

AWARD NUMBER: W81XWH-14-2-0191

TITLE: A Multicenter, Randomized Controlled Trial of Cerebrospinal Fluid Drainage in Acute Spinal Cord Injury

PRINCIPAL INVESTIGATOR: Nicholas Theodore, MD

CONTRACTING ORGANIZATION: Dignity Health  
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| REPORT DOCUMENTATION PAGE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |              |                          |                            | Form Approved<br>OMB No. 0704-0188            |                                           |
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| 6. AUTHOR(S)<br>Nicholas Theodore, MD<br><br>E-Mail: Nicholas.Theodore@bnaneuro.net                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |              |                          |                            | 5d. PROJECT NUMBER                            |                                           |
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| 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)<br>Dignity Health<br>185 Berry St Ste 300<br>San Francisco, CA 94107-1773                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |              |                          |                            | 8. PERFORMING ORGANIZATION REPORT NUMBER      |                                           |
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| 13. SUPPLEMENTARY NOTES                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |              |                          |                            |                                               |                                           |
| 14. ABSTRACT<br>The purpose of this randomized clinical trial is to evaluate the safety and efficacy of cerebrospinal fluid drainage (CSFD) and to provide a preliminary clinical efficacy evaluation of the combination of CSFD and elevation of mean arterial pressure (MAP) in patients with acute spinal cord injury. Enrollment has not started for this study; we are awaiting Office of Research Protections (ORP) Human Research Protections Office (HRPO) authorization to begin study activities.                                                                                                                                                                                                                                                                                                                                                                                                                                               |              |                          |                            |                                               |                                           |
| 15. SUBJECT TERMS<br>acute spinal cord injury, cerebrospinal fluid drainage, mean arterial pressure, intrathecal pressure, improving neurologic motor outcomes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |              |                          |                            |                                               |                                           |
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| a. REPORT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | b. ABSTRACT  | c. THIS PAGE             |                            |                                               | USAMRMC                                   |
| Unclassified                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Unclassified | Unclassified             | Unclassified               | 10                                            | 19b. TELEPHONE NUMBER (include area code) |

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## 1. INTRODUCTION

In the United States, 10,000-14,000 people per year suffer acute spinal cord injuries. These injuries incur significant costs to the individual and society that are expected to increase with better long term care technologies. The purpose of this randomized clinical trial is to evaluate the safety and efficacy of cerebrospinal fluid drainage (CSFD) and to provide a preliminary clinical efficacy evaluation of the combination of CSFD and elevation of mean arterial pressure (MAP) in patients with acute spinal cord injury. This investigational method for treating acute spinal cord injury patients aims to reduce cell death and axonal damage leading to improved neurological function in patients.

## 2. KEYWORDS

acute spinal cord injury, cerebrospinal fluid drainage, mean arterial pressure, intrathecal pressure, improving neurologic motor outcomes

## 3. ACCOMPLISHMENTS

### What Were The Major Goals Of The Project?

- *Prepare Research Protocol & Study Documents*
  - *Projected Completion: March 2015*
  - *Actual Completion: March 2015*
- *Contract the Sites and Vendors*
  - *Projected Completion: February 2015*
  - *Actual Completion: WIP, 75%*
- *Obtain Regulatory Approvals*
  - *Initial Approvals*
    - *Projected Completion: March 2015*
    - *Actual Completion: WIP, 67%*
  - *Continuing Approvals*
    - *Ongoing throughout study*
- *Develop & Validate eCRF*
  - *Projected Completion: March 2015*
  - *Actual Completion: April 2015*
- *Program Clinical Data in SAS®*
  - *Projected Completion: February 2016*
  - *Actual Completion: Not Started*
- *Initiate Sites*
  - *Projected Completion: March 2015*
  - *Actual Completion: WIP, 67%*
- *Enroll Subjects, Deliver Study Treatment, Perform Evaluations*
  - *Projected Completion: January 2018*
  - *Actual Completion: Not Started*
- *Monitoring & Data Management*
  - *Projected Completion: January 2018*
  - *Actual Completion: Ongoing throughout study*
- *Close the Study & Lock the Database*
  - *Projected Completion: January 2018*
  - *Actual Completion: Not Started*

