September 13, 2009 #1

# Abstract Title: Analysis of long-term curative effect on syringomyelia in surgery

Primary Presenter: Guo Jian, M.S Primary Presenter Institution: 401 hospital of PLA,Qingdao,Shandong Presenting author's full street address and e-mail address: No 22.Minjiang Road, Qingdao, China <u>E-mail:guozzq@yahoo.com.cn</u>

### Introduction

An analysis of the effectiveness of surgical treatment on syringgomyelia in order to determine more effective treatment methods.

#### Materials and Methods

500 surgeries performed on patients between 11/1990 to 12/1996 were followed up by appointment. The factors of influence the long-term curative effect were analyzed .

#### Results

After operation a year inside, curative effect is 92.7%. The age, disease distance, empty type, surgical operation method is the main factor of the near period in influence curative effect. The adhesion of posterior fossa, empty extend again and the spinal cord atrophy may be main factors to affect the long-term curative effect.

#### Conclusion

The traditional surgical operation method is better to near period curative effect in syringomyelia.the long-term curative effect then can't guarantee.

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Time	Effective	Invalid	Deterioration
1 year	293_92.72%_	15_4.75%_	8_2.53%_
After 1 year	216_68.35%_	85_31.65%_	15_7.29%_
After 3 year	140_44.30%_	35_42.72%_	18_12.97%
After 5 year	102_32.28%_	15_47.47%_	23_20.25%

Post-operative effect of 316 patients of syringomyelia in different periods

Note: Effective: refers to mitigation or disappearance of symptoms; Invalid: no means to reduce; Deterioration: increasing the mean postoperative symptoms.

### Learning Objectives:

1. The latest research on Spinal cord disease

# September 13, 2009 #3

Abstract Title: Procedure- and Device-Related Complications of Intrathecal Baclofen Administration for Management of Adult Hypertonia: A Review Primary Presenter: Ivana Stetkarova, MD, PhD Department of Neurology, Na Homolce Hospital Prague, Czech Republic Email: ivana.stetkarova@homolka.cz

### Co-presenter(s):

- 1. Name: Stuart A. Yablon Credentials: MD
- 2. Name: Markus Kofler Credentials: MD
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3. Place of Employment: Center for Neuroscience and Neurological Recovery, Methodist Rehabilitation Center City: Jackson State: MS Country: USA

#### Introduction

Intrathecal baclofen is an effective therapy for managing moderate to severe spasticity of spinal and cerebral origin both in children and adults. However, various complications have been encountered which may hinder success and acceptance of this form of treatment. The purpose of this study was to provide a systematic literature review of procedure- and device-related

complications associated with ITB administration for adult muscle hypertonia of spinal or cerebral origin.

#### **Materials and Methods**

We searched PubMed database for full-length articles written in English since 1987 that reported complications in adults 19 years and older. Of nearly 150 articles retrieved, 32 full-length manuscripts and 9 case reports described various procedure- and device-related ITB complications.

### Results

In aggregate, 557 complications were reported following 1,361 pump implants (overall complication rate of 0.41 per implant). The rates of complications varied greatly between different studies, however, ranging from 0 to 2.24 per implant. Of those 557 complications, 148 (27%) were related to surgical procedures, 39 (7%) were due to pump problems, and 368 (66%) were associated with catheter malfunctions. The overall rate of complication was significantly higher for 15 studies that followed-up patients for more than 18 months on average (mean 0.56/implant), compared to 15 studies with the mean follow-up of less than 18 months (0.23/implant, p<0.05).

### Conclusion

Device-related complications, primarily catheter problems, are relatively common and more frequent than surgical procedure complications after ITB pump implantation for management of adult spasticity. Higher rate of complications should be expected in centers that implant more pumps and follow-up patients for a longer period of time. To raise the awareness and minimize the risks of procedure- and device-related complications standardized data collection and reporting procedures along with appropriate training should be implemented in centers offering ITB treatment for management of muscle hypertonia.

#### Learning Objectives:

1. Intrathecal baclofen treatment in adult muscle hypertonia

2. A systematic literature review of procedure- and device-related complications due to ITB treatment

3. Management of ITB complications

September 13, 2009 #4

**Abstract Title:** Preliminary analysis of Lidocaine as an intrathecal (IT) agent in patients unresponsive to chronic IT opioids.

Primary Presenter: Marc A Russo MBBS FANZCA FFPMANZCA

**Primary Presenter Institution:** Hunter Pain Clinic, Broadmeadow, Newcastle, NSW, Australia.

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#### Introduction

Whilst intrathecal (IT) analgesia with opioids may provide partial relief from chronic pain in some patients, a subset does not respond to dosages that do not impair quality of life. We present our experience of including IT Lidocaine in such patients.

#### **Materials and Methods**

Patients were considered refractory to IT analgesia after initially responding to IT opioids but subsequently failing to maintain this response despite increasing opioid doses and remaining unresponsive at a dosage of hydromorphone (2mg/day) in combination with clonidine (300ug/day) and ropivacaine (25mg/day). Following analgesic failure IT drug doses were decreased to eliminate undesired drug side-effects before introducing IT Lidocaine. 8 patients (5 males and 3 females) were trialled and had a mean age of 62.5 years, an average of 25.75 years of persistent pain; and IT analgesia commencing an average of 5 years prior to Lidocaine treatment. The treatment group reported an average of 2.5 separate pain areas and a mean pain VAS of 60/100 prior to Lidocaine treatment.

### Results

Data represent a group (n=8) treated with IT lidocaine for an average of  $0.52 \pm 0.25$  years (SD). 4 patients (mean Lidocaine dose of 41.3 mg/day) demonstrated substantial improvement with the VAS score for this subgroup decreasing from an average of 72.5 to 45. In contrast, the remaining 4 patients did not show improvement i.e. average VAS increased from 47.5 to 50. However, the latter 4 patients were still in the titration phase of their IT Lidocaine treatment (average dose of 20mg/day). Overall, the sample (n=8) showed a VAS decrease from 60 to 47.5 with a mean Lidocaine dosage of 30.6 mg/day.

### Conclusion

Lidocaine may be a useful IT agent to manage chronic pain in patients who have become refractory to standard IT analgesics including amide-based local anaesthetics. This may be related to Lidocaine's ability to decrease opioid-induced hyperalgesia via an inhibitory action on glial upregulation of the dorsal horn.

#### Learning Objectives:

1. To observe the responses of a refractory group of persistent pain patients to intrathecal Lidocaine.

2. To understand the preliminary nature of these findings and that more work in this area is required.

3. To understand that Lidocaine has a specific effect on hyperalgesia and on glial regulation of the central nervous system.

# September 13, 2009 #5

# A retrospective study of long term continuous intrathecal infusions of opioid and/or bupivicaine in refractory non-malignant pain.

Hosam Al-Jehani, Tania DiRenna, Jacques Line

Abstract Title A retrospective study of long term continuous intrathecal infusions of opiod and/or bupivicaine in refractory non malignant pain. Primary presenter: Line Jacques MD,FRCS(c) Montreal Neurological Hospital and Institute Montreal,Canada Ljacques2@yahoo.com Co-presenter Tania Di Renna MD Ottawa Civic Hospital Ontario Canada Introduction: We investigated, in a retrospective manner, the long-term efficacy and safety of continuous intrathecal opioids with or without bupivicaine in patients with chronic non-malignant pain. This study summarizes the clinical data and the personal experience of the principal author with long-term intrathecal infusion therapy.

Materials and Methods: After obtaining ethical board review permission, the charts of 57 patients with intrathecal narcotic pumps were examined. Measured outcomes include patient satisfaction according to pre and post infusion visual analogue pain scores (VAS) ,oral opioid supplementation, return to work rates, post operative complications, device related complications requiring repeat operations, pharmacological side effects, drug titration and combinations. Success with combinations of intrathecal pumps and spinal cord stimulators was also analyzed. The paired t test was used to analyze statistical significance.

Results: The patients had a mean age of 47 with 38 (67%) males and 19 (33%) females. Indications for pump insertion include Failed Back Surgery Syndrome (FBSS) in 45 (79%) patients, Chronic Regional Pain Syndrome (CRPS) in 5(9%) patients or peripheral neuropathy, brachial plexopathy, abdominal pain and phantom limb pain in 7 (12%) patients that was refractory to medical treatment. Opioid and other drug combinations comprised of morphine 24(42%), hydromorphone 8 (14%), fentanyl 9 (16%) and opioid and bupivicaine mixtures 14 (24%). Oral or transdermal opioid supplementation was reduced by 64% (p<0.0001) after pump insertion. Mean VAS pre-implant was 8.6 and post VAS implant was 4.7 with a difference of 3.9 that is statistically significant (p<0.001). Post operative complications included self limited post operative headache, csf leak, catheter migration and blockage and pump infection. Pharmacological side effects included constipation, urinary retention, nausea, pruritis and sedation. Success with combinations of intrathecal pumps and SCS was found in 14% of patients. A total of 12% of patients were able to return to work.

Conclusion: With the data from this experience we conclude that continuous intrathecal opioid with or without bupivicaine can be a safe, effective therapy for the management of nonmalignant pain among a carefully selected patient population. Patient satisfaction from continuous intrathecal narcotic administration is evidenced by a significant decrease in oral narcotic consumption and improved VAS scores. We also appreciate that further clinical research is needed in order to provide stronger evidence for the usefulness of a number of drugs currently used for intrathecal therapy.

#### Learning Objectives

1-To be able to review the efficacy of intrathecal drug infusions in patient with mainly failed back surgery syndrome in the long term basis

2-Review the pharmacological options for patient with refractory chronic non malignant pain

September 13, 2009 #6

Abstract Title: Intrathecal Morphine (ITM) infusion for Chronic Back Pain: pain and functional status evaluation Primary Presenter: Genni Duse, MD Ospedale Sant'Antonio, Padova, Italy <u>genniduse@libero.it</u>' Co-presenter: Giorgio Davià, MD Introduction: ITM infusion can be considered an effective treatment for chronic non oncologic pain. This ongoing prospective data collection aims to investigate the effect of ITM also in the functional status.

Materials and Methods: Since September 2007, 11 patients have been included (72.7% females, 27.3% males). Mean age at implant was 73.9±8.3 years. Every patient had both back and lower limbs pain (36.3% only right limb) for 57.8±28.8mos. In this population, chronic pain is due to Failed Back Surgery Syndrome (36.4%), to Lumbar Spinal Stenosis (27.2%), and to others Spine disorders (36.4%). 36.4 % of patient is obese and 36.4% is over-weight but nobody suffers of diabetes. 2 patients experienced vascular disease complications: 1 acute myocardial infarction and 1 stroke; nobody experienced transient ischemic attack. 2 patients suffer of dyslipidemia. Pain, with Numeric Rating Scale NRS, pharmacological therapy and clinical-functional status are recorded at baseline and every 6mos after implant. Results: Every patient performed a trial test with continuous test, having a positive response at 2.0±0.9 mg/day in three weeks. Every patient initially using opioids, antidepressant and pain relieving drugs, stopped oral opioids medication. All the patients were implanted with a Synchromed II pump (Medtronic, Inc) and morphine average dose at implant was 242.3±85.3 µg/die. 7 pts performed the 6mos follow-up visit; the initial dose increases 6 months after implant up to 568.4±776.2 µg/day. The NRS scale decreases from 79.1±31.4 to 39.0±33.4 and from 71.8±31.2 to 39.0±36.5 in the back and in the lower limbs, respectively. We observed 1 adverse event related to drug withdrawal symptoms.

Conclusion: These preliminary data revealed a reduction in chronic pain in patients treated with ITM, where the conventional medical treatment is not effective or has intolerable side effects. The impact on the quality life will be deeper investigate during data collection.

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# September 13, 2009 #7

#### Abstract Title:

A Prospective, Multi-Centered Clinical Evaluation of A Newly Released 16-Channel Implantable Pulse Generator (IPG) for the Management of Chronic Pain of the Trunk and/or Limbs: Final Results.

#### **Primary Presenter:**

Roni Diaz

#### **Primary Presenter Institution:**

St. Jude Medical Neuromodulation Division, Plano, TX

#### Co-presenter(s):

Edward A. Lewis, MD Timothy Deer, MD Tory McJunkin, MD Klee Bethel, MD Brad Sisson, MD Shane Brogan, MD

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Carolina Center for Advanced Management of Pain, Asheville, NC The Center for Pain Relief, Charleston, WV Arizona Pain Specialists, Scottsdale, AZ The Beth-El Clinic, Mesa, AZ Colorado Pain Clinic, Ft. Collins, CO University of Utah, Salt Lake City, UT

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#### Introduction

Spinal Cord Stimulation (SCS) is a proven treatment for chronic pain, but there is still a need of additional high-quality prospective clinical study data. The study being presented is a prospective, multi-centered, 45 day follow-up study using the Eon<sup>®</sup> Mini implantable pulse generator (IPG; St. Jude Medical Neuromodulation; Plano, TX).

#### Methods

This IRB-approved study was a prospective, multi-centered, 45 days post implantation study. After informed consent was obtained, patients were screened according to the inclusion criteria. Following system implantation, patients were seen at initial programming, 21 days and 45 days post-implantation. The primary objective was to demonstrate that the Eon Mini is equivalent to the Eon in recharging intervals. Data collected included: device programming and stimulation coverage, pain evaluation, battery recharging information and patient satisfaction.

#### Results

Preliminary data analysis from 36 patients at the 45 day time-point showed that 75% of patients

reported 50% pain relief or better and the mean overall patient reported pain relief was 61.0% in these patients. Most patients (83.3%) were either very satisfied or satisfied with their SCS device and most (80.6%) patients say their quality of life has either greatly improved or improved since SCS implantation. The majority of patients (44.4%) recharged on a weekly basis and it took less than 1 hr to recharge in most patients (80.6%). Over the course of the study, 40.3% of patients utilized the portability of the system. No patients reported any lack of adequate pain relief while recharging. Final data will be presented.

#### Conclusion

To date, patients have experienced good battery recharging intervals with the Eon Mini when compared with the Eon IPG in the management of chronic pain of the trunk and or limbs.

#### Acknowledgements

This work was supported by St. Jude Medical Neuromodulation Division through a sponsored clinical research study. Dr. Deer is a paid consultant of St. Jude Medical Neuromodulation.

September 13, 2009 #8

### Abstract Title:

An evaluation of the effect of stimulation parameters on efficacy measures in spinal cord stimulation for chronic pain

**Primary Presenter:** 

Jon Ruais

#### **Primary Presenter Institution:**

St. Jude Medical Neuromodulation Division, Plano, TX

#### Co-presenter(s):

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#### Introduction

There has been little examination of the impact of stimulation parameters including, frequency, pulse width, and amplitude settings in relation to spinal cord stimulation (SCS) efficacy for chronic pain. Previous work on the strength duration curve and calculation of the chronaxie has been published, but this has not been related to SCS efficacy measures. The following analysis was undertaken to examine whether specific stimulation parameters were correlated with better SCS efficacy.

#### **Material and Methods**

Data is presented an ongoing, IRB-approved, clinical research study conducted with patients implanted with a rechargeable implantable pulse generator (IPG; Eon® St. Jude Medical

Neuromodulation Division, Plano, TX). Mean pulse width for each patient at each visit was calculated using the patients 1 or 2 favorite programs. For each patient visit, measures of pain relief, patient satisfaction, and quality of life were available. Analysis of variance was used to determine if there was any difference in average pulse width between patients with varying levels of pain relief, satisfaction, and quality of life. Also, the relationship between frequency, pulse width, amplitude and patient reported percent pain relief was explored using a Pearson correlation.

### Results

The mean frequency, pulse width and amplitude for patients were 66.2 Hz, 319.6  $\mu$ s, and 7.5 mA, respectively. Analysis of variance found no significant difference in frequency, pulse width, or amplitude among patients who reported varying levels of satisfaction, pain relief, and improvements in quality of life (all *p*s > 0.05). There was no trend observed of increasing pulse width in increasing satisfaction, quality of life, or pain relief. In addition, Pearson correlations for each of the stimulation parameters were not significant.

### Conclusion

Frequency, pulse width, and amplitude settings do not appear to have any effect or relationship to efficacy measures among patients with rechargeable IPGs.

