

Positioning Method Based on Infrared Spectrum Detection of Neurotransmitters for Electrical Nerve Stimulation after Spinal Cord Injury

Nie Min, Yang Guang

School of Communication and Information Engineering
Xi'an University of Posts and Telecommunications
Xi'an, China

Abstract. Spinal cord injury is one of the most painful wounds in human bodies, and also is a problem difficult to solve in the medical science field. Electrical nerve stimulation bridging is a hot research topic for limb function reconstruction after spinal cord injury, most important of which is to determine the location of the “Pier”. In other words, how to find the accurate position of the stimulation is the key factor of the nerve bridging. This study proposes a novel method based on infrared spectrum detection technology, by measuring the spectrum absorption of 6 kinds of neurotransmitters in the injured area, to determine the activity of neurons in spinal cord injured areas quickly and accurately, thus to determine the exact position of the nerve stimulation. Animal experiment results show that our method has the advantages of accurate, reliable, efficient, with a detection rate of 96.67%. It provides the basis of positioning for electrical nerve stimulation bridging after spinal cord injury to reconstruct the limb function of the patients.

Keywords: spinal cord injury; infrared spectrum detection; activity of neurons; electrical nerve stimulation; positioning for nerve bridging

1 Introduction

Sports hurts, mechanical hits, falling down from high places or other reasons, could result in human spinal cord injury^[1-3] (SCI). In recent years, with the rapid growth of the number of the vehicles, traffic accidents occur frequently, which cause a significant increase in the number of the patients who suffered spinal cord injuries. SCI interrupts the transmission channel of human neural signals^[4-7]. Most patients become paraplegic, and lose their limb feeling and the ability to care for themselves. These may finally cause a lifelong physically disabilities. As one of the most serious wounds in human body, SCI brings great mental anguish and economic burden not only to the patient himself, but also to the family and the society.

Nerve regeneration and neural stem cell transplantation are the frontier research in the field of SCI^[8-12]. Currently in the medical field, it is mainly through drug therapy, surgery and nerve graft to solve the problem of nerve regeneration^[13-16]. However,

due to the complexity of the structure and conduction of nerve, these studies have not yet achieved a breakthrough. Recovery of limb functions in patients with SCI is still a difficult problem in the world. Recently, electrical nerve stimulation bridging becomes a hot topic to help the reconstruction of limb functions after SCI. Related study has achieved encouraging results^[17~21]. Through electrical stimulation, drug treatment and rehabilitation exercise, some patients have recovered the pain feeling and part of the physical function gradually^[22~25].

In electrical nerve stimulation bridging, how to determine the position of electrical stimulation accurately is the key issue. However, research on this issue has not been carried out^[26~28]. Since it is bridging, we must first determine the exact position of the “pier”. In other words, how to find the exact position of electrical stimulation of the nerves is the key to success. For this purpose, we adopt infrared spectrum detection technology, by measuring the spectrum absorption of 6 kinds of neurotransmitters in the injured area, to determine the activity of neurons in spinal cord injured area quickly and accurately, thus to determine the exact position of the nerve stimulation. The results of animal experiments show a detection rate of 96.67%. This method is proved to be accurate, reliable, efficient and effective.

The rest of this paper is organized as follows. In section 2, we summarize the conventional routine examination methods for SCI. In section 3, we analyze the advantages and disadvantages of the conventional examinations and diagnosis. In section 4, we provide the method and system implementation for testing the activity of neurons in SCI areas based on infrared spectrum detection of neurotransmitters. In section 5, we give the neuronal activity detection principle based on Infrared spectrum analysis. In section 6, we give the procedure of our infrared spectrum detection method. In section 7, we describe the animal experiments using our method and the results of the experiments. In section 8, we give a brief discussion of our method and other method in principle. In section 9, we give the conclusion of this paper.

2 Conventional routine examination methods for SCI

Conventional routine clinical examinations^[32-34] to diagnose SCI usually use the following methods and equipment:

(1) X-ray examination. Regularly it needs to make the lateral view of the spine, and the oblique view when necessary. When inspecting the photo, measure the height of the front of the vertebra and the back of the vertebra, then compare the results with adjacent vertebra; measure the distance between the pedicles and measure the width of the vertebra; measure the spinous pitch and the width of the intervertebral disc gap, and compare the results with adjacent vertebra; measure the height of lateral pedicle. Through the X-ray examination, the location and type of spinal fracture can be determined roughly.

