results obtained at this field strength. Previous work at 9.4T has focused on human postmortem samples17 injured SC in squirrel monkeys,18,19 and SC in mice20 and rats.21

A comprehensive overview on 7T SC coils13 demonstrated that the majority of these designs had only posterior elements on a holder adapted to the neck and utilized only surface-loop receive elements.10,11,13 In this work, a new approach to SC RF coil design is introduced that combines transceiver surface-loop elements with additional receive-only vertical loops and contains anterior as well as posterior coverage to increase the central SNR. This coil design was originally suggested for improved central SNR in human brain scans. The increase in central SNR is also beneficial for imaging the cervical SC because of its central position in the head and neck. Anatomical images of the cervical SC were measured with a T2*-weighted GRadient-Echo (GRE) sequence.23 To address the SC MRI inherent issue of periodic B0 inhomogeneities caused by the intervertebral discs,24,25 the literature provides solutions as “electrocardiogram-triggered, higher order, projection-based B0 shimming”26 or z-shim gradient pulses.25 To minimize the influence of these B0 inhomogeneities, four different B0 shimming routines were tested and compared during this work. Intrinsic SNR maps were calculated and the impact of different echo times (TEs) on image quality and contrast was investigated to find optimal sequence parameters.

Recently, anatomical SC images with an in-plane resolution of 0.18 × 0.18 mm² have been published,10,27 which is the highest resolution of in vivo human SC measurement in the literature. In this study, the resolution could be further improved and anatomical images with an in-plane resolution of 0.15 × 0.15 mm² are presented.

Additionally, algorithmic SC detection and GM/WM segmentation was performed, as well as calculation of T2*—relaxation-time maps of the human SC at 9.4T.

2 | METHODS

2.1 | Radiofrequency coil

All measurements in this study were performed with an in-house-built 16-channel tight-fit array coil.22 This array consists of eight transceiver surface loops and eight receive-only loops. The eight transceiver surface loops are placed on a cylindrical holder. Each of the eight vertical receive-only loops is positioned along the central axis of a transceiver loop, perpendicular to its surface. Figure 1A consists of a photograph of the coil and some of the transceiver and receive-only loops.

This coil was originally constructed for human brain scans with an emphasis to enhance the SNR in deep brain structures and high-transmission efficiency. The addition of the vertical loops has no measurable effect on the Tx efficiency of the array. However, the 16-channel set-up provides an improvement of the SNR in vivo of approximately 30% in the center of the brain, compared with the surface-loops-only set-up.

The central SNR improvement was the motivation for testing the coil for SC data acquisition. The coil array and its housing geometry is cylindrical, with openings at top and bottom. This geometry makes it possible to place the subject further inside the coil than originally intended and allow the cervical SC to be imaged. Figure 1B depicts the subject positioning for brain scans versus that for SC scans. For brain scans, the subject’s brain is placed in the center of the loop array; however, for cervical SC measurements in this study each subject was positioned further into the coil until the shoulders contacted the coil housing. In that position, the upper cervical SC is located in the center of the loop array.
During RF transmission, the array was driven in the circular polarized mode with a 45° phase shift between adjacent transceiver loops. This was achieved with an eight-way splitter box, with corresponding phase shifts incorporated.

A comprehensive set of safety tests of the RF coil has been performed according to our internal standard operational procedures approved by the local institutional review board; the coil was certified for in vivo use in human subjects as described earlier. The specific absorption rate was continuously monitored and supervised by means of the k-factor, which is incorporated in the coil file. Sequence parameters that would exceed the specific absorption-rate limit are hence not allowed, and the parameters have to be adjusted accordingly prior to the scan. In case the specific absorption rate is still exceeded during the scan, it is stopped automatically by the vendor-integrated specific absorption-rate–monitoring system.

2.2 Volunteer scans

Ten healthy volunteers (eight men, two women, age: 27.4 ± 4.72 years, weight: 75.4 ± 11.77 kg) were scanned on a 9.4T whole-body MR scanner (Siemens Healthcare, Erlangen, Germany) equipped with a SC72 whole-body gradient system with a maximum amplitude and slew rate of 40 mT/m and 200 mT/m/ms, respectively.

All experiments were performed with the approval of the local ethics committee. Informed signed consent was obtained from each volunteer before each MR experiment.

2.3 Study design

Each in vivo scan session was performed with the following routine. A localizer sequence was applied and used to position the B₀ shimming volume (Figure 1C). The tested B₀ shim approaches are explained in the B₀ shimming comparison subsection below.

After B₀ shimming, a flip-angle (FA) map using the AFI (Actual Flip-angle Imaging) sequence (field of view (FOV): 243 × 243 mm², in-plane resolution: 1.68 × 1.68 mm², number of slices: 12, slice thickness: 5 mm, repetition time (TR) = 20/100 ms, TE = 4 ms, FA: 53 degree, acquisition time: 1:47 minutes:seconds, dimension: 3D, R = 2 [Gene Ralized
Autocalibrating Partially Parallel Acquisitions (GRAPPA)) acceleration) was acquired to check the achieved mean FA at the SC position (see FA map in Figure 1D). If the mean FA was unequal to the desired one, the transmit voltage was adjusted according to the proportion of desired and measured FA. After adjustment of the transmit voltage, the AFI sequence was applied and the mean FA was evaluated again to ensure correct FA adjustment. The FA homogeneity within the SC was assessed visually in the FA map.

All anatomical images were acquired with an axial T2*-weighted GRE sequence. The sets of parameters used during this study are listed in Table 1. Every time sequence A, B, C, D, E, F, G, H, or I is mentioned in the text, respectively, a GRE sequence with the parameters displayed in Table 1 is referred to. All sequences acquired one average, and phase stabilization was active. Each parameter set was tested on at least three subjects. Sequence B was applied with a slice oversampling of 66%.