#### Acknowledgements

This work was supported by St. Jude Medical Neuromodulation Division through sponsored clinical research studies.

#### September 13, 2009 #9

Abstract Title: Percentage of Paresthesia Overlap and Successful Spinal Cord Stimulation at 1-year Follow-up Primary Presenter: Roni Diaz Primary Presenter Institution: St. Jude Medical Neurmodulation Division, Plano, TX Co-presenter(s): Cheryl Monroe, MPH Stephanie Washburn, PhD Co-presenter(s): St. Jude Medical Neuromodulation Division, Plano, TX St. Jude Medical Neuromodulation Division, Plano, TX Presenting author's full street address and e-mail address: 6901 Preston Road Plano, TX 75024 roni.diaz@sjmneuro.com

# Introduction

Spinal cord stimulation (SCS) is used to treat specific types of chronic pain. It requires implantation of an electrical generator and leads that send pulses of current to the spinal cord. A successful trial is used as a method of selection for SCS candidacy. A successful trial, however, does not always assure SCS success. Paresthesia coverage of a patient's painful area is considered crucial to SCS success. This analysis evaluated the relationship between

paresthesia coverage of original painful areas and successful treatment with spinal cord stimulation at 1-year.

# Materials and Methods

Results were gathered from an interim analysis of four ongoing IRB-approved clinical studies. Patients were screened according to the inclusion/exclusion criteria. If the patient experienced a successful SCS trial, defined as a 50% reduction of pain, the patient was subsequently implanted with a rechargeable implantable pulse generator (Eon®, St. Jude Medical Neuromodulation Division, Plano, TX).

Percent of paresthesia overlap was calculated as the number of painful areas designated at the baseline visit with paresthesia coverage at the 1-year visit divided by the total number of painful areas. Treatment success was determined in two ways: patients reporting at least a 50% reduction in the overall numerical rating scale pain score and patients reporting their quality of life as "improved" or "greatly improved".

# Results

Preliminary analysis showed that 74.1% of patients achieved pain relief of at least 50% and these patients had average paresthesia coverage of 74.2%. Patients rated their quality of life as "improved" or "greatly improved" (81.4%) had average paresthesia coverage of 73.4%. At least 25% paresthesia coverage of pain areas was required to achieve 50% pain relief. Patient reported percent pain relief was significantly positively correlated with paresthesia coverage (r = 0.23).

### Acknowledgements

This work was supported by St. Jude Medical Neuromodulation Division through a sponsored clinical research study.

# Learning Objectives:

- 1. Define paresthesia coverage.
- 2. Understand how paresthesia coverage is related to patient outcome measures.

September 13, 2009 #10

# Abstract Title:

Beneficial results from lidocaine infusion pump implantation and obturators neurotomies for intractable pain and adductors spasticity in one patient after 36 months follow-up. **Primary Presenter:** José D. Carrillo-Ruiz, MD & PhD Mexico General Hospital. Department of Neurosurgery. Unit of Stereotaxy, Functional Neurosurgery and Radiosurgery. Mexico City, D.F. Mexico Email: josecarrilloruiz@yahoo.com **Co-presenter(s):** 1. Pablo Andrade, MD

- 2. Nora Godínez-Cubillos, MD
- 3. María L. Montes-Castillo, MD
- 4. Fiacro Jiménez, MD & PhD

Ana L. Velasco, MD & PhD
 Guillermo Castro, MD & MSc
 Francisco Velasco, MD
 Co-presenter(s):
 Mexico General Hospital, Mexico City, D.F., Mexico

### Introduction (History and Physical examination)

Spastic diplegia represents 75% of patients' prevalence with cerebral palsy. It affects lower extremities disturbing locomotion and very often associated with intense pain. This is the case of a 28-years-old woman with background of perinatal hypoxia, subsequent cerebral palsy and severe spastic diplegia, without the capacity to walk, clinical scales of Ashworth 4 and Held-Tardieu 5, and mixed pain in the left hip and knee with visual analogue scale (VAS) score of 10/10. Previous multiple treatments without success were performed.

#### **Results (Operation and Post-operative Course)**

For the spasticity, the patient underwent partial bilateral adductors myotomies; evident results were obtained since the first 3 months after surgery, showing significant improvement on the clinical field (Ashworth 0, Tardieu 0 up to the 36<sup>th</sup> month of evaluation). For the pain, after 12 months of insidious results obtained from lidocaine peripheral nerve application, it was decided the implantation of an infusion pump for intrathecal lidocaine 2% rate 0.3 mL/day application at T-7 level (Isomed Implantable Infusion Pump, Medtronic Inc. Model 8472-35-10). Immediately after the catheter was implanted VAS diminished dramatically to 0, and remained continuous and sustained at the long-term evaluations.

#### Conclusions

These results represent a promising indication for commercialized infusion pumps in the treatment field for neuropathic pain. This case is the first report of an infusion pump used with lidocaine to treat pain, combined with spasticity surgery obtaining highly positive results.

#### Acknowledgements

This work was partially supported by the National Research System of Mexico.

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# Learning Objectives:

- 1. Use of lidocaine in an infusion pump administered intrathecally in neuropathic pain abolition in a patient with resistance to therapeutics.
- 2. Combination of two different modalities to treat at the same time pain and spasticity with neuromodulation and lesion procedures.
- 3. In long-term evaluation lidocaine was safety a safety drug to the nervous system, at least at 36 months follow-up.

# September 13, 2009 #11

**Abstract Title:** Rate of device contamination or infection during transcutaneous spinal neurostimulation trial

Primary Presenter: Alessandro Dario M.D.

**Primary Presenter Institution:** Neurosurgical Clinic, Varese Regional Hospital. Varese. Italy **Co-presenter(s):** Federico Pessina M.D., Giustino Tomei M.D.

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#### Introduction

The aim of this paper is to evaluate the rate of infection and the possible door of entrance of bacteria during spinal neurostimulation trial

#### **Materials and Methods**

Twenty patients underwent implantation of spinal epidural lead to perform trial. Six electrodes were surgical paddle, fourteen were percutaneous leads. All electrodes were connected to temporary transcutaneous extension sited in lateral subcutaneous pouch. The perioperative antibiotic prophylaxis was carried out by intravenous cefazoline 2 milligrams one hour before surgery. All brand of spinal neurostimulators were implanted. The neurostimulation trial period was between 3 or 4 weeks. All patients but two underwent permanent implantation. At definitive IPG implantation or electrode removal for ineffectiveness the pouch containing temporary extension was opened and a two specimens were cultured to find bacteria.

#### Results

In all patients but one the specimens were negative for bacteria. In the positive specimen due to *S. epidermidis* no clinical and blood test infection was reported after 12 months. None of the negative patients developed device infection at follow-up (mean 16 months).

### Conclusion

In this series there was not device contamination or infection during transcutaneous spinal neurostimulation trial. The pouch containing the transcutaneous temporary extension does not appear to be a *locus minoris resistentiae* for device contamination.

#### Learning Objectives:

1. To clarify the rate of infection and the possible door of entrance of bacteria during spinal neurostimulation

trial

September 13, 2009 #12

**Abstract Title:** Pulsed radiofrequency improves experimental neuropathic pain but is not a neuromodulation technique

Primary Presenter: Alessandro Dario M.D.

**Primary Presenter Institution:** Neurosurgical Clinic, Varese Regional Hospital. Varese. Italy **Co-presenter(s):** 

Elisa Borsani M.D.<sup>1</sup>,Marina Protasoni M.D.<sup>2</sup>, Marcella Reguzzoni M.D.<sup>2</sup>, Claudio Reverberi M.D.<sup>3</sup>,Simone Sangiorgi M.D. °Giustino Tomei M.D.°, Luigi Rodella M.D.<sup>1</sup>

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# Introduction

To evaluate the effect of PRF on nitroxidergic neurons of lumbar DRGs, spinal cord (L4-L6) and brain PAG area in a rat model of chronic pain as well as the histological changes on spinal ganglia

#### Materials and Methods

The rat group was subdivided in: control (NAIVE) group; PRF treated group; chronic constriction sciatic nerve injury (CCI) group; CCI group treated with PRF. The histological examination was performed one hour after PRF treatment by light microscopy and transmission electron microscopy (TEM) analysis. At the end of the experiment, DRGs, spinal cord (L4-L6) and brain PAG area were processed for nNOS and iNOS immunohistochemistry. The animals were behavioural tested (plantar test) during the experimental period.

#### Results

At light microcopy no particular histological alterations were found while at TEM analysis T gangliar cells presented abnormal smooth reticulum and myelinated axons had myelinic damage. DRG and spinal cord we observed a similar modulation of nitroxidergic system. The NAIVE and the sham groups showed the same pattern of nNOS and iNOS expression. The PRF group was not statistically different from NAÏVE group. The CCI group showed a significant increase of nNOS and iNOS staining respect to NAÏVE group. The CCI+PRF group showed a significant decrease of the nNOS and iNOS staining respect to CCI group.

In the PAG dorsolateral area the CCI group showed a significant increase of Fos and nNOS staining respect to NAÏVE whereas in the CCI+PRF group a pattern like to NAIVE group was seen. These data are supported by evidences in plantar test, where the PRF is able to increase the thermal withdrawal latency in CCI animals.

### Conclusion

Yet the pulsed radiofrequency improves the experimental neuropathic pain the histological alterations are not compatible with the term "neuromodulation technique"

#### Learning Objectives:

- 1. To clarify the histological changes on spinal ganglia as well as on nitroxidergic neurons of the CNS due to pulsed radiofrequency in a model of neuropathic pain
- 2. To clarify the improvement due to this technique in a neuropathic pain model of the rat.

# September 13, 2009 #13

**Abstract Title:** Subcutaneous peripheral nerve stimulation for unilateral face, head and neck pain – a case report

**Primary Presenter:** Bruce Mitchell, MD Metro Spinal Clinic Melbourne, VIC, Australia Email: bmitchell@metrospinal.com.au

### Co-presenter(s):

Name: Adele Barnard Credentials: BSc, Hons
 Co-presenter(s):
 Place of Employment: Metro Spinal Clinic City: Melbourne State: VIC Country: Australia

# Introduction

Subcutaneous stimulation in occipital and trigeminal nerve distributions are widely reported treatments for neck and head pain (1, 2). The presented patient had unilateral face, head and neck pain treated by novel placement of leads at the vertex and parietal/temporal areas.

#### Materials and Methods

Patient had 9 year history of daily, right-sided head pain behind the eye, face and neck pain spreading into shoulder and scapula; initially dull then becoming severe (8/10) with sharp jabbing. Physiotherapy, acupuncture and neck joint mobilisation provided relief. Medial branch blocks and facet joint injections provided little relief. Trial stimulation with 4x 8-contact leads over occiput and shoulder was equivocal. Another trial with leads over the vertex, lateral neck and trapezius gave good relief, but not of face pain. Final trial was performed with vertex and temporal lead (stimulating the ophthalmic and maxillary branches of the trigeminal nerve) within the hair line, this gave good relief. Leads were implanted in this position with the IPG implanted in the right axilla. At ten days, the vertex lead tip had nearly eroded through the skin; this was re-buried and anchored at the tip.

# Results

At 39 days patient reported she was delighted with stimulation (used for 22.9 hrs/day) and pain relief. At 7 months patient reported a VAS pain score of 1 (8 pre-implant), 90-95% improvement in pain, and complete satisfaction with the procedure and outcomes. Daily activities were no

longer limited and now full-time employed. Analgesic use decreased significantly, occasionally taken for shoulder pain.

#### Conclusion

Subcutaneous stimulation of occipital and trigeminal nerve branches can achieve excellent pain relief to the face, head and neck, whilst avoiding visible (& potentially disfiguring) lead placements.

#### Acknowledgements

We would like to acknowledge Robert Gorman and Philippa Marks from Boston Scientific for providing technical information

#### References

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2) Slavin KV, Colpan ME, Munawar N, Wess C, & Nersesyan H. Trigeminal and occipital peripheral nerve stimulation for craniofacial pain: a single-institution experience and review of the literature. Neurosurg Focus 2006. 21:E5

#### Figure Legend:

Fluoroscopic images of the implanted vertex and parietal/temporal leads.

#### Learning Objectives:

- 1. Vertex and Parietal/Temporal lead placement for face, head and neck pain
- 2. Lead placement within the hair-line for face pain

September 13, 2009 #14

Abstract Title: A MEMS-based fully-integrated wireless neurostimulator Primary Presenter: Will Rosellini, MS Neuroscience Primary Presenter Institution: MicroTransponder Inc. Dallas, Texas USA Presenting author's full street address and e-mail address: 12147 Leuders Ln. Dallas TX 75230 will@microtransponder.com

#### Introduction

We report design, fabrication and *in-vivo* animal testing of a MEMS-based fully-integrated fullybiocompatible minimally-invasive wireless battery-free neurostimulator (3.1 x 1.5 x 0.3 mm) for chronic pain relief application. The device consists of spiral coil for inductive power coupling, rectification diodes, an ASIC neurostimulator circuit chip, biphasic platinum-iridium (PtIr) stimulation electrodes, interconnection between parts, and biocompatible SU-8 [1] packaging. The wireless neurostimulator was implanted subcutaneously in a rat and cortical responses evoked by wireless stimulation were repeatedly recorded.

Electrical stimulation has widely used to elicit or modify certain behaviors, to restore sensory perception, or to treat neurological disorders. Predominant methods of electrical stimulation involve delicate surgical procedure to implant relatively large electrodes with long electrical lead wires to connect with bulky electronic controllers. Such methods can cause the risk of infection

and reduction of the functional reliability related to problems with wiring or physical motion of the implanted device. Inductively coupled wireless power transmission is a promising solution to address such issues. However, sizes of reported wireless inductive power devices [2, 3] are relatively large.

A schematic view of the wireless neurostimulator is shown in Figure1. It consists of a round spiral inductor as a coupling element, diodes responsible for rectifying induced AC voltage, an ASIC chip to control stimulus current, and bipolar stimulating electrodes as neural interfaces. SU-8 was used as packaging material due to its biocompatibility. For the purpose of compact integration of those components, a SU-8 based socket platform was devised to tightly fit in rectifying diodes and the ASIC chip. A 1 mm diameter spiral inductor was embedded in the platform. The socket dimensions were decided by the dimensions of commercially available Schottky diodes ( $830_300_95 \mu m$ ) and the ASIC chip ( $1_10.15 mm$ ). The contact pads at the bottom floor of each socket are to make interconnection between each component. Tiny amount of conductive epoxy was applied on each contact pad, and the ASIC and diodes were slid into the fabricated sockets. After integration process was completed, the whole device was completely sealed by another layer of SU-8. Finally, 1 mm diameter PtIr stimulating electrodes were attached on both sides of the device. Figure 2 illustrates fabrication sequence and Figure 3 shows the successfully fabricated SU-8 based wireless neurostimulator ( $3.1_1.5 \times 0.3 mm$ ).

Prior to the animal study, wireless stimuli were recorded during open-air tests for calibration across RF power levels at different separation distances between the wireless simulator and RF power coil as shown in Figure 4. The stimulus discharge time constant was consistently about 1 µs, decaying from a peak stimulus voltage which depended upon the applied RF power level and separation distance up to a maximum of about 6.5 V at 1 Watt power and 1 mm separation down to stimulus failure at distances over 5 mm. After open-air tests, the fabricated device was placed subcutaneously upon the peroneal nerve of a rat and recorded the cortical responses to wireless stimulation powered by an external RF coil applied to the skin over the implant. Figure 5 illustrates the subcutaneous placement of a wireless stimulator and the external RF coil on the skin overlying the implant, which was prepared to mimic the configuration planned for human trials. As can be seen in Figure 6, increasing wireless stimulation intensity by increasing external RF power resulted in an increase in the amplitude of the evoked cortical responses. Fairly substantial cortical response was detected with wireless RF power as low as 21 dBm (125 mW) at 394 MHz.

