SUNDERLAND SOCIETY MEETING
December 4 - 6, 2016
Frankfurt a.M., Germany

QUO VADIMUS?

Programme & Abstracts
SUNDERLAND SOCIETY MEETING
December 4 – 6, 2016
Frankfurt a.M., Germany
Meeting Venue:
Grandhotel Hessischer Hof
Friedrich-Ebert-Anlage 40
60325 Frankfurt / Main

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Frankfurt am Main, Germany
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www.sunderlandsociety.org
Dear Members and Guests of the Sunderland Society,

Dear Friends,

Welcome to the 22nd Sunderland Society Meeting!

It is a great honor to be your hosts this year. With particular joy and pride we look forward to meet, exchange, discuss and enjoy with you 4 tightly packed days in the Centre of Frankfurt. We envision a stimulating meeting that covers a wide range of peripheral nerve topics, such as laboratory & clinical research, techniques and innovations.

The mother universities of our two hospitals have quite diverse backgrounds. The Justus Liebig University of Giessen is one of the oldest, most esteemed and traditional universities in Germany. Located in the Federal State of Hesse, the university was founded in 1607 for the education of vicars and civil servants; soon academic work had to be halted during 30 years of war and restarted only after the treaty of Westphalia in 1650. In the 17th and 18th centuries, the then called Ludoviciana was a typical small university with four faculties: theology, jurisprudence, medicine, and philosophy. After WWII and near-complete destruction of Giessen, the university was reestablished as the Justus von Liebig University of Giessen, named after its most famous collegiate son, a naturalist, chemist and pharmacist. Today, Giessen’s medical school follows a traditional curriculum.

The Carl von Ossietzky University, located in the northwest of Germany, close to the Dutch border and the shoreline of the northern sea, had its beginnings as a teacher training college in the 1920’s. The University of Oldenburg was established in 1973 by the State of Lower-Saxony, and soon began work in different faculties.
In contrast to Giessen, the history of Oldenburg’s medical school and faculty for human and health related sciences at the Carl von Ossietzky University could not be shorter. To date, it is the youngest Federal State sponsored medical faculty in Germany, and most likely its smallest. It was founded in 2012. In a collaborative effort it forms the European Medical School-EMS, together with its partner, the University of Groningen in the Netherlands. The EMS follows a model curriculum with problem based learning as its core, which incorporates student-patient interaction right from the beginning.

It is our ambition and sincere hope that you will enjoy this year’s Sunderland Society Meeting at a personal, social and intellectual level.

Your hosts,

Thomas Kretschmer  
Kartik G Krishnan
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SCIENTIFIC PROGRAMME
**Sunderland Society Meeting • Frankfurt • Germany**

## Scientific Programme

**Venue:** Empire Salon, Grandhotel Hessischer Hof

### Saturday, December 3rd, 2016

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<tr>
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<td>Welcome &amp; Introduction</td>
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<td></td>
<td>Kartik Krishnan, Eberhard Uhl &amp; Thomas Kretschmer</td>
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<tr>
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<tr>
<td>08:50</td>
<td>Scientific Session 1</td>
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<tr>
<td>09:00 – 10:00</td>
<td>Nerve Regeneration I</td>
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<td>Chair: Lynda Yang</td>
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<tr>
<th>Time</th>
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<tr>
<td>09:00</td>
<td>Rajiv Midha: Isolation and characterization of myelinating schwann cells from adult human skin</td>
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<td>09:10</td>
<td>Thomas Kretschmer: BIOBOI – a multi-layered nerve data-bank of grafted patients</td>
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<td>09:20</td>
<td>Huan Wang: Proteome of the distal nerve: its implication in delayed repair and poor functional recovery</td>
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<tr>
<td>09:30</td>
<td>Patrick Dömer: Analysis of regeneration and myelination associated proteins in human neuroma in continuity and discontinuity (BIOBol Mol)</td>
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<tr>
<td>09:40</td>
<td>Discussion</td>
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<td>10:00 – 10:30</td>
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<tr>
<td>10:30 – 11:30</td>
<td>Imaging &amp; Clinical I</td>
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<td>Chair: Michel Kliot</td>
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<tr>
<th>Time</th>
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<tbody>
<tr>
<td>10:30</td>
<td>Henrich Kele: Fascicular neuritis- novel imaging diagnosis that prevents unnecessary peripheral nerve surgery</td>
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<tr>
<td>10:40</td>
<td>Henrich Kele: Peripheral nerve imaging is indispensable for correct diagnosis and therapy in certain neuropathies</td>
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<tr>
<td>10:50</td>
<td>Christian Heinen: Ultrasound imaging of grafted patients – morphological changes over time (BIOBol-nerve)</td>
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<tr>
<td>11:00</td>
<td>Dimitri Anastakis: Evaluation of Ontario provincial wait-times for delayed traumatic preiperal nerve surgery</td>
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<tr>
<td>11:10</td>
<td>Jörg Bahm: Nerve transfers in upper limb arthrogryposis</td>
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<td>Scientific Session 3</td>
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<td>11:30 – 12:30</td>
<td>Chair: Thomas Kretschmer</td>
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<td>13:30 – 14:00</td>
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11:30 **KeyNote Lecture:** Jörg Schorer: Movement Analysis – a primer
12:00 **Jörg Bahm:** Movement analysis in upper limb dysfunction
12:10 **Tom Quick:** A study of hand held dynamometry assessments of peak force generated fatigability and related surface EMG assessed co-contraction
12:20 **Judith Tirp:** Movement analysis of dart players
12:30 Discussion
12:50 – 13:30 *Take lunch to session room*
13:30 – 14:00 **Tom Quick:** Group discussion: how do we assess motor recovery

