



2018

## Multicenter, randomized, double-blind placebo-control intramedullary decompression for acute complete spinal cord contusion injury

Lin Chen

*Department of Neurorestoratology, Neurosurgery Center, Tsinghua University Yuquan Hospital, Beijing, China*

Yaping Feng

*Department of Neurosurgery, the 920th Hospital of the PLA Joint Logistics Support Force, Kunming, China*

Yuqi Zhang

*Department of Neurorestoratology, Neurosurgery Center, Tsinghua University Yuquan Hospital, Beijing, China*

Hongyun Huang

*Institute of Neurorestoratology, General Hospital of Chinese People's Armed Police Forces, Beijing, China  
Beijing Hongtianji Neuroscience Academy, Beijing, China*

Follow this article and additional works at: <https://tsinghuauniversitypress.researchcommons.org/journal-of-Neurorestoratology>  
*Department of Orthopaedics, Union Hospital, Tongji Medical College, Huazhong University of Science & Technology, China*

Part of the [Biomedical Engineering and Bioengineering Commons](#), [Nervous System Diseases Commons](#), [Neurology Commons](#), [Neurosciences Commons](#), and the [Neurosurgery Commons](#)

### Recommended Citation

Lin Chen, Yaping Feng, Yuqi Zhang et al. Multicenter, randomized, double-blind placebo-control intramedullary decompression for acute complete spinal cord contusion injury. *Journal of Neurorestoratology* 2018, 6(1): 165-170.

This Research Article is brought to you for free and open access by Tsinghua University Press: Journals Publishing. It has been accepted for inclusion in *Journal of Neurorestoratology* by an authorized editor of Tsinghua University Press: Journals Publishing.

CLINICAL TRIAL DESIGN

# Multicenter, randomized, double-blind placebo-control intramedullary decompression for acute complete spinal cord contusion injury

Lin Chen<sup>1</sup>, Yaping Feng<sup>2</sup>, Yuqi Zhang<sup>1</sup> (✉), Hongyun Huang<sup>3,4</sup> (✉), Xiaodong Guo<sup>5</sup>

<sup>1</sup> Department of Neurorestoratology, Neurosurgery Center, Tsinghua University Yuquan Hospital, Beijing, China

<sup>2</sup> Department of Neurosurgery, the 920th Hospital of the PLA Joint Logistics Support Force, Kunming, China

<sup>3</sup> Institute of Neurorestoratology, General Hospital of Chinese People's Armed Police Forces, Beijing, China

<sup>4</sup> Beijing Hongtianji Neuroscience Academy, Beijing, China

<sup>5</sup> Department of Orthopaedics, Union Hospital, Tongji Medical College, Huazhong University of Science & Technology, China

## ARTICLE INFO

**Received:** 15 November 2018

**Revised:** 16 December 2018

**Accepted:** 24 December 2018

© The authors 2018. This article is published with open access at <http://jnr.tsinghuajournals.com>

## KEYWORDS

intramedullary decompression surgery;  
complete acute spinal cord contusion injury;  
protocol;  
multicenter;  
RCT clinical trial

## ABSTRACT

**Introduction:** Spinal cord injury is one of the main causes of severe neurological trauma and disability. Intramedullary decompression of acute spinal cord contusion in acute phase is one of the important therapeutic exploration methods. Due to the lack of multicenter, randomized, double-blind, placebo-controlled clinical studies, true effect of this treatment remains controversial.

**Objective of the study:** This design of the study is to explore the safety and neuro-restorative effects of intramedullary decompression for acute complete spinal cord contusion injury.

**Design of the study:** We design the prospective, multicenter, randomized, double-blind placebo-controlled trial (MRDPT) for acute (less than 24 hours after injury) spinal cord contusion injury. Sixty patients with acute complete spinal cord contusion injury (20 in cervical 4 to thoracic 1, 20 in thoracic 2 to thoracic 9, and 20 in thoracic 10 to lumbar vertebra 1) are selected according to the selected conditions. All patients receive conventional treatments such as reduction and fixation of spinal fractures and/or spinal spondylolisthesis, bone external decompression relieves spinal cord compression. At the same time, group A ( $n = 30$ , 10 of each segment group) undergoes intramedullary decompression surgery and group B ( $n = 30$ ) does not undergo intramedullary decompression. All relevant functional changes before, after, and during the follow-up period are recorded to ensure objective evaluation of the results of the treatment.