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# Acknowledgements

MicroTransponder Inc., University of Texas at Dallas, Texas Emerging Technology Fund

September 13, 2009 #15

Title: MOTOR CORTEX STIMULATION (MCS) FOR PAIN: INTRAOPERATIVE IDENTIFICATION OF OPTIMAL ELECTRODE POSITION Primary Presenter: Meglio M, MD Primary Presenter Institution: Neurochirurgia Funzionale e Spinale – Università Cattolica – Roma - Italy Neurochirurgia Funzionale e Spinale - Università Cattolica – Policlinico Gemelli - Lg Gemelli, 8 – 00168 Roma – Italy <u>mmeglio@rm.unicatt.it</u> Co-presenter(s): Cioni B, MD, De Simone C, MD, Conforti G, MS, \*Perotti V,MD Co-presenter(s) Institution: Neurochirurgia Funzionale e Spinale e \*Anestesiologia – Università Cattolica – Roma - Italy

**Introduction:** The optimal contact position in order to obtain the best pain relief by MCS, is still matter of debate. In 2007 Yamamoto et al found a significant direct correlation between D-wave amplitude and VAS reduction. Holsheimer et al found that the anode providing the largest muscle response in the area of pain gave the best pain relief. But the muscle response shows a very high variability from trial to trial, and D wave, very stable, does not give somatotopic information. To overcome these disadvantages we combined the two technique, but the placement of an epidural spinal cervical electrode is an invasive, sometimes time-consuming procedure. We developed a novel methodology for the intraoperative identification of the best spot to be chronically stimulated.

**Material and method:** After a small craniotomy, under TIVA, we identify the central sulcus by the SEP phase reversal. We stimulate the motor cortex by a monopolar handheld probe using the high frequency short train technique with increasing current and we record the muscle response in order to select the area somatotopically corresponding to the body region of pain with the lowest motor threshold.

Here we place the electrode paddle perpendicular to the central sulcus with at least one contact over the sensory cortex. We stimulate the spot with the lowest motor threshold as a cathode, while the contact over the sensory cortex is used as an anode.

**Results:** The target for stimulation has been clearly identified and the procedure is relieble and reproducible.

**Conclusions:** This methodology is simple and safe, comfortable for the patient because under general anesthesia and seems to improve the efficacy of MCS for pain.

#### **References:**

Yamamoto T, Katayama Y, Obuki T, Kano T, Kobayashi K, Oshima H, et al. Recording of cortico-spinal evoked potential for optimum placement of motor cortex stimulation electrodes in the treatment of post-strke pain Neurol Med Chir 2007. 47:409-414  Holsheimer J, Lefaucheur JP, Buitenweg JR, Guij0n C, Nineb A, Ngujen JP The role of intraoperative motor evoked potentials in the optimization of chronic cortical stimulation for the treatment of neuropathic pain Clin Neurophysiol 2007.118(10):2287-96

**Learning objectives:** the goal of the presentation is to teach how to identify the exact neurophysiological localization of electrodes on the cortex

September 13, 2009 #16

**Title:** INTRATHECAL BACLOFEN INFUSION IN SEVERE SPASTICITY DUE TO ACQUIRED BRAIN INJURY

Primary Presenter: M Meglio, MD Primary Presenter Institution: Neurochirurgia Funzionale e Spinale – Università Cattolica – Roma- Italy Co-presenter(s): B Cioni, MD, C De Simone, MD, G Conforti, MS Co-presenter(s) Institution: Neurochirurgia Funzionale e Spinale – Università Cattolica – Roma- Italy Presenting author's full street address and e-mail address: Neurochirurgia Funzionale e Spinale - Università cattolica – Policlinico Gemelli - Lg Gemelli, 8 – 00168 Roma – Italy mmeglio@rm.unicatt.it

**Introduction:** We report our experience with intrathecal Baclofen (ITB) infusion in the treatment of severe spasticity due to acquired brain injury.

**Material and method** The study included 15 patients. The etiology of hypertonia was a severe brain trauma in 11 cases and a cerebral focal anoxia following subarachnoid hemorrhage in 4 cases. Other inclusion criteria were: age 15years or older, spasticity resistant to other pharmacological and physical modalities, no allergy to Baclofen, signed informed consent. The mean time since the injury was 52months, in 6 cases being </= 12 months. ITB was continuously infused via an implantable electronic pump. Mean follow-up was 65 months (min 12, max 152 months). The clinical evaluation included: muscle tone utilizing the Ashworth scale, painful spasms, neurovegetative storms, as well as functional assessment, and adverse events.

**Results:** The initial mean daily dose of ITB was 142ug, and at maximum follow it was 285ug. Muscle hypertonia significantly decreased both at upper and lower extremities, painful spasms disappeared in 8 cases and were reduced in 7. Neurovegetative storms, present in 4 cases before ITB, disappeared in 3 cases, while in the forth case were greatly reduced. A functional improvement was present in terms of caring, dressing, skin ulcers, wheelchairing, walking, sleeping. In the 8 cases of minimal consciousness, a more evident relationship with the environment was referred by the caring persons. Only minor adverse events occurred.

**Conclusions:** Our experience confirms the clinical usefulness of ITB in hypertonia due to acquired brain injury: in 13/15 cases, relatives, caregivers and /or patients were satisfied and would reimplant the pump.

#### **References:**

- Hsieh JC, Penn RD Intrathecal Baclofen in the treatment of adult spasticity Neurosurg Focus 2006. 21(2):E5
- Koulousakis A, Kuchta J Intrathecal antispastic drug application with implantable pumps: results of a 10 year follow up study Acta Neurochir 2007. Suppl 97:181-184

**Learning objectives:** The goal of this paper is to discuss how neuromodulation with intrathecal baclofen can significantly improve hypertonia following brain injury.

September 13, 2009 #17

Abstract Title: Intrathecal baclofen treatment for disorders other than spasticity **Primary Presenter:** Takaomi Taira

**Primary Presenter Institution:** Department of Neurosurgery, Tokyo Women's Medical University, Tokyo, Japan

**Co-presenter(s):** Hiroyuki Akagawa, Shinichi Goto, Tsuyoshi Nakajima, Taku Ochiai **Co-presenter(s):** Department of Neurosurgery, Tokyo Women's Medical University, Tokyo, Japan

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#### Introduction

Intrathecal baclofen therapy (ITB) is well established for control of intractable spasticity of various origins and secondary dystonia in cerebral palsy. However, little is known about indications and efficacy of ITB in other neurological disorders such as intractable pain, idiopathic dystonia and other rare conditions.

#### Materials and Methods

We have tried ITB for otherwise intractable complex regional pain syndrome (CRPS, 5 cases), fixed dystonia (2 cases), stiff-person syndrome (one), and intractable tremor (one). These patients had been treated with other conventional method (both conservative and surgical including spinal cord stimulation, deep brain stimulation), but the symptoms were intractable.

#### Results

In CRPS, ITB was effective to relieve fixed dystonic posture in all (100%) and pain in two (40%). However, ITB did not affect swelling or edema of the extremities (Fig.1). Fixed dystonia (Fig 2) that did not fulfill the diagnostic criteria of CRPS responded effectively. During the follow-up period of 1-3 years, dystonia progressed to other parts of the body in three patients and ITB no longer was effective despite increase of daily baclofen dose up to 600 micrograms. The effect on stiff-person syndrome was dramatic. The patient had been under intravenous anesthesia and on respirator for three months. After ITB, she returned to school normally. Probably because of drug tolerance, we had increase the dose up to 2000 micrograms per day afterwards. One patient with intractable tremor who had undergone bilateral thalamic deep brain stimulation only with transient effect showed remarkable long-term suppression of the symptom after desperately performed ITB.

#### Conclusion

Both CRPS and fixed dystonia can be benefited with ITB, though we cannot control the disease progression of such disorders with ITB. Because bolus trial injection is safe, we consider trying ITB for intractable neurological symptoms such as muscle stiffness, dystonia and tremor.

Baclofen may affect on dystonia and tremor by modulating the peripheral input at the spinal cord level.

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Fig 2: fixed dystonia

Fig 1: Abnormal swelling in CRPS

# Learning Objectives:

- 1. To understand general indication of intrathecal baclofen treatment
- 2. To know special and exceptional application of ITB treatment
- 3. To consider possible future treatment of intractable neurological disorders

#### September 13, 2009 #18

Abstract Title: Spinal Cord Stimulation versus Spinal Nerve Root Stimulation in Management of Neuropathic Pain of the Lower Limb. (Preliminary Report) Primary Presenter: Adnan Al Kaisy, MB ChB FRCA FFPMRCA St Thomas' Hospital, London, UK Email: alkaisy@aol.com

# Co-presenter(s):

1. Name: Teo Goroszeniuk	Credentials: FCARSI
2. Name: Adam Woo	Credentials: MBBS FRCA
3. Name: V Munukutla	Credentials: MBBS FRCA

#### Co-presenter(s):

1. Place of Employment: St Thomas' Hospital City: London State: London Country: UK

#### Introduction

Spinal cord stimulation (SCS) is a well established practice in the management of neuropathic pain of the lower limb. Stimulation-induced paresthesia in the painful area is essential for effectiveness of SCS therapy. Lead migration has been accounted as single most common complication associated with this technique (1). This is an ongoing study comparing SCS with retrograde spinal nerve root stimulation technique in the management of neuropathic pain of the lower limb.

### **Materials and Methods**

Two separate quad leads inserted simultaneously: one in a retrograde fashion to stimulate spinal nerve roots of L5-S1 (for foot pain) or L3 (for knee pain), the other lead is inserted in a anterograde to the level of T12/L1 (for foot pain) or T11/T12 (for knee pain).

The trial period of two weeks consisted of separate stimulation of the leads for one week each. We measured VAS, patient satisfaction, constancy of paresthesia coverage with postural changes and voltage requirements.

#### Results

Our initial findings in four patients was that there was significant pain reduction in the two techniques but the leads stimulating the nerve roots produced more constant paresthesia in the area intended with low amplitudes of stimulation. The spinal nerve root stimulation lead gave high patient satisfaction as it covered the area required only.

#### Conclusion

Despite this small number of cases, spinal nerve root stimulation may be the preferable method of stimulation in neuropathic lower limb pain. Larger numbers will be required to refine the best method of stimulation for this condition.

#### References

1. Turner JA, Loeser JD, Deyo RA, Sadders SB. Spinal cord stimulation for patients with failed back surgery syndrome; Systematic review of effectiveness and complications. Pain 2004; 108:137-147.

#### Learning Objectives:

1. Comparison of spinal nerve roots versus spinal cord stimulation

September 13, 2009 #19

Abstract Title:

Does olfactory ensheathing cells therapy have any role in the management of neuropathic pain following spinal cord injury in humans?

# Primary Presenter: Haitao XI, Attending Physician

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Co-presenter(s):
1. Name: Hongyun HUANG Credentials: Prof.
2. Name: Lin CHEN Credentials: Associate Prof.

### Co-presenter(s):

1. Place of Employment: Beijing Hongtianji Neuroscience Academy, Department of Neurosurgery, Beijing Rehabilitation Center - Beijing, China

### Introduction

Many patients following peripheral and central neural injuries continue to suffer from intractable chronic pain. To date, there are no published successful methods to treat human SCI pain with olfactory ensheathing cells. To explore the feasibility and potential benefit of olfactory ensheathing cell (OEC) intraspinal transplantation in the treatment of intractable chronic neuropathic pain after spinal cord injury (SCI).

### **Materials and Methods**

This open and self-controlled clinical study was carried out in Beijing Hongtianji Neuroscience Academy, during November, 2004 to March, 2007. Of the total fourteen patients, thirteen were male and one was female. Ages ranged from 18 to 68 years (mean 42.1 years). The etiology of cord impairment included car accidents, falls, radiation damage, machine extrusion, gun-shot, and diving. The procedures were performed on patients ranging from, 12 to 312 months (mean 120.9 months), after their injuries. The damaged segments located at cervical spinal cord in 8 patients and at thoracic cord in residue. Olfactory bulbs were harvested and trypsinized down to single fetal OECs. They were cultured for 12-17 days and to be ready for use. The fetal OECs were transplanted by injection into spinal cord at opposing ends of the injury site. The degree of pain was assessed and compared before operation, after operation, and long-term following up according to the *International Association of Neurestoratology Spinal Cord Injury Functional Rating Scale*, i.e., 0 point means extreme pain, uncontrolled, 1 point severe pain, narcotics required, 2 points mild pain, ordinary pain killer effective, 3 points No pain.

# Results

The reevaluations and follow-up were performed at 1 to 21 months with an average of 7.5 months after cells transplantation. The pain scores of *International Association of Neurestoratology Spinal Cord Injury Functional Rating Scale* increased from  $1.4\pm0.6$  to  $2.6\pm0.5$  points (*p*=0.000).

Conclusion

The result shows that the OEC intraspinal transplantation appears to have a positive role in treatment of intractable chronic pain after the SCI. The long-term outcome and mechanism is worth to be further studied.

# Acknowledgements

Beijing Hongtianji Neuroscience Academy Funding

# References

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Huang HY, Wang HM, Xiu B. Preliminary report of clinical trial for olfactory ensheathing cell. J General Naval Hospital PLA 2002; 15: 18-21

Li Y, Field PM, Raisman G. Repair of adult rat corticospinal tract by transplants of olfactory ensheathing cells. Science 1997; 277: 2000-2002

International Association of Neurorestoratology Spinal Cord Injury Functional Rating Scale. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi 22(8): 1021-1023; 2008.

# Learning Objectives:

1. This study provides an evidence of effect of olfactory ensheathing cell intraspinal transplantation on neuropathic pain.

2. Olfactory ensheathing cell therapy is a promising regime for intractable pain following spinal cord injury.

3. Olfactory ensheathing cell therapy is safe and feasibility.

# September 13, 2009 #20

**Abstract Title:** Impact of Sacral surface therapeutic electrical stimulation on early recovery of urinary continence after radical retropubic prostatectomy: a pilot study.

# Primary Presenter: Haruo Nakagawa M.D.

# **Primary Presenter Institution:**

Department of Urology Tohoku University Graduate School of Medicine, Sendai Japan **Co-presenter(s):** 

Yasuhiro Kaiho M.D., Syunichi Namiki M.D., Shigeto Ishidoya M.D., Seiichi Saito M.D.v and Yoichi Arai M.D.

# Co-presenter(s):

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#### Introduction

Urinary incontinence and sexual dysfunction are representative long-term complications of radical prostatectomy. During several months after radical prostatectomy, some degrees of urinary incontinence develop in most patients, significantly lowering their quality of life. The aim of this study is to investigate whether sacral surface therapeutic electrical stimulation (SSTES) initiated during the early postoperative period would be effective towards early recovery of postprostatectomy urinary continence.

### **Materials and Methods**

A total of 35 consecutive patients who underwent nerve sparing radical retropubic prostatectomy by a single surgeon were enrolled in this study. Twenty early patients began pelvic floor muscle exercise (PME) a day before the surgery. Fifteen subsequent patients received SSTES postoperatively with no instruction for PME provided. For SSTES, a pair of plate electrodes was placed on the sacral skin surface. Pulses of 30-Hz, 200-µs were used for 15 minutes, twice a day for 1 week. Immediate urinary function just after catheter removal was evaluated with frequency-volume chart and 24-hour pad test. The urine loss ratio (ULR) was defined as the weight of urine loss in the pad divided by the daily urine volume.

### Results

There were no differences between the SSTES and PME groups in maximum bladder capacity and ULR on the first day after removal of urethral catheter. However, these parameters improved rapidly in the SSTES group. On day 3 maximum bladder capacity was significantly larger in the SSTES compared with the PME group (315.0±59.9 ml vs. 268.1±94.6 ml, p<0.05,Fig-1). ULR was also significantly lower in the SSTES group (1.18±1.36 % vs. 10.32±22.7 %, p<0.05,Fig-2).

# Conclusion

SSTES treatment is feasible and appears to be effective for early recovery of urinary continence after radical prostatectomy. A randomized controlled trial with large study population is warranted to confirm the effectiveness.

# Acknowledgements

This study was supported by Suzuken Memorial Foundation

# Figure and Table Legend

Fig-1: Maximum functional bladder capacity at day 1, 2 and 3 after removal of the urethral catheter. Error bars represent SEs.

Fig-2: Percentage of urine loss ratio at day 1, 2 and 3 after removal of the urethral catheter. The urine loss ratio was defined as the weight of urine loss in the pad divided by the daily urine volume. Error bars represent SEs.

