Rapid High Resolution MR Neurography with a Diffusion-weighted Pre-pulse

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Purpose: To introduce, optimize, and assess the feasibility of a new scheme to rapidly acquire high-resolution volumetric neurographic images using a three-dimensional turbo spin-echo sequence combined with a diffusion-weighted pre-pulse called improved motion-sensitized driven equilibrium (iMSDE): Diffusion-prepared MR Neurography (D-prep MRN).

Methods: In order to optimize the signal suppression of blood vessels and muscle at D-prep MRN, coronal lumbosacral plexus images were acquired in five volunteers at 3T, and the following parameters were examined: iMSDE gradient-strength (b-value) of 0, 2 and 10 s/mm² (with the aim to suppress blood vessels) and iMSDE preparation duration (iMSDEprep-time) of 18, 50 and 100 ms (with the aim to suppress muscle signal). Subsequently, the feasibility of the optimized D-prep MRN sequence in visualizing the brachial plexus, lumbosacral plexus, and cranial nerves was evaluated in 5 healthy volunteers.

Results: A higher b-value of 10 s/mm² was better in signal suppression of blood vessels, whereas an intermediate iMSDEprep-time of 50 ms provided the best compromise between suppression of muscle signal and minimization of signal loss of nerves. With these parameters, the normal nerve structures showed high signal intensity, while the blood vessels and muscles were effectively suppressed. The optimized D-prep MRN sequence clearly showed the three-dimensional trajectory of the brachial plexus, lumbosacral plexus, and cranial nerves.

Conclusion: D-prep MRN was introduced and optimized, and clearly showed detailed anatomy of the brachial plexus, lumbosacral plexus, and cranial nerves. These results suggest that the D-prep MRN can be used for fast, high-resolution, volumetric imaging of the peripheral nervous system.

Keywords: motion-sensitized driven equilibrium, MR neurography, peripheral nervous system, 3D turbo spin-echo
tensity structures while most background tissue, including blood vessels, can be suppressed. Thus, nerves can be easily separated from surrounding structures and visualization of the 3D trajectory of the entire nerve system has become possible with DWI. However, DWI suffers from a relatively low spatial resolution and image distortion. Both are non-negligible issues, especially when aiming to visualize fine peripheral nerve structure or to obtain close-up views to evaluate focal pathology. The 3D DW-SSFP sequence provides superb visualization of thin peripheral nerves, but suffers from relatively stronger background signal that requires time-consuming image post-processing. Moreover, and perhaps most importantly, the 3D DW-SSFP sequence requires a long scan time of around 10 min. Thus, the development of a better MRN sequence in terms of high-speed and high-contrast is still needed.

In this study, we propose a new scheme to rapidly acquire high-resolution, and volumetric neurographic images using a 3D turbo spin-echo sequence combined with a diffusion-weighted pre-pulse called improved motion-sensitized driven equilibrium (iMSDE): Diffusion-prepared MRN (D-prep MRN). The purpose of this study was to introduce and optimize the D-prep MRN sequence, and to perform an initial evaluation in healthy volunteers.

**Materials and Methods**

**Theory**

The pre-pulse section of D-prep MRN consists of two parts; a fat-suppression pre-pulse and the iMSDE pre-pulse to suppress signal from vessels, followed by a readout sequence with a 3D tissue-specific variable refocusing flip-angle rapid acquisition with relaxation enhancement (RARE) sequence to acquire contrast-efficient T2-weighting. The most important component, the iMSDE pre-pulse, is based on a T2-preparation (T2-prep) pulse and therefore T2-contrast is affected by the duration time of the pre-pulse (iMSDEprep-time). A long iMSDEprep-time may be effective to reduce signal from background tissue with short T2 value such as muscle. Consequently, D-prep MRN is able to emphasize the nerve-sheath thanks to reduction of the signal from fat, vessels, and muscles. Figure 1 shows the concept and sequence diagram of D-prep MRN.