### 2.4 B0 shimming comparison

Along the SC the B0 field varies dramatically because of transitions between bone and intervertebral discs; these “B0 field distortions interfere with encoding of contrast and spatial origin of the MR signal, commonly causing artifacts in the form of signal loss and geometric distortion, but can also contribute to ghosting, blurring and distorted excitation volumes, amongst other effects.” Thus, as input for the scan protocol optimization for anatomical SC imaging, multiple B0 shimming algorithms were compared to investigate the influence of the B0 shim performance on SC image quality. In particular, the primary focus evaluating B0 shim performance by the severity of signal dropouts that occur periodically in the intervertebral disc-located slices.

#### Table 1 Description of the parameters of the gradient echo sequences

| Sequence | FOV (mm²) | In-plane resolution (mm²) | No. of slices | Slice thickness (mm) | TR (ms) | TE (ms) | FA (degree) | Acq. time (min:s) | Dim | Acq. BW (Hz/vox) |
|----------|-----------|--------------------------|---------------|---------------------|---------|---------|-------------|------------------|-----|-----------------|
| A        | 133 × 133 | 0.22 × 0.22              | 9             | 3                   | 365     | 9       | 50          | 03:40            | 2D  | 155             |
| B        | 189 × 189 | 1.68 × 1.68              | 12            | 5                   | 8.7     | 2       | 6           | 00:20            | 3D  | 580             |
| C        | 150 × 150 | 0.47 × 0.47              | 1             | 3                   | 250     | 5 or 9 or 14 or 19 | 25 | 01:20            | 2D  | 155             |
| D        | 140 × 140 | 0.23 × 0.23              | 12            | 3                   | 500     | 4 and 10 and 16 and 22 | 50 | 05:04            | 2D  | 316             |
| E        | 140 × 140 | 0.23 × 0.23              | 12            | 3                   | 500     | 5.1 and 9.4 and 13.8 and 17.7 | 50 | 05:04            | 2D  | 316             |
| F        | 147 × 147 | 0.15 × 0.15              | 10            | 3                   | 259     | 12      | 25          | 04:14            | 2D  | 158             |
| G        | 147 × 147 | 0.15 × 0.15              | 10            | 3                   | 500     | 5.1 and 13.8 | 50 | 07:46            | 2D  | 220             |
| H        | 147 × 147 | 0.15 × 0.15              | 10            | 3                   | 500     | 9.4 and 17.7 | 50 | 07:46            | 2D  | 220             |
| I        | 160 × 160 | 0.50 × 0.50              | 128           | 1                   | 2800    | 10      | 50          | 15:00            | 2D  | 300             |

Acq. BW: acquisition bandwidth in Hz per voxel; Acq. time: acquisition time; FA: flip angle; FOV: field of view; TE: echo time; TR: repetition time
2.5 Calculation of the intrinsic signal-to-noise ratio

To create intrinsic SNR maps (“the SNR that would be obtained with a homogeneous FA of 90°, an infinite repetition time and an echo time of zero”)14, signal measurements were acquired using sequence B. Afterwards a corresponding noise scan was performed by applying the same sequence with the transmit voltage set to zero. Based on the noise data, the noise covariance matrix33 was calculated. Analogous to Pohmann et al.14 the pseudo-multiple replica approach34 was employed. Experimental SNR was then computed with the formulation from Roemer et al35 for phased array root-sum-of-squares magnitude image combination. Afterwards, these SNR values were corrected with Equation 1 from Pohmann et al.14 to achieve the intrinsic SNR. The correction was done based on the FA map acquired with the AFI sequence mentioned in the Study design subsection. The intrinsic SNR in the SC was averaged for each slice, respectively.

2.6 Sequence parameter optimization and high-resolution anatomical images

To show that the RF coil can be used to acquire high-quality anatomical images of the SC, single low-resolution axial slices were acquired with sequence C, utilizing each time another TE (5, 9, 14, or 19 ms) as initial input for scan parameter optimization.

Following the feasibility test, multiecho sequences, where the signal is measured at four different TEs, were applied (sequence D and E). Within these sequences, 12 different transversal slices with an in-plane resolution of 0.23 × 0.23 mm² were acquired along the upper cervical SC (level C1, C2, C3, and partly C4). The parameters of sequence E were set analogously to those set in Massire et al.27 because these TEs produced good results at 7T. The data from both sequence D and E were combined to create MEDIC (Multi Echo Data Image Combination)36 images and to calculate T₂* maps. MEDIC images were obtained by computing the sum of squares of the image from each TE. To assess the GM/WM contrast for different TEs, the contrast-to-noise ratio (CNR) for each TE and each slice was calculated. We defined the CNR (analogously to Bachmann et al.9 Fushimi et al.,37 and Constable and Henkelman38) as the difference between the mean signal of GM and WM, divided by the standard deviation of artifact free background noise. To average the signal intensities, the GM and WM tissue masks resulting from image segmentation (see Segmentation subsection) were utilized.

By means of the intrinsic SNR, statements for the experimental SNR of acquisitions with different sequence parameter values can be derived. For various values of TE, TR, or FA, Equation 1 from Pohmann et al.14 were employed to calculate the experimental SNR from the intrinsic SNR. For various voxel sizes, matrix sizes, or sequence dimensions, the rules from Constable and Henkelman,38 Hendrick,39 Edelstein et al.,40 and Brown et al.41 were applied. Following these rules, the experimental SNR for the parameters of sequence D and E was derived.

To observe the benefits of very high-resolution images, measurements (sequence F, G, and H) with the highest axial in-plane resolution (0.15 × 0.15 mm²) achievable with the proposed sequence settings and gradient timings, were performed to make the small SC structures visible. The scanner did not allow the measurement of higher resolutions because the gradients could induce too severe peripheral nerve stimulation. Although sequence F is a single-echo sequence, the sequences G and H are multiecho sequences, with two echoes, respectively. For that high resolution, the scanner did not permit the measurement of four echoes in one sequence because of the risk of too strong nerve stimulation. The data from both sequences G and H were combined to create MEDIC images.