(2) CT (computer tomography) examination. It is helpful to determine the degree that the displaced fracture fragments invades the spinal canal, and to find the changes of the bone blocks or the intervertebral discs that have entered into the spinal canal.

(3) MRI (Magnetic resonance imaging) examination. It is of great value to determine the degree of the SCI. MRI can display early spinal cord injury edema, hemorrhage, and also can display spinal cord compression, spinal cord transaction, spinal cord atrophy and cystic lesions after SCI.

(4) SEP (Somatosensory Evoked Potential) and MEP (Motor Evoked Potential) examination. This is a test method to examine the conduction function of the sensory system of the body, and is help to determine the degree of SCI.

(5) Jugular venous pressure experiments and myelography. Jugular venous pressure experiment is of certain value to judge the degree of spinal cord injury and compression. Myelography is meaningful to diagnose the old traumatic spinal stenosis.

3 Advantages and disadvantages of the conventional examinations and diagnosis

Limited by the current conditions, only five kinds of routine examinations above can be carried out in hospitals.

The advantages are as follows.

(1) These methods are applicable to the condition that the patients with SCI go to hospital in time. They provide first-hand information for clinical diagnosis and treatment.

(2) They can be used to determine the degree of acute SCI immediately and accurately, thus to draw up the emergency treatment plan.

The disadvantages are as follows.

(1) These methods are not applicable to patients who have been spinal cord injured for many years, and it is difficult to accurately observe the injured spinal cord cavity and crusting.

(2) They can not provide comparable image data for the recovery of the patients.

(3) They can neither reflect the activity of the neurons in spinal cord injured areas, nor the types of the neurotransmitter in the injured areas. For these reasons, it is difficult to give a targeted treatment plan.

(4) It is hard to determine the position where the neurons live or apoptose accurately.

4 Method and system implementation for testing the activity of neurons in spinal cord injured areas based on infrared spectrum detection of neurotransmitters

In order to detect the activity of neurons in spinal cord injured area of patients who experienced long-term paraplegia, through which to determine the position of electrical nerve stimulation, we use infrared spectrum analysis techniques. We detect the infrared absorption spectrum of 6 kinds of neurotransmitters in SCI area, then we analyze the distribution of wavelengths of infrared light absorption of neurotransmit-

ters including GABA (gamma-aminobutyric acid), Glu (Glutamate acid), 5-HT (5 hydroxytryptamine), Ach (acetylcholine), NE (norepinephrine) and DA (dopamine). According to the results, it is possible to accurately determine the neuronal activity in injured areas of patients. This method has high detection accuracy, detection time is short, analysis is quick, and there is no new trauma. It provides important basis to analyze the conditions of SCI and to take targeted recovery treatments for patients.

Fig.1 is the structure of the system used to implement the detection of the neurons' activity in SCI area based on infrared spectrum analysis.

In Fig.1, A means the infrared spectrum database, B means the computer, C means the monitor, D means the infrared spectrometer, F means the patient with SCI.

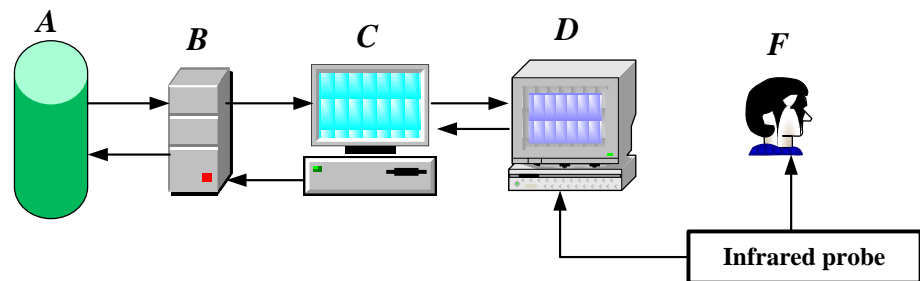


Fig. 1. Structure of the system used to detect the neurons' activity in SCI area. A means the infrared spectrum database, B means the computer, C means the monitor, D means the infrared spectrometer, F means the patient with SCI.

The function of A is to store detailed infrared absorption spectrum data of 6 kinds of neurotransmitters in normal bodies. These neurotransmitters are: GABA, Glu, 5-HT, Ach, NE, and DA. Each kind of neurotransmitter has a unique infrared absorption spectrum. These important data are stored in database, ready to be read and written by the computer in any time.