**Experiments**

This study was approved by the local institutional review board, and written informed consent was obtained from all subjects. A total of 5 healthy volunteers were examined with a 3.0-Tesla whole-body clinical imager (Achieva, Philips Healthcare, Best, the Netherlands) using a 16-element phased-array surface coil (for imaging of the brachial plexus), a 32-element phased-array surface coil (for imaging of the lumbosacral plexus), and an 8-element head coil (for imaging of the cranial nerves). The study consisted of two parts; (1) parameter optimization of the D-prep MRN sequence and (2) evaluation of the feasibility of the optimized D-prep MRN sequence in visualizing the brachial plexus, lumbosacral plexus, and cranial nerves.

The imaging parameters common to all methods were 3D volume isotropic turbo spin-echo acquisition (VISTA) sequence with spectral attenuated inversion recovery (SPAIR) fat suppression pre-pulse, repetition time (TR) of 2500 ms, effective echo time (TE) (TEeff) of 63 ms, echo train length (ETL) of 100, echo spacing of 4.0 ms, voxel size of $1 \times 1 \times 1 \text{ mm}^3$, 3D volume size of 220 mm (foot to head [FH]) $\times 310 \text{ mm (right to left [RL])} \times 100 \text{ mm (anterior to posterior [AP])}$ mm (brachial plexus)/280 $\times 280 \times 100 \text{ mm (lumbosacral plexus)}/240 \times 180 \times 240 \text{ mm (cranial nerves)}$, and scan duration of 4 min 57 s to 5 min 47 s.

**Suitable parameters of iMSDE gradient strength and iMSDE preparation duration**

The iMSDE is a specific pre-pulse for suppressing signal from flowing blood and has previously been used for black-blood imaging. The scheme of the iMSDE preparation pulse is shown in Fig. 2. The iMSDE preparation consists of a 90° excitation
Fig. 2. Scheme of the improved motion-sensitized driven equilibrium (iMSDE) preparation pulse. Motion-sensitizing gradients were applied in 3 axes (frequency, phase, and slice direction) in all experimental studies.

pulse, two 180° Malcom-Levitt (MLEV) refocusing pulses and a −90° flip-back pulse with motion sensitizing gradients sandwiched in between the radio-frequency pulses. Moreover, additional bipolar gradients were inserted at front for eddy currents compensation.16,17

To analyze the suitable iMSDE preparation with regard to the suppression of blood vessels and muscle signals, coronal lumbosacral plexus images were acquired in five volunteers.

Examined parameters of iMSDE gradient-strength (b-value) were 0, 2 (target flow velocity, 5 cm/s), and 10 s/mm² (target flow velocity, one cm/s; maximum value of the present sequence), with the aim to suppress blood vessels. Note that the b-value in this study, it shows the total value of the three axes. In order to suppress the vessel signal at any flow directions, motion sensitizing gradients were applied in 3-axes (frequency, phase, and slice direction), in all experimental studies. On the other hand, examined parameters of iMSDE preparation duration (iMSDEprep-time) were 18 (shortest value), 50 and 100 ms, with the aim to suppress muscle signal.

Quantitative analysis of the effect of iMSDE gradient strength

We attempted to evaluate the effect of the iMSDE in suppression of blood vessels. However, it is difficult to directly measure the signal of serpentine and fine blood vessels without contamination of the background such as muscle and fat. Here, the important point is that the signal of muscle and fat can be regarded as steady during the iMSDE preparation, because there structures do not move during the iMSDE. On the other hand, the signal of blood vessels should be suppressed by the iMSDE. Consequently, the standard deviation (SD) of all these tissues together (consisting of blood vessels, muscle and fat) should be decreased if iMSDE works well. Thus, for the purpose of assessing the effect of iMSDE in suppression of blood vessels, the SD of all regions in the field of view (FOV) outside the nerve (SDbackground) was measured. More specifically, a square-shaped region of interest (ROI) with an area of 200 cm² was placed in the both the left and right background tissue at the level from L1 to S1.

Meanwhile, the signal intensity of the nerve should not be suppressed by iMSDE. To confirm that the iMSDE does not affect the nerve signals, signal-to-noise-ratio (SNR) of the nerves (SNRNerve) was measured/calculated as follows:

$$\text{SNR}_{\text{Nerve}} = \frac{\text{SI (nerve)}}{\text{SD (noise)}}$$

where SI (nerve) is signal intensity of the nerves, and SD (noise) is the standard deviation of the noise measured outside the body.