#### Learning Objectives:

1.New rehabilitation method preventing urinary incontinence after radical prostatectomy using neuromodulation

# #21

Abstract Title: Migraines and Gastroparesis: A Histologic, Physiologic, and Clinical Analysis with Temporary Gastric Stimulation

Primary Presenter: Mubina Isani, B.A.

Primary Presenter Institution: University of Mississippi Medical Center, Jackson, MS.

Co-presenter(s): Christopher Lahr, Truptesh H. Khotari, Robert Schmieg, Danielle Spree, Vetta Vedanarayanan, Archana Kedar, Charu Subramony, Thomas Abell

Co-presenter(s): Medical Center, University of Mississippi, Jackson, MS. James J. Peters VA Medical Center, Bronx, NY.

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#### Introduction

A relationship between migraines and gastroparesis (GP) has been observed, but the pathophysiology and mechanisms are unknown. We compared histologic, electrophysiologic, and clinical outcomes to define any differences between drug refractory GP patients with Migraines and those with No Migraines, undergoing temporary gastric electrical stimulation (GES).

#### Materials and Methods

We reviewed data on 80 consecutive patients: 28 Migraine (35%) and 52 No Migraine (65%); 13 males, 67 female, mean age of 43 (26 diabetic, 53 idiopathic, 1 post surgical) undergoing temporary and latter permanent GES for drug refractory GP. Symptoms evaluated included vomiting, nausea, epigastric pain, bloating/distension, and anorexia/early satiety (scored from 0 to 4 for each) and total symptom score (TSS) with a max of 20. Vomiting score and TSS were measured before treatment and during treatment with temporary GES. Four hour Gastric Emptying Time (GET) % retention before and during treatment along with cutaneous, mucosal, and serosal EGG was also measured, reported as frequency and amplitude. Outcomes were reported as change in vomiting scores, change in TSS, and change in 4 hour GET. A full thickness gastric biopsy was performed at the time of subsequent permanent GES placement and was analyzed for S-100 (neuronal) and CD-117 (Cajal) cells. Two tailed unpaired t tests were performed for each category.

#### Results

Vomiting and TSS scores at baseline were higher among patients with migraines. Also the migraine patients had more improvement in vomiting scores with temporary GES. Patients with migraines had more normal gastric emptying scores at baseline and a greater change after temporary GES. The amplitude of mucosal EGG in patients with Migraines was higher than in the No Migraine group. There was no statistical difference between the Migraine group and the No Migraine group in outer or inner S-100 cells (neuronal) outer or inner CD-117 (Cajal) cells, cutaneous EGG frequency and amplitude, or serosal EGG frequency and amplitude. (See Table)

#### Conclusion

GP Patients with Migraines have different baseline physiology as well as better symptom improvement from temporary GES compared with No Migraine GP patients.

#### References

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  - non cyclic patients undergoing gastric electrical stimulation.
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	Migraine	No Migraine	P value of Difference
Baseline Vomiting	2.91	1.87	0.002*
Treatment Vomiting	0.34	0.43	0.71
Vomiting Change	-2.50	-1.34	0.002*
Baseline TSS	15.61	13.68	0.03*
Treatment TSS	5.48	4.41	0.34
TSS Change	-10.44	-9.12	0.27
Baseline 4 hour GET scan	0.13	0.25	0.02*
Treatment 4 hour GET	0.16	0.26	0.08**
4 hour GET Change	0.02	0.01	0.89
Muc EGG Freq.	5.36	5.14	0.64
Muc EGG AMF	1.12	0.74	0.05*

Table: Comparison of Migraine vs. No Migraine

(\*p-value ≤0.05; \*\*p-value <0.10)

Learning Objectives:

1. A relationship between migraines and gastroparesis (GP) has been observed, but the pathophysiology and mechanisms are unknown.

2. Vomiting and TSS scores at baseline were higher among patients with migraines. Also the migraine patients had more improvement in vomiting scores with temporary GES. Patients with migraines had more normal gastric emptying scores at baseline and a greater change after temporary GES. The amplitude of mucosal EGG in patients with Migraines was higher than in the No Migraine group.

3. GP Patients with Migraines have different baseline physiology as well as better symptom improvement from temporary GES compared with No Migraine GP patients.

Abstract Title: Gastric Pacemaker Interstitial Cells of Cajal - Reduced in Patients with Chronic Nausea and Vomiting

# Primary Presenter: Christopher Lahr, MD

Primary Presenter Institution: The University of Mississippi Medical Center, Mississippi, USA Co-presenter(s): \*Truptesh H. Kothari MD, \*\*Christopher Lahr, MD, \*\*Lindsey Halley, \*\*Stacy Hood, \*\*Benoit Blondeau MD, \*\*Robert Schmieg MD, \*\*Charu Subramony MD, \*\*Thomas Abell MD

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# Introduction

Loss of gastric neurons and interstitial cells of Cajal (ICC) has been postulated as an etiology of diabetic gastroparesis. This study was undertaken to evaluate this hypothesis

# **Materials and Methods**

Two surgeons performed full thickness gastric biopsies at the time of permanent gastric electrical stimulator implantation for drug refractory gastroparesis in 81 patients. Biopsies were stained for S100 and CD117 cells. Investigators counted and averaged the stained cells in ten high-powered fields in both outer muscle layer and the inner muscle layer for each patient. They examined specimens from seven autopsy controls in a similar fashion. Patients were categorized by etiology as either idiopathic (n=59) or diabetes mellitus (n=24). Un-paired T tests were used to compare groups.

# Results

Diabetic gastroparesis patients had a mean of 6.13 cells/hpf in the outer muscle layer and a mean of 10.70 cells/hpf in the inner muscle layer with a maximum of 16 cells/hpf and a minimum of 1 cell/hpf in both the layers on an average. Autopsy control patients had a mean of 17.62 cajal cells/hpf in the outer muscle layer and a mean of 23.24 cajal cells/hpf in the inner muscle layer with a maximum of 50.4 cells/hpf and a minimum of 11.9 cells/hpf in both the layers. Other group comparisons were not statistically significant.

# Conclusion

Quantitative immunohistological evaluation of full thickness gastric biopsies in patients undergoing gastric electrical stimulator implantation for diabetic gastroparesis reveals significant reduction in the number of neurons and interstitial Cajal cells when compared with nongastroparetic controls. Similar reductions in neurons and Cajal cells were not seen in patients undergoing gastric electrical stimulation for idiopathic gastroparesis.

# #22

The presence of reduced neurons in the stomachs of diabetic gastroparetics is evidence that the cause of diabetic gastroparesis is locally mediated cell damage and does not arise in the central nervous system.

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	Diabetic Gastroparesis	Controls
Mean	6.1312	17.6286
SD	4.6984	6.1622
Ν	24	7

S-100 Outer Muscle Layer – Diabetic Gastroparesis Vs Controls P < 0.0001

# Learning Objectives:

1. Diabetics have reduced S-100 cells count which corresponds to neuronal and Cajal cell loss statistically more than autopsy controls.

Neuronal cell loss in idiopathics was not significantly different from autopsy controls
 Longitudinal muscle layer is more important than the circular muscle layer of the stomach in causing nausea, vomiting and gastroparesis in diabetes mellitus.

September 13, 2009 #23

Abstract Title: Depression and Gastroparesis: A Histological, Physiological and Clinical Outcome Analysis in Response to Gastric Stimulation Primary Presenter: Joy Hughes, BA Primary Presenter Institution: University of Mississippi Medical Center, Jackson, MS Presenting author's full street address and e-mail address: 1037A Whitworth St Jackson, MS 39202

#### Introduction

Gastroparetic (GP) patients often present with gastrointestinal symptoms perceived to be psychiatric or psychosomatic in origin. We hypothesized differences in treatment outcomes, as well as in depressed patients' gastric histology and physiology compared to those without self-reported depression.

### **Materials and Methods**

We reviewed prospective data on 80 patients (47 depressed and 33 not depressed by selfidentification)\_(67 f, 13 m, mean age of 43, with 26 diabetic, and 53 idiopathic and 1 postsurgical) undergoing temporary and later permanent gastric electrical stimulation (GES) for drug refractory gastroparesis. Symptoms evaluated included nausea, vomiting, epigastric pain, bloating, and early satiety. Each symptom was scored from 0 to 4 based upon frequency and severity, and total symptom score (TSS) is the sum of the five symptom scores with a maximum of 20. Vomiting and TSS were measured before treatment and during treatment with temporary GES. Four hour Gastric Empting Time (GET) was measured before and during treatment. Outcomes were reported as change in: vomiting scores, TSS, and 4 hour GET. Evaluation included cutaneous, mucosal, and serosal EGG reported as frequency and amplitude and full thickness gastric biopsies done at the time of subsequent GES placement for the number of CD117 cells (Cajal) and S100 (neurons) cells per high powered fields (hpf) from 10 hpf. Two tailed unpaired t tests were performed for each clinical and treatment outcome (See Table). {may be too long}

### Results

The depressed patients had greater baseline TSS and greater change in TSS in response to temporary GES. There was no difference between the post-treatment TSS scores of the depressed and non-depressed patients. There were no statistically significant differences in gastric emptying times between the two groups. We found no stastically significant histological differences between the two groups, although the depressed patients averaged less neurons in both inner and outer layers.

#### Conclusion

In this group of GP patients undergoing GES, depressed patients appear to have some symptom differences at baseline when compared to non-depressed patients. In addition, depressed patients improved more than non depressed patients after GES. Depression, although common in GP patients, appears not to be a contraindication to a temporary GES or subsequent permanent GES.

#### References

Truptesh H. Kothari, Joy Hughes, Christopher J. Lahr, Robert Schmeig, Danielle Spree, Gabriel Uwaifo, Archana Kedar, Charu Subramony, Thomas Abell

		No	P-value of	
Data Measured	Depression	Depression	difference	
Baseline Vomiting	2.04	2.43		0.14
Change in				
Vomiting	-1.31	-1.88		0.13
Treatment				
Vomiting	0.41	0.4		0.97
Baseline TSS	15.46	12.7		0.001

#### Table: Comparison of GP Patients Means by Depression

Change in TSS	-10.69	-7.93	0.0495
Treatment TSS	5.09	4.14	0.38
Baseline 4hr GET	0.22	0.2	0.67
Baseline TGET	1.6	1.51	0.86
Treatment TGET	1.22	1.43	0.19
Cut EGG Freq	5.43	5.11	0.45
Cut EGG Amp	0.11	0.15	0.22
Muc EGG Freq	5.18	5.27	0.84
Muc EGG Amp	0.81	0.96	0.43
Ser EGG Freq	5.51	5.74	0.48
Ser EGG Amp	0.59	0.45	0.29
Outer S-100	6.69	11.44	0.14
Inner S-100	11.72	16.58	0.23
Outer CD-117	8.33	10.25	0.38
Inner CD-117	12.02	11.17	0.63

#### Learning Objectives:

1. Learn whether or not patients with gastroparesis presenting with depression compare in their baseline symptom scores to patients without depression.

2. Learn whether or not patients presenting with depression benefit from treatment with gastric pacemakers.

3. Learn whether or not patients with depression and gastroparesis exhibited no statistically significant histological changes compared to non-depressed patients with gastroparesis.

September 13, 2009 #24

**Abstract Title:** Diabetes and Gastroparesis: A Histologic, Physiologic and Clinical Analysis in Response to Temporary and Subsequent Permanent Gastric Stimulation **Primary Presenter:** Joy Hughes, BA

Primary Presenter Institution: University of Mississippi Medical Center, Jackson, MS Presenting author's full street address and e-mail address:

1037A Whitworth St Jackson, MS 39202 Joyandjosh.hughes@yahoo.com

#### Introduction

Diabetes mellitus (DM) is commonly associated with gastroparesis (GP) and is associated with significant attendant morbidity and mortaility (DIG, 75 (2-3): 83-89, 2007). Gastric electrical stimulation (GES) is used for both DM and non-DM GP, but detailed pathophysiologic comparisons between diagnostic groups are lacking. We aimed to compare clinical outcomes, electrogastrography, and histology of diabetics vs. non-diabetics among GP patients treated with temporary GES.

#### **Materials and Methods**

We prospectively collected data on 80 patients (26 diabetic, 54 non-diabetic, 67 f, 13 m, mean age of 43 with GP ) undergoing temporary and subsequent permanent GES for drug refractory GP. Symptoms evaluated were nausea, vomiting, epigastric pain, bloating/distension, and

anorexia/early satiety and Total symptom score (TSS) he sum of the five aforementioned symptom scores from 0 to 4 for each, max. 20. Total gastric emptying time (TGET) (the sum of percent of retained isotope at 1, 2, and 4 hours) were measured before and during treatment with temporary GES and cutaneous, mucosal, and serosal EGGs were measured, reported as frequency and amplitude. Full thickness biopsy was done with subsequent implantation of permanent GES and showed the number of CD-117 (Cajal) cells and S-100 (neuronal) cells per hpf from 10 high powered field. Two tailed unpaired t tests were performed for each category (see table).

#### Results

The two groups had similar improvement in vomiting and TSS. Both baseline 4 hr GET and post-treatment TGET were greater in diabetics than non-diabetics. The serosal EGG frequency was significantly lower in diabetic patients. The mucosal EGG frequency was also lower in the diabetic patient group, although this difference failed to satisfy statistical significance. The diabetic group demonstrated lower numbers of neurons and Cajal cells in both inner and outer muscle layers, but the only parameter that satisfied statistical significance was the outer CD-117 (Cajal) cells, which were lower in the diabetic group. See Table.

### Conclusion

In this group of patients undergoing temporary and later permanent GES, a number of difference exist between DM and non-DM groups both baseline physiologic measures and treatment effects for temporary GES.

#### References

Truptesh H. Kothari, Joy Hughes, Christopher J. Lahr, Robert Schmeig, Danielle Spree, Gabriel Uwaifo, Archana Kedar, Charu Subramony, Thomas Abell

	Not		
Data Measured	Diabetic	Diabetic	P-value
Baseline Vomiting	2.28	2.14	0.68
Change in Vomiting	-1.74	-1.52	0.58
Treatment Vomiting	1.18	1.47	0.72
Baseline TSS	14.65	13.72	0.31
Change in TSS	-9.52	-9.38	0.83
Treatment TSS	4.88	4.46	0.71
Baseline 4hr GET	0.18	0.28	0.05*
Baseline TGET	1.6	1.51	0.86
Treatment TGET	1.18	1.47	0.06**
Cut EGG Freq	5.22	5.5	0.53
Cut EGG Amp	0.12	0.16	0.26
Muc EGG Freq	5.42	4.79	0.18
Muc EGG Amp	0.87	0.88	0.93
Ser EGG Freq	5.83	5.14	0.04*
Ser EGG Amp	0.52	0.54	0.83
Outer S-100	9.85	6.01	0.26
Inner S-100	14.31	12.38	0.65
Outer CD-117	10.78	5.7	0.03*
Inner CD-117	12.49	9.95	0.17

#### Table: Comparison of Means for GP patients

#### <0.05 \*\*0.05<p<0.1

#### Learning Objectives:

1. Learn whether or not GP patients with diabetes exhibit histological changes compared to GP patients without diabetes.

2. Learn whether or not GP patients presenting with diabetes have different therapeutic benefit from gastric electric stimulation.

3. Learn whether or not GP patients presenting with diabetes have different physiologic recording than GP patients without DM.

September 13, 2009 #25

Abstract Title: Pain and Gastroparesis: Not a Contraindication for a Trial of Gastric Electrical Stimulator Primary Presenter: Lindsey Halley, B.S. Primary Presenter Institution: University of Mississippi Medical Center 2500 N State St. Jackson, MS 39216 Presenting author's full street address and e-mail address: 3795 I55-N Apt. B-4 Jackson, Ms 39219 Ihalley@psychiatry.umsmed.edu

#### Introduction

Many patients with gastroparesis (GP) have abdominal pain and many other GP patients undergo GES. However the characteristics and responses of abdominal pain to gastric electrical stimulation (GES) have not been defined.

