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Do Susceptibility-Weighted Imaging and Multi-Shot Echo Planar Imaging Optimally Demonstrate and Predict Outcome for Spinal Cord Injury?

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14. ABSTRACT

Multiple detector computed tomography is the imaging modality of choice to demonstrate spinal fractures. Conventional magnetic resonance imaging (MRI) is useful to evaluate the anatomical location of spinal cord contusion, demonstrate hemorrhage, and associate injury to ligaments, discs, and other soft tissue that are crucial for planning optimal surgery and rehabilitation. However, conventional MRI or multiple detector computed tomography provides no vital information regarding the extent of axonal injury at the site of spinal cord injury (SCI). The goals of this study were to compare two advanced diffusion tensor imaging (DTI) parameters in predicting longitudinal neurological and functional outcome at 1 year and to compare the performance of susceptibility-weighted imaging (SWI) and gradient echo (GRD) sequences in demonstrating spinal cord hemorrhage. In this prospective longitudinal study, 30 patients and 15 control subjects underwent conventional and advanced cervical spine MRI within 24 hours of injury. DTI values and hemorrhage volumes were measured from hand-drawn regions of interest. The association between DTI measurements and functional outcomes at 1 year was determined. Hemorrhage volumes measured using SWI and GRD were compared. We observed no differences in mean diffusivity, axial diffusivity (AD), or radial diffusivity between the two DTI sequences except for an increased fractional anisotropy calculated from the spin echo sequence ($p=0.006$) in patients. In a regression model, AD provided the best correlation with the International Standards for Neurological Classification of Spinal Cord Injury motor ($r^2=0.93$, $p=0.0019$) and Spinal Cord Independence Measure III scores at 1 year ($r^2=0.77$, $p=0.0004$). SWI was more sensitive and volumes of hemorrhage were significantly larger than GRD ($p=0.001$). The shorter acquisition times with spin echo DTI make this the technique of choice to obtain DTI measurements. AD measurements at the SCI site represent a potential imaging biomarker to predict long-term functional and neurological outcome. SWI is more sensitive in demonstrating hemorrhage within SCI.

15. SUBJECT TERMS
Spinal cord injury, diffusion tensor imaging, DTI, susceptibility-weighted imaging, SWI, spinal cord hemorrhage

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1.0 SUMMARY

Multiple detector computed tomography is the imaging modality of choice to demonstrate spinal fractures. Conventional magnetic resonance imaging (MRI) is useful to evaluate the anatomical location of spinal cord contusion, demonstrate hemorrhage, and associate injury to ligaments, discs, and other soft tissue that are crucial for planning optimal surgery and rehabilitation. However, conventional MRI or multiple detector computed tomography provides no vital information regarding the extent of axonal injury at the site of spinal cord injury (SCI). Advanced MRI sequence using diffusion tensor imaging (DTI) has the potential to measure parameters within the SCI that help to predict the amount of axonal injury. Susceptibility-weighted imaging (SWI) is a new sequence that is highly sensitive to demonstrate products of hemorrhage. We proposed to investigate how the extent of axonal injury measured using DTI predicts longitudinal outcome and hemorrhage demonstrated with SWI within SCI. Specifically, we had two main goals: 1) compare two advanced DTI parameters in predicting longitudinal neurological and functional outcome at 1 year, and 2) compare the performance of SWI and gradient echo (GRD) sequences in demonstrating spinal cord hemorrhage.

In this prospective longitudinal study, 30 patients and 15 control subjects underwent conventional and advanced cervical spine MRI within 24 hours of injury. DTI values and hemorrhage volumes were measured from hand-drawn regions of interest. Measurements made from two DTI sequences (spin echo (SE) and RESOLVE) were compared. The association between DTI measurements and functional outcomes at 1 year was determined. Hemorrhage volumes measured using SWI and GRD were compared.

We observed no differences in mean diffusivity, axial diffusivity (AD), or radial diffusivity between the two DTI sequences except for an increased fractional anisotropy calculated from the SE sequence ($p=0.006$) in patients. In a regression model, AD provided the best correlation with the International Standards for Neurological Classification of Spinal Cord Injury motor ($r^2=0.93$, $p=0.0019$) and Spinal Cord Independence Measure III scores at 1 year ($r^2=0.77$, $p=0.0004$). SWI was more sensitive and volumes of hemorrhage were significantly larger than GRD ($p=0.001$).

The shorter acquisition times with SE DTI make this the technique of choice to obtain DTI measurements. AD measurements at the SCI site represent a potential imaging biomarker to predict long-term functional and neurological outcome. SWI is more sensitive in demonstrating hemorrhage within SCI. Therefore, this study provides convincing evidence that DTI and SWI sequences used routinely in clinical MRI protocols for SCI measure axonal injury and the amount of hemorrhage accurately to predict long-term functional and neurological outcome.