Circular-shaped ROIs with a diameter of 5 mm were placed in the left and right lumbosacral trunks and sciatic nerves on coronal source images of D-prep MRN. Another circular-shaped ROI with a diameter of 30 mm was placed in the noise outside the body.

The SDbackground and SNRNerve were assessed by using one-way repeated measures analysis of variance (ANOVA) and post-hoc Tukey test, because the data fitted a normal distribution (Shapiro-Wilk normality test).

Quantitative analysis of the effect of iMSDEprep-time

Since the iMSDEprep-time gives a T₂-weighted contrast, the muscle may lose its signal with a medium or longer duration of the iMSDEprep-time. Since the nerve has a longer T₂ value than the muscle, it may lose its signal with a longer duration of the iMSDEprep-time. We evaluated what length of iMSDEprep-time gives the best contrast between nerve and muscle. To that end, the SNR of the nerve (SNRNerve) and the contrast-ratio (CR) between the nerve and the muscle (CRNerve-Muscle) were measured/calculated as follows:
where $SI$ (nerve) is the signal intensity of the nerves, and $SI$ (muscle) is the signal intensity of the muscles. For the ROIs of the nerves, a circular-shaped ROI with a diameter of 5 mm was manually placed in the both the left and right lumbosacral trunks and sciatic nerves on coronal source images of D-prep MRN datasets. For the ROIs of the muscles, a circular-shaped ROI with a diameter of 20 mm was manually placed in the both the left and right psoas muscle at the level of L5.

The $CR_{\text{Nerve-Muscle}}$ and $SNR_{\text{Nerve}}$ were also assessed by using one-way repeated measures ANOVA and post-hoc Tukey test, because the data fitted a normal distribution (Shapiro-Wilk normality test).

**Feasibility evaluation**
An initial evaluation of the optimized D-prep MRN sequence for visualization of the brachial plexus, lumbosacral plexus, and cranial nerves was performed in 5 healthy volunteers.

**Results**
In this study, D-prep MRN acquisitions were successfully acquired in all subjects.

**Quantitative analysis of the effect of iMSDE gradient strength**
Regarding the suppression of blood vessels, $SD_{\text{background}}$ for the different iMSDE gradient-strengths (b-values) of 0, 2 and 10 s/mm² were $131.80 \pm 5.81$, $118.60 \pm 6.71$ and $103.72 \pm 3.50$ among five volunteers (Fig. 3a). Therefore, the $SD_{\text{background}}$ gradually decreased as the b-value increased.

On the other hand, corresponding $SNR_{\text{Nerve}}$ were $62.2 \pm 13.1$, $57.6 \pm 10.5$ and $56.3 \pm 10.1$, respectively (Fig. 3b). This means that the changes in $SNR_{\text{Nerve}}$ were ignorable with any of the b-values. Thus, a higher b-value of 10 s/mm² was better in suppression of blood vessels. Representative images are shown in Fig. 4.

**Quantitative analysis of the effect of iMSDE$_{\text{prep-time}}$**
Regarding the suppression of muscle signal, $CR_{\text{Nerve-Muscle}}$ for iMSDE$_{\text{prep-time}}$ of 18, 50 and 100 ms were $0.61 \pm 0.16$, $0.75 \pm 0.11$ and $0.79 \pm 0.09$, respectively (Fig. 5a). The $CR_{\text{Nerve-Muscle}}$ clearly increased as the iMSDE$_{\text{prep-time}}$ was changed from shortest value (18 ms) to intermediate (50 ms) and long (100 ms). On the other hand, corresponding $SNR_{\text{Nerve}}$ were $56.3 \pm 10.1$, $44.3 \pm 8.9$ and $37.5 \pm 8.7$, respectively (Fig. 5b). The $SNR_{\text{Nerve}}$ significantly decreased at longer iMSDE$_{\text{prep-time}}$ (100 ms). Therefore, an intermediate iMSDE$_{\text{prep-time}}$ of 50 ms provided the best compromise between suppression of muscle signal and minimization of signal loss of nerves. Representative images are shown in Fig. 6.