15:00 Bus pick-up at Grandhotel Hessischer Hof
Social Programme (see page 72)

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**MONDAY, DECEMBER 5TH, 2016**

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<tbody>
<tr>
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<td>Chair: Howard Clarke &amp; Robert Schmidhammer</td>
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08:30 **Michael Fox:** Effects of surgical decompression on neuropathic pain in patients with infraclavicular brachial plexus injuries
08:40 **Lukas Rasulic:** Impact on quality of life, disability and patient satisfaction after severe brachial plexus injury followed by surgical repair
08:50 **Robert Schmidhammer:** The correlation of reduced clavicle growth to pathological scapula positioning, and –rotation in brachial plexus birth palsy. A retrospective study
09:00 **Mario Siqueira:** Functional outcome of accessory-suprascapular nerve transfer for restoration of shoulder function in traumatic brachial plexus palsy in adults
09:10 **Mukund R Thatte:** Distal transfers as a primary treatment in obstetrical brachial plexus palsy – a series of 20 cases
09:20 **Howard Clarke:** Sensory outcome in children with obstetrical brachial plexus palsy following microsurgical reconstruction
09:30 **Howard Clarke:** Pain in infants with obstetrical brachial plexus palsy following primary microsurgical reconstruction
09:40 **Mukund R Thatte:** A prospective study comparing classical intraplexal repair v/s primary distal transfer in Narakas group I babies with a four year follow up
09:50 Discussion
10:00 – 10:30 Coffee break
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<tr>
<th>Scientific Session 2</th>
<th>Nerve Regeneration II</th>
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<tbody>
<tr>
<td>10:30 – 11:30</td>
<td>Chair: Mikael Wiberg</td>
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<tr>
<td>10:30</td>
<td><strong>Tessa Gordon</strong>: The significance of muscle fiber type grouping in skeletal muscles reinnervated after nerve injury and surgical repair</td>
</tr>
<tr>
<td>10:40</td>
<td><strong>Christine Radtke</strong>: CNPase expression in olfactory ensheathing cells</td>
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<tr>
<td>10:50</td>
<td><strong>Christine Radtke</strong>: Analysis of motor hand recovery in a nonhuman primate following median nerve repair as a preclinical model for nerve conduit implantation</td>
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<tr>
<td>11:00</td>
<td><strong>Zhongyu Li</strong>: Aging influences the expression of energy sensor SIRT1 during wallerian degeneration</td>
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<td>11:10</td>
<td>Discussion</td>
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<td>11:30 – 12:40</td>
<td>Chair: Eric Zager</td>
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<tr>
<td>11:30</td>
<td><strong>Kartik G Krishnan</strong>: A comparative evaluation of the method of innervation in microneurovascular reanimation (FMT) in unilateral facial palsy</td>
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<tr>
<td>11:40</td>
<td><strong>Kartik G Krishnan</strong>: Case Presentation Facial Reanimation</td>
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<tr>
<td>11:50</td>
<td><strong>Alexander Cárdenas-Mejia</strong>: Clinical and neurophysiological findings of facial palsy patients related to oculoauriculo-vertebral spectrum</td>
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<tr>
<td>12:00</td>
<td><strong>Alexander Cárdenas-Mejia</strong>: Surgical strategies in moebius patients: lessons learned after 128 cases</td>