#### **Materials and Methods**

We reviewed data on 80 patients (13 males, 67 female, mean age of 43, 26 diabetic, 53 idiopathic, 1 post surgical) undergoing temporary gastric electrical stimulation for drug refractory gastroparesis. The patients were categorized into two groups, severe pain (pain scores >3) and mild to moderate pain (pain scores <3) on a scale of 0-4, none to worse. Symptom scores and 4 hour Gastric Empting Times (GET) were measured before and during treatment with temporary GES. Outcomes were measured as change in vomiting score, change in abdominal pain, and change in total symptom scores (TSS). Two tailed unpaired t tests were performed for each category.

Low amplitude, high frequency settings were employed (current 5-10 amps, frequency 14-55 Hz, 330 microseconds pulse width, cycle on time 0.1-4 seconds, cycle off time 5-1 seconds).

#### Results

Patients with severe pain had more vomiting at baseline and their improvement in vomiting score was greater than patients with mild to moderate vomiting. Patients with severe pain showed more improvement in pain than the mild to moderate group as well. Patients with severe pain also had a significantly greater baseline TSS than patients with mild to moderate pain but the improvement was greater for the severe pain group.

### Conclusion

In this group of GP patients with severe abdominal pain the improvement in vomiting, pain and gastric emptying times were greater than patients with mild to moderate pain with GES. Therefore, severe abdominal pain should not be a contraindication for a trail of gastric electrical stimulation.

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### Acknowledgements

Lindsey Halley, Christopher Lahr, Truptesh Kothari, Robert Schmieg, Danielle Spree, Ike Eriator, Christine Kasser, Archana Kedar, Charu Subramony, Thomas Abell

	Mild to Moderate Pain	Severe Pain	P value of difference		
Baseline Vomiting	1.5	2.3	0.02		
Treatment Vomiting	0.45	0.36	0.75		
Vomiting Change	-0.97	-1.9	0.02		
Baseline Pain Score	1.2	3.6	< 0.0001		
Treatment Pain Score	0.56	1.1	0.15		
Pain Change	-0.44	-2.5	<0.0001		
Baseline TSS	10.9	15.1	<0.0001		
Treatment TSS	4.5	4.8	0.80		
TSS Change	-6.4	-10.4	0.002		

# TABLE

# Learning Objectives:

1. The characteristics and responses of abdominal pain to gastric electrical stimulation (GES) have not been defined.

2. Abdominal pain is not a contraindication for GES.

September 13, 2009 #26

Abstract Title: Pain and Gastroparesis: Not a Contraindication for a Trial of Gastric Electrical Stimulator Primary Presenter: Lindsey Halley, B.S. Primary Presenter Institution: University of Mississippi Medical Center 2500 N State St. Jackson, MS 39216 Presenting author's full street address and e-mail address: 3795 I55-N Apt. B-4 Jackson, Ms 39219 Ihalley@psychiatry.umsmed.edu

### Introduction

Many patients with gastroparesis (GP) have abdominal pain and many other GP patients undergo GES. However the characteristics and responses of abdominal pain to gastric electrical stimulation (GES) have not been defined.

#### **Materials and Methods**

We reviewed data on 80 patients (13 males, 67 female, mean age of 43, 26 diabetic, 53 idiopathic, 1 post surgical) undergoing temporary gastric electrical stimulation for drug refractory gastroparesis. The patients were categorized into two groups, severe pain (pain scores >3) and mild to moderate pain (pain scores <3) on a scale of 0-4, none to worse. Symptom scores and 4 hour Gastric Empting Times (GET) were measured before and during treatment with temporary GES. Outcomes were measured as change in vomiting score, change in abdominal pain, and change in total symptom scores (TSS). Two tailed unpaired t tests were performed for each category.

Low amplitude, high frequency settings were employed (current 5-10 amps, frequency 14-55 Hz, 330 microseconds pulse width, cycle on time 0.1-4 seconds, cycle off time 5-1 seconds).

#### Results

Patients with severe pain had more vomiting at baseline and their improvement in vomiting score was greater than patients with mild to moderate vomiting. Patients with severe pain showed more improvement in pain than the mild to moderate group as well. Patients with severe pain also had a significantly greater baseline TSS than patients with mild to moderate pain but the improvement was greater for the severe pain group.

#### Conclusion

In this group of GP patients with severe abdominal pain the improvement in vomiting, pain and gastric emptying times were greater than patients with mild to moderate pain with GES. Therefore, severe abdominal pain should not be a contraindication for a trail of gastric electrical stimulation.

#### References

1. Ayinala S, Batista O, Goyal A, Al-Juburi A, Abidi N, Familoni B, Abell T. Temporary gastric electrical stimulation with orally or PEG-placed electrodes in patients with drug refractory gastroparesis. Gastrointestinal Endoscopy 2005; 61: 455-461.

- Jennifer Maranki, Vanessa Lytes, John Meilahn, Sean Harbison, Frank Friedenberg, Robert Fisher, Henry Parkman. Predictive Factors for Clinical Improvement with Enterra Gastric Electric Stimulation Treatment for Refractory Gastroparesis. Springer Science+Business Media 2008; 2072-2078
- W. A. Hoogerwerf, M.D., P. J. Pasricha, M.D., A. N. Kalloo, M.D., and M. M. Schuster, M.D. Pain: The Overlooked Symptom in Gastroparesis. The American Journal of Gastroenterology 1999: Vol 94, No. 4; 1029-1033

# Acknowledgements

Lindsey Halley, Christopher Lahr, Truptesh Kothari, Robert Schmieg, Danielle Spree, Ike Eriator, Christine Kasser, Archana Kedar, Charu Subramony, Thomas Abell

IABLE				
	Mild to Moderate Pain	Severe Pain	P value of difference	
Baseline Vomiting	1.5	2.3	0.02	
Treatment Vomiting	0.45	0.36	0.75	
Vomiting Change	-0.97	-1.9	0.02	
Baseline Pain Score	1.2	3.6	< 0.0001	
Treatment Pain Score	0.56	1.1	0.15	
Pain Change	-0.44	-2.5	<0.0001	
Baseline TSS	10.9	15.1	<0.0001	
Treatment: TSS	4.5	4.8	0.80	
TSS Change	-6.4	-10.4	0.002	

# Learning Objectives:

1. The characteristics and responses of abdominal pain to gastric electrical stimulation (GES) have not been defined.

2. Abdominal pain is not a contraindication for GES.

# September 13, 2009 #27

# Abstract Title:

Modeling motor cortex stimulation to excite the Subthalamic nucleus via different pathways in human.

Primary Presenter: D.G.M. de Klerk, MSc.

Institute for Biomedical Technology, Department of Electrical Engineering, Mathematics and Computer Science, Biomedical signals and systems group, University of Twente Enschede, the Netherlands

Email: d.g.m.deklerk@utwente.nl

# Co-presenter(s):

1. Name: T. Heida Credentials: Dr.ir.

1. Place of Employment: Institute for Biomedical Technology, Department of Electrical Engineering, Mathematics and Computer Science, Biomedical signals and systems group, University of Twente City: Enschede Country: the Netherlands

#### Introduction

Deep brain stimulation of the Subthalamic nucleus is widely applied to treat Parkinson's disease. In order to locate the motor part of the Subthalamic nucleus, motor cortex stimulation can be applied and the response in the Subthalamic nucleus-motor part can be sensed. The corticosubthalamic connections consist of a hyperdirect and indirect pathway (Figure 1A). The hyperdirect pathway originates in deep layer V pyramidal tract neurons [1] (Figure 1B). In contrast, the intratelecenphalic neurons from layer III and superficial layer V presumably provide the main excitatory input to the indirect pathway [2], but see [3]. Selective cortical stimulation can be used to preferentially excite either the hyperdirect or indirect pathway, which will evoke different responses in the Subthalamic nucleus [4].

#### Materials and Methods

A 3D finite-element volume conduction model of the motor cortex was built to compute the potential field following cortical stimulation (Figure 2). In addition, a neuron model was developed using the McNeal-type cable model [5]. Both models were merged and activation fields in the cortex were calculated.

#### Results

Activation fields following different stimulation configurations were analyzed. Our proposed configurations selectively excite distinct cortical neuronal populations in order to separately excite pathways to the Subthalamic nucleus. The hyperdirect pathway is preferentially excited by low-amplitude monopolar stimulation (Figure 3).

#### Conclusion

Selective cortical stimulation of the hyperdirect and indirect pathway can be achieved by different stimulation configurations, which will lead to different Subthalamic responses. Our proposed configuration preferentially excites the hyperdirect pathway, which conveys information directly related to movement [1]. Hypothetically, this will provide a Subthalamic response, which is most optimally located in the motor part. Analyzing these responses reveals information about differently connected parts in the Subthalamic nucleus and can aid better localization of the Subthalamic nucleus-motor part, the main target in deep brain stimulation.

#### Acknowledgements

The authors gratefully acknowledge the support of the BrainGain Smart Mix Programme of the Netherlands Ministry of Economic Affairs and the Netherlands Ministry of Education, Culture and Science.

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### Figure Legend:

1A. The hyperdirect pathway consists of a direct connection between the cortex and Subthalamic nucleus (STN). The indirect pathway goes via the striatum and Globus Pallidus externus (GPe).

1B. The hyperdirect pathway originates in layer III and superficial layer V (Va) intratelecenphalic (IT) neurons. The indirect pathway originates in deep layer V (Vb) pyramidal tract (PT) neurons.

2. The 3D finite-element volume conduction model of the motor cortex.

3. Activation of cortical neurons following monopolar motor cortex stimulation at 1 V and a pulsewidth of 90  $\mu$ s. Green neurons are activated, while blue neurons are not. The figures show that a large population of PT neurons is activated, while only a small number of IT neurons is activated.

### Learning Objectives:

1. Excitability of different pathways to the Subthalamic nucleus (selectivity of stimulation)

2. Localization of the motor part of the Subthalamic nucleus

# September 13, 2009 #28

**Title**: Neural Sensing and Stimulation with IrO<sub>2</sub>/Au Nanowires and Nanocavity Ensemble **Primary Presenter**: Hargsoon Yoon

**Primary Presenter Institution**: Innovative Nano/Bio Devices and System Laboratory, Electrical Engineering Dept., University of Arkansas, 700 Research Center Blvd., Fayetteville, AR, 72701, USA

**Co-Presenter**: Phillip Hankins<sup>1</sup> and Vijay K. Varadan<sup>1,2</sup>

# **Co-Presenter Institution:**

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# Abstract:

High frequency deep brain stimulation has been applied as a clinical treatment for abnormal brain activity in Parkinson's patients and substantial efforts have focused on the treatment of pharmacologically intractable epilepsy using the technology. The aim of this research is to

develop a reliable neural stimulation system using nanotechnology. This presentation specifically focuses on the development of neural stimulating, recording and sensing electrodes with heterostructured IrO<sub>2</sub>/Au nanoelectrodes. The uniqueness of this research is the use of nanoscale electrodes as the interfacing surface with neurons. These electrodes have been developed on flexible neural probes with both titanium and polyimide substrates. The outer, functional layer of the nanoelectrodes, made of iridium oxide, provided high charge storage capacity, 48.6 C/cm<sup>2</sup> which can enhance neural signal sensing and stimulating efficiency. We will also discuss the analysis of neural cell interactions with the nanoelectrodes and *in-vivo* recording from hippocampal rat neurons using the nanoelectrode probes. To investigate the correlation between stimulation and neurochemical response in the brain, neurotransmitter sensing electrodes have been developed in this research. By using a 3-dimensional cavity structure of two working electrodes, collection efficiency in redox cycling of dopamine is enhanced. Analysis results from dopamine sensing and the collection efficiency will be presented as well.

# September 13, 2009 #29

Abstract Title: Requirements for the safety and compatibility of MRI for patients with a neuromodulaton device; Progress report on behalf of the ISO MRI Joint Working Group Primary Presenter: Prof. Robert A. Stevenson, PE Primary Presenter Institution: Greatbatch Medical, Inc. 10,000 Wehrle Drive, Clarence, NY 14031 Presenting author's full street address and e-mail address: 15349 Iron Canyon Road, Santa Clarita, CA 91387 rstevenson-gb-sierra@socal.rr.com

Introduction: Manufacturers are working to design active implantable medical devices (AIMDs) including neurostimulators that are Magnetic Resonance Imaging (MRI) compatible. This is because MRI has become one of medicine's most valuable diagnostic tools and is also used in real time medical procedures. MRI is contraindicated for most neurostimulator patients due to concerns that the powerful electromagnetic fields produced by MRI could cause malfunction of the implanted device, and/or could induce undesirable heating in implanted leads.

Methods: The International Standards Organization (ISO) has formed a joint working group (TC150; JWG2) involving over 50 MR physicists, MR manufacturers, implant manufacturers and regulatory experts from the FDA. The JWG2 is working on a technical specification (TS) which defines comprehensive bench top testing to assure the safety and compatibility of AIMDs in 1.5 Tesla MR environments. As more is learned, the TS will evolve into a formal ISO Standard for MRI Safety and Compatibility of AIMDs.

Results: The JWG has documented a comprehensive list of variables that affect how the MR static, gradient and RF fields can interact with AIMDs and their implanted lead systems. Previous reports of MRI scans being safely performed on neurostimulator patients should be considered anecdotal at this time. For example, SAR is a very poor predictor of the energy that can be induced in an implanted lead (up to 40% variability). A better indicator is B1 RMS which MRI manufacturers have agreed to add to their equipment displays.

Conclusions: The first draft of the ISO MRI TS is expected to be completed in the third quarter of 2009. Included are in-vitro tests for lead heating, EMI, gradient and static field induced effects. Also included

is a discussion of how much heat can occur in certain situations and novel lead designs that significantly reduce implanted lead heating during MRI scans.

#### Acknowledgements

I would like to acknowledge the more than 50 members of the ISO MRI Task Force, ISO Technical Committee TC-150, Subcommittee 6, Joint Working Group 2 who have been meeting several times per year for the last three years in locations all around the world to produce a draft of the new MRI Technical Specification (TS). I would like to particularly acknowledge the Conveynors and Subcommittee Chairs of JWG2: Curt Sponberg - Medtronic; Hans Engels - Philips; Michael Streckner – Toshiba, Dave Manahan – Medtronic (Gradient Subgroup Chairman); and Niels Kuster – IT'IS (RF Subgroup Chairman) and Bob Stevenson (myself) – Greatbatch Medical (EMC Subgroup Chairman).

# Learning Objectives:

1. Learn about the technical challenges in design and implant of neurostimulators such that they may safely receive one or more MRI scans.

2. Learn about the work of the ISO MRI Joint Working Group and their progress on producing a technical specification to set the standards for assuring that an active implantable device may be safely scanned under specific conditions.

3. Learn about the variables and the specific conditions that must be specified to safely perform MRI scans on AIMDs such as neurostimulators.

4. Learn about novel new design techniques of leads and devices to make them MRI compatible under these "certain specific condition."

# September 13, 2009 #30

**Abstract Title:** Medio-lateral field steering in spinal cord stimulation (SCS) using triple leads with longitudinal guarded cathodes

Primary Presenter: V.Sankarasubramanian Msc

**Primary Presenter Institution:** Institute of Biomedical technology, Department of Electrical engineering, University of Twente, Enschede, Netherlands.

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#### Introduction

In spinal cord stimulation (SCS) clinical practice, longitudinal guarded cathode (+-+) stimulation by a single electrode, symmetrically placed over the dorsal columns provides the broadest paresthesia coverage. Off-midline lead migrations often do not result in this paresthesia sufficiently covering the pain area. Dual-leads with medio-lateral cathodal field steering can offer a higher degree of control over the electrical fields in targeting the desired paresthesia back to the pain location but at the cost of a reduced dorsal column width. To improve the coverage, a triple lead aligned configuration is modeled in this study and to specifically

1. Compare the influence of transversal separation between the leads on the activated dorsal column fibers.

2. Observe the effects of anodal currents (constant and variable) on the medio-lateral steering of dorsal column activation.

### Materials and Methods

Triple aligned parallel leads, with longitudinal guarded cathode configuration (with the center lead placed on the spinal cord midline) were modeled for various transversal lead separations (1.0, 1.5, 2.0 and 2.5 mm). Medio-lateral cathodal field steering, with and without the steering of anodes was performed by changing the current ratios between the midline and the lateral lead. The usage range (UR) and the recruited dorsal column area was determined for all current ratios.