2.0 INTRODUCTION

The overarching goal of this study was to investigate the clinical utility of two advanced magnetic resonance imaging (MRI) sequences to determine the extent of axonal injury to the spinal cord in patients with blunt spinal cord injury (SCI). The first objective was to assess the ability of susceptibility-weighted imaging (SWI) to demonstrate hemorrhage within the SCI. Specifically, we hypothesized that hemorrhages within the zone of injury (ZOI) in the spinal cord would be better visualized using SWI compared to conventional MRI. The second objective was to determine if multi-shot echo planar imaging (MS-EPI) sequences (RESOLVE) improved the accuracy of diffusion tensor imaging (DTI) measurements compared to the conventionally

used single-shot EPI sequences. Specifically, we hypothesized that MS-EPI sequences would provide more accurate diffusion-weighted measurements within the ZOI compared to single-shot EPI sequences and these measurements would, therefore, show greater correlations with clinical measurements.

3.0 BACKGROUND

According to the 2008 census, it was estimated that in the United States approximately 250,000 Americans have obtained SCIs. Roughly 47% of these injuries result in substantial enough damage to leave the individuals as quadriplegics. This is a growing problem, as it is estimated that each year 11,000 new SCIs will occur. The majority of these SCIs impact young adults, making the situation all the more tragic for the individuals and the financial burden to society all the greater, resulting in an average cost of care per year for these individuals that ranges anywhere from $236K to $801K [1].

The ability to noninvasively determine the extent of damage to the spinal cord, ligaments, discs, and other soft tissue is crucial for the clinical management of these patients. While, computed tomography (CT) has been conventionally used to determine the extent of injury, MRI allows more direct visualization of the spinal cord and other tissues than CT [2-8]. Different MRI techniques are required to optimally visualize the injured spinal cord, ligaments, and soft tissues due to different magnetic properties between various tissue types [4,5,8]. Conventional MRI, consisting of T1- and T2-weighted imaging, is currently the standard of care to demonstrate the ZOI following an SCI that has a neurological deficit localized to the spinal cord [4,6,9-12]. However, conventional MRI techniques have various limitations, and perhaps advanced techniques, such as DTI and SWI, may provide additional information regarding the scope of the ZOI following SCI.

In recent years, diffusion-weighted MRI has become an influential tool in studying subtle central nervous system injuries because of the technique's ability to provide in vivo measurements of microstructural alterations that conventional MRI and CT lack the sensitivity to detect. The ability to study the change in random motion of protons in water in vivo is the basis for diffusion-weighted MRI and DTI [13-18]. Restricted proton motion results in a decrease in the apparent diffusion coefficient of water and results in greater signal intensity on diffusion-weighted images. DTI measures this signal change across multiple spatial directions and identifies the preferential directions of water diffusion, thus obtaining accurate measurements of water diffusion both longitudinally and transversely to spinal cord tracts. Fractional anisotropy (FA) is another important DTI parameter that measures the disproportion of the diffusion along the longitudinal vs. transverse directions and is reflective of cord integrity. More specifically, the diffusion along and perpendicular to the axons can be independently measured through axial diffusivity (AD) and radial diffusivity (RD), respectively. AD has been linked to axonal injury, while RD has been linked to myelin disruption and axonal swelling [13,14,18]. These measures can provide important information about the microstructure of the local tissue environment following spinal cord injury.

This study attempted to optimize the latest advances in MRI technology to identify optimal biomarkers to predict long-term functional outcome and to assess the true extent of SCI. Techniques such as MS-EPI can be used to study disruptions in microarchitecture and to visualize microhemorrhages with SWI at the ZOI that are not evident in conventional CT or MRI measurements.

4.0 METHODS

4.1 Participants

Thirty patients were enrolled in this study. All participants were admitted to the R Adam Cowley Shock Trauma Center for SCIs between January 2013 and March 2015. All patients had an acute subaxial blunt cervical SCI resulting in an American Spinal Injury Association (ASIA) impairment scale A, B, C, or D injury. Inclusion criteria were as follows: (**a)** age ≥ 18 years old, both genders, (**b)** admitted following blunt trauma, (**c)** a neurological deficit that could be localized to the cervical spine on clinical examination, **(d)** a spinal cord contusion demonstrated on conventional MRI performed within 24 hours of injury. Exclusion criteria were as follows: **(a)** age < 18 years, **(b)** penetrating mechanism, **(c)** moderate or severe traumatic brain injury, cerebrovascular accident, **(d)** concomitant extremity fractures preventing neurological assessment, **(e)** neurological deficit without cervical spinal contusion, **(f)** peripheral cord or nerve injury.

Each patient underwent both CT and MRI examination of the cervical spine following admission. Axial, sagittal and coronal multi-planar reformatted CT images were used for determining morphology of cervical spine fracture.