**Ethics and dissemination:** The clinical study protocol and consent form were approved by China Branch of International Association of Neurorestoratology and the ethics committees of the hospitals which join this trial. Registration No. of this study is ChiCTR1800020458. Findings will be published in peer-reviewed journals.

## 1 Background and introduction

Spinal cord injury (SCI) is one of the main causes of severe neurological trauma and disability. Patients

with acute complete SCI can cause complete loss of sensory, motor and sphincter function below the injured segment, which seriously affects the patients' quality of life and imposes a huge burden on families and

Corresponding authors: Yuqi Zhang, E-mai: [yuqi9597@sina.com](mailto:yuqi9597@sina.com); Hongyun Huang, E-mail: [hongyunh@gmail.com](mailto:hongyunh@gmail.com)

society [1, 2].

At present, neurorestorative therapy such as cell therapy, nerve bridges, neuromodulation and brain-computer interface can improve the function for patients with SCI to a certain extent, but the effective degree of neurorestoration still needs to be improved [3–8]. The professional circle has also been searching for better neurorestorative methods. Procedure of intramedullary decompression preventing the spinal cord compartment syndrome has long history [9–16]. It may be one of the important potential therapeutic methods for acute spinal cord contusion injury [15–23]. Due to the lack of multicenter, randomized, double-blind, controlled clinical studies, so far this treatment technology remains controversial whether it is truly effective.

On May 26, 2018, the China Branch of International Association of Neurorestoratology (IANR) discussed and decided to organize a clinical trial which is prospective multicenter, randomized, double-blind intramedullary decompression for acute complete spinal cord contusion injury. The aim of this study is to explore the safety and neurorestorative effects of intramedullary decompression for patients with acute complete spinal cord contusion injury.

## 2 Research protocol

This trial is designed and run by The China Branch of International Association of Neurorestoratology (IANR).

This trial got approved by the ethics committee of participating hospitals.

### 2.1 Preliminary work

Participated hospitals focus on holding meetings and training.

The evaluation criteria focus on training and discussion of clinical examination and evaluation criteria for acute complete spinal cord contusion injury (less than 24 hours after injury), which include neurological physical strength score, ASIA-SCI score, IANR-SCI function evaluation scale, and intraspinal decompression surgery operation method. The evaluation, data collection and operative methods should be surely kept with same or unifying standards.

### 2.2 Study design

That is a prospective, multicenter, randomized, double-blind controlled study (MRDCS) of intramedullary decompression for complete acute (less than 24 hours after injury) spinal cord contusion injury (IDCASCSCI). Sixty patients suffering from acute complete spinal cord injury (20 with cervical segment 4-thoracic 1, 20 with thoracic 2-thoracic 9, and 20 with thoracic 10-lumbar vertebra 1) are collected according to the selected conditions and randomized dividing into two groups in above listed three segment injury area. All patients receive conventional treatments including reduction and fixation of spine fractures and/or spine spondylolisthesis, bone external decompression relieves spinal cord compression. At the same time, group A ( $n = 30$ ) undergoes intramedullary decompression and group B ( $n = 30$ ) does not undergo intramedullary decompression. All relevant evaluated functions are recorded before, after, and during the follow-up period.

### 2.3 Subjects

Number of samples: 60 patients who meet the inclusion criteria with acute (less than 24 hours after injury) complete spinal cord contusion injury in three injured areas are involved.

#### 2.3.1 Inclusion criteria

- (1) Age: 18 to 60 years old; fully capable; willing to participate in the study and can participate in the follow-up of this study.
- (2) The spinal cord injury score in three injury areas was ASIA-A grade: 20 in cervical 4-thorax 1, 20 in thoracic vertebra 2-thoracic vertebra 9, and 20 in thoracic 10-lumbar vertebra 1, other neurologically stable.
- (3) Non-coma patients, cooperate when checking.

#### 2.3.2 Exclusion criteria

- (1) Coma or accompanied by severe brain injury.
- (2) Accepting other clinical trials.
- (3) Blood glucose  $< 2.7$  mmol/L or  $> 22.2$  mmol/L. Blood pressure  $> 150/90$  mmHg, does not continue to decline after the medication.
- (4) Heart, lung, liver or kidney failure, or blood transfusion due to severe anemia. Or a disease

that has been diagnosed (such as a mental illness), it is difficult to complete a study for up to 1 year.

