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Value of MRI and DTI as Biomarkers for Classifying Acute Spinal  
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<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b> The purpose of this study is to determine if diffusion tensor imaging (DTI) in conjunction with conventional magnetic resonance imaging (MRI) can reliably forecast neurologic recovery after spinal cord injury (SCI).  As we are still early in phase of patient recruitment, there are no significant findings to report.					
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## **Introduction**

Use of MRI/DTI may improve accuracy in stratifying SCI patients that are being selected for clinical trials to test novel therapies. Trials which utilize MRI/DTI at the point of entry have the potential to demonstrate therapeutic efficacy with fewer patients. The objective of our proposal is to prove that the MRI features of SCI and DTI when used in conjunction with the initial neurologic assessment will provide a better method to classify patients during their initial hospitalization and will better discriminate patients that have capacity for spontaneous functional recovery from those with no inherent capacity for recovery. The results derived from this project have the capacity to radically alter the methods by which we categorize SCI at the point of entry into the healthcare system by more accurately characterizing the extent of their injuries and providing the opportunity to administer appropriate therapies in the critical few hours after injury. This has direct benefit to the individual patient and their families in gauging expectations for recovery and in selecting patients for novel therapies. The goal of this study is to combine the information obtained from the physical examination of the SCI patient at the time of injury with the anatomic and physiologic information provided through MRI and DTI to better predict which patients might realize the most benefit from a new medication. If the added value of MRI and DTI improves the pre-selection process of patients for a new medication, this could also provide a secondary benefit in helping to expedite the drug approval process by decreasing the number of patients required to prove that the drug actually benefits patients.

## Body

Regarding the Task 2 items, 19 spinal cord injury patients have been successfully enrolled thus far since approval for open enrollment (item 2a & 2d). We have successfully identified twenty trauma patients with no neurologic deficit who have been screened with MRI as per 2b of the SOW. Most significant challenge for this year has been patient recruitment. Vagaries of the regional referral patterns have shifted a considerable number of potential patients outside of our referral network which has substantially limited the number of patients that could be considered for enrollment. Nevertheless we have managed to enroll the majority of patients who meet inclusion criteria over the past year.

Details of patient enrollment:

- Date last patient enrolled: October 15th, 2013
- Total number of patients enrolled: 19
- Demographics of those patients: 13 white males, 2 black females, 2 white females, 1 black male, 1 Hispanic male
- # patients who have completed data accrual: 13
- # patients still on follow-up (and with details of where there are on follow-up):
  - All 5 patients require 6 month clinical evaluation.
- Withdrawals or lost to follow-up: 1 patient death from underlying disease.

For the enrolled patients, all of the Task 3 specifications were completed including the conventional anatomic MRI (3a) and the diffusion tensor imaging acquisition (3b).

For the enrolled patients, the initial clinical assessments were performed (specified in 4a and 4c). Recovery calculations (4b, 4d and 4e) are deferred pending subsequent neurologic assessments.

Assessment of the conventional MRI studies (Task 5) were performed on the six enrolled patients by neuroradiologists. Length, location and morphology of the cord lesion was recorded (5a, 5b, 5c).

For the 19 enrolled SCI patients and the 20 patients without neurologic injury, the data was transferred to a workstation for custom post-processing (6a). An automated co-registration algorithm was implemented (6b) to preferentially filter for preserved white matter fibers in each axial section. Slice by slice FA, MD, LD and TD were calculated for each contiguous axial slice covering the entire cervical spinal cord (6c). Comparative and group analysis (6d) is deferred pending more patient accrual.

This report fulfills the requirement of SOW Task 7b.

## **Key Research Accomplishments**

- Developed a validated, reproducible DTI protocol that request less than five minutes of acquisition time.
- Trained an entire pool of MR technologists to perform the protocol autonomously.
- Developed a data management plan to transfer raw data to the analysis platform.
- Developed an automated quality control process to rapidly process the DTI data to assess for flaw/errors which might prohibit patient enrollment.
- Developed an enrollment strategy with the rehabilitation co-investigators to ensure capture of all potential patient candidates that meet inclusion criteria.
- Continued to refine the DTI protocol as needed to minimize distortion and statistical variability.
- Are now utilizing three distinct methods to analyze DTI data to better understand variations contributed by algorithms.
- Continued to collective normative DTI data for age-matched controls.

## Reportable Outcomes

- Presentation at the 2013 American Society of Neuroradiology (ASNR) Annual Meeting in San Diego, California (attached) using preliminary data obtained during protocol development.
  - Reliability of Diffusion Tensor Imaging Values in Spinal Cord Injury: Analytical Variations and Effects from Injury Severity (O-137).

## **Conclusion**

We are behind on SCI patient enrollment principally due to idiosyncratic changes in referral patterns to our Level I trauma and SCI center. We have managed to capture the majority of potential patients that meet our entry criteria. The research team has continued to focus on novel methods to analyze existing DTI datasets and analytical tools on retrospective clinical data to ensure that our acquisition methodology and analytical tools are sound.

## Reference

Not applicable.

## **Appendices**

Not applicable.

## Supporting Data

Not applicable