In addition, 15 neurologically intact healthy volunteers with comparable age and gender were recruited to obtain normative data.

4.2 Clinical Variables

Patients underwent comprehensive clinical assessment using the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) protocol prior to discharge from the hospital [14,15]. In addition, a subset of patients (n=16) received a clinical assessment at 12 months following injury [14,15]. The Spinal Cord Independence Measure III (SCIM) was administered at 12 months to assess functional outcome [14,16]. The assessment was performed by a trained certified physical therapist with at least 7 years of experience evaluating SCI patients without the knowledge of the type of SCI (hemorrhagic vs. nonhemorrhagic contusion) or DTI measurements. Both these scores range from 0 to 100, with a higher score indicating greater ability.

4.3 MRI Acquisition

MRI imaging was performed acutely within 24 hours of injury. All imaging was performed on a 1.5-T Avanto scanner (Siemens Medical Solutions, Erlangan, Germany) with parallel imaging capability. Conventional MRI included sagittal T2 (echo time (TE)/repetition time (TR): 109/4,000 ms), fluid-attenuated inversion recovery (TE/TR: 102/8,000 ms, echo train length: 13), and axial T2 and T2* three-dimensional SWI (TE/TR: 16/30 ms, FA: 20°) images. Two DTI sequences were acquired on each participant. Single-shot DTI (spin echo [SE]) were acquired at a TE/TR of 87/2800 ms and a resolution of 128 × 128 over a 20-cm field of view. Diffusion weighting was applied in 20 directions with an effective b-value of 700 s/mm^2 and 3 averages. In total, 20 axial slices at 4 mm slice thickness were acquired centered at the location of the contusion for patients. Imaging time was 3 minutes 6 seconds. A second DTI sequence was obtained using a multi-shot readout-segmented EPI sequence (RESOLVE) with the same

resolution, diffusion encoding directions, and number of averages at TE1/TE2/TR of 67 ms/95 ms/2800 ms and 7 segments. Imaging time was 8 minutes 32 seconds. For volunteers, three acquisitions were performed with slices placed at upper (lower brainstem to C2), mid (C3-C5), and lower (C6 to T1) sections. A 12-channel head and 4-channel neck array coil was used on all patients, and parallel imaging with an acceleration factor of 2 was used with phase encoding in the anterior-to-posterior direction. Sagittal T2-weighted short tau inversion recovery (STIR) images and b = 0 s/mm^2 images from the DTI scan were used for anatomic reference.

4.4 MRI Analysis

4.4.1 DTI Analysis. DTI data were reconstructed offline using Diffusion Toolkit (www.trackvis.org) for mean diffusivity (MD), FA, AD, and RD maps. A single radiologist used soft copy T2 and fluid-attenuated inversion recovery images to identify the anatomical location and extent of injury. Spinal cord edema was diagnosed when increased intramedullary signal was seen both on T2 and STIR sequences. Spinal cord hemorrhage was diagnosed using the presence of decreased intramedullary signal on SWI or T2* images. A single measurement was made within the SCI using regions of interest (ROIs) drawn on mid-sagittal diffusion-weighted image maps by the radiologist (blinded to clinical data), carefully placed to avoid cerebrospinal fluid and areas of hemorrhage; the area of edema was confirmed using T2 and STIR sequences, and sites of hemorrhage were confirmed using SWI and T2* sequences.

In the control population, three ROIs were drawn on upper (lower brainstem – lower C2), mid (upper C3 – lower C5), and lower (upper C6 – lower T1) sections of the C-spine. For outcome prediction in patients, the DTI values within the lesion were normalized by control DTI values based on lesion location due to the potential diffusion tensor differences based on anatomical location in the cervical spine.

Differences between the two DTI sequences (SE and RESOLVE) were determined using paired t-tests for MD, FA, AD, and RD for each of the three ROIs (upper, middle, and lower) within the control population and within the single ROI within the patient population. In addition, differences in DTI parameters between the SCI patients with hemorrhagic contusion (HC) compared to those without hemorrhagic contusion (non-HC) were determined using t-tests for each parameter.

4.4.2 DTI Outcome Prediction. Using the outcome data from the 16 patients who returned for their 1-year follow-up, stepwise regression analysis was performed to find relevant parameters (normalized DTI values, age, gender, HC or non-HC) that correlated with patient ASIA motor score and SCIM III scores at 12 months.

4.4.3 SWI Analysis. ROIs to include the volume of hemorrhage were drawn by a radiologist on both the SWI and gradient echo (GRD) images on an application that enables quantitative analysis and visualization of MR sequences (MIPAV, version 7.2.0., http://mipav.cit.nih.gov/). The total hemorrhage volume per individual was determined for each sequence. Paired t-tests determined the difference in hemorrhage volume measured by SWI and GRD sequences.