### Results

A smaller transversal separation between the leads results in a larger usage range, providing deeper and wider dorsal column activation, and larger paresthesia area. The electrical field was displaced smoothly along the adjacent cathodes in the medio-lateral direction, when the transversal spacing between the leads was small. Steering of anodes combined with the cathodal steering provides a greater control of the activated dorsal column area.

#### Conclusion

The transversal separation between the leads is a major determinant of the area and distribution of paresthesia. Balancing of currents in the longitudinal direction by steering the anodes is preferable in dorsal column activation, more than the shielding effect of anodes on the dorsal root fibers, when not steered. A triple lead configuration can provide greater post-operative flexibility in covering a larger width of the low-thoracic dorsal columns.

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#### Acknowledgements

The authors gratefully thank Boston Scientific Neuromodulation (Valencia, CA, USA) for their grant to support this research

### Learning Objectives:

1. The transversal separation between the leads is a major determinant of the area and distribution of paresthesia.

2. Balancing of currents in the longitudinal direction by steering the anodes is preferable in dorsal column activation, more than the shielding effect of anodes on the dorsal root fibers, when not steered.

3. A triple lead configuration can provide greater post-operative flexibility in covering a larger width of the low-thoracic dorsal columns.

# September 13, 2009 #31

Abstract Title: A Programmable Multi-Channel Stimulation IC for Neuromodulation Primary Presenter: Kyou Sik Min, Ph.D. candidate

**Primary Presenter Institution:** School of Electrical Engineering and Computer Science, Seoul National University, Seoul, Republic of Korea

**Co-presenter(s):** Choong Jae Lee<sup>1</sup>, Se Ik Park<sup>1, 2</sup>, Sung Eun Lee<sup>1</sup> and Sung June Kim<sup>1</sup> **Co-presenter(s):** 

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#### Introduction

Deep Brain Stimulation (DBS) therapy has been a successful treatment for patients with Parkinson's Disease(PD) for decades[1]. Thanks to the success of DBS, neurosurgeons are now researching new neuromodulational methods to overcome neuronal diseases. Various neuromodulational therapies showed possibilities to alleviate symptoms of neuropathic pain, depression, and even dementia[2-4]. As neuronal diseases require different stimulation parameters respectively, applying a generic stimulation system can be helpful to optimize modulation parameters for specific neuronal disease. We have developed 4-channel programmable generic stimulation IC for neuromodulation. Neurosurgeons are able to set modulating sites and parameters for specific case through direct cable, IR transceiver, RF-coil communication, and so on.

#### **Materials and Methods**

Silicon based chip was fabricated by Austria Microsystems in Austria. Data receiver uses pulsewidth modulation(PWM) and pulse counting scheme. Each channel can be programmed in 24-bipolar and 24-monopolar stimulation modes respectively. Stimulation strategy uses four consecutive trigger signals and assigns channels to signals at which the channel delivers stimulation current.

#### Results

Simulation results showed that the chip can span frequency from 20Hz to 230Hz in 5Hz step. The current levels were quantized in 1024 steps from 10uA to 10.23mA. Consecutive four trigger signals determine the duration of stimulus, which can be different from each other. Duration can be set from 10us to 630us in 10us steps.

#### Conclusion

We developed multi-channel stimulation IC, which is applicable to neuromodulation research. This IC can be used developing neural pre-prosthetic system for searching appropriate modulation parameters for various neuronal diseases. In addition, by inserting channels to brain sites which is assumed neuronal circuit failure, neurosurgeons can implement artificial consecutive neuronal circuits.

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### Acknowledgements

This work was financially supported by the grant from the Industrial technology development program (10031270) of the Ministry of Knowledge Economy(MKE) of Korea.

### Learning Objectives:

- 1. Programmable Stimulation IC
- 2. Stimulation Strategy

Neuromodulation Device

September 13, 2009 #32

### Abstract Title: An "AC logic" concept for low cost, but safe neuro-stimulator system Primary Presenter: Kyou Sik Min, Ph.D. candidate

**Primary Presenter Institution:** School of Electrical Engineering and Computer Science, Seoul National University, Seoul, Republic of Korea

**Co-presenter(s):** Choong Jae Lee<sup>1</sup>, Sung Eun Lee<sup>1</sup>, Se Ik Park<sup>1, 2</sup>, and Sung June Kim<sup>1</sup>

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#### Introduction

Neuro-stimulator device requires hermetic package that seals implant circuit against the body fluids for the durability of the circuit and safety of the tissue [1]. This package is costly to make and difficult to maintain [2, 3]. New approach to make simple and low-cost package has been studied, but the package still has leakage of water and ions. [4] Thus, this research investigate electrochemical safety in the leakage condition and propose novel Alternative Current (AC) logic

concept which means the possibility of Direct Current (DC) is eliminated for safe neurostimulator system.

### **Materials and Methods**

We conducted the soak test of the working neuro-stimulator IC in the 1% Phosphate Buffered Saline (PBS). In the test, we observed the pH shift of the solution when the soaked IC began to work. We also monitored electrochemical reactions by measuring the accumulated charge at 1.5 mm X 0.5 mm Au metal sites soaked in the PBS solution. We compared the soak test results of AC logic condition with conventional DC condition in order to verify enhancement of safety.

### Results

In DC condition, exposed metal of the neuro-stimulator generated bubbles implying irreversible Faradaic reaction to be avoided.[5] The pH dropped from pH 7 to pH 2 and accumulated charge measured 6 uC. In AC condition, on the contrary, no bubble was observed and the pH shift and averaged accumulated charge were 0.1 and 5 nC, respectively.

### Conclusion

We have showed the electrochemical safety of neuro-stimulator by quantitative measurement and demonstrated distinguished decrease of the pH shift and accumulated charge in the AC logic condition. This finding is of importance to suggest the electrical method to enhance the durability of the circuit and safety of the tissue.

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# Acknowledgements

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#### Learning Objectives:

- 1. Hermetic package
- 2. Electrochemical safety
- 3. AC logic concept

September 13, 2009 #33

# Abstract Title: Hydrogel based *in vitro* neuronal network design for Neuron-on-a-Chip technology

Primary Presenter:

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#### **Primary Presenter Institution:**

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#### Co-presenter(s):

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### Introduction

The electrical measurement of neural network culture on microelectrode array is widely used neuroscience, specifically for study of neural network functionality characterization. With controllable morphology of neural network, the interface between neurons and microelectrodes can be enhanced and the network functionality can be studied in response to specific connectivity or electrical, chemical stimulations. Here we report a efficient neuron patterning method to control the network morphology of cultured neural networks *in vitro*.

#### **Materials and Methods**

The design of network pattern is varying from simple independent well array type to complicated network composed of several nodes and connecting bridges. Using soft-lithography, PDMS mold which has intended pattern design is fabricated and selectively treated with air plasma. After attaching the PDMS mold on microelectrode array, agarose hydrogel structures were molded using MIMIC (Micromolding in capillaries). The reason that agarose was selected is that agarose effectively prevents binding of neurons onto undesired area and physically block the neurite growth.

The patterns were aligned with microelectrodes, and E18 rat hippocampal neurons were cultured for a 3 weeks. The development of network activity was investigated by electrical and optical techniques between 14~21 days *in vitro* (DIV).

# Results

Resulted neural network has captured cell bodies only in nodes and neurites in connecting bridges. The spontaneous activity of neural network is measured with calcium imaging technique and MEA from 7 DIV, and the synchronization of activity in connected network has been discovered.

The network connectivity is confirmed through measuring evoked response from electrical stimulation from 10 DIV to 15 DIV. Also chemical stimulation is conducted with pharmacological agents which has changed the spontaneous activity pattern and network connectivity.

### Conclusion

This reliable neuron patterning method in combination with optical and electrical interfaces would serve as powerful tool to study the synaptic plasticity and functional electric stimulations for neural prostheses.

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#### Acknowledgements

This work was supported by the Korea Research Foundation Grant (KRF-2009-313-D00614) and the Korea Science and Engineering Foundation (2009-0080081) funded by the Korean Government (MEST). This work was also supported by System IC 2010 Program.



Fig. 1. Fabricated neuronal network of paired two-node clustered network structure on microelectrode array.

# Learning Objectives:

1. Develop a efficient and reliable method for making *in vitro* neuronal network of fixed morphology.

2. Make sure that the growth of neuronal network is confined by designed network structure and the spontaneous activity of network is correlated to the specific network connectivity.

3. Measure the activity and connectivity change evoked from electrical and chemical stimulation that proves the functionality of neuronal network.

# September 13, 2009 #34

**Abstract Title:** The Development of Diagnostic and Therapeutic System for Brain Disease Using Probe Pin Device (PPD)

**Primary Presenter:** Uhn Lee(M.D)

Primary Presenter Institution: Department of Neurosurgery, Incheon

**Co-presenter(s):** Young Mi Yoo<sup>1</sup>(Ph.D.), Yong Jung Kim<sup>1,2</sup> (Ph.D.), Hyun Tae Yoo<sup>1</sup>(B.S) **Co-presenter(s):** 

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### Introduction

During the last decade, Deep brain stimulation (DBS) has been increasingly accepted as an adjunct therapy for Parkinson's disease (PD), obsessive-compulsive disorder (OCD), and even major depression. The treatment of these diseases using DBS involves the insertion of electrodes with probes incorporated deep in the brain to hit a precise neuro-anatomical target that is central to the disease.

In the conventional system, a stimulator is connected to electrodes by the wiring for power supply. Although the wiring that runs from a stimulator to electrodes appears to be a quick solution for clinical trial, it causes unbearable discomforts to a patient and is also often vulnerable to disconnection of the implanted wire under the skin. The disconnection of wire or power drainage requires repeated surgical procedures.

#### **Materials and Methods**

MEMS Passive and Active Wireless Sensors, Nanowire electrode arrays for PPD, High efficient MEMS antennas, Wireless Implantable Neural Probes

#### Results

The proposed technique to feed power wirelessly requires no wiring whatsoever because of wireless power transmission to implanted electrodes. The feature of wireless powered probe-pin device (PPD) that will be embedded inside the brain will incorporate a number of sensory systems to monitor the neural functions of internal brain.

#### Conclusion

The site-specific function of brain requires a precise amount of control signal and power. Accordingly, a mapping of site-specific power requirement of brain will determine a probe-pin device with specific sensing capabilities.

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# Acknowledgements

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# Learning Objectives:

1. The aim of this proposal is to *deliver* a complete wireless control of neural functionality that will alleviate neurally dysfunctional elements or enhance all functionality of weakened neural elements.

# September 13, 2009 #35

Abstract Title: Voltage- vs. Current-controlled Stimulation in SCS: Effect of Pulse Shape on Neural Response in a Computational Model Primary Presenter: Dongchul C. Lee, PhD **Primary Presenter Institution:** Boston Scientific Neuromodulation, Valencia, CA, USA Co-presenter(s): Kristen Lechleiter, MS Kerry Bradley, MS Dave Peterson, PhD Co-presenter(s): Boston Scientific Neuromodulation, Valencia, CA, USA Presenting author's full street address and e-mail address: **Boston Scientific Neuromodulation** 25155 Rye Canyon Loop Valencia, CA, 91355 Dongchul.Lee@bsci.com

# Introduction

It has been established that the delivery of current over time in pulsatile stimulation varies when using different stimulator types: current-controlled (CC) stimulators deliver a 'square' current pulse that has a constant amplitude during the stimulating pulse, where voltage-controlled (CV) stimulators have a diminishing current delivery during the pulse phase [Holsheimer et al 2000; Merrill et al 2005]. Recently, clinical studies in spinal cord stimulation (SCS) for stimulation preference (CC vs CV) were performed by different researchers but the results were not consistent [Schade et al, Alo et al]. In this mathematical modeling study, we sought to understand the neural response to the electric field generated from different pulse shapes using a computational model with realistic fiber diameter distribution [Lee et al 2007].

#### **Materials and Methods**

The mathematical model of SCS consisted of a volume conductor model based on human morphometric data, and non-linear myelinated fiber models with a range of sizes and densities observed in human histological studies [Feirabend et al 2002]. Two different pulse shapes (tilted exponential and square, with 1000\_s pulse width) were applied to the model (rostrocaudal guarded cathode configuration; 8 mm anode-cathode spacing) and distribution of stimulated fibers of several diameters were computed.

#### Results

At the threshold amplitude of dorsal root (DR) fibers, the square waveform recruited more fibers by activating abundant small diameter dorsal column (DC) fibers. However, the difference was small at 1.4xDCth. The model showed that threshold ratio (DRth/DCth) was higher for square pulse (1.83) than tilted exponential (1.72). At the amplitude of DRth, total number of stimulated fibers was higher for square pulse (900) than tilted exponential (348).

# Conclusion

The clinical effect of pulse shape may vary with amplitude, contact impedance and discomfort fiber source. One SCS clinical study has shown that pain coverage was similar for CC vs CV, but that CC provided a preferred sensation. The model is limited to direct effect of electric field

on fiber, but the major effect on sensational difference may originate from neural networks in the spinal cord and the brain.

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**Figure 1**. Expected fiber recruitment with different shape of waveform. **A**: Effect of different waveforms from CV vs CC devices on DC stimulation at amplitude of DR threshold. **B**: Threshold ratio (DRth/DCth) was dependent on pulse shape. **C**: Total number of fibers, recruited at different amplitude relative to DCth, This suggests a potential source for discrepancy in the observations from clinical studies.

### Learning Objectives:

1. To understand the neural response to the electric field generated from different pulse shapes 2. To quantify the effect of different pulse shapes on dorsal column stimulation

September 13, 2009 #36

Abstract Title: Liquid Crystal Polymer based Deep Brain Stimulation electrode for animals

Primary Presenter: Sung Eun Lee, M.S. candidate

**Primary Presenter Institution:** School of Electrical Engineering and Computer Science, Seoul National University, Seoul, Republic of Korea.

#### Co-presenter(s):

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### Introduction

Conventional electrodes of animal Deep Brain Stimulation (DBS) systems have limitations. A parylene coated tungsten which is a conventional material of single-channel electrode cannot be used for multi-channel with MRI compatibility **[1~2]**. Alternative materials for multi-channel electrode have other problems. The silicon and SOI **[3~5]** are brittle, and polyimide **[6]** has high moisture absorption implying low durability.

In this research, we propose multi-channel electrodes based on Liquid Crystal Polymer (LCP), which has biocompatibility, sufficient stiffness and high stability in aqueous environments for long term durability [7].

#### Materials and Methods

We fabricated two-channel electrodes based on LCP using micro-fabrication technology. By the dimensional control, the electrical and mechanical characteristics of the electrodes were measured for verifying the feasibility of the LCP electrode. The electrode was implanted in the rodent Subthalamic nucleus (STN, AP - 3.6 mm, ML 2.5 mm related to bregma and DV - 8.2 mm from dura, PD model) and the rodent Ventral posteromedial nucleus (VPM, AP - 3.6 mm, LR 2.8 mm related to bregma and DV 6.0 mm from the dura, Pain model) and we confirmed the verticality of the implanted electrode-track using cresyl violet staining.

#### Results

Newly suggested LCP electrode showed sufficient charge storage capacity ( $156.6\pm31 \text{ uC/cm}^2$ ) and charge injection ( $28 \text{ uC/cm}^2$ ) for established stimulation parameters. We confirmed that the LCP electrode has adequate stiffness to insert into the brain without damage of brain.

#### Conclusion

We introduced new LCP based multi-channel electrodes for animal DBS experiments. We observed the electrical and mechanical characteristics of the LCP electrode to demonstrate the feasibility as a DBS electrode. We will report on the behavioral experiments.