2.7 Segmentation

Using the Spinal Cord Toolbox (v.4.0; sourceforge.net/projects/spinalcordtoolbox),42 algorithmic SC detection, as well as GM/WM segmentation within the SC, was performed. The Spinal Cord Toolbox is a comprehensive software program used to process MRI SC data. From the wide range of applications and algorithms implemented in the Spinal Cord Toolbox, the propagated cord segmentation (function sct_propseg)43 for detecting the SC within the full FOV and the deep-learning algorithm with dilated convolutions (function sct_deepseg_gm)44 to segment the GM within SC were employed. Once the SC detection and the GM segmentation were executed successfully, the WM segments were detected by subtracting the GM mask from the full SC mask. To test the SC detection algorithm, a GRE sequence acquiring 128 slices (sequence I, slice thickness: 1 mm) was applied. With these 128 transversal slices, it was possible to create sufficient sagittal and coronal coverage to visualize the SC detection result in all three dimensions. The SC detection algorithm was also tested on the data acquired with sequence D and E. Additionally, on this data the GM segmentation algorithm was applied.

2.8 T₂*-time calculation for gray matter and white matter

To perform pixel-wise T₂*-time calculations, the multiecho results from sequences D and E were employed. In addition
to the four TEs adopted from Massire et al.\textsuperscript{27} (sequence E), another four TEs (sequence D) were measured. This yielded eight, instead of four, sample points per pixel to calculate a more accurate mono-exponential fit. The fitting was performed with a nonlinear least squares algorithm using MATLAB (MathWorks, Natick, MA).

To calculate the average $T_2^*$-relaxation times of GM and WM separately, the segmented GM and WM tissue masks were applied to $T_2^*$ maps. All the fitted $T_2^*$ values of GM and WM pixels from three subjects were pooled to calculate mean GM and WM specific $T_2^*$-relaxation times and a two-sample $t$ test was performed with MATLAB to investigate statistically significant differences.

3 | RESULTS

3.1 | $B_0$ shimming comparison

Figure 2 presents the results acquired with sequence A. The Siemens shim routine offered the images with the best quality and was consequently utilized for all of the following measurements. Most notably, the Siemens shim performed much better in the first and second slice. Signal dropouts, which are visible for the other three set-ups, arose just marginally for the Siemens shim. For slices three to six, all routines provided excellent image quality. The Tune-Up shim, which consists of a fixed set of shim values, delivered similar image quality to those of other shimming routines. For slice seven, the Siemens shim again offered the best image quality. Because this slice touched a disc, a slight signal dropout occurred in the lower area of the SC and cerebrospinal fluid (CSF). This dropout worsened for Tune-Up, FASTESTMAP, and ConsTru shim relative to the Siemens shim. For slices eight and nine, again all routines provided similar, sufficient image quality.

3.2 | Calculation of the intrinsic signal-to-noise ratio

Figure 3A shows a map of the intrinsic SNR, represented by 6 out of the 12 measured slices. For the two presented subjects, the highest SNR in the SC was achieved in slices 3 to 10, with values mostly observed between 6600 and the maximum of 8060 (subj.1, slice 4). For slices positioned further in the head direction than slice 3 and placed further in the feet direction than slice 10, the SNR dropped dramatically (Figure 3B).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{A: Comparison of the influence of different shimming routines. All images were acquired with gradient echo (GRE) sequence A. The table of images presents different slices (labeled with the yellow numbers) acquired with the same shim set-up in the columns and same slices acquired with different shim set-ups (Sh.1 = Siemens shim, Sh.2 = TuneUp, Sh.3 = fast, automatic shim technique using echo-planar signal readout for mapping along projections [FASTESTMAP], Sh.4 = ConsTru) in the rows. Enlargements of the full field of view are shown. B: The top (bottom) image presents the central sagittal (coronal) slice. The yellow lines mark the position of the transversal slices, depicted in A.}
\end{figure}
3.3  |  Sequence parameter optimization and high-resolution anatomical images

First, a single slice with a low in-plane resolution of $0.47 \times 0.47 \text{ mm}^2$ was measured four times, each time with a different TE. Figure 4 displays the FOV of one volunteer. Anteriorly, the teeth can be seen and on the posterior side, the neck muscles are visible. In the center of the FOV, the SC is surrounded by CSF (yellow box) and the vertebrae. In the four surrounding images in Figure 4, enlargements from the...
FOV at the SC location at different TEs are displayed. At a short TE of 5 ms, a high signal with low GM/WM contrast is visible. With increasing TE, the signal has partially decayed and GM/WM contrast has increased. The “butterfly” shape of the GM is clearly visible and distinguishable from the WM for a TE of 9 ms and 14 ms; furthermore, nerve roots at the left and right side of the SC are apparent. A TE of 19 ms seems to be too long, as GM/WM contrast has diminished and magnetic susceptibility effects appear, especially in the CSF.

In Figure 5A, the results of the two multiecho GRE sequences D (TEs: 4/10/16/22 ms) and E (TEs: 5.1/9.4/13.8/17.7 ms) with an in-plane resolution of 0.23 × 0.23 mm² are depicted. Figure 5B shows the corresponding CNR for each slice and TE. Figure 5C illustrates the averaged experimental SNR in the SC for each TE recalculated from the intrinsic SNR depicted in Figure 3B (Subj.1).