5.0 RESULTS

5.1 Participants

Table 1 shows the demographics of patients included in this study. As has been previously reported, males were more likely to receive an SCI [2]. All MRI examinations were obtained within 24 hours of the injury (range 3-17 hours).

Table 1. Demographics and Clinical Parameters

Demographic	Study Group n=30	Control Group n=15
Age (yr), median (range)	53 (20-79)	46 (26-69)
Male	24 (80%)	12 (80%)
Mechanism		
Fall	14 (46.6%)	N/A
Motor vehicle collision	8 (26.6%)	
Bicycle	1 (3.3%)	
Diving accident	4 (13.3%)	
Object fallen on head	2 (6.6%)	
Pedestrian struck	1 (3.3%)	
Injury to MRI (time)	(3:30 ~17:18 h)	N/A
Morphology of Injury		
Distraction	8 (50.0%)	N/A
Rotation	3 (6.25%)	
Disc/osteophyte complex	19 (43.75%)	
Cord contusion		
Hemorrhagic	14	
Nonhemorrhagic	16	
Injury Severity Score, mean (SD)	26.47	N/A
Trauma Injury Severity Score, mean (SD)	0.83	N/A
Revised Trauma Score admission, mean (range)	7.47 (6.17-7.84)	N/A
ASCOT, mean (range)	0.81 (0.5-0.99)	N/A
Systolic blood pressure, mean (range)	115.87 (79-144)	N/A
Glasgow Coma Scale, mean (range)	13.67 (9.00 -15.00)	N/A
Motor Glasgow Coma Scale, mean (range)	5.8 (5-6)	N/A
Carotid or vertebral artery injury	3	N/A
Intensive care unit length of stay (days), mean (range)	12.42 (3.34-21.56)	N/A
Hospital length of stay (days), mean (range)	14.55 (4-31.9)	N/A

ASCOT = a severity classification of trauma; SD = standard deviation.

5.2 Single-Shot EPI (SE) vs. Multi-Shot EPI (RESOLVE) DTI Acquisition

In the control population, no differences were noted between the SE and RESOLVE DTI sequences for MD, AD, RD, or FA for any of the ROIs (upper, middle, lower) investigated (all p-values > 0.05) (Table 2). However, in the SCI population, while no differences were noted between the SE and RESOLVE sequences for MD, AD, or RD, the FA calculated from the

RESOLVE sequence was significantly higher than the FA calculated from the SE sequence (p=0.006) (Figure 1; Table 2).

Table 2. DTI Parameters for Study Population

Parameter	SE DTI	RESOLVE DTI	p-value
Control Population			
Lower ROI			
MD ($x10^{-3}$ mm^2/s)	0.00077 ± 0.00011	0.000756 ± 0.00013	0.603
FA	0.62326 ± 0.06006	0.641060 ± 0.03615	0.201
AD ($x10^{-3}$ mm^2/s)	0.00136 ± 0.00012	0.001350 ± 0.00017	0.472
RD ($x10^{-3}$ mm^2/s)	0.00047 ± 0.00012	0.000460 ± 0.00012	0.675
Middle ROI			
MD ($x10^{-3}$ mm^2/s)	0.00074 ± 0.00010	0.000710 ± 0.00010	0.164
FA	0.66993 ± 0.04364	0.688680 ± 0.05358	0.120
AD ($x10^{-3}$ mm^2/s)	0.00137 ± 0.00013	0.001340 ± 0.00012	0.154
RD ($x10^{-3}$ mm^2/s)	0.00042 ± 0.00010	0.000390 ± 0.00010	0.175
Upper ROI			
MD ($x10^{-3}$ mm^2/s)	0.00075 ± 0.00013	0.000760 ± 0.00012	0.787
FA	0.66851 ± 0.04971	0.675170 ± 0.04182	0.559
AD ($x10^{-3}$ mm^2/s)	0.00139 ± 0.00016	0.001410 ± 0.00017	0.308
RD ($x10^{-3}$ mm^2/s)	0.00044 ± 0.00014	0.000430 ± 0.00011	0.845
SCI Population			
MD ($x10^{-3}$ mm^2/s)	0.00068 ± 0.00013	0.000700 ± 0.00020	0.475
FA	0.56466 ± 0.06290	0.606620 ± 0.07876	**0.006**[a]
AD ($x10^{-3}$ mm^2/s)	0.00113 ± 0.00019	0.000190 ± 0.00026	0.066
RD ($x10^{-3}$ mm^2/s)	0.00045 ± 0.00011	0.000450 ± 0.00018	0.921

[a]FA calculated from the RESOLVE sequence was significantly higher than the FA calculated from the SE sequence.