Computer B has the responsibility to calculate and analyze the infrared spectrum data. It gets data from A, then analyzes and compares the data.

The Monitor C displays the infrared waveforms and the calculation results.

The infrared spectrometer D detects the infrared signals of the SCI area of the patients.

5 Neuronal activity detection principle based on Infrared spectrum analysis

The 6 kinds of neurotransmitters GABA, Glu, 5-HT, Ach, NE, and DA in normal human body are the indispensable substances to maintain a normal neural activity. Each kind of neurotransmitter is produced by neurons. If all kinds of the neurotransmitters exist, then the neurons act normally. If some of the neurotransmitters do not

exist, then the neurons apoptose. So, we can determine the activity of neurons by detecting the existence of the neurotransmitters^[28-31].

When an infrared beam with a continuous wavelength goes through neurotransmitters, molecules of different neurotransmitters will resonate with the infrared signal if they have the same vibration frequency. This will result in energy absorption^[9]. After the molecules of neurotransmitters have absorbed infrared energy, they produce molecular vibrations and energy transitions. Infrared spectrum of the corresponding wavelength will be absorbed by the molecules of the neurotransmitters^[10]. Each kind of neurotransmitter has a unique molecule structure, so the distribution of infrared absorption spectrum is unique. Thus, infrared absorption wavelength distributions of six kinds of neurotransmitters have six different infrared absorption spectrums in normal bodies. Therefore, by detecting the infrared absorption spectrum of neurotransmitters, we can accurately determine the activity of neurons^[11-13].

6 Detection procedure

First step, wipe the spinal cord injured area of the patient with alcohol swab to make it disinfected; second step, place the infrared probe in SCI area, record the infrared waveform data in different test points with the infrared spectrometer, then record the position of the test points; third step, use the computer to get the infrared absorption spectrum data of all kinds of neurotransmitters previously stored in the database A, compare the infrared data obtained from test with the data stored in database A; fourth step, display results of the analysis and the test, print the results when necessary; fifth step, record the correlations between the result of each detection and the position of each test point; sixth step, extract the accurate information of the neuronal activity in different SCI areas according to above procedures, thus to provide accurate positioning information for electrical nerve stimulation bridging.

7 Animal experiments

7.1 The formation of the reference samples in the database

The reference samples stored in the database are the infrared absorption spectrums of 6 kinds of neurotransmitters and the combined spectrums of some of the neurotransmitters of healthy SD rats.

Fig.2 to Fig.7 are the infrared absorption spectrums of six kinds of neurotransmitters GABA, Glu, 5-HT, Ach, NE, and DA. The X-axis of Fig.2 to Fig.7 is the infrared power spectrum of the neurotransmitter, and the unit is dbm. The Y-axis of Fig.2 to Fig.7 is wavelength, and the unit is nm.

To get the infrared absorption spectrums of the six kinds of neurotransmitters, we first extract the mixed neurotransmitters from the spinal cords of healthy SD rats. Then, we separate each neurotransmitter from the mixture through medical method. After these procedures, we use the infrared spectrometer to measure the infrared absorption spectrum of each neurotransmitter. To eliminate the interference of noise, we

use some data processing method such as wavelet method. At last, we get Fig.2 to Fig.7.

Because of the different structures of different molecules, each kind of neurotransmitter has a unique infrared absorption spectrum. Since the neurotransmitters are produced by the neurons, then through the infrared spectrum analysis technology, we can get the survival information of the neurons in SCI areas, thus to provide accurate positioning information for electrical nerve stimulation.

Using the same method, we also get the combined spectrums of some of the neurotransmitters, for example, the combined spectrum of GABA and Glu, or the combined spectrum of GABA, 5-HT and Ach. These combined spectrums are also stored in the database as reference samples. Fig.8 is the combined infrared absorption spectrum of 6 kinds of neurotransmitters of SD rats.

By comparing the infrared absorption spectrums of the spinal cord injured animals with the reference samples, we can determine the activity of the SCI areas.