**Feasibility evaluation**
Representative images acquired with the optimized D-prep MRN sequence (iMSDE gradient-strength [b-value] of 10 s/mm² and iMSDE$_{\text{prep-time}}$ of 50 ms) are shown in Fig. 7 (brachial plexus), Fig. 8 (lumbosacral plexus), and Fig. 9 (cranial nerves). These examinations consistently resulted in high-quality images, with high SNR and excellent con-

![Fig. 3.](image-url)
Fig. 4. Representative diffusion-prepared magnetic resonance neurography (D-prep MRN) images with different improved motion-sensitized driven equilibrium (iMSDE) gradient strengths (b-values) of 0 (a), 2 (b) and 10 s/mm² (c). A b-value of 10 s/mm² (c) image was considered best for signal suppression of blood vessels.

Fig. 5. Quantitative comparison of diffusion-prepared magnetic resonance neurography (D-prep MRN images) with different improved motion-sensitized driven equilibrium preparation times (iMSDEprep-time) of 18 (shortest), 50, and 100 ms. (a) The contrast ratio between nerve and muscle (CRNerve-Muscle) clearly increased as the iMSDEprep-time was changed. (b) The corresponding signal-to-noise ratio of nerve (SNRNerve) significantly decreased with longer iMSDEprep-time. Therefore, an intermediate iMSDEprep-time of 50 ms provided the best compromise between suppression of muscle signal and minimization of signal loss of nerves.

Discussion

The concept of MRN was introduced in 1993 by Filler et al., who demonstrated the utility of fat suppressed T2-weighted images for this purpose.1 Although this technique succeed to visualize the peripheral nerve with moderately suppressed background thanks to use of a long TE, only a short range of the nervous system can be visualized because of poor differentiation from blood vessels which run parallel to the nerves. The development of DWI for MRN solved this issue.7 DWI can simultaneously suppress blood vessels and show the nerves as high signal intensity structures. Consequently, DWI allowed visualization of the nerves over long trajectories on maximum intensity projection (MIP) images, which is advantageous to understand the distribution/extent of lesions. Another useful MRN technique, the 3D DW-SSFP sequence, was reported by Zhang et al. in 2008.10 Since this technique uses a short TR, and motion probing gradients (MPGs) have to insert within it, a high b-value cannot be achieved. Therefore, some background signal remains with this technique, which causes a need for careful post-processing with cutting of unnecessary surrounding structures to obtain selective MIP. However, thanks to its
Fig. 6. Representative diffusion-prepared magnetic resonance neurography (D-prep MRN) images with different improved motion-sensitized driven equilibrium preparation times (iMSDEprep-time) of 18 (shortest) (a), 50 (b), and 100 ms (c). An intermediate iMSDEprep-time of 50 ms provided the best compromise between suppression of muscle signal and minimization of signal loss of nerves.

Fig. 7. Optimized diffusion-prepared magnetic resonance neurography (D-prep MRN images) of the brachial plexus. The 3-dimensional trajectory of the nerves is shown beautifully without vessel signals. Scan parameters: repetition time (TR), 2500 ms; effective echo time (TEeff), 61 ms; echo train length (ETL), 100; spectral attenuated inversion recovery (SPAIR); improved motion-sensitized driven (iMSDE) (motion-sensitized gradients applied in 3 axes; b-value, 10 s/mm²; iMSDEprep-time [preparation time], 50 ms); scan duration, 5 min 30 s.

high spatial resolution, it is advantageous to evaluate focal nerve pathology. Nevertheless, the 3D DW-SSFP sequence is of little practical use because it suffers from a long acquisition time of around 10 min due to the need to insert MPGs for every TR. Thus, a high-speed sequence with high spatial resolution is still needed.