As Figure 4 has already shown, as TE increases, the signal decays and GM/WM contrast grows. While a TE of less than 9.4 ms seems too short to achieve a strong visual GM/WM contrast, a TE of between 9.4 ms and 13.8 ms provided the best compromise between signal intensity and tissue contrast as illustrated in Figure 5A. Confirming this observation, the CNR between GM and WM is increasing from a TE of 4 ms until 13.8 ms for most slices. After 13.8 ms, the CNR is decreasing or rises only marginally.

Slice five is located at an intervertebral disc location. With increasing TE, a signal dropout occurred here. While this dropout does not or only marginally occurs for the first four TEs, it became severe for a TE of 13.8 ms and longer. To not adulterate the CNR of that slice, the GM and WM masks were corrected manually to exclude the pixels where the dropout occurs (see Supporting Information Figure S1 for the CNR values including signal dropout).

The experimental SNR is decreasing along an exponential curve with increasing TE. In slice three (which had one of the highest intrinsic SNR values of 8000 as seen in Figure 3) the highest experimental SNR was acquired.

The MEDIC images offer excellent GM/WM contrast, as it can be seen in the images in Figure 5A, as well as from the CNR values in Figure 5B. For instance, slice three provides a CNR of 4.95 at a TE of 13.8 ms and a CNR of 7.95 for the MEDIC image.

The results given in Figure 5 were acquired with a TR of 500 ms and a FA of 50°; the results given in Figure 4 were acquired with a TR of 250 ms and a FA of 25°. After a proper scaling, there is no visible difference in the image quality.

As TEs between 9 and 13.8 ms are good compromises between tissue contrast and minimal magnetic susceptibility effects, a TE of 12 ms was chosen for the single-echo measurements with an in-plane resolution of 0.15 × 0.15 mm² (sequence F). In all depicted slices (Figure 6A), high-quality images of the SC are visible. GM and WM can be distinguished. Nerve roots and blood vessels are shown in excellent detail in most of the slices. The anterior median fissure and the posterior median septum are recognizable. The same is valid for the MEDIC images (Figure 6B) created out of the measurements acquired with multiecho sequences G and H. The MEDIC images offer improved GM/WM contrast compared with the single-echo measurements, while showing similar sharpness and number of details.

For comparison, Figure 6C,D show 7T GRE acquisitions from Sigmund et al.10 and Massire et al.27 with an in-plane resolution of 0.18 × 0.18 mm².

3.4 | Segmentation

The white-colored pixels in Figure 7 mark the SC, as it was masked by the SC detection algorithm. All white-colored pixels mark the location of the spinal cord in each perspective correctly, except for the bottom slices, where the SC was not detected.
On the slices acquired with sequence D and E, the SC detection algorithm and the GM segmentation algorithm were applied. Figure 8 shows three segmented example slices. The algorithm detected the SC and segmented GM and WM correctly. The typical butterfly shape is observed as depicted by white pixels in the GM mask.

3.5 | $T_2^*$-time calculation for gray matter and white matter

For each of the three subjects that were measured with multiecho sequences D and E (12 slices acquired per sequence), a $T_2^*$ map was calculated. Figure 9 shows an example slice, where the CSF and the SC are distinguishable; to some extent, the GM and WM within the SC are also discernible. $T_2^*$ slices, in which these tissue types were not recognizable because of midvertebra disk-related signal dropouts, were excluded from averaging. Based on the created GM and WM masks, mean $T_2^*$ values were calculated. For the cervical SC at 9.4T, the calculated $T_2^*$ value for GM is 24.88 ms ± 6.68 ms and for WM 19.37 ms ± 8.66 ms.

A two-sample $t$-test results in $p$ value of $1.6233 \times 10^{-271}$ for the null hypothesis (“The mean of the GM sample is equal to the mean of the WM sample.”). For that reason, the null hypothesis needs to be rejected. Thus, the means of GM and WM $T_2^*$-relaxation times differ significantly.
DISCUSSION

This work presents the first in vivo MR images of the human SC measured at the B0 field strength of 9.4T. An RF coil optimized for central SNR in the human brain was employed to acquire in vivo cervical SC images.

A TE between 9 and 13.8 ms was found to offer the best image quality with an excellent contrast between CSF, GM, and WM (Figures 4 and 5). That TE recommendation is slightly higher in comparison with what Sigmund et al10 suggested at 7T with their SC-dedicated coil (GRE sequence with TE = 4.91 ms). In comparison with the noncombined data, the combined MEDIC images36 show improved image quality in terms of tissue contrast. Because the acquisition of multiecho data does not require additional scan time, MEDIC is an attractive alternative to single-echo measurements. Slice one in Figure 5A shows high contrast between CSF and the SC largely independent of TE, which possibly occurs because of the reduction in transmit $B_1^+$ field at the edge of the FOV of the RF coil in that slice position.

The highest axial in-plane resolutions (in vivo) acquired prior to this work were 0.18 × 0.18 mm² by Sigmund et al10 (Figure 6C) and Massire et al27 (Figure 6D) at a field strength of 7T with SC-dedicated coils. We presented
an improved resolution of 0.15 × 0.15 mm$^2$. That means in the 9.4T images (Figure 6A,B) the area of each pixel is decreased by approximately 30% from 0.0324 mm$^2$ to 0.0225 mm$^2$ compared with the 7T acquisitions. The 9.4T results show the small SC structures in excellent detail. The quality of these images seems to outperform the 7T results, as the nerve roots are also visible at 7T, but are not as sharp as at 9.4T. Moreover, the anterior median fissure and the posterior median septum are recognizable in $T_2^*$-weighted images at 9.4T, whereas they are hard to detect at 7T.$^{10,27}$ In the most recent work from Massire et al.,$^{45}$ these two structures are recognizable on 7T $T_1$ maps of the SC, but again difficult to detect on $T_2^*$-weighted images, as is possible at 9.4T.