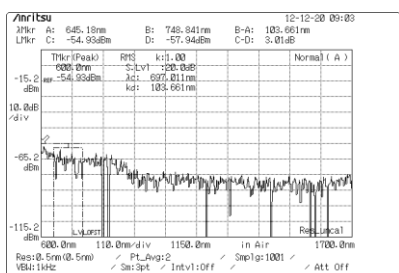


Fig.2. Infrared absorption spectrum of GABA

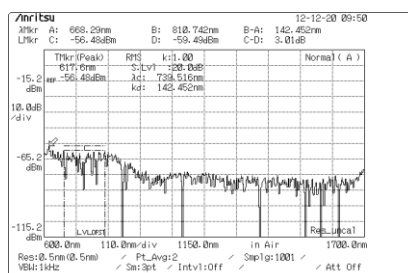


Fig.3. Infrared absorption spectrum of GLU

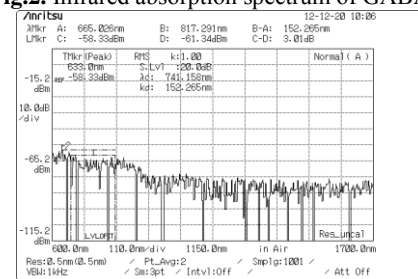


Fig.4. Infrared absorption spectrum of 5-HT

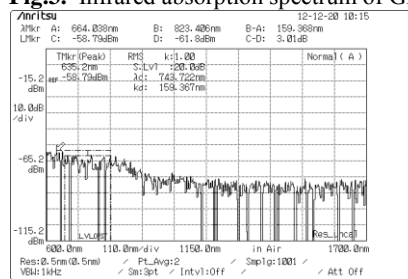


Fig.5. Infrared absorption spectrum of Ach

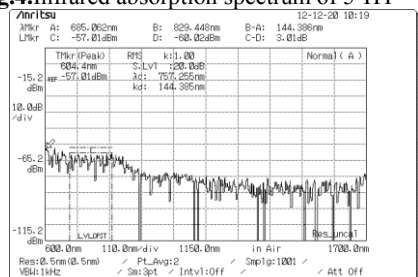


Fig.6. Infrared absorption spectrum of NE

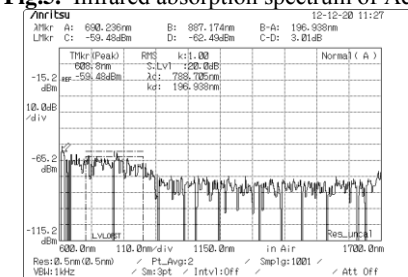


Fig.7. Infrared absorption spectrum of DA

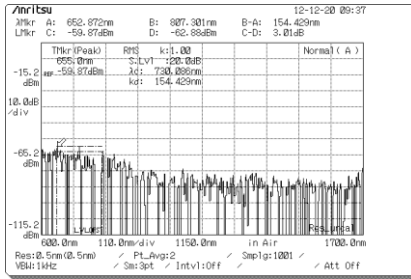


Fig.8. Combined infrared absorption spectrum of SD rat

7.2 The results of the animal experiments

The animal experiments use 60 adult SD rats provided by School of Medicine of Xi'an Jiaotong University. The weights of them are 280 to 300 grams. The rats are divided into two groups, the experimental group (group A) and the control group (group B), each group has 30 rats. All of the 60 rats were transected at the T10 to T11 vertebrae, so as to make a spinal cord injury model. Two weeks later, the electrical stimulation bridging was performed in both groups. For group A, we use the infrared absorption spectrum test method to detect the activity of the neurotransmitters in SCI areas, through which to determine the accurate position of the electrical stimulation. For group B, we only perform the electrical stimulation in the area near to the T10 to T11 vertebrae, and no positioning is used.

Six weeks later, there are 29 rats in group A who have rapid escape behavior on acupuncture, 1 rat does not have any response behavior. In group B, there are 11 rats who have rapid escape behavior on acupuncture, 19 rats do not have any response behavior. Fig.9 is the recovery results of group A and group B.

This experiment shows that, the electrical nerve stimulation bridging has obvious effect on the limb recovery after SCI. Use the infrared spectrum analysis to determine the activity of the neurons in SCI area, so as to provide the accurate positioning information for electrical stimulation, is a key technology for the limb function recovery.