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<td>12:10</td>
<td><strong>Fernando Guedes</strong>: Misdiagnose in biopsied tumors of peripheral nerves – consequences and lessons from a surgical series</td>
</tr>
<tr>
<td>12:20</td>
<td><strong>Gregor Antoniadis</strong>: Pudendal neuralgia. Fact or fiction? Our experience using the transgluteal decompression of the pudendal nerve</td>
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<tr>
<td>12:30</td>
<td>Discussion</td>
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<td>12:40 – 13:00</td>
<td>Lunch</td>
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<tr>
<th>Scientific Session 4</th>
<th>Innovation</th>
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<td>Chair: Allan Belzberg</td>
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<td>13:00</td>
<td><strong>Tom Quick</strong>: Reanimated elbow flexion – when is good enough? And how much better than better is better?</td>
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<tr>
<td>13:10</td>
<td><strong>Urs Schneider</strong>: Approaches to powered hand-arm orthotics as a synergetic treatment to neurosurgery</td>
</tr>
<tr>
<td>13:20</td>
<td><strong>Andrew Hart</strong>: Establishing an ethical and financially self-supporting system to provide viable human dorsal root ganglion neurons for in vitro pain research</td>
</tr>
<tr>
<td>13:30</td>
<td><strong>Simon Archibald</strong>: Fabricated 3D matrix basal lamina construct for promoting schwann cell migration and proliferation</td>
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<tr>
<td>Time</td>
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<tr>
<td>13:40</td>
<td><strong>Shimon Rochkind</strong>: Guiding regenerative gel (GRG) and anti-gliotic GRG (AGRG) for reconstruction of severely injured peripheral nerve and spinal cord</td>
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<td>13:50</td>
<td>Discussion</td>
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<td>2nd Business Meeting – Members only</td>
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<tr>
<td><strong>Scientific Session 1</strong></td>
<td><strong>Brachial Plexus II</strong> Chair: David G Kline</td>
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<tr>
<td>09:00 – 10:00</td>
<td><strong>Willem van Ouwerkerk</strong>: Change of cortical motor program in magnetencephalography (MEG) studies in late accessory to suprascapular nerve transfer in obstetric brachial plexus lesions</td>
</tr>
<tr>
<td>09:10</td>
<td><strong>Debora Garozzo</strong>: A clinical study on deafferentation pain following brachial plexus injuries</td>
</tr>
<tr>
<td>09:20</td>
<td><strong>Lynda Yang</strong>: Nerve transfer of ulnar fascicle to musculocutaneous nerve (Oberlin Transfer) significantly improves forearm supination as compared to nerve graft repair in neonatal brachial plexus palsy</td>
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<tr>
<td>09:30</td>
<td><strong>Israel Chambi</strong>: Recurrence of thoracic outlet syndrome following a trans-axillary first rib resection</td>
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<tr>
<td>09:40</td>
<td><strong>Eric Zager</strong>: Outcomes after surgical treatment of pediatric neurogenic thoracic outlet syndrome</td>
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<tr>
<td>09:50</td>
<td>Discussion</td>
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<tr>
<td>10:10 – 10:30</td>
<td>Coffee break</td>
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**Scientific Session 2**