Compared with the acquisitions with an in-plane resolution of 0.23 × 0.23 mm$^2$ (Figure 5A), the 0.15 × 0.15 mm$^2$ images present the SC in slightly improved acuity. However, the enhancement may not be as strong as expected from the difference between both spatial resolutions. A possible reason for this is the physiological SC motion (between 0.40 and 0.50 mm in superior/inferior, 0.60 ± 0.34 mm in anterior/posterior, and 0.17 ± 0.09 mm in right/left direction$^{46,47}$), which possibly blurs images, especially in cases of very high spatial resolutions. Cardiac triggering or prospective motion correction$^{48}$ could be an option to mitigate the influence of motion; however, it was not applied during this study. Future work should test whether image acuity at a spatial resolution of 0.15 × 0.15 mm$^2$ can be improved and even higher spatial resolutions are feasible by including optimized motion compensation methods and encoding schemes that prevent excessive peripheral nerve stimulation. Even if a higher spatial resolution would be possible technically, it remains to be clarified whether this can further improve diagnostic specificity and sensitivity.

$T_2^*$ maps were derived from multiecho GRE images and showed clear distinction between GM, WM, and CSF. By means of the Spinal Cord Toolbox, masks for GM and WM were calculated, and the $T_2^*$ times for all GM and WM voxels inside the respective masks were averaged. Although an uncertainty remains when using this pixel-by-pixel fit method (see noise in Figure 9 and the resulting relatively high SD) the first estimate of $T_2^*$ times in the human SC at 9.4T has been presented (GM 24.88 ms ± 6.68 ms and for WM 19.37 ms ± 8.66 ms) and a statistically significant difference was found between GM and WM. These results are consistent with the literature. While Massire et al.$^{27}$ presented the
expected slightly higher $T_2^*$ times from the cervical SC at 7T (GM: 29.3 ms ± 4.5 ms, WM: 23.5 ms ± 5.7 ms), Pohmann et al$^{14}$ published $T_2^*$ times at 9.4T for the human brain (GM: 23.8 ms ± 1.0 ms, WM: 19.2 ms ± 0.9 ms), which are very similar to the values calculated for the SC at 9.4T.

Periodic signal dropouts were observed in slices near intervertebral discs, possibly due to strong magnetic susceptibility between soft tissue and bone.$^{24,25}$ Although among the herein investigated $B_0$ shimming approaches, the vendor-implemented second-order $B_0$ shimming offers the best image quality for slices next to intervertebral disks; in general, the differences within the four different shimmmed images are not very prominent (Figure 2). Even the TuneUp shim, which is a fixed set of shim values, does not have a substantially poorer performance in most slices in comparison with FASTEST MAP and ConsTru. Although the vendor shim mitigates the dropouts, it did not obliterate it. Tackling the $B_0$ inhomogeneities for SC imaging remains a future challenge. A possible solution could be dedicated $B_0$ shim hardware.$^{49-53}$ In addition, a 3T study showed improved $B_0$ homogeneity within the neck by placing pyrolytic graphite foam behind the neck$^{54}$; this could also be worth investigating at ultrahigh field.

The simplicity of the utilization of a 16-channel transceiver array RF coil driven in circular polarized mode for SC imaging that was originally optimized to yield high SNR in central brain structures and high transmit efficiency for brain MRI and MRS is worth noting. Utilizing the same coil for both brain and cervical SC applications is cost-efficient and offers the opportunity to tackle “the lack of commercial SC-receiver array RF coil driven in circular polarized mode for SC imaging that was originally optimized to yield high SNR in central brain structures and high transmit efficiency for brain MRI and MRS is worth noting. Utilizing the same coil for both brain and cervical SC applications is cost-efficient and offers the opportunity to tackle “the lack of commercial SC-dedicated coils” as reported in Massire et al.$^{27}$ There is no costly development of a SC-dedicated coil needed to achieve comparable results for the cervical SC. Two of the 10 subjects reported that the positioning inside the coil was not as comfortable as for brain scans; however, no subject needed to interrupt or abort a scan session.

We chose to investigate the intrinsic SNR of the SC (ie, the SNR in the situation of a homogeneous FA of 90°, an infinite TR and an TE of zero) to achieve a normalized SNR value that allows for the comparison between different field strength and hardware set-ups by correcting for the influence of the sequence parameters. It is worth noting that the reported intrinsic SNR values featured in Figure 3 are not achievable in experiments.

The intrinsic SNR reported in Pohmann et al$^{14}$ (approximately 3000 in brain center at 9.4T, but smaller voxel size as in sequence B) can be recalculated with respect to the parameter values from sequence B by multiplying it with a factor of 3.2 (eq. 7.12 from Hendrick$^{39}$). With the coil$^{55}$ used in Pohmann et al$^{14}$ and the settings from sequence B, the intrinsic SNR in the brain center theoretically would be 9600. This value is higher than the intrinsic SNR that was acquired in the SC during this study (Figure 3; SNR between 6600 and 8060 in slices 3 to 10). The lower SNR in the SC compared with the brain center at 9.4T is most likely caused by the different coil set-ups utilized. The dedicated brain coil$^{55}$ has 31 receive channels arranged on a close-fitting helmet to maximize SNR. The coil employed in this study was a single row eight-channel transceiver coil with eight additional receive-only elements and has, therefore, a limited coverage, which negatively impacts central SNR.$^{15}$ On the other hand, the combination of transceiver loops and dipolar receive-only elements was designed to enhance the SNR in deep-brain structures.$^{22}$ The design of the coil used herein allows SC applications, which is not the case for the dedicated brain coil design in Pohmann et al.$^{14}$ However, the coil loading differs between the subject position for SC imaging and brain imaging (Figure 1B), which may also lead to SNR losses. All these influence factors could be reasons for the slightly lower SNR in the SC as compared with the central brain at 9.4T.$^{14}$