- (5) The patient or his or her guardian is unable or unwilling to sign an informed consent form.
- (6) Completely transverse injury of the spinal cord.
- (7) Spinal cord firearm or sharp weapon injury.
- (8) Spinal cord shock.
- (9) More than 24 hours after injury or incomplete injury.

### 2.3.3 Subject withdrawal criteria

- (1) The subject formally withdraws their consent (in writing).
- (2) The complication that is not caused by this study, and the comorbidity will affect the research effect.
- (3) Patients were treated with unconventional drugs (neurotrophic factors, etc.) that should be banned in the study during the observation period; serious adverse reactions of drugs unrelated to the study occurred; serious physical illnesses occurred; and failure to follow the doctor's advice. Failure to adhere to the completion of follow-up studies. The terminating researchers are not included in the final result statistics.
- (4) Postoperative spinal or intracranial infection.
- (5) Death of a patient unrelated to the study.

**Signed Informed Consent Form:** All selected patients are signed a written informed consent form from the study subject or their legal guardian.

## 2.4 Research methods

Comprehensive treatment of acute complete spinal cord contusion injury is an essential for patients involving in this clinical study. They will be ensured not to delay routine treatment or affect the prognosis as far as possible due to participation in the study, in line with the principles of science and ethics.

### 2.4.1 Intervention program

- (1) Selected patients: acute spinal cord contusion injury with ASIA A in cervical vertebra 4-thoracic vertebra 1, thoracic vertebra 2-chest 9 and thoracic spine 10-lumbar 1.
- (2) Sample size: 20 people in each injury segment group, a total of 60 patients.
- (3) Patients in each segment group were randomly

divided into 2 sub-groups, 10 patients in each sub-group.

- (4) Routine basic treatment: spinal fractures and/or spondylolisthesis are routinely restored, fixed, and to remove the extramedullary bone fragments, intervertebral discs, ligamentum flavum and hematoma in the spinal cord injury segment for all patients and were enrolled in the routine neurological rehabilitation treatment of spinal cord injury for 1 year: (a) Group 1 conventional basic treatment + intramedullary decompression; (b) Group 2 conventional basic treatment.

### 2.4.2 Operation technique of intramedullary decompression

- (1) Following extramedullary decompression, the intramedullary surgical procedures described below should be under the operating microscope.
- (2) Suspend the dura mater, and cut the dura mater with the spinal cord injury segment as the center to expose to the upper and lower normal spinal cord. If the dura mater is damaged, it is enlarged along the middle longitudinal line.
- (3) If the spinal cord is contused, the spinal cord is swollen with the most severe blood vessels. The spinal cord is cut longitudinally with a sharp blade to a length of about 0.3–0.5 cm. The nerve stripper is used to gently scrape the hematoma and wash the shredded necrotic spinal cord tissue by using 0.9% sodium chloride. Since the injury boundary is often unclear, the intramedullary decompression should be stopped when the spinal cord resumes pulsation; if the spinal cord has been exposed to laceration, the injured spinal cord tissue and hematoma can be washed directly by using 0.9% sodium chloride.
- (4) After intramedullary decompression and pulsation recovery of the spinal cord, intermittent or continuous suture of the dura mater should be done. If the dural defect or local spinal cord pressure is high, artificial dura mater should be used and enlarged to suture the dura in order to prevent cerebrospinal fluid leakage, residual spinal cord and surrounding tissue to form scar adhesion, etc.
- (5) The rest of the surgical procedures are routinely processed.

### 2.4.3 Observing items

#### Neurological physical strength score:

- ASIA-SCI score;
- IANR-SCI Function Assessment Scale;
- Kunming Walking Classification (KLS);
- MRI scan: thin scan at the lesion (2mm), DTI.

**There are 5 time observation: before treatment, and 1 month, 3 months, 6 months, 1 year after treatment.**

#### Check item:

##### Pre-treatment examination (before treatment):

Routine laboratory tests (blood routine, coagulation mechanism, urine routine, liver function, renal function, hepatitis B, anti-HIV, anti-HCV, syphilis antibody, chest X-ray, ECG);

- MRI examination;
- Neurological physical strength score;
- ASIA-SCI score;
- IANR-SCI Function Assessment Scale;
- Video of physical examination;
- Photo of special signs;

**1 month, 3 months, 6 months, and 12 months after treatment:**

Routine laboratory tests (blood routine, liver function, renal function, hepatitis B, anti-HIV, anti-HCV, syphilis antibodies);

- Neurological physical strength score;
- ASIA-SCI score;
- IANR-SCI Function Assessment Scale;
- Kunming Walking Classification (KLS);
- Medical examination video;
- Patient sign photo.