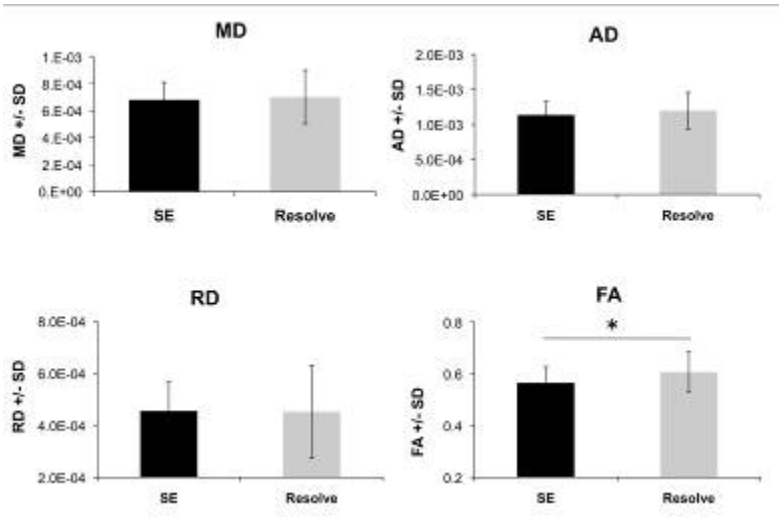

Figure 1. DTI measurements between SE and RESOLVE in SCI patients.

There were no differences in MD, AD, RD, or FA between HC and non-HC groups for either the SE or RESOLVE sequence (Figure 2). However, as expected, the extent of the lesion as measured by ROI sizes was greater in the HC group compared to the non-HC group for both the SE sequence (p=0.003) and the RESOLVE sequence (p<0.001).

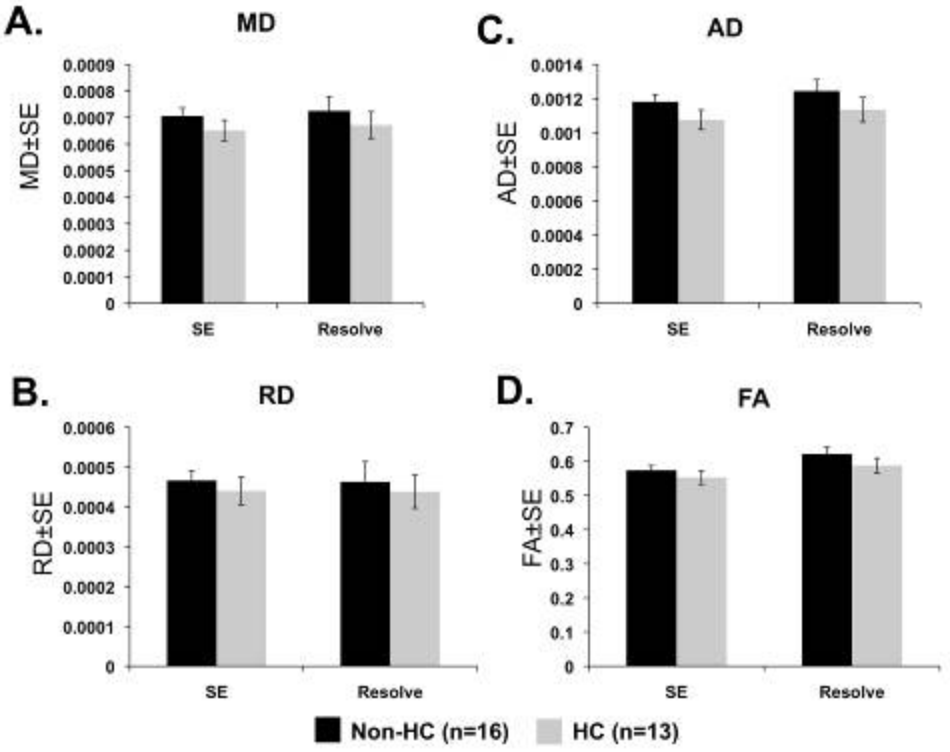

Figure 2. Differences in DTI measurements between non-HC and HC SCI patients.

5.3 DTI and Outcome

The results of the stepwise regression demonstrate that age and gender had no effect for neurological outcome for prediction of motor scores at the 1-year follow-up, while presence of hemorrhage within the SCI (HC) and DTI parameters was an important factor in patient outcome (p<0.0001). Among the four DTI parameters, including AD in the regression model provided the best results (r^2=0.93, p=0.0019). Other significant DTI parameters included MD (r^2=0.89, p=0.0027) and RD (r^2=0.86, p=0.014). FA was not a significant factor. Figure 3 shows the correlation between DTI parameters with follow-up ISNCSCI motor score at 1 year for HC and non-HC SCI patients. Both non-HC and higher MD, AD, or RD are indicative of higher ASIA motor score at 1 year. In HC patients, significant positive correlations between ISNCSCI motor scores and MD, AD, and RD were noted.