- *Analysis & Reporting*
  - *Projected Completion: April 2018*
  - *Actual Completion: Not Started*

### **What Was Accomplished Under These Goals?**

- *Prepare Research Protocol & Study Documents*
  - *Research Protocol and Study Documents finalized.*
- *Contract the Sites and Vendors*
  - *Barrow Neurological Institute, University of Arizona, University of Alabama and Nor Consult (CRO) have finalized contracts.*
- *Obtain Regulatory Approvals*
  - *Initial Approvals*
    - *Barrow Neurological Institute has received initial and continuing IRB approval for this study.*
    - *University of Arizona has received initial IRB approval for this study.*
    - *University of Alabama submitted for IRB approval.*
  - *Continuing Reviews / Amendments*
    - *Barrow Neurological Institute has received IRB approval for version 2.0 of this protocol.*
    - *Barrow Neurological Institute has received approval for their annual continuing review.*
- *Develop & Validate eCRF*
  - *The Electronic Data Capture (EDC) system that will be utilized for this study has been developed and validated.*
- *Initiate Sites*
  - *Site Initiation Visits (SIV) occurred at Barrow Neurological Institute and University of Arizona.*
- *Monitoring & Data Management*
  - *Data management data checks and risk-based data checks have been written.*

### **What Opportunities For Training And Professional Development Has The Project Provided?**

Nothing to Report.

### **How Were The Results Disseminated To Communities Of Interest?**

Nothing to Report.

### **What Do You Plan To Do During The Next Reporting Period To Accomplish Goals?**

During the next reporting period we plan to begin enrolling subjects at Barrow Neurological Institute and University of Arizona pending approval from the ORP HRPO Administrative Review. We anticipate the receipt of this authorization for Barrow Neurological Institute within the next week. One investigational site (University of Alabama, Birmingham) is awaiting initial IRB approval. Once they receive their IRB approval we will conduct a Site Initiation Visit.

#### **4. IMPACT**

##### **What Was The Impact On The Development Of The Principal Discipline(S) Of The Project?**

Nothing to Report.

##### **What Was The Impact On Other Disciplines?**

Nothing to Report.

##### **What Was The Impact On Technology Transfer?**

Nothing to Report.

##### **What Was The Impact On Society Beyond Science And Technology?**

Nothing to Report.

#### **5. CHANGES/PROBLEMS**

##### **Changes in approach and reasons for change:**

Nothing to Report.

##### **Actual or anticipated problems or delays and actions or plans to resolve them:**

The delay in this study has been with the USAMRMC ORP HRPO Administrative Review. There was a change to the Investigational Protocol (now version 2.0) and the Informed Consent Document that was required for approval. Once these changes were made, it required approval from the IRB at Barrow Neurological Institute. These changes were approved and the approval documents forwarded to the USAMRMC ORP HRPO. At this time, I have been informed that our Human Protections Scientist has recommended approval and is waiting on the Signatory Official to send out the authorization to enroll at Barrow Neurological Institute. The other two investigational sites (University of Arizona, Tucson and University of Alabama, Birmingham) are submitting the updated documents to their IRBs. Once they receive the IRB approval, we will then forward all documents to the USAMRMC ORP HRPO for review and authorization to begin enrolling.

##### **Changes that had a significant impact on expenditures:**

Nothing to Report.

##### **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents:**

Nothing to Report.

## 6. PRODUCTS

**Publications, conference papers, and presentation**

**Journal publications.**

Nothing to Report.

**Books or other non-periodical, one-time publications.**

Nothing to Report.

**Other publications, conference papers, and presentations.**

Nothing to Report.