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<tr>
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<tr>
<td>10:30 – 12:30</td>
<td><strong>Anatomy, Surgical Technique &amp; Innovation</strong> Chair: Rajiv Midha</td>
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<tr>
<td>10:30</td>
<td><strong>Danzhu Guo</strong>: A new technique for ultra-minimally invasive surgery</td>
</tr>
<tr>
<td>10:40</td>
<td><strong>Christian Heinen</strong>: Variations in lumbar plexus anatomy – a cadaver study</td>
</tr>
<tr>
<td>10:50</td>
<td><strong>Mariano Socolovsky</strong>: Transgluteal approach to the sciatic nerve: an anatomical and clinical study</td>
</tr>
<tr>
<td>11:00</td>
<td><strong>Amgad Hanna</strong>: The lateral femoral cutaneous nerve canal</td>
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<tr>
<td>11:10</td>
<td><strong>Amgad Hanna</strong>: Preoperative ultrasound-guided wire localization of the lateral femoral cutaneous nerve</td>
</tr>
<tr>
<td>11:20</td>
<td><strong>Michel Kliot</strong>: Testing flexible integrated chips (biostamp) placed on the skin to monitor nerve-muscle function during peripheral nerve, spine, and cranial nerve surgery</td>
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<tr>
<td>Time</td>
<td>Speaker(s)</td>
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<tr>
<td>11:30</td>
<td><strong>Danqing Guo:</strong> The needle-to-needle inserting approach for thread trigger finger release (TTFR)</td>
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<td>11:40</td>
<td><strong>Wilson Zack Ray:</strong> Resorbable Electronics for Peripheral Nerve Interfacing</td>
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<td>11:50</td>
<td><strong>Mark Mahan:</strong> Biomechanical dynamics of rapid-stretch nerve injury animal model</td>
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<tr>
<td>12:00</td>
<td><strong>Mark Mahan:</strong> Histologic evaluation of rapid-stretch nerve injury animal model</td>
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<tr>
<td>12:10</td>
<td>Discussion</td>
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<td>12:30</td>
<td>Lunch</td>
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**Scientific Session 3**  
**Nerve Regeneration III**  
**Chair:** Allan Belzberg

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<th>Time</th>
<th>Speaker(s)</th>
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<tbody>
<tr>
<td>13:00</td>
<td><strong>Mikael Wiberg:</strong> A comparison of an artificial nerve repair construct and nerve grafting when used in combination with intramuscular injections of stem cells for reduction of muscle atrophy</td>
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<td>13:10</td>
<td><strong>Tom Quick:</strong> Human in vivo schwann cell change. An immunohistochemical assessment comparing innervated and denervated human nerve</td>
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<tr>
<td>13:20</td>
<td><strong>Joost Verhaagen:</strong> Gene therapy for GDNF with a stealth gene switch promotes long-distance axon regeneration and functional recovery</td>
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<td>13:30</td>
<td><strong>Christine Radtke:</strong> Enhanced nerve regeneration of critical size nerve defects following implantation of a biomimetic nerve conduit based on spider silk</td>
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<td>13:40</td>
<td>Discussion</td>
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<td>Closing remarks</td>
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<td>15:00</td>
<td>Bus pick-up at Grandhotel Hessischer Hof &amp; Transfer to Idstein</td>
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ABSTRACTS
Dimitri ANASTAKIS, CB Novak, HL Baltzer
University of Toronto (CAN), Dimitri.anastakis@utoronto.ca

**EVALUATION OF** O**NTARIO PROVINCIAL WAIT TIMES FOR DELAYED TRAUMATIC PERIPHERAL NERVE SURGERY**

**Aim:** The main objective of this study was to evaluate the Ontario provincial wait times (wait time between the surgeon’s decision to treat date and the date of surgery) and the distribution of cases for delayed traumatic peripheral nerve surgery (PNS) performed by Plastic & Reconstructive Surgery (PRS) and Neurosurgery.

**Materials & Methods:** The wait time data were retrieved from Ontario Ministry of Health and Long-Term Care databases. Delayed traumatic PNS data included all cases that were (1) performed in fully equipped operating rooms, (2) performed in patients >18 years of age and (3) excluded nerve injuries acutely repaired within 24 hours. The data were collected from April 2009 to March 2016 and included total cases, mean and median wait times, and percentage of cases performed within the provincial target time. The data were categorized by provincial geographic regions known as Local Health Integration Networks (LHIN).

**Results:** In total, 31,211 peripheral cases were performed by PRS (n = 28,925) and Neurosurgery (n = 2,286). Of these, there were 5,245 cases of delayed traumatic PNS with variability in the case distribution across Ontario. The highest volume of delayed traumatic PNS cases was performed in the Toronto Central LHIN (n = 2,145) and the lowest volume Waterloo Wellington and North Simcoe Muskoka (n = 2). Toronto Central was the largest referral centre in Ontario drawing patient from across the province. The Ontario mean and median wait time was 44 and 25 days, respectively. The highest mean wait time was 205 days in North East LHIN and the shortest mean wait time 13 days in Erie St. Clair LHIN; both occurred in LHINs with low volume. Men in all age groups had lower wait times for consultation and surgery dates. The provincial access target wait time for delayed traumatic PNS was 182 days. The percentage completed within the provincial target time ranged from 78% (Southwest LHIN) to 100% (Erie St. Clair LHIN).