In the regression analysis comparing DTI parameters with SCIM III scores at the 1-year follow-up, the best results were with AD (r^2=0.77, p=0.0004). Other significant DTI parameters included RD (r^2=0.50, p=0.0483) and MD (r^2=0.66, p=0.0047).

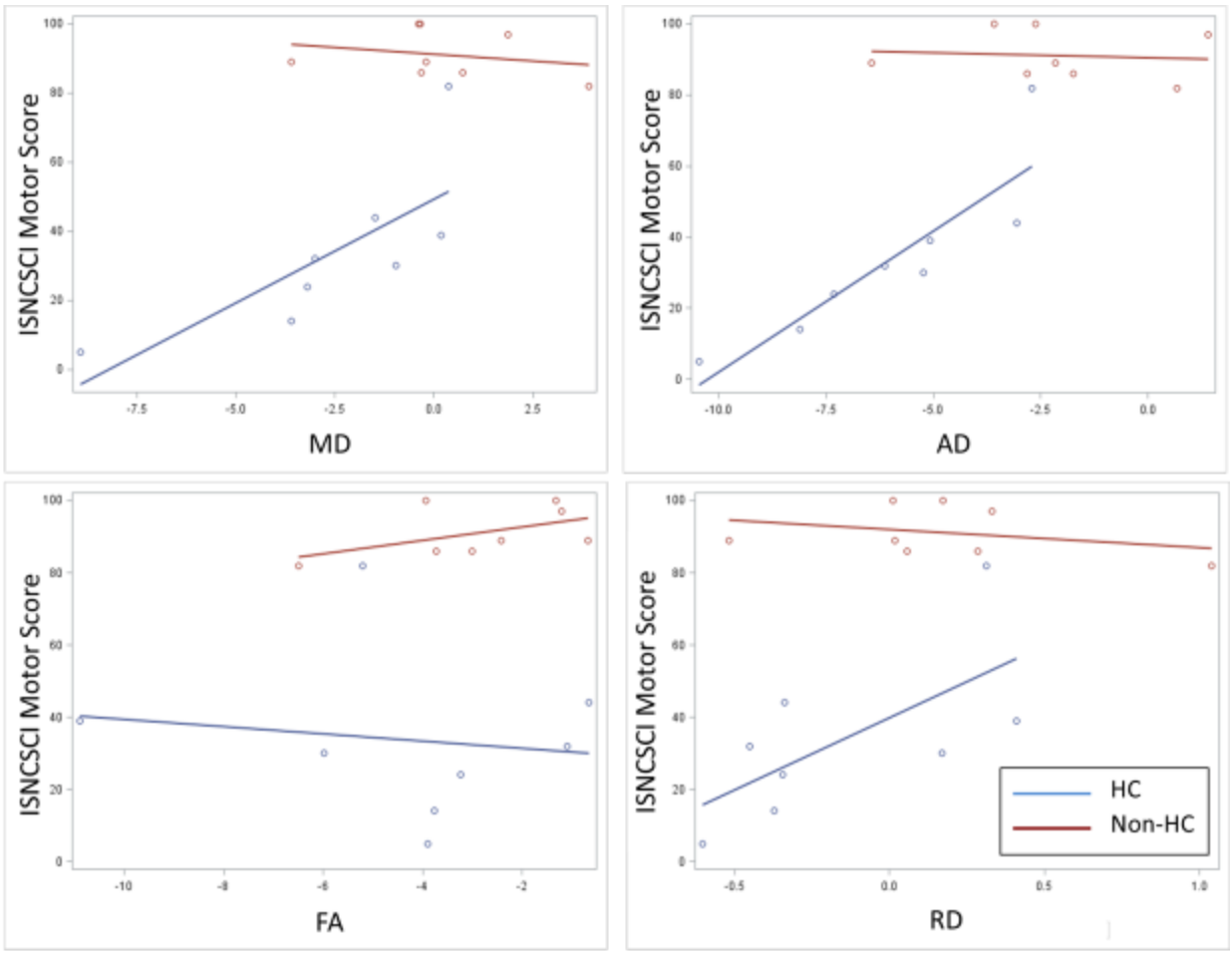

Figure 3. Correlations between normalized DTI measurements and ISNCSCI motor score at 12 months.

5.4 GRD vs. SWI

MRI demonstrated spinal cord HC within the site of SCI in 14 out of the 30 patients. Fourteen patients had hemorrhage within the site of SCI on SWI. Only 11 (79%) of these hemorrhages were visualized on conventional GRD sequence, indicating that SWI is a more sensitive sequence to demonstrate spinal cord hemorrhage compared to GRD (Figure 4).

Furthermore, the mean volume of hemorrhage was greater when measured on SWI compared to GRD (Figure 5A). Figure 5B shows the individual hemorrhage volumes for each of the 14 patients.