In Sigmund et al$^{10}$, the authors report an average experimental SC SNR in vivo of 227 at 7T. If we recalculate the intrinsic SNR from this study (Figure 3, slices 3 to 10) with respect to the sequence parameter from Sigmund et al$^{10}$ (utilizing eq. 7.12 from Hendrick$^{39}$ and eq. 1 from Pohmann et al$^{14}$ acquisition bandwidth was not mentioned; therefore, we assumed the same bandwidth as in sequence B) and we achieved an experimental SNR between 265 and 324. The SNR increase was expected; however, it is not as high as the change from 7T to 9.4T may imply.$^{14,15}$

In general, an increase of the static magnetic $B_0$ field strength leads theoretically to an almost quadratic increase of SNR and thus doubles the SNR at 9.4T versus 7T for similar sequences and coils.$^{14,15}$ Furthermore, at high field a combination of surface loops and dipolar elements is needed for SNR optimization in central regions.$^{15}$ In addition, wrap-around coils (such as the coil in Zhang et al$^{56}$), tend to provide higher SNR compared with the neck coils used by Sigmund et al$^{10}$ and Zhao et al$^{11}$ with only posterior elements. Both advantages are incorporated in the coil proposed herein.

The decreased SNR in slices 1, 2, 11, and 12 (Figure 3), as well as the failed SC detection in the lowest positioned slices in Figure 7, indicates a drawback of the proposed coil: the relatively small longitudinal coverage for areas that are not placed in the center of the loops. Vertebrae C1, C2, C3, and to some extent, C4 can be covered excellently, but reaching any lower vertebra seems to be problematic. In addition, measuring the brain and the SC within the same scan is not possible. To achieve extended coverage, other array architectures (eg, with dipole receive elements instead of loops$^{57}$ or SC-dedicated coils (eg, see Sigmund et al$^{10}$, Zhao et al$^{11}$, Kraff et al$^{58}$ or Barry et al$^{15}$ for an overview of all 7T SC coils) need to be employed. Having a coil design that considers the principles of the proposed coil, but is further optimized for SC imaging could improve results with respect
to longitudinal coverage, SNR, and subject comfort. With an extended longitudinal coverage, the brain and the SC could be imaged in the same experiment, as it is necessary to assess the functional connectivity between both regions.

With this work, we have taken the first step into SC research at a B₀ field strength higher than 7T. By testing and optimizing other sequences (eg, magnetization-prepared 2 rapid gradient echoes [MP2RAGE], T2W, echo planar imaging, MRS, or the AMIRA approach in the future, anatomical image quality could be further improved and multimodal SC imaging at 9.4T can be enabled. Furthermore, T₁⁻ and T₂⁻ relaxation-time measurements need to be performed to complete the set of tissue relaxation times as input for sequence optimization and quantitative MRI for the SC at 9.4T.

5 CONCLUSION

With this work, the first step into SC research at a B₀ field strength of 9.4T was performed. With an RF coil, originally optimized for maximal SNR and transmit efficiency in deep brain structures, we were able to acquire high-resolution (in-plane: 0.15 × 0.15 mm²) anatomical SC data in excellent detail and quality. Algorithmic SC detection, as well as GM/WM segmentation, reliably works on the data. The T₂* times of GM and WM in the human SC at 9.4T were presented. Such high-resolution images at ultrahigh field of the human SC might open new possibilities in the field of SC research and clinical patient care. Knowing the T₂*-relaxation time allows optimization of imaging parameters and potentially enables improvements in sensitivity and contrast.

ACKNOWLEDGMENTS

Funding by the European Union (ERC Starting Grant, SYNAPLAST MR, Grant Number: 679927) and the Cancer Prevention and Research Institute of Texas (Established Investigator Award RR180056) is gratefully acknowledged. We would like to thank Rolf Pohmann for supporting us with the SNR maps. In addition, we appreciate the help from Andrew Wright and Saipavitra Murali Manohar for text proofreading. Open access funding enabled and organized by Projekt DEAL.

ORCID

Ole Geldschläger https://orcid.org/0000-0002-8400-0635
Nikolai I. Avdievich https://orcid.org/0000-0001-7608-0869

REFERENCES

1. Ciccarelli O, Werring DJ, Barker GJ, et al. A study of the mechanisms of normal-appearing white matter damage in multiple sclerosis using diffusion tensor imaging. J Neurol. 2003;250:287-292.

2. Ciccarelli O, Wheeler-Kingshott CA, McLean MA, et al. Spinal cord spectroscopy and diffusion-based tractography to assess acute disability in multiple sclerosis. Brain. 2007;130:2220-2231.

3. Kearney H, Schneider T, Yiannakas MC, et al. Spinal cord grey matter abnormalities are associated with secondary progression and physical disability in multiple sclerosis. J Neurol Neurosurg Psychiatry. 2014;86:608-614.

4. Sach M, Winkler G, Glauhe V, et al. Diffusion tensor MRI of early upper motor neuron involvement in amyotrophic lateral sclerosis. Brain. 2004;127:340-350.

5. Demir A, Ries M, Moonen CTW, et al. Diffusion-weighted MR imaging with apparent diffusion coefficient and apparent diffusion tensor maps in cervical spondylotic myelopathy. Radiology. 2003;229:37-43.

6. Mahmood NS, Kadavigere R, Ramesh AK, Rao VR. Magnetic resonance imaging in acute cervical spinal cord injury: A correlative study on spinal cord changes and 1 month motor recovery. Spinal Cord. 2008;46:791-797.

7. Gilmore CP, Geurs KG, Evangelou N, et al. Spinal cord grey matter lesions in multiple sclerosis detected by post-mortem high field MR imaging. Mult Scler J. 2008;15:180-188.

8. Sicotte NL, Voskuhl RR, Bouvier S, Klutch R, Cohen MS, Mazzotta JC. Comparison of multiple sclerosis lesions at 1.5 and 3.0 Tesla. Invest Radiol. 2003;38:423-427.