##### Follow-up plan:

Patients will be regularly followed up and evaluated 1 year after treatment. At the beginning of the study, we will get: (1) patient's mailing address, phone number, email address and WeChat. (2) Contact telephones such as home phones and mobile phones. At the beginning of the follow-up, the patient will be notified by phone in advance. The researchers will contact the patient at least once a month and make adjustments to the study plan if necessary.

### 2.4.4 Random method and blind method:

According to the uniform serial number and random double-blind form for the eligible patients, two groups

of patients are to be treated in the enrolled hospitals. The independent third-party does evaluation in pre-treatment, post-treatment following-up.

**Safety evaluation:** All selected patients should record adverse events after treatment, such as fever, new neurological symptoms, etc.

## 3 Possible complications and treatment strategies

### 3.1 Complications

They include surgical area bleeding, cerebrospinal fluid leakage, operative injury, and rejection of implants.

### 3.2 Countermeasures

The operative procedures must be precise and gentle. Gelatin sponge and cotton pad is used to stop bleeding. Stitching and repairing the dura mater should be strict.

Postoperative complications such as cerebrospinal fluid leakage, surgical infection should be prevented through strictly aseptic and high quality dural repair.

## 4 Data analysis

The SPSS statistical software will be used for data analysis of this subject research. One-way ANOVA was used for the measurement data plan, and there was a significant difference at  $P < 0.05$ .

## 5 Attribution of this research results

This study, IDCASCCI-MRCS, was organized and implemented by the China Branch of International Association of Neurorestoratology (IANR), but the results of each project belonged to the specific units and individuals involved in the study. The size of the contribution, that is, the number of cases in each selected hospital, determines the order of the articles and achievements. The postscript of the article indicates that the China Branch of International Association of Neurorestoratology (IANR) approves and leads the implementation, and lists supporting units of research fee source.

## 6 Patient compensation

The patients in treatment group may get some benefits in this trial. The patients in control group may be no longer able to get those benefits if the results of treatment are confirmed to be statistically better than that of control at the end of the study. The China Branch of IANR will have priority to give other effective treatment if patients in the control group are willingness to get.

## 7 Discussion

This study IDCASCCI-MRCS is the first multi-center randomized double-blind clinical study for acute (less than 24 hours after injury) spinal cord contusion injury in the world, and hopes to obtain a clearer conclusion.

The characteristics of this study are:

- (1) Although the study of intramedullary decompression for acute spinal cord injury has been studied for decades, it is still controversial. The main reason is that most of the results are single-center studies and lacking a higher level of evidence-based medical evidence. Therefore, this trial is designed a multicenter randomized double-blind and placebo-control clinical study.
- (2) The SCI types are complex, including contusions, bullet wounds, transverse injuries, ischemic injuries, and traction injuries. This study tests whether the spinal cord contusion injury (the most common cases) in clinical practice can get benefits from intramedullary decompression. The results will have more practical guiding significance for complete acute SCI [15–23].
- (3) In this study, the patient's inclusion criteria and exclusion criteria are clear, reducing the confusing effects on the final outcome judgment.
- (4) The third-party independent evaluation in this study can make the results more objective
- (5) The operative procedure of this study was performed under a microscope, which can avoid the extra procedure damage and affect the results.

## 8 Ethics and dissemination

The clinical study (IDCASCCI-MRCS) protocol and

consent form were approved by China Branch of International Association of Neurorestoratology and the ethics committee of the hospitals which join this study. Registration No. of this study is ChiCTR1800020458. Findings will be published in peer-reviewed journal.

## Disclosure

The authors report no conflicts of interest in this work.