**Conclusions:** The provincial distribution of delayed traumatic PNS was variable and the highest volumes were in the LHINs with the highest populations. Men are treated quicker than women. Precise reporting of these surgeries from all hospitals is necessary to accurately capture and understand delivery of care regarding PNS. Efforts are underway to improve delayed traumatic PNS wait times across Ontario.
Gregor ANTONIADIS, MT Pedro, L Federle, HP Richter  
Peripheral Nerve Surgery Unit, Department of Neurosurgery, University of Ulm (GER); 
gregor.antoniadis@uni-ulm.de

**PUDENDAL NEURALGIA: FACT OR FICTION? OUR EXPERIENCE USING THE TRANSGLUTEAL DECOMPRESSION OF THE PUDENDAL NERVE**

**Aim:** Pudendal neuralgia is chronic pain related to the pudendal nerve. The pudendal nerve originates from the lumbo-sacral plexus (L4-S4). It consists of both sensory fibers (80%) and motor fibers (20%). The pudendal nerve divides into 3 branches: the inferior rectal nerve, the dorsal nerve of the clitoris or penis, and the perineal nerve that supplies the perineum and the genital area. The pudendal nerve is the only peripheral nerve that has both somatic and autonomic fibers. Irritation of the pudendal nerve (pudendal neuralgia) may result in sensory symptoms, like burning, crushing, shooting or prickling sensation. Any of the areas supplied by the pudendal nerve can be affected. The pain may be worse when sitting down and improve when standing or lying down. We would like to present our experience with the surgical transgluteal treatment.

**Materials & Methods:** Between 2003 and 2016 we treated 16 patients suffering from pudendal neuralgia. 15 Patients (12 women and 3 men; age range 39-76 yrs) with chronic perineal pain at least of one year duration (range 1-40 yrs) underwent decompression of the pudendal nerve via a transgluteal approach. Decompression was performed on the left side in 9 cases, on the right in 6 and on both sides in one. One patient underwent left pudendal nerve stimulation. All patients underwent MRI to exclude space-occupying lesions around the pudendal nerve and pelvis area and had a thorough clinical, neurophysiological, urological, gynecological investigations, and neuropsychological treatment. All patients showed a positive transrectal test (pressing against the sacrospinal ligament). CT-guided nerve blocks were performed in all. 14 out of 15 patients had at least two positive blocks.

**Results:** 14 /16 patients were evaluated per questionnaire. Two were lost to follow-up. Mean follow-up was 108 months. 3/15 patients (23%) reported global improvement, 4/15 (30.8%) had more than 50% improvement and 1/15 (7.7%) – less then 50%. 5/15 (38.5%) showed no improvement at all. In all 61.5% improved after surgery. The patient with pudendal nerve stimulation was painfree in the first year and remained painfree even after explantation of the device. The quality of life was not restricted in 2 patients, slightly restricted in 5 and severely restricted in 6. The patient with the neuromodulation showed a normal life activity.

**Conclusions:** Pudendal neuralgia can be a cause of chronic, disabling perineal pain more in women than in men. Symptomatic patients must have urological, gynecological & neurophysiological examinations, and neuropsychological treatment prior to surgery. A reliable preoperative diagnostic protocol should be established. Selection of candidates for surgery should be very meticulous. Surgical decompression of the pudendal nerve can be a therapeutical option in patients refractory to conventional treatment.
Simon ARCHIBALD, F O'Brien, A Matsiko  
Integra Life sciences (USA) and Drexel University (IRL), sarchibald@integralife.com

**Fabricated 3D matrix basal lamina matrix for promoting Schwann cell migration and proliferation**

**Aim:** Synthesize a 3D basal lamina construct incorporating structural and biochemical elements of the Schwann cell basal lamina to promote Schwann cell migration and proliferation in the repair of peripheral nerve defects at a rate equivalent or superior to autologous nerve grafts.