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# Learning Objectives:

- 1. Liquid Crystal Polymer
- 2. Liquid Crystal Polymer based DBS electrode
- 3. Polymer based DBS electrode

September 13, 2009 #37

**Abstract Title:** The Comprehensive Solution to Prevent Neurostimulator Lead Migration in the Epidural Space

**Primary Presenter:** Anthony Alexander, MD, DABPM, MPD (Master of Product Development) **Primary Presenter Institution:** Pain Medicine and Rehabilitation Center, Inc., Seymour, IN **Presenting author's full street address and e-mail address:** 1425 Corporate Way, Seymour, IN 47274

**Introduction:** Without question, one of the most frustrating problems with current epidural Neuromodulation is lead migration in the immediate post-operative period. It has been estimated that 11-30% of all epidural lead have some degree of caudal-cephalad or transverse lead migration. Base on current efficacy of Neuromodulation technology a reduction in the lead migration would result in improved acceptance and greater utilization by all four of the customers involved in this technology; the patient, provider, insurance company and hospital administrator.

**Materials and Methods:** A theoretical mechanical engineering structural approach using CAD technology to examine the epidural spaces to determine the causes of lead migration was utilized. These results were then analyzed using current animation technology to determine the usefulness of new design technique created. Once these design techniques were confirmed by engineering theory the designs were utilized to create prototypes for a new base anchor and porous neurostimulator lead. This would theoretical allow neurostimulator anchoring in the epidural space to begin at the time of surgery and finalize within 5-7 days from the initial operation.

**Results:** The mechanical engineering structural approach to development of new innovative anchor is sound and produces anchoring systems that will result in improved lead anchoring system that will decrease the anchor time from its current 6-8 weeks, independent of the manufacturer; to 5-7 days with the new base anchor and porous neurostimulator lead.

**Conclusion:** The current neurostimulator lead migration rate is unacceptable by all customers involved in the technology. The post-op restriction placed on patient for 6-8 weeks interferes with their everyday life and in many cases results in job loss or reduction in income. The physician frustrated with migration results in fewer worthy patient receiving the technology because of the possibility of future operations being need to maintain satisfaction with the technology. The insurance companies are beginning to reclassify the technology as experimental because migration in some cases prevent long term study evaluation that show patient satisfaction outcomes that justify the cost. The hospital administrator cannot justify the cost of keeping neurostimulator leads in stock if they are unsure the physician will utilize the leads in patient.

The technology utilized to create the base anchor and porous lead insures decrease cephalocaudal and transverse lead migration, which will improve acceptance by all customers.

#### Acknowledgements

Alexander Medical Anchors, Inc. owned by the author provided all funding sources. There were no other contributors to the research in this section with the exception of employees and subcontractors of Alexander Medical Anchors, Inc.

### Learning Objectives:

1. Current Neurostimulation Lead Migration is unacceptable to all four customers

2. Mechanical Structural Engineering Approach is useful in understanding the epidural space that causes neurostimulator lead migration and were useful in the development of a base anchor and porous neurostimulator lead

3. The combination of CAD and mechanical structural engineer is useful in the development of a base anchor and porous neurostimulator lead that potential reduce lead anchoring time from the current 6-8 weeks to the new design 5-7 days.

# September 13, 2009 #38

**Title of presentation:** Decoding of retinal ganglion cell activities of photoreceptor-degenerated retina evoked by temporally-patterned electrical stimulation

**Name and institution of presenter(s):** Sang Baek Ryu<sup>1,2</sup>, Jong Seung Lee<sup>1,2</sup>, Jang Hee Ye<sup>3,2</sup>, Yong Sook Goo<sup>3,2</sup>, Kyung Hwan Kim<sup>1,2</sup>

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3. Department of Physiology, Chungbuk National University Medical School

### Introduction

To evoke meaningful visual percept via visual prosthesis, it is necessary to develop a proper electrical stimulation strategy. We suggest the quantification of the accuracy of encoding visual information in RGC responses for this purpose based on spike train decoding.

#### **Materials and Methods**

We constructed an *in-vitro* model of retinal visual prosthesis using planar multi-electrode array (MEA) and investigated whether the quantitative information on input electrical stimulus can be decoded from retinal ganglion cell (RGC) spike responses. *Rd*1 mouse was used as an animal model of photoreceptor degeneration. Assuming that pulse amplitude modulation is utilized for the encoding of light intensity variation, amplitude-modulated electrical pulses were generated and applied to one channel of the MEA on which retinal patch was attached. Multiple single unit activities from evoked RGCs were recorded simultaneously from other channels.

#### Results

Oscillatory activities (8~10 Hz) were observed in the background of extracellular neural signals. Rhythmic burst of spontaneous RGC spikes were also found with same frequency. Evoked RGC activities were found to be consistently modulated by the pulse amplitudes. The poststimulus histogram (PSTH) showed multiple peaks with oscillatory behavior which was similar to the rhythm in spontaneous activities. When the amplitudes of electrical pulses trains were modulated according to predetermined temporal patterns in 2~20 uA range, the firing rate of RGC responses were significantly correlated with the temporal pattern of the pulse amplitude. Spike train decoding also showed that information on pulse amplitude time-series was faithfully represented in RGC responses.

#### Conclusions

The results indicated that RGC activities in degenerated retina could be reliably modulated by pulse amplitude variation, just as in normal retina. We expect that it is possible to encode temporal visual information faithfully by amplitude-modulated pulse trains, in spite of abnormal rhythmic spontaneous RGC activities.

#### September 13, 2009 #39

Abstract Title: Real-time and training-free control of a prosthetic robot arm using human electrocorticograms Primary Presenter: Masayuki Hirata Primary Presenter Institution: Osaka University Medical School, Suita, Osaka, Japan Co-presenter(s): Takufumi Yanagisawa, Youichi Saitoh, Tetsu Goto, Ryohei Fukuma, Haruhiko Kishima, Hiroshi Yokoi, Yukiyasu Kamitani, Toshiki Yoshimine Co-presenter(s): Osaka University Medical School, Suita, Osaka, Japan ATR Computational Neuroscience Laboratories, Seikacho, Kyoto, Japan The University of Electro-Communications Presenting author's full street address and e-mail address: 2-2 Yamadaoka, Suita, Osaka, Japan

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# Introduction

Training-free manipulability is one of the most important factors in clinical application of functional restoration with Brain-Machine Interface (BMI). Here, we present a BMI system that permits a person to control a prosthetic robot arm using electrocortcicogram (ECoG) without patients' trainings.

### **Materials and Methods**

Three post-stroke patients participated in this study. Subdural electrodes were temporarily implanted over the sensorimotor cortices for the treatment of intractable pain. They were instructed to perform three types of simple upper limb movements following a sound cue to train the two decoders which predicted the onset timing and the type of movement based on linear support vector machine<sup>1</sup>. The powers of four frequency bands (theta, alpha, beta, gamma) during an 1-s movement period were used as the input features to the decoders. The decoding performances with the four features were compared with each other. With the trained decoder, a novel ECoG signals were analyzed on line to control a prosthetic robot arm by a patient's intention to move his hand.

# Results

Among the four band powers, the gamma power was the most informative feature to infer the upper limb movements. With the trained decoders, the movement parameters were accurately decoded from ECoG signals in real time even when the subject performed self-paced movements without onset cues without any prior training. Our ECoG-based BMI system successfully controlled the prosthetic robot arm according to the patient's motion in real time without requiring any prior patients' training.

#### Conclusion

ECoG-based BMI is a clinically-feasible method for motor restoration.

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#### Acknowledgements

This work was supported in part by the Strategic Research Program for Brain Sciences of MEXT, Grants-in-Aid for Scientific Research (17591512, 18300184, 19390378, 19650153, 20300199) from JSPS.

September 13, 2009 #40

**Abstract Title:** Fetal olfactory ensheathing cells intracerebral implantation in patient with sequela of stroke: dream or reality?

Primary Presenter: Hongyun HUANG, Prof. PhD, MD.

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#### Co-presenter(s):

1. Name: Lin CHEN Credentials: Associate Prof.

#### Co-presenter(s):

1. Place of Employment: Beijing Hongtianji Neuroscience Academy, Department of Neurosurgery, Beijing Rehabilitation Center City: Beijing State: Country: China

#### Introduction

To study the feasibility and efficacy of olfactory ensheathing cell (OEC) intracranial implantation in the treatment of sequela of stroke.

#### **Materials and Methods**

Between November, 2003 and November, 2006, six patients with sequela of stroke were treated at our clinic. Of them, four were man and two were women. Ages ranged from 40 to 72 years (mean 52.9 years). The type of stoke were infarct (n=3 patients and hemorrhage (n=3). The transplant procedures were done on patients at 2 to 14.25 years (mean 6.6 years), after their injuries. The impaired loci located in the basal ganglia and hemisphere (n=5), and medulla oblongata (n=1). Olfactory bulbs were harvested and trypsinized down to single fetal OECs. They were cultured for 12-17 days and to be ready for use. The fetal OECs were transplanted into one or two targets at the corona radiate or the anterior and posterior border of the cerebromalacia focus by using the stereotactic technique. The neurologic function were evaluated before operation, after operation (3-4 weeks, n=5), and long-term following up (2 years, n=1) according to Barthel Index and patients clinical status.

#### Results

No complication was observed during the admission and follow-up. The assessment of Barthel Index were accomplished in five patients, with the amelioration of scores from  $68.2\pm27.4$  to  $72.2\pm29.7$  points (*t*=-2.138, *p*=0.099). Clinical neurologic function improvements including speech (*n*=2), power of limbs (*n*=3), muscle tone (*n*=2), balance (*n*=1), pain relief (*n*=1), and respiration (*n*=1).

#### Conclusion

The preliminary result appears to suggest that novel therapeutic strategy of OEC intracranial implant might have a potential role in patients of sequela following hemorrhagic and ischemic stroke.

### Acknowledgements

Beijing Hongtianji Neuroscience Academy Funding

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### Learning Objectives:

1. The olfactory ensheathing cells intracerebral implantation is a promising treatment for stroke.

2. This novel method is safe.

3. This is one of neuronrestorative operation.

September 13, 2009 #41

**Abstract Title:** Long-term result of deep brain stimulation for pain relief **Primary Presenter:** Hyung-seok Kim, MD

**Primary Presenter Institution:** Dept. of Neurosurgery, St. Vincent's Hospital, The Catholic Universit of Korea, Suwon, Republic of Korea

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93-6, Chi-dong, Paldal-gu, Suwon, Gyeonggi-do, Republic of Korea, 442-723 Dept. of Neurosurgery, St. Vincent's Hospital, nshs@catholic.ac.kr

#### Introduction

Chronic intractable pain syndromes have been treated by electrical stimulation of deep brain structures for the decades. There is a debate regarding the longterm effectiveness of deep brain stimulation for the treatment of chronic pain. We report our long-term result of sensory thalamic nucleus/periventricular gray matter/ hypothalamic deep brain stimulation.

#### Materials and Methods

Since May 2003, We performed deep brain stimulation for patients with chronic intractable pain. Inclusion criterias were: chronic pain duration > at least 6 mo, visual analogue scales(VAS) >7/10, identifiable anatomic cause of pain, medically inctractable pain. Preoperative mean VAS was about 7.5/10. The result was assessed with VAS and patients assessment of pain relief (percentage pain relief (PPR)).

# Results

DBS was effective in 9 out of 12 patients in initial trial, then chronic stimulation was given. At 6 months follow-up, the mean PPR at 6 months was about 58.75 %. However, the analgesic efficacy declined after 6-12 months in most cases. At long-term follow-up (32 months), DBS was

effective in only 3 out of 9 patient (33 %) with mean PPR of 56.6 %. The analgesic effect was lost in 6 chronic stimulation patients with less than 30 % pain relief.

#### Conclusion

In our results, the analgesic effect of DBS was not maintained for more than initial 6-12 months after surgery in more than half of patients. The longterm effect was observed in one thirds of intractable pain. A more sophisticated trial and study of DBS for pain relief should be warranted.

#### Acknowledgements

No financial support or relationship in this paper.

#### Learning Objectives:

- 1. Chronic intractable pain syndromes
- 2. Deep brain stimulation

# September 13, 2009 #42

**Abstract Title:** Brain Penetration Effects of Microelectrodes and DBS Leads in Ventral Intermediate Nucleus (Vim) Stimulation for Essential Tremor **Primary Presenter:** Takashi Morishita, M.D.

#### **Primary Presenter Institution:**

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#### Introduction

Microelectrode recording (MER) and macrostimulation (test stimulation) are utilized to refine the optimal DBS lead placement. The aim of this study was to determine how intraoperative MER and lead placement affects tremor severity in a cohort of essential tremor (ET) patients.

#### Materials and Methods

Consecutive ET patients undergoing unilateral DBS (ventral intermediate nucleus stimulation) for medication refractory tremor were evaluated. Tremor severity was measured at five time points utilizing a modified Tremor Rating Scale (mTRS): 1) immediately before MER 2)

immediately post-MER, 3) immediately post lead collision/implantation, 4) six months post DBS implantation in the DBS off condition, and 5) six months post implantation on DBS. To investigate the impact of the MER and lead placement, Wilcoxon signed rank tests were applied to test changes in tremor severity scores over the surgical course. In addition, a generalized linear mixed model including factors which potentially influenced the impact of the microlesion was also used for analysis.

#### Results

Nineteen patients were evaluated. There was improvement in total mTRS, postural, and action tremor scores (p<.05) as a result of MER and lead placement. The improvements observed following lead placement were similar in magnitude to what was observed in the chronically programmed clinic setting parameters at six months post implantation. Improvement in tremor severity was maintained over time even in the "off" DBS condition at 6 months. The number of macrostimulation passes, the number of MER passes, and disease duration were not related to the change in tremor severity score over time.

### Conclusion

Immediate improvement in postural and intention tremors may result from MER and lead placement in patients undergoing DBS for ET. Clinicians should be aware of these effects, and should consider pre- and post-lead placement rating scales to take these effects into account when evaluating outcome in and out of the operating room.

### Learning Objectives:

- 1. Importance of evaluating the microlesion effect in the operative settings.
- 2. Microlesion effect can be a predictor of successful DBS lead placement.

# September 13, 2009 #44

Abstract Title: Unusual case of methylmalonic aciduria (MMA) with spasticity treated with success with Intrathecal Baclofen through infusion pump Primary Presenter: Massimo Mearini, MD Primary Presenter Institution: Neurosurgical Clinical, University of Brescia, Italy Co-presenter(s): G. M. Sicuri MD, M. Scagnet MD, P. d'Auria MD, and M. Cenzato MD Co-presenter(s): Neurosurgical Clinical, University of Brescia, Italy Presenting author's full street address and e-mail address:

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#### Introduction

The aim is to evaluate the effects of Intrathecal Baclofen (ITB) on patient with severe spasticity deriving from Methylmalonic Aciduria. No other cases are present in literature.

MMA is a metabolic metabolic disorder that comes from a defect in the metabolism of Vitamin B12.

Adolescent variant with psychiatric syndrome or spinal cord degeneration is milder of *neonatal* type.

There are only 5 cases in Europe about which 2 in Italy.

#### Materials and Methods

Woman of 26-years–old. In 1999 appeared weariness, reduced concentration, dystonia and four limbs spasticity. Brain CT and Brain/Spine MRI didn't give relevant results. Symptomatic therapy with oral Baclofen was started. In 2000 was diagnosed MMA and she began intramuscular infusion of Hydroxicobalamine with general improvement of symptoms.

The spasticity at inferior limbs didn't respond to oral Baclofen.

After a positive sub-arachnoid test, in June 2003 spinal subarachnoid infusion system was implanted with tip of catheter at D10 level and Synchromed-EL Medtronic 18 ml pump. It was replaced with Synchromed-II Medtronic 20ml at November 2007.

### Results

Ashworth: improvement from 3 to 1 Muscular spasms: improvement from 3 to 1 FIM: improvement from 116 to 122 Hygiene level and sphincter control scale: improvement from 1 to 0 Dose was progressively reduced from 80 to 53 mcg die. No adverse events were communicated.

Patient's judgement is optimum with improvement of quality of life.

### Conclusion

ITB is a very effective spasticity treatment in our rare case of adolescent form of MMA. It is important to underline the progressive dose decrease, with result preserved, in an evolutionary neurologic disease.