6.0 DISCUSSION

The results from this study have provided multiple lines of evidence suggesting that advanced MR imaging techniques such as DTI and SWI are better able to detect the extent of axonal injury compared to conventional MRI techniques.

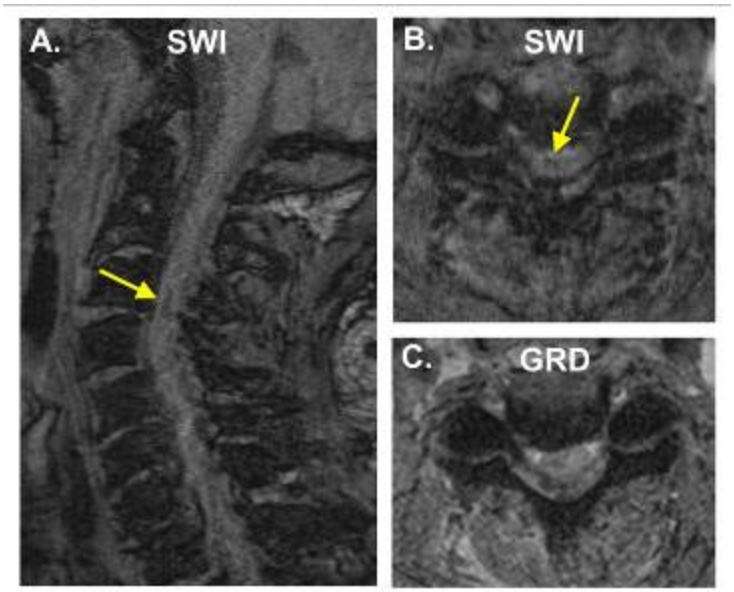

Figure 4. Example of hemorrhage visualized on SWI but not GRD.

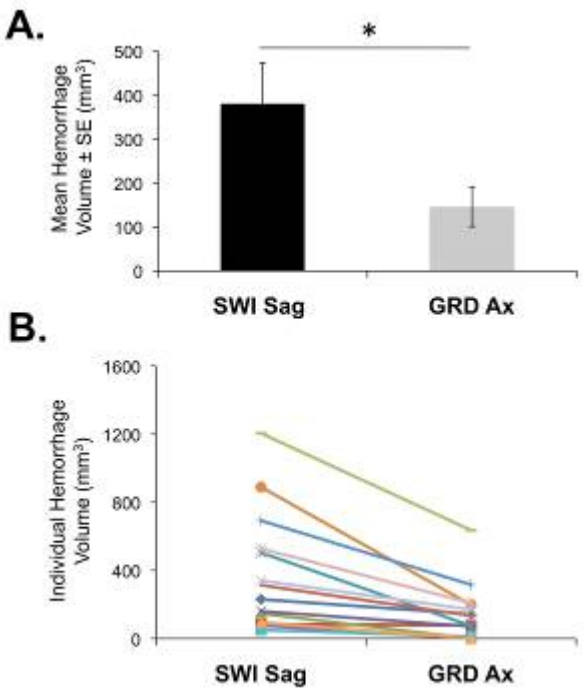

Figure 5. Hemorrhage volume as measured by SWI and GRD.

6.1 SE vs. RESOLVE

In our study, we compared measurements at the injury site using two different DTI sequences, SE and RESOLVE. No differences in any of four DTI parameters investigated were noted between the SE and RESOLVE sequences in the control population, suggesting that the two techniques are comparable. A significant difference between the two sequences was in FA in SCI patients, suggesting a difference in these two techniques. However, FA was not useful to predict long-term outcome in this study. Since the DTI measurements were comparable between the two techniques, and the shorter acquisition times associated with the SE sequence are likely to result in less motion artifact, our results suggest that the SE sequence is the preferred DTI sequence for future studies. However, recent advances in MRI technology indicate an extension of the DTI model, known as diffusion kurtosis imaging (DKI), can provide more accurate measurement of the amount of axonal injury at the site of SCI because it takes into consideration tissue heterogeneity, which may be reflective of cord inflammation. DKI will also allow calculation of all the DTI measurements (FA, MD, RD, AD) used in this study. There are challenges applying DKI in cervical spine due to the low signal-to-noise ratio and potential motion in the spinal cord due to prolonged acquisition time. Future studies will include DKI imaging of the cervical spinal cord to obtain DKI measurements at the injury site. They may serve as early robust imaging biomarkers to predict longitudinal outcome in SCI.