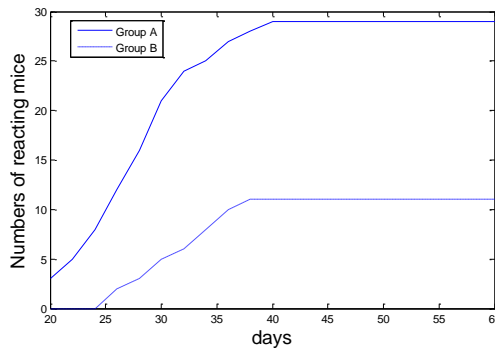


Fig.9. Recovery results of group A and group B in the animal experiments.

8 Discussion

Due to the limitation of experiment conditions, we have not done the experiments using the conventional positioning methods mentioned in section 2. We can only give an analysis in principle. The conventional examination methods for SCI such as X-ray examination and MRI can only tell the physical morphology of the SCI area. They can not tell the activity of the neurons in spinal cord injured area. It is blind to some extent to only use the physical morphology as the basis for the positioning of electrical stimulation in nerve bridging. For example, even the physical morphology of the vertebra is normal, while the activity of the neurons in it may be lost. So the effects of these methods in electrical stimulation nerve bridging are similar to the method used in the animal experiments of group B.

9 Conclusion

Electrical nerve stimulation bridging brings hope to the recovery of limb functions after spinal cord injury for patients. How to determine the position of the stimulation is the key factor of nerve bridging. For this purpose, we proposed a method based on infrared absorption spectrums detection of neurotransmitters to determine the accurate position of the electrical stimulation. Animal experiments show this method is accurate, reliable and obvious.

Acknowledgements

We thank Dr. Yan Yaosheng and Dr. Han Shuiping for their help in experiments. This work was supported by the National Natural Science Foundation of China (Grants No. 61172071, 61201194).

References

1. Susan Harkema, Yury Gerasimenko, Jonathan Hodes, Joel Burdick, Claudia Angeli, Yangsheng Chen, Christie Ferreira, Andrea Willhite, Enrico Rejc, Robert G Grossman, V Reggie Edgerton, Effect of epidural stimulation of the lumbosacral spinal cord on voluntary movement, standing, and assisted stepping after motor complete paraplegia: a case study. *www.thelancet.com* Vol.377. June 4, 2011
2. Grillner S. Neurobiological bases of rhythmic motor acts invertebrates. *Science* 1985; 228: 143–49.
3. Fuentes R, Petersson P, Siesser WB, Caron MG, Nicolelis MA. Spinal cord stimulation restores locomotion in animal models of Parkinson's disease. *Science* 2009; 323: 1578–82.
4. Gerasimenko Y, Roy RR, Edgerton VR. Epidural stimulation: comparison of the spinal circuits that generate and control locomotion in rats, cats and humans. *Exp Neurol* 2008; 209: 417–25.
5. Rossignol S, Barriere G, Frigon A, et al. Plasticity of locomotor sensorimotor interactions after peripheral and/or spinal lesions. *Brain Res Rev* 2008; 57: 228–40.