#### Learning Objectives:

1. Good results of ITB in spasticity in an adolescent form of MMA.

2. Particular case of progressive Baclofen dose decrease with results preserved in an evolutionary disease

September 13, 2009 #45

**Abstract Title:** Early somatosensory symptoms in refractory temporal epilepsy. **Primary Presenter:** Alexander G. Weil, MD

**Primary Presenter Institution:** Department of Surgery, Division of Neurosurgery, Notre Dame Hospital, University of Montreal, Montreal, Qc, Canada

#### Co-presenter(s):

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#### Introduction

Surgery is an important treatment option for refractory temporal lobe epilepsy (TLE), relieving patients from disabling seizures in 58%. Several causes have been identified to explain temporal lobe surgery failures or why successful cases cannot be weaned completely off antiepileptic drugs. Recent evidence suggest that failure to recognize insular seizures could explain part of these failures. Insular cortex epilepsy should be suspected when viscerosensitive, motor and especially somatosensory symptoms (SSS) are combined early in the attack. We sought to determine the prevalence and prognostic value of early SSS in patients with refractory TLE.

### **Materials & Methods**

We performed a retrospective chart analysis of patients who underwent temporal lobe surgery for refractory epilepsy at Notre-Dame Hospital from September 2000 to October 2007. Each patient underwent a comprehensive epilepsy surgical workup. Collected data included duration of epilepsy, seizure type, frequency and semiology, results from preoperative investigations, type of surgery and outcome. Particular attention was put on the presence of early SSS.

### Results

Fifty patients underwent temporal lobectomy for drug-resistant TLE (26 males). Mean duration of epilepsy was 18,9 yrs and mean age at surgery was 39,71 years. There were 21 anterior temporal lobectomies (ATL), 23 selective amygdalo-hippocampectomies (SAH), 5 lesionectomies , and 2 ATL plus insulectomy. Hippocampal sclerosis was diagnosed at pathology either alone (n=34) or with other diagnosis (n=4). Other pathologies included cavernoma (n=2), astrocytoma (n=1), FCD (n=2), DNET (n=1), cortical gliosis (n=2) or were non-conclusive (n=5). Eleven (21,5%) patients reported experiencing early somatosensory symptoms during their seizures. Engel 1a outcome was 53% (n=27) overall, 33% (n=9) in the group with early SSS, 55% (n=40) in the group without early SSS, and 100% (n=2) in the group with early SSS with additional insulectomy.

# Conclusion

These preliminary observations suggest that the presence of early ictal SSS in apparent refractory TLE predicts a poorer surgical outcome. Potential explanations include unrecognized insular or parietal lobe seizures.

# September 13, 2009 #46

**Abstract Title:** Repetitive transcranial magnetic stimulation (rTMS) for neuropathic pain **Primary Presenter:** Youichi Saitoh, M.D., Ph.D. Department of Neurosurgery, Osaka University Graduate School of Medicine Suita, Osaka, Japan Email: neurosaitoh@mbk.nifty.com

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- 2. Name: Haruhiko Kishima Credentials: M.D., Ph.D.
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#### Co-presenter(s):

1. Place of Employment: Osaka Univ Grad Sch Med City: Suita State: Osaka Country: Japan

#### Introduction

The objective of this retrospective study was to confirm the pain relief with repetitive transcranial magnetic stimulation (rTMS) for neuropathic pain mainly post-stroke pain. Preliminarily, in 20 neuropathic pain patients, only rTMS of the primary motor cortex (M1) significantly reduced pain for 3 hours among the targets of M1, S1, premotor and SMA (Pain, 2006). Next, we compared the effectiveness of sham, 1-Hz, 5-Hz and 10-Hz for pain relief. Five and 10-Hz rTMS reduced pain significantly but 1-Hz and sham did not (J Neurosurg, 2007). Therefore, we had kept 5-Hz rTMS of M1 for neuropathic pain patients.

### **Materials and Methods**

The neuropathic pain patients were totally 86 who underwent 5Hz-rTMS of M1 and evaluation of that efficacy with visual analogue scale (VAS) and Short-form of McGill Pain Questionnaire (SF-MPQ). The patiens were consisted of 48 post-stroke, 15 spinal cord injury, 7 phantom-limb, 7 root avulsion, 6 peripheral nerve injury, 3 trigeminal nerve injury. Forty three of 86 patients underwent both real and sham rTMS.

#### Results

Regarding real rTMS in all the patients, the mean reduction rate in VAS and SF-MPQ was 23.3% and 33.1% respectively, and 28 (32.6%) and 26 (45.6%) showed  $\geq$ 30% pain reduction in VAS and SF-MPQ respectively. Among the 43 patients who underwent both real and sham rTMS, the pain reduction of real rTMS was greater than that of sham (mean reduction rates of VAS; 30.3%, 14.4%, p=0.0003), and 21 patients (48.8%) showed  $\geq$ 30% pain reduction in VAS after real rTMS, while six patients (14.0%) after sham (p=0.0005).

#### Conclusion

These results confirmed that 5Hz-rTMS of the M1 could provide pain relief in patients with neuropathic pain. Intractable neuropathic pain may be treatable by everyday 5-Hz rTMS.

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Saitoh Y, Hirayama A, Kishima H, Shimokawa T, Oshino S, Hirata M, et al. Reduction of intractable deafferentation pain due to spinal cord or peripheral lesion by high-frequency repetitive transcranial magnetic stimulation of the primary motor cortex. J Neurosurg 2007. 107: 555-559.

# Learning Objectives:

Transcranial magnetic stimulation
 Neuropathic pain
 Post-stroke pain

September 13, 2009 #47

**Abstract Title:** Application of focal brain cooling to the treatment of intractable epilepsy **Primary Presenter:** Masami Fujii, MD

**Primary Presenter Institution:** Departments of Neurosurgery, Graduate School of Medicine Yamaguchi University, Ube, Yamaguchi, JAPAN

# Co-presenter(s):

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# Introduction

Although epilepsy patients are generally treated by medicines or surgical techniques, these treatments are not always successful. Under these circumstances, focal brain cooling has recently gained much attention because it has a potential to terminate epileptiform discharges (EDs) in the brain. This report describes precisely the effect of the focal cooling on seizures and the influence of the focal cooling on the normal brain in experimental models and in human.

# **Materials and Methods**

The experiments were performed on adult male Sprague-Dawley rats under halothane anesthesia. After a craniotomy, the cooling device (Peltier chip) was placed on the surface of the cortex or inserted in the hippocampus. The kainic acid (KA) was injected into the cortex or hippocampus to provoke EDs. Clinically, a cooling device was also applied in 4 patients with intractable epilepsy after obtaining informed consent. During surgery, cooling was performed for 20 minutes in the cortex where EDs were recorded and therefore it had to be resected.

# Results

Experimentally, the EDs, which appeared after KA injection, began to decrease in amplitude immediately after the start of cooling and continued to decrease as the temperatures of the cortex or hippocampus decreased (20-23°C). Histologically, no apparent damages were observed in the brain structures after cooling. Sensorimotor functions were preserved after cooling of cortex for 1 hour above 20°C. Clinically, EDs diminished during the cooling process when the temperature of the brain surface reached less than 25°C in all cases.

### Conclusion

We demonstrated the termination of neocortical and hippocampal seizures by focal brain cooling without any irreversible brain damages. Owing to recent advances in the precision machinery industry, an implantable focal cooling system is expected to become a new and potentially effective minimally-invasive treatment for epilepsy in the near future.

#### References

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2) Tanaka N, Fujii M, Imoto H, Uchiyama J, Saito T, Suzuki M, et. al.: Effective suppression of hippocampal seizures in rats by direct hippocampal cooling using a Peltier chip. J Neurosurg 108: 791-797, 2008 \_

3) Oku T, Fujii M, Tanaka N, Imoto H, Saito T, Suzuki M, et al.: The influence of focal brain cooling on the neurophysiopathology -Validation for clinical application-. J Neurosurg 2009 (in press)

### Acknowledgements

This work was supported in part by a Grant-in-Aid for Specially Promoted Research (Project No.20001008) granted by Japan Ministry of Education, Culture, Sports, Science and Technology.

### Learning Objectives:

focal brain cooling
 seizure suppression
 implantable cooling device

September 13, 2009 #48

**Abstract Title:** Motor cortex stimulation for central pain and peripheral neuropathic pain **Primary Presenter:** Byung-chul Son, MD, PhD

**Primary Presenter Institution:** Dept. of Neurosurgery, St. Vincent's Hospital, The Catholic Universit of Korea, Suwon, Republic of Korea

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93-6, Chi-dong, Paldal-gu, Suwon, Gyeonggi-do, Republic of Korea, 442-723 Dept. of Neurosurgery, St. Vincent's Hospital, <u>sbc@catholic.ac.kr</u>

#### Introduction

The authors report our experience of motor cortex stimulation (MCS) in patients with medically intolerable central and peripheral neuropathic pain.

#### **Materials and Methods**

During the last 4 years, 10 patients underwent MCS trial for intractable central and peripheral neuropathic pain. The cause of central pain was traumatic brain contusion (2), spinal cord injury (2 cervical, 1 thoracolumbar), iatrogenic surgical cervical cord injury (postcordotomy dysesthesia), brachial plexus injury, complex regional pain syndrome type II, poststroke pain (3). Under the 3D neuronavigational guidance, epidural SEP monitoring and direct cortical stimulation were done to localize the exact somatotopy of motor homunculus. If the patient's pain relief was more than 50 %, the implantable pulse generator was implanted.

#### Results

For hemibody pain following TBI, MCS showed exellent pain relief with more than 3 years follow-up. For arm pain with iatrogenic cervical cord injury, postcordotomy dysesthesia and brachial plexus injury pain MCS was effective with 50 % pain relief with more than 1 year follow-up. In patients with leg pain following spinal cord injury, MCS was effective in one of three patients. MCS was effective in one of poststroke pain with more than 2 years follow-up. In our trial MCS, trial success was about 60 % (6/10) and in the early responders, 2 patients showed varying degree of tolerance, and one needed revision. There was no complication related to the procedure or stimulation itself (mean follow-up 18 months).

### Conclusion

As shown in these patients, MCS was effective in some patients with intractable central and peripheral neuropathic pain. We felt that MCS was more effective for peripheral neuropathic pain than the central pain syndromes and arm pain responded better than leg pain.

#### Acknowledgements

No financial support or relationship in this paper.

#### Learning Objectives:

1. central and peripheral neuropathic pain

2. motor cortex stimulation.

September 13, 2009 #49

Abstract Title: Neurorestoratological unit Primary Presenter: Lin CHEN, Associate Prof. Doctor Beijing Hongtianji Neuroscience Academy, Department of Neurosurgery, Beijing Rehabilitation Center, Beijing, China Email: chenlin\_china@163.com Co-presenter(s): 1. Name: Hongyun Huang Credentials: Prof.

1. Name: Hongyun Huang Credentials: Prof.

# Co-presenter(s):

1. Place of Employment: Beijing Hongtianji Neuroscience Academy, Department of Neurosurgery, Beijing Rehabilitation Center, Beijing, China

# Introduction

To introduce the new theory and concept of neurorestoratological unit (NRU).

#### **Materials and Methods**

The definition, the component elements, the personnel allocation, the work flow, the intervention plan, the therapeutic scope of NRU was elucidated systematically.

#### Results

NRU is a medical integrated unit for the management of sub-acute stage, chronic stage, and/or sequela of central nervous system impairment, which has the diagnosing and treating standard and is clear about the treatment goal. The professional in NRU are commonly included the physicians, nurses, and therapists who come from department of neurorestoratology, department of neurosurgery, department of neurology, department of orthopedics, department

of neurological rehabilitation, and department of traditional Chinese medicine, etc.. Their work is to implement the comprehensive neurorestoratological clinical solution with the ultimate goal to improving the patient's neurological function for maximal degree and increasing the quality of life for maximal degree.

# Conclusion

Establishment, development, and consummation of NRU will be sure to impel the progress of neurorestoratology, urge the treatment of nervous system disease more scientific, the systematization, the standardization, and increase the effective degree unceasingly.

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# Learning Objectives:

1. This a first report of the new concept of Neurorestoratological unit.

2. To establish Neurorestoratological unit will be sure to promote of progress of Neurorestoratology.

3. Neurorestoratologist will be new specialist as the neurologist and neurosurgeon.

# September 13, 2009 #50

**Abstract Title:** Key points for neural network restoration (KPNNR): theoretical exploration and clinical practice

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# Introduction

The theory of key point for neural network restoration (KPNNR) was first proposed by Professor Huang Hongyun in 2003 and successfully used in clinical practice. According to the theory, the key target where the cells were implanted into is located at anterior 1/4-1/3 of the body of lateral ventricle and 23-27mm away from the midline. This site mainly is the pathway of frontal corona radiata pyramidal tract, along with the convergence point of numerous projection fibers, association fibers, and commissural fibers. In theory, after the cells was transplanted into this brain important "points", extensive twoway adjustment will occur to the entire neural network including cerebrum, cerebellum, and spinal cord. Various central nervous system diseases such as cerebral palsy (CP), amyotrophic lateral sclerosis (ALS), ataxia, hereditary spastic paraplegia (HSP), multiple system atrophy (MSA), multiple sclerosis (MS), dementia, sequelae of kernicterus, corticobasal degeneration (CBD), adrenoleukodystrophy, Parkinsonism plus syndrome, non-specific encephalitis sequelae, and epilepsy, etc, ultimately involved a number of similar neural network sites including the neurons and fibers of cerebral cortex, spinal cord, cerebellum, pons, the brainstem nuclei, red nucleus, substantia nigra and basal ganglia, although its etiology and pathologic findings vary. Thus, the key point of cell transplantation should have a role for neurorestoration. To explore the objectivity, authenticity and practicality of the theory of KPNNR by clinical data analysis.

#### **Materials and Methods**

Between May of 2003 and January of 2009, 636 patients with central nervous system diseases underwent the olfactory ensheathing cell (OEC) graft into KPNNR. Of them, 609 patients had complete clinical information: 392 male and 217 female. Their age ranged from 1.2 to 84 (mean 42.87±19.64) years and course of disease from 0.4 to 35 with an average of 5.11±5.46 years. Disease distribution: 432 patients suffered ALS, 110 CP, 25 MS, 12 ataxia, 7 MSA, 6 HSP, 6 persistent vegetable state (PVS), 2 dementia, 2 sequela of cerebral anoxia, 2 Parkinsonism plus syndrome, 1 non-specific encephalitis sequelae, 1 adrenoleukodystrophy, 1 kernicterus equelae, and 1 CBD. The patients came from 75 countries or regions.

# Results

The patients were followed up for 2 to 8 weeks, an average of four weeks, after cell transplantation. Among 609 cases, 526 cases had neurological function improvements at different levels. The overall improvement rate was 86.37%. Of them, the effective rate in ALS was 87.96% with ALS-FRS increased from  $20.12\pm8.37$  pre-transplant to  $22.31\pm8.61$  points post-transplant and Norris score increased from  $38.34\pm27.23$  to  $41.87\pm28.99$  points (p\_0.000); The improvement rate in CP was 82.73% together with GMFM score decreased from  $42.95\pm49.25$  to  $45.73\pm49.76$  points (p\_0.000), especially, 4 patients who accompanied with epilepsy reduced attack significantly; The improvement rate in ataxia was 83.3% with ICARS decreased from  $45.67\pm19.28$  to  $40.42\pm19.87$  points (p\_0.005); The improvement rate in HSP was 83.3% with ICARS decreased from  $36.17\pm22.44$  to  $32.50\pm22.69$  points. Perioperative adverse events occurred at a total of 33 cases, the occurrence rate of 5.42%, mainly headache, fever and so on, which were cured by symptomatic treatment.

### Conclusion

The therapeutic method of OEC transplanted into KPNNR is simple, safe, and feasible, which can improve the function of patients with a variety of central nervous system of neurological diseases and/or slow down the progressive deterioration of some degenerative diseases. At present, we assumed that that the implanted cells into KPNNR play the positive effects through the activation, integration, regulation and control neural networks. The novel theory of KPNNR has important significance to guide the future clinical treatment of nerve repair and is worthy of further study and exploration.

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# Learning Objectives:

1. The concept of "*Key points for neural network restoration*" is first reported in this paper.

- 2. This concept is very essential for guidance of neural network surgery.
- 3. It may be useful for selection of some target of neuromodulation.