**Materials & Methods:** Collagen nerve guide conduits were fabricated at RCSI from type 1 atelo-collagen supplied by Integra LifeSciences. An acetic acid collagen dispersion was precipitated with ammonia and the fibres spun onto a mandrel to form conduits. Tubes were cross-linked with formaldehyde and freeze dried. Tubes were subjected to cyclic compression and suture pull-out mechanical testing. Tubes were filled with a 0.5% w/v type 1 collagen dispersion that was axially frozen, freeze dried and cross-linked to create longitudinal pores (diameter 50-80 μm) in the matrix, simulating Bands of Bungner. Additional component were introduced into the matrix composition, individually and in combination: chondroitin-6-sulphate proteoglycan (C6S) (5μg/ml), hr fibronectin (5μg/ml), hr laminin-1 (5μg/ml), hr laminin-2 (5μg/ml). Sections of the tube matrix construct were assessed in-vitro over 7 days for cell proliferation (total DNA content) and morphologically for promotion of cell migration and axonal extension using rat neonate DRG explants and primary Schwann cell cultures.

**Results:** Mechanical testing of the filled collagen tube construct demonstrated that the tube wall had a pull-out strength greater than could be exerted with a 9-0 nylon suture. Cyclic compression demonstrated an elastomeric hysteresis and the tubes maintained rebound to original dimension over 100 cycles. Compared to collagen (C) matrix alone the addition of C6S and any one of laminin-1 (L1), laminin-2 (L2) or fibronectin (F) had no significant positive or negative effect on Schwann cell proliferation. In combination these components had a very significant effect on Schwann cell proliferation, C+C6S+L1+F= 179% increase, C+C6S+L2+F= 295% increase, C+C6S+L1+L2+F= 471% increase. From the morphological assessment there was significant improvement in axonal extension and organization on substrates containing combinations of fibronectin and either laminin-1 or laminin-2 compared to the collagen/C6S substrate alone.

**Conclusions:** This study demonstrates a proof of concept in the synthetic fabrication of Schwann cell basal lamina mimic incorporating components individually and in synergy that are found in nature. A powerful synergic interaction between basal lamina components (fibronectin, laminin-1 and laminin-2) has been demonstrated to promote Schwann cell proliferation, whereas in singular presentation these components have no significant effect. Further work is required to fine tune these materials and confirm the benefits for peripheral nerve repair in animal models and the clinic.
Disclosures: I serve as the Chief Scientist for Integra Lifesciences Corp. This study conducted at the Royal College of Surgeons Ireland in collaboration with Professor Fergal O’Brien and Amos Matsiko, PhD

Jörg BAHM, C Disselhorst-Klug
Franziskushospital Aachen (GER), jorg.bahm@belgacom.net

MOVEMENT ANALYSIS IN UPPER LIMB DYSFUNCTION

Aim: Movement analysis is based on a video-assisted recording of infrared makers fixed on the skin while a defined limb movement is performed (Vicon-technology). We apply this technology since 15 years to examine children suffering from obstetric brachial plexus palsy.

Materials & Methods: Since 2000, we cooperate with the movement analysis lab of the AME Institute of RWTH Aachen University, examining different patterns of complex upper limb motion, biceps triceps co-activation, and shoulder rotational balance. Additionally, force transducers and robob (standardized motion) are used.

Results: Multifunctional analysis of recorded motion data allows a better understanding of muscle co-activation, forces and torques acting on normal or dysplastic glenohumerale joints and complex motion “chains” in patients suffering from various severity of brachial plexus palsy.

Conclusions: Movement analysis is a scientific research tool which allows reliable and repetitive analysis of complex upper limb movement characteristics in healthy volunteers and brachial plexus patients.

Jörg BAHM, C Hagemann
Franziskushospital Aachen (GER), jorg.bahm@belgacom.net

NERVE TRANSFERS IN UPPER LIMB ARTHROGRYPOSIS

Aim: Arthrogryposis multiplex congenita (AMC) is a multifactional neuro-orthopedic entity responsible for severe upper and lower limb motion including joint stiffness, limb malposition and various expressions of palsy. Early nerve transfers in selected cases may reanimate key functions.

Materials & Methods: In the last 4 years 5 children with “atypical” AMC and major upper limb palsy have been operated by classic nerve transfer to reanimate shoulder abduction and elbow flexion.

Results: We show video documented results of shoulder and elbow function after nerve transfers; the mean follow-up is 2 years.
**Conclusions:** Early nerve transfer in selected cases of upper limb AMC without major ankylosis gives good functional results and should be added to the complex neuro-orthopedic strategy in these children.