Recently, the concept of “low b-value DWI” was proposed for several clinical applications such as suppression of hepatic vessels, avoidance of signal loss in the left hepatic lobe, and suppression of intestinal luminal fluid to highlight hypokinetic intestinal loops.18 Although the images acquired with a low b-value do not contain as much diffusion effect as images acquired with a high b-value, a low b-value is still very effective in suppressing different physiological phenomena such as perfusion or turbulence of (semi-) liquid substances in the body. Therefore, this concept is symbolically/practically called “low b-value DWI”. The concept of the D-prep MRN sequence is similar to that of low b-value DWI, but also different in that it employs the diffusion effect in a pre-pulse with motion-sensitized gradients. The main sequence that follows the
pre-pulse can be selected/designed freely. Therefore, it provides both high speed and high resolution for MRN in a relatively short scan time of around 5 min as we did in this study. Our study showed that the combination of an appropriate iMSDE gradient-strength (b-value) and an appropriate iMSDE prep-time could suppress the vessel signal and the muscle signal effectively.

Regarding the main sequence, a tissue-specific variable refocusing flip-angle TSE technique, which is a variant of the RARE sequence allowing extremely large ETL \( \geq 100 \),\(^{14,15}\) was employed. It enables acquisition of high-resolution isotropic 3D datasets with contrasts similar to those obtained with “conventional 2D T\(_2\)-weighted images” with a relatively shorter scan time than with a SSFP sequence. Furthermore, theoretically, it is less likely to affect by magnetic susceptibility effects compared with DW-SSFP, because DW-SSFP is based on gradient-echo sequence. Therefore, it may potentially avoid to deterioration of image quality at location near the air (e.g., hypostatic cranial nerves, brachial plexus) than DW-SSFP.

The new technique that was proposed for MRN in this study has several limitations. First, the D-prep MRN sequence is theoretically susceptible to magnetic field inhomogeneities. Therefore, it may cause artifact in clinical patient studies. Since the initial evaluation was only done in volunteers, further investigation is needed. Second, we could only apply a weak value for diffusion-weighting. Although this provided effective suppression of blood vessels and cerebrospinal fluid, the suppression of other background tissue may not be sufficient. This, in turn, causes the need for sophisticated selective MIP post-processing procedures (instead of the full MIP technique) to eliminate unwanted normal structures surrounding the nerves in D-prep MRN, resulting in longer post-processing time. Moreover, complete separation of the nerves from surrounding structures may not be successful when nerves are closely encompassed by surrounding tissue. Since D-prep MRN can be done in a short scan time (\(<5\) min), complementary use of DWI based MRN (i.e. single-shot spin-echo echo-planar imaging at high b-value) may be useful, with the former potentially providing good evaluation of focal nerve pathology and the latter providing a more global overview of the nerve region of interest. Third, there is another additional limitation which may be related to the weak diffusion-weighting; the D-prep MRN sequence may suffer from some contamination of fluid signal especially if steady in motion, which may occur in the fluid is just adjacent to the nerve sheath. Therefore, further technical exploration is necessary. In addition, clinical studies are required to validate its utility in the evaluation of pathologic conditions involving nerves, such as...
Fig. 9. Optimized diffusion-prepared magnetic resonance neurography (D-prep MRN) images of cranial nerves (V3: mandibular nerve, 3rd branch of the trigeminal nerve; VII: facial nerve; IX: glossopharyngeal nerve; X: vagus nerve; XII: hypoglossal nerve). The 3-dimensional trajectory of the nerves is shown beautifully without vessel signals. Scan parameters: repetition time (TR), 2500 ms; effective echo time (TE_{eff}), 63 ms; echo train length (ETL), 100; spectral attenuated inversion recovery (SPAIR); improved motion-sensitized driven (iMSDE) (motion-sensitized gradients were applied in 3 axes; b-value, 10 s/mm²; iMSDE_{prep-time} [preparation time], 50 ms); scan duration, 5 min 47 s.

tumors, inflammation, and trauma. Finally, a thorough comparison of proposed D-prep MRN and conventional methods (DW-MRN, DW-SSFP) was not performed in this study and therefore further comparative study is needed.

In conclusion, a new scheme of iMSDE prepared 3D-RARE based D-prep MRN sequence was introduced and optimized, and clearly showed detailed anatomy of the brachial plexus, lumbar-sacral plexus, and cranial nerves. These results suggest that the D-prep MRN can be used for fast, high-resolution, volumetric imaging of the peripheral nervous system.

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