6.2 Predicting Outcome

Our study provides new insight into the gaps in knowledge in the utility of DTI measurements made at the SCI seen by conventional MRI (STIR and T2-weighted sequences) performed during the hyperacute stage following SCI that can be a sensitive biomarker to predict neurological and functional outcome at 1 year. Among the four measurements made (AD, RD, MD, and FA), AD best predicted both neurological and functional outcome at 1 year. A decrease in AD is a measure of the diffusion properties of water parallel to the white matter tracts associated with axonal injury in preclinical studies [19-23]. These studies report excellent correlation between reduced AD and histological analysis of the extent of injured spinal cord within preclinical models. For example, the reduction in AD measurements observed at the contusion epicenter following graded injury to mouse spinal cord demonstrated correlations with amount of cytotoxic edema and white matter necrosis on spinal cord histology. In our study, there was optimum correlation between admission AD measurements within the ZOI and both the 12-month ASIA motor and SCIM III scores, suggesting that admission AD may be the best DTI predictor of functional outcome. To our knowledge, this is the first study to demonstrate that admission AD has the potential to be a DTI biomarker that could be used to predict both long-term functional and neurological outcome. Therefore, DTI has the potential to be used in the future to prospectively triage patients into the appropriate new therapeutic intervention and plan long-term rehabilitation. However, these novel results need further validation using a larger sample size.

All the patients included in our study came directly from the accident scene to our hospital. This enabled us to obtain the MRI examination for the entire study group within 24 hours of the accident. The neurological assessment due to spinal shock during this period typically is unreliable in predicting long-term outcome [24,25]. The technique we use to obtain both conventional and DTI sequences is quickly obtainable on most clinical MR scanners in the

acute post-injury period in trauma centers in the United States. This technique could be easily applicable in clinical practice to individual patients. The DTI measurements we report in our study were obtainable on standard workstations provided by all MR vendors and will be the only biomarker available immediately following the MR examination. It has the potential to help with the unmet need to prognosticate functional outcome, help with formulating optimum definitive therapy, and triage patients to novel new therapy. Providing accurate long-term functional and neurological outcome early after SCI may also help to alleviate the immense anguish most patients and families face during this period.

6.3 GRD vs. SWI

SWI is a high-spatial-resolution, three-dimensional gradient echo sequence with phase post-processing [26]. Accentuating paramagnetic properties of products of hemorrhage, including deoxyhemoglobin, methemoglobin, and hemosiderin, increases its conspicuity within a lesion. These properties make SWI a very sensitive sequence that increases the conspicuity in demonstrating hemorrhage within various lesions compared to GRD or T1- or T2-weighted sequences [27]. The unique contrast provided by this sequence has the potential to provide additional clinically useful diagnostic and prognostic information [26,28]. In this study, we demonstrate that SWI is more sensitive than GRD in demonstrating hemorrhage within SCI. The volume of hemorrhage measured within identical SCI lesions using SWI was significantly larger than measured on GRD (Figure 5). The ability to accurately identify hemorrhage in spinal cord patients is crucial to guide clinical care and formulate the best rehabilitation plan to maximize recovery. In addition, accurately demonstrating sites of hemorrhage within SCI using the SWI sequence was helpful in our study to avoid hemorrhage when placing an ROI to measure DTI parameters. Therefore, this study provides convincing evidence that the SWI sequence should be included in clinically acquired spinal cord MRI protocols to provide a more complete picture of the spinal cord injury.

7.0 CONCLUSIONS

The findings presented in this report lead to three main conclusions. First, AD measurements from DTI made at the site of SCI have the potential to be an accurate imaging biomarker to predict long-term functional and neurological outcome. Second, since the two DTI sequences present comparable measurements, the shorter acquisition time associated with the SE sequence compared to the RESOLVE sequence makes it the technique of choice to obtain DTI measurements in patients with SCI. Finally, our results demonstrate that SWI is a more sensitive technique compared to conventional MRI sequences in demonstrating both the presence and extent of hemorrhage within SCI. Therefore, this study provides convincing evidence that the advanced MRI sequences should be included in clinically acquired spinal cord MRI protocols to provide additional information on the precise damage associated with the SCI as well as aid in the clinician’s prediction of functional and neurological outcome.

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LIST OF ABBREVIATIONS AND ACRONYMS

AD	axial diffusivity
ASIA	American Spinal Injury Association
CT	computed tomography
DKI	diffusion kurtosis imaging
DTI	diffusion tensor imaging
FA	fractional anisotropy
GRD	gradient echo
HC	hemorrhagic contusion
ISNCSI	International Standards for Neurological Classification of Spinal Cord Injury
MD	mean diffusivity
MRI	magnetic resonance imaging
MS-EPI	multi-shot echo planar imaging
non-HC	nonhemorrhagic contusion
RD	radial diffusivity
ROI	region of interest
SCI	spinal cord injury
SCIM	Spinal Cord Independence Measure
SE	spin echo
STIR	short tau inversion recovery
SWI	susceptibility-weighted imaging
TE	echo time
TR	repetition time
ZOI	zone of injury