6. Grillner S, Wallen P. Central pattern generators for locomotion, with special reference to vertebrates. *Ann Rev Neurosci* 1985;8: 233–61.
7. Grillner S. The motor infrastructure: from ion channels to neuronal networks. *Nat Rev Neurosci* 2003; 4: 573–86.
8. Grillner S, Zangger P. On the central generation of locomotion in the low spinal cat. *Exp Brain Res* 1979; 34: 241–61.
9. de Leon RD, Hodgson JA, Roy RR, Edgerton VR. Locomotor capacity attributable to step training versus spontaneous recovery after spinalization in adult cats. *J Neurophysiol* 1998; 79: 1329–40.
10. de Leon RD, Hodgson JA, Roy RR, Edgerton VR. Full weight-bearing hindlimb standing following stand training in the adult spinal cat. *J Neurophysiol* 1998; 80: 83–91.
11. Barbeau H, Rossignol S. Recovery of locomotion after chronic spinalization in the adult cat. *Brain Res* 1987; 412: 84–95.
12. Courtine G, Gerasimenko Y, van den Brand R, et al. Transformation of nonfunctional spinal circuits into functional states after the loss of brain input. *Nat Neurosci* 2009; 12: 1333–42.
13. Ichihama RM, Courtine G, Gerasimenko YP, et al. Step training reinforces specific spinal locomotor circuitry in adult spinal rats. *J Neurosci* 2008; 28: 7370–75.
14. Wernig A, Muller S. Laufband locomotion with body weight support improved walking in persons with severe spinal cord injuries. *Paraplegia* 1992; 30: 229–38.
15. Wernig A, Nanassy A, Muller S. Maintenance of locomotor abilities following Laufband (treadmill) therapy in para- and tetraplegic persons: follow-up studies. *Spinal Cord* 1998; 36: 744–49.
16. Harkema S, Schmidt-Read M, Lorenz D, Edgerton VR, Behrman A. Balance and ambulation improvements in individuals with chronic incomplete spinal cord injury using locomotor training-based rehabilitation. *Arch Phys Med Rehab* (in press).
17. Dietz V, Colombo G, Jensen L. Locomotor activity in spinal man. *Lancet* 1994; 344: 1260–63.
18. Harkema SJ, Hurley SL, Patel UK, Requejo PS, Dobkin BH, Edgerton VR. Human lumbosacral spinal cord interprets loading during stepping. *J Neurophysiol* 1997; 77: 797–811.
19. Harkema SJ. Plasticity of interneuronal networks of the functionally isolated human spinal cord. *Brain Res Rev* 2008; 57: 255–64.
20. Dimitrijevic MR, Gerasimenko Y, Pinter MM. Evidence for a spinal central pattern generator in humans. *Ann NY Acad Sci* 1998; 860: 360–76.
21. Gerasimenko Y, Daniel O, Regnaud J, Combeaud M, Bussel B. Mechanisms of locomotor activity generation under epidural spinal cord stimulation. In: Dengler R, Kossev A, eds. *Sensorimotor control*. Washington, DC: IOS Press, 2001: 164–71.
22. Minassian K, Gilge B, Rattay F, et al. Stepping-like movements in humans with complete spinal cord injury induced by epidural stimulation of the lumbar cord: electromyographic study of compound muscle action potentials. *Spinal Cord* 2004; 42: 401–16.
23. Minassian K, Persy I, Rattay F, et al. Human lumbar cord circuitries can be activated by extrinsic tonic input to generate locomotor-like activity. *Hum Mov Sci* 2007; 26: 275–95.
24. Gilge B, Minassian K, Rattay F, et al. Initiating extension of the lower limbs in subjects with complete spinal cord injury by epidural lumbar cord stimulation. *Exp Brain Res* 2004; 154: 308–26.
25. Kuhn RA. Functional capacity of the isolated human spinal cord. *Brain* 1950; 73: 1–51.
26. Nadeau S, Jacquemin G, Fournier C, Lamarre Y, Rossignol S. Spontaneous motor rhythms of the back and legs in a patient with a complete spinal cord transection. *Neurorehabil Neural Repair* 2010; 24: 377–83.

27. Calancie B. Spinal myoclonus after spinal cord injury. *J Spinal Cord Med* 2006; 29: 413–24.
28. Marino RJ, Barros T, Biering-Sorensen F, et al. International standards for neurological classification of spinal cord injury. *J Spinal Cord Med* 2003; 26 (suppl 1): S50–56.
29. Beres-Jones JA, Johnson TD, Harkema SJ. Clonus after human spinal cord injury cannot be attributed solely to recurrent muscle-tendon stretch. *Exp Brain Res* 2003; 149: 222–36.
30. Maegele M, Muller S, Wernig A, Edgerton VR, Harkema SJ. Recruitment of spinal motor pools during voluntary movements versus stepping after human spinal cord injury. *J Neurotrauma* 2002; 19: 1217–1229.
31. Jankowska E. Spinal interneuronal systems: identification, multifunctional character and reconfigurations in mammals. *J Physiol* 2001; 533: 31–40.
32. Macdonald R.L, Schwartz M.L, Mirich D.M.D et al. Diagnosis of Cervical Spine Injury in Motor Vehicle Crash Victims: How Many X-rays Are Enough? *Journal of Trauma-Injury Infection & Critical Care*, April 1990, vol.30.
33. Bondurant Fonda J, Cotler Howard B, Kulkarni Madan V, et al. Acute Spinal Cord Injury: A Study Using Physical Examination and Magnetic Resonance Imaging. *Journal of Spinal Disorder & Techniques*. March 1990, vol.15.
34. Burns AS, Marino RJ, Flanders AE, Flett H. Clinical diagnosis and prognosis following spinal cord injury. *Handb Clin Neurol*, 2012;109:47-62.