9. Bachmann R, Reilmann R, Schwindt W, Heindel W, Krämer S. FLAIR imaging for multiple sclerosis: A comparative MR study at 1.5 and 3.0 Tesla. Eur Radiol. 2005;16:915-921.

10. Sigmund EE, Suero GA, Hu C, et al. High-resolution human cervical spinal cord imaging at 7 T. NMR Biomed. 2011;25:891-899.

11. Zhao W, Cohen-Adad J, Polimeni JR, et al. Nineteen-channel receive array and four-channel transmit array coil for cervical spinal cord imaging at 7T. Magn Reson Med. 2013;72:291-300.

12. Dula AN, Pawate S, Dortch RD, et al. Magnetic resonance imaging of the cervical spinal cord in multiple sclerosis at 7T. Mult Scler J. 2015;21:320-328.

13. Barry RL, Vannesjo SJ, By S, Gore JC, Smith SA. Spinal cord MRI at 7T. NeuroImage. 2018;168:437-451.

14. Pohmann R, Speck O, Scheffler K. Signal-to-noise ratio and MR tissue parameters in human brain imaging at 3, 7, and 9.4 Tesla using current receive coil arrays. Magn Reson Med. 2015;75:801-809.

15. Ptrommer A, Henning A. The ultimate intrinsic signal-to-noise ratio of loop- and dipole-like current patterns in a realistic human head model. Magn Reson Med. 2018;80:2122-2138.

16. Geldschläger O, Manohar SM, Wright A, Avdievitch N, Henning A. First MRI of the human spinal cord at 9.4T. In 27th ISMRM; Montreal, Canada. 2019. Abstract number: 1585.

17. Schoeltes F, Adriaensens P, Storme L, et al. Correlation of postmortem 9.4 Tesla magnetic resonance imaging and immunohistopathology of the human thoracic spinal cord 7 months after traumatic cervical spine injury. Neurosurgery. 2006;59:671-678.

18. Chen LM, Mishra A, Yang PF, Wang F, Gore JC. Injury alters intrinsic functional connectivity within the primate spinal cord. Proc Natl Acad Sci USA. 2015;112:5991-5996.

19. Wang F, Qi HX, Zu Z, et al. Multiparametric MRI reveals dynamic changes in molecular signatures of injured spinal cord in monkeys. Magn Reson Med. 2014;74:1125-1137.

20. Bilgen M, Al-Hafez B, Berman NEJ, Festoff BW. Magnetic resonance imaging of mouse spinal cord. Magn Reson Med. 2005;54:1226-1231.
21. Ellingson BM, Kurpad SN, Li SJ, Schmit BD. In vivo diffusion tensor imaging of the rat spinal cord at 9.4 T. *J Magn Reson Imaging*. 2008;27:634-642.

22. Avdievich NI, Giapitzakis IA, Pfrommer A, Borbath T, Henning A. Combination of surface and “vertical” loop elements improves receive performance of a human head transceiver array at 9.4 T. *NMR Biomed*. 2017;31:e3878.

23. Bernstein M, King K, Zhou X. *Handbook of MRI Pulse Sequences*. Oxford: Elsevier; 2004.

24. Cooke FJ, Blamire AM, Manners DN, Styles P, Rajagopalan B. Quantitative proton magnetic resonance spectroscopy of the cervical spinal cord. *Magn Reson Med*. 2004;51:1122-1128.

25. Finsterbusch J, Eippert F, Büchel C. Single, slice-specific z-shim gradient pulses improve $T_2^*$-weighted imaging of the spinal cord. *NeuroImage*. 2012;59:2307-2315.

26. Hock A, Fuchs A, Boesiger P, Kollias SH, Henning A. Electrocardiogram-triggered, higher order, projection-based B0-shimming allows for fast and reproducible shim convergence in spinal cord 1H MRS. *NMR Biomed*. 2012;26:329-335.

27. Massire A, Taso M, Besson P, Guye M, Ranjeva JP, Callot V. High-resolution multi-parametric quantitative magnetic resonance imaging of the human cervical spinal cord at 7T. *NeuroImage*. 2016;143:58-69.

28. Hoffmann J, Henning A, Giapitzakis IA, et al. Safety testing and operational procedures for self-developed radiofrequency coils. *NMR Biomed*. 2015;29:1131-1144.

29. Yarnykh VL. Actual flip-angle imaging in the pulsed steady state: A method for rapid three-dimensional mapping of the transmitted radiofrequency field. *Magn Reson Med*. 2007;53:192-200.

30. Bruder H, Fischer H, Graumann R, Deimling M. A new steady-state imaging sequence for simultaneous acquisition of two MR images with clearly different contrasts. *Magn Reson Med*. 1988;7:35-42.

31. Gruetter R, Tkac I. Field mapping without reference scan using asymmetric echo-planar techniques. *Magn Reson Med*. 2000;43:319-323.

32. Nassirpour S, Chang P, Fillmer A, Henning A. A comparison of optimization algorithms for localized in vivo B0 shimming. *Magn Reson Med*. 2017;79:1145-1156.

33. Kellman P, McVeigh ER. Image reconstruction in SNR units: A general method for SNR measurement. *Magn Reson Med*. 2005;54:1439-1447.

34. Robson PM, Grant AK, Madhuranthakam AJ, Lattanzi R, Sodickson DK, McKenzie CA. Comprehensive quantification of signal-to-noise ratio and g-factor for image-based and k-space-based parallel imaging reconstructions. *Magn Reson Med*. 2008;60:895-907.

35. Roemer PB, Edelstein WA, Hayes CE, Souza SP, Mueller OM. The NMR phased array. *Magn Reson Med*. 1990;16:192-225.

36. Held P, Dorenbeck U, Seitz I, Fründ R, Albrich H. MRI of the abnormal cervical spinal cord using 2D spoiled gradient echo multiecho sequence (MEDIC) with magnetization transfer saturation pulse: A $T_2^*$-weighted feasibility study. *J Neuroloradiol*. 2003;30:83-90.