**Website(s) or other Internet site(s).**

Nothing to Report.

**Technologies or techniques.**

Nothing to Report.

**Inventions, patent applications, and/or licenses.**

Nothing to Report.

**Other Products.**

Nothing to Report.

## 7. Participants & Other Collaborating Organizations

**What individuals have worked on the project?**

Name: Nicholas Theodore, MD, no change

Name: Bridget Dancs, no change

Name: Anna McCann, no change

Name: Stan Abramov, no change

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Nothing to Report.

**What other organizations were involved as partners?**

**Organization Name:** University of Arizona, Tucson  
**Location of Organization:** 1501 N. Campbell Ave, LSN 416 Bldg 221, Tucson, Arizona 85724  
**Partner's Contribution:** Other (Investigational Site)

**Organization Name:** University of Alabama, Birmingham  
**Location of Organization:** 510 20<sup>th</sup> Street South, FOT 1030, Birmingham, Alabama 35233  
**Partner's Contribution:** Other (Investigational Site)

**Organization Name:** Nor Consult, LLC  
**Location of Organization:** 677 Strander Blvd, Suite F, Seattle, WA 98188  
**Partner's Contribution:** Other (Contract Research Organization)

## 8. Special Reporting Requirements

### Quad Chart:

A Multicenter, Randomized, Controlled, Trial of Cerebrospinal Fluid Drainage in Acute Spinal Cord Injury

CDMRP Log Number: SC130237

Grants.gov ID Number: GRANT11501120

PI: Nicholas Theodore, MD

Org: St. Joseph's Hospital & Medical Center Award Amount: \$1,653,993

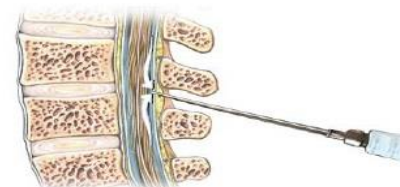


#### Study/Product Aim(s)

- The purpose of this RCT is to evaluate the safety and efficacy of cerebrospinal fluid drainage (CSFD) and to provide a preliminary clinical efficacy evaluation of combination of CSFD and elevation of Mean Arterial Pressure (MAP) in patients with acute spinal cord injury.

#### Approach

Subjects randomized to the Control Arm will receive elevation of MAP. Subjects randomized to the Experimental Arm will receive an intensive regimen of CSFD and elevation of MAP. The duration of the study treatments will be 120 hours in both arms counting from the time when the study treatment has been initiated.



Accomplishments: The major accomplishments were the completion of all study documents and the approval from the USAMRMC ORP HRPO for the main protocol and the first study site (Barrow Neurological Institute).

#### Timeline and Cost

| Activities                     | CY | 14  | 15  | 16  | 17  |
|--------------------------------|----|-----|-----|-----|-----|
| Study Start Up                 |    |     |     |     |     |
| Enrollment and Follow-up       |    |     |     |     |     |
| Enrollment and Follow-up       |    |     |     |     |     |
| Trial Termination and Analyses |    |     |     |     |     |
| Estimated Budget (\$K)         |    | 504 | 310 | 308 | 339 |

Updated: October 14, 2015

#### Goals/Milestones

Quarter 3, 2014 – Quarter 3 2015:

- ☒ Prepare Research Protocol & Study Documents
- ☐ Contract Sites & Vendors
- ☐ Obtain Regulatory Approvals
- ☒ Develop & Validate eCRF
- ☐ Initiate Sites

#### Comments:

Regulatory approvals were delayed due to additional USAMRMC ORP HRPO regulatory requests. Site Initiation Visits (SIV) were completed at two out of the three investigational sites. We expect to have both University of Arizona and University of Alabama open for enrollment by the end of Q4 2015.

#### Budget Expenditure to Date

Projected Expenditure (direct costs): \$737,923

Actual Expenditure: \$548,093

## 9. Appendices

None