## References

- [1] Eckert MJ, Martin MJ. Trauma: Spinal cord injury. *Surg Clin North Am.* 2017, **97**(5): 1031–1045.
- [2] Kumar R, Lim J, Mekary RA, et al. Traumatic spinal injury: Global epidemiology and worldwide volume. *World Neurosurg.* 2018, **113**: e345–e363.
- [3] Gazdic M, Volarevic V, Harrell CR, et al. Stem cells therapy for spinal cord injury. *Int J Mol Sci.* 2018, **19**(4): E1039.
- [4] Huang H, Young W, Chen L, et al. Clinical cell therapy guidelines for neurorestoration (IANR/CANR 2017). *Cell Transplant.* 2018, **27**(2): 310–324.
- [5] Fox IK, Miller AK, Curtin CM. Nerve and tendon transfer surgery in cervical spinal cord injury: individualized choices to optimize function. *Top Spinal Cord Inj Rehabil.* 2018, **24**(3): 275–287.
- [6] Yozbatiran N, Keser Z, Davis M, et al. Transcranial direct current stimulation (tDCS) of the primary motor cortex and robot-assisted arm training in chronic incomplete cervical spinal cord injury: A proof of concept sham-randomized clinical study. *Neuro Rehabilitation.* 2016, **39**(3): 401–411
- [7] Ajiboye AB, Willett FR, Young DR, et al. Restoration of reaching and grasping movements through brain-controlled muscle stimulation in a person with tetraplegia: a proof-of-concept demonstration. *Lancet.* 2017, **389**(10081): 1821–1830.
- [8] Lebedev MA, Nicolelis MA. Brain-machine interfaces: from basic science to neuroprostheses and neurorehabilitation. *Physiol Rev.* 2017, **97**(2): 767–837.
- [9] Galanda M, Nádvořník P, Fröhlich J. Surgical treatment of spasticity in spinal cord injuries (critical comments on longitudinal myelotomy). *Bratisl Lek Listy.* 1974, **61**(5): 589–594.
- [10] Yamada S, Perot PL Jr, Ducker TB, et al. Myelotomy for control of mass spasms in paraplegia. *J Neurosurg.* 1976, **45**(6): 683–691.
- [11] Borovich B, Peyser E, Gruskiewicz J. Acute central and

- intermediate cervical cord injury. *Neurochirurgia (Stuttg)*. 1978, **21**(3): 77–84.
- [12] Wu G, Zhao L. *Field Surgery*. Shanghai Scientific and Technologic Press, 1981.
- [13] Tachibana S, Okada K, Ohwada T, et al. Posterior longitudinal myelotomy as a surgical treatment of acute cervical spinal cord injury. *No Shinkei Geka*. 1984, **12**(2): 183–188.
- [14] Koyanagi I, Iwasaki Y, Isu T, et al. Myelotomy for acute cervical cord injury. Report of four cases. *Neurol Med Chir (Tokyo)*. 1989, **29**(4): 302–306.
- [15] Cao XJ, Feng SQ, Fu CF, et al. Repair, protection and regeneration of spinal cord injury. *Neural Regeneration Research* 2015, **10**(12): 1953–1975.
- [16] Qu YZ, Luo Z, Guo XD, et al. The durotomy or myelotomy for the spinal cord extensive swelling with/without intramedullary hemorrhage. *Chinese Journal of Orthopaedics* 2015, **35**(7): 707–713.
- [17] Zhu H, Feng YP, Young W, et al. Early neurosurgical intervention of spinal cord contusion: an analysis of 30 cases. *Chin Med J (Engl)*. 2008, **121**(24): 2473–2478.
- [18] Kim M, Hong SK, Jeon SR, et al. Early ( $\leq 48$  Hours) versus Late ( $>48$  Hours) surgery in spinal cord injury: Treatment outcomes and risk factors for spinal cord injury. *World Neurosurg*. 2018, **118**: e513–e525.
- [19] Sewell MD, Vachhani K, Alrawi A, et al. Results of early and late surgical decompression and stabilization for acute traumatic cervical spinal cord injury in patients with concomitant chest injuries. *World Neurosurg*. 2018, **118**: e161–e165.
- [20] Ahuja CS, Schroeder GD, Vaccaro AR, et al. Spinal cord injury-what are the controversies? *J Orthop Trauma*. 2017, **31**(Suppl 4): S7–S13.
- [21] Tykocki T, Poniowski Ł, Czyż M, et al. Intraspinous pressure monitoring and extensive duroplasty in the acute phase of traumatic spinal cord injury: A systematic review. *World Neurosurg*. 2017, **105**: 145–152.
- [22] Huang H, Sun T, Chen L, et al. Consensus of clinical neurorestorative progresses in patients with complete chronic spinal cord injury. *Cell Transplant*. 2014, **23**: S1–13.
- [23] Feng Y, Sun T, Chen L, et al. Clinical therapeutic guideline for neurorestoration in spinal cord injury (Chinese version 2016). *J Neurorestoratology* 2017, **5**: 73–83.