37. Fushimi Y, Miki Y, Si U, et al. Gray matter-white matter contrast on spin-echo $T_1$-weighted images at 3 T and 1.5 T: A quantitative comparison study. *Eur Radiol*. 2007;17:2921-2925.

38. Constable RT, Henkelman RM. Contrast, resolution, and detectability in MR imaging. *J Comput Assist Tomogr*. 1991;15:297-303.

39. Hendrick ER. *Breast MRI: Fundamentals and Technical Aspects*. New York: Springer Science and Business Media; 2008.

40. Edelstein WA, Glover GH, Hardy CJ, Redington RW. The intrinsic signal-to-noise ratio in NMR imaging. *Magn Reson Med*. 1986;3:604-618.

41. Brown RW, Cheng YCN, Haacke EM, Thompson MR, Venkatesan R, editors. *Magnetic Resonance Imaging*. Hoboken, NJ: John Wiley & Sons Ltd; 2014.

42. Leener BD, Lévy S, Dupont SM, et al. SCT: Spinal cord tool box, an open-source software for processing spinal cord MRI data. *NeuroImage*. 2017;145:24-43.

43. Leener BD, Kadoury S, Cohen-Adad J. Robust, accurate and fast automatic segmentation of the spinal cord. *NeuroImage*. 2014;98:528-536.

44. Perone CS, Calabrese E, Cohen-Adad J. Spinal cord gray matter segmentation using deep dilated convolutions. *Sci Rep*. 2018;8:1–13.

45. Massire A, Rasoanandrainanina H, Guye M, Callot V. Anterior fissure, central canal, posterior septum and more: New insights into the cervical spinal cord gray and white matter regional organization using T1 mapping at 7T. *NeuroImage*. 2020;205:116275.

46. Figley CR, Stroman PW. Investigation of human cervical and upper thoracic spinal cord motion: Implications for imaging spinal cord structure and function. *Magn Reson Med*. 2007;58:185-189.

47. Mikulis DJ, Wood ML, Zerdoner OA, Poncelet BP. Oscillatory motion of the normal cervical spinal cord. *Radiology*. 1994;192:117-121.

48. Eschelbach M, Aghaeifar A, Bause J, et al. Comparison of prospective head motion correction with NMR field probes and an optical tracking system. *Magn Reson Med*. 2019;81:719-729.

49. Topfer R, Starewicz P, Lo KM, et al. A 24-channel shim array for the human spinal cord: Design, evaluation, and application. *Magn Reson Med*. 2016;76:1604-1611.

50. Topfer R, Foias A, Stikov N, Cohen-Adad J. Real-time correction of respiration-induced distortions in the human spinal cord using a 24-channel shim array. *Magn Reson Med*. 2018;80:935-946.

51. Germain G, Stockmann J, Topfer R, Wald LL, Stikov N, Cohen-Adad J. Optimization of geometry for combined RF/shim coil arrays for the spinal cord. In Proc. ISMRM; 2016;24:1154.

52. Walter S, Perl R, Notohamiprodjo M, Nikolau K, Gatidis S. Improvement of EPI-based DWI of the head/neck region using additional local shim coils at 3 Tesla. In Proc. ISMRM; 2019;27:3521.

53. Biber S, Wohlforth K, Kirsch J, Schmidt A. Design of a local shim coil to improve B0 homogeneity in the cervical spine region. In Proc. ISMRM. 2012;20:2746.

54. Lee G, Jordan C, Tiet P, et al. Improved frequency selective fat suppression in the posterior neck with tissue susceptibility matched pyrolytic graphite foam. *J Magn Reson Imaging*. 2014;41:684-693.

55. Shajian G, Kozlov M, Hoffmann J, Turner R, Scheffler K, Pohmann R. A 16-channel dual-row transmit array in combination with a 31-element receive array for human brain imaging at 9.4 T. *Magn Reson Med*. 2013;71:870-879.

56. Zhang B, Seifert AC, Kim JW, Borrello J, Xu J. 7 Tesla 22-channel wrap-around coil array for cervical spinal cord and brainstem imaging. *Magn Reson Med*. 2016;78:1623-1634.

57. Avdievich NI, Solomakha G, Ruhm L, Scheffler K, Henning A. Evaluation of short folded dipole antennas as receive elements of ultra-high-field human head array. *Magn Reson Med*. 2019;82:811-824.

58. Kraff O, Bitz AK, Kruszona S, et al. An eight-channel phased array RF coil for spine MR imaging at 7T. *Invest Radiol*. 2009;44:734-740.

59. Marques JP, Kober T, Krueger G, Zwaag W, Moortele PFV, Gruetter R. MP2RAGE, a self bias-field corrected sequence for gradient pulses improve $T_2^*$-weighted imaging of the spinal cord. *NeuroImage*. 2012;59:2307-2315.
improved segmentation and T1-mapping at high field. NeuroImage. 2010;49:1271-1281.
60. Weigel M, Bieri O. Spinal cord imaging using averaged magnetization inversion recovery acquisitions. Magn Reson Med. 2017;79:1870-1881.

SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section.

FIGURE S1 Plot of the CNR-values for all of the SC images shown in Figure 5A, from the main document, but without removing the signal dropout in slice 5 from the signal averaging. Each line presents the CNR-values of a certain slice at different TEs and in the MEDIC image.

How to cite this article: Geldschläger O, Bosch D, Avdievich NI, Henning A. Ultrahigh-resolution quantitative spinal cord MRI at 9.4T. Magn Reson Med. 2021;85:1013–1027. https://doi.org/10.1002/mrm.28455