Alexander CARDENAS-MEJIA, JTTarriba, E Velazquez, E de La Concha
Hospital General Dr Maniel Gea Gonzalez, Mexico-City (MEX); alexcardenas@hotmail.com

**SURGICAL STRATEGIES IN MOBIUS PATIENTS: LESSONS LEARNED AFTER 128 CASES**

**Aim:** Mobius syndrome is a clinical condition that involves facial and abducens nerves. Clinically the patient is unable to move the eyes laterally and unilateral or bilateral facial palsy are evident. The syndrome may be associated with craniofacial and musculoskeletal malformations and ophtalmic comorbidities.

**Materials & Methods:** Between 2008 and 2016, we evaluated all patients diagnosed as mobius syndrome that attend the facial palsy clinic in our hospital and underwent facial reanimation procedures. We reviewed charts and complimentary exams and patients with no follow up or incomplete information was eliminated.

**Results:** We reviewed 124 records and charts with diagnosis of mobius syndrome (45 males and 79 females), age groups were distributed: under 4 y/o: (40 cases), between 5-15 y/o (63 cases) and older than 15: (21 cases), age average was 8.61, we divided patients in three different groups according with type of mobius: complete mobius 88, incomplete 28 and like 8. We included 76 cases (88 procedures) with facial reanimation surgeries. Segmental gracilis as a free functional muscle transfer was the most popular procedure in 46 cases, temporalis muscle transfer was performed in 15 cases, nerve transfers 15 cases and staccic procedures in 12 cases. COMPLETE MOBIUS GROUP Segmental gracilis was done in 34 cases using as a donor nerve hypoglossal nerve 7 cases, masseter nerve 18 cases and spinal accesory 9 cases), in those cases the muscle was performed bilaterally in 4 cases, unilateral 20 and bilaterally alternanting one side after other side 10 cases), we had 8 re-explorations, 4 re-insetting gracilis flap, 1 failure and 1 haematoma. INCOMPLETE MOBIUS GROUP, we included 13 cases, and we performed segmental gracilis in 9 of those patients (donor nerves were facial-masseter in 6 cases and spinal accesory in 3 cases), cross facial nerve graft 2 cases and temporalis muscle transfer 2 cases. MOBIUS LIKE GROUP we had 5 cases, and we did 3 segmental gracilis (donor nerve was masseter nerve in 3 cases) one bilateral and 2 unilateral and 2 cross facial nerve grafts.

**Conclusions:** Mobius syndrome is a rare condition, this is one of he biggest cohorts in the world. Preoperative planning including donor nerve evaluation and neurophysiological studies are helpful to get better results. Our study describes our algorithm and strategies in these kind of patients.
Alexander CARDENAS-MEJIA, SR Maniardi, E Velazquez, E de La Concha
Hospital General Dr Maniel Gea Gonzalez, Mexico-City (MEX); alexcardenas@hotmail.com

CLINICAL AND NEUROPHYSIOLOGICAL FINDINGS OF FACIAL PALSY PATIENTS RELATED TO OCULOAURIULOVERTEBRAL SPECTRUM

Aim: To describe the clinical and neurophysiological findings of patients with facial palsy related to oculoauriculovertebral spectrum in our Hospital between 2010 and 2015.

Materials & Methods: We conducted an observational, descriptive study and included all patients with facial palsy associated to the oculoauriculovertebral spectrum. We reviewed the information from clinical records and neurophysiological studies.

Results: We included 32 patients, 12 men and 20 women, with an average age of 11.46 years. 17 had left facial palsy, 14 were right affected and 1 bilateral. The upper branches of the facial nerve were involved in 6 patients, the lower branches in 3 patients and all branches in 23 patients. We identified auricular malformations in 32 patients, orbital in 4, and mandibular hypoplasia in 21. We used the eFace system to evaluate results. An average score of 74 at rest was obtained, a dynamic score of 56, periorcular score of 72, midface and smiling score of 68 average and lower third score of 79. Neurophysiological studies of facial nerve reported a mixed motor axonopathy, compromise of 3 branches in 23 patients, 2 branches in 5 individuals and 1 branch in 4 cases. We identified motor branch of trigeminal nerve dysfunction in 13 patients and hypoglosal nerve involvement in 4 cases.

Conclusions: Clinical and electrophysiological characterization of facial palsy patients related to oculoauriculovertebral spectrum allows determining the extent of clinical and subclinical compromise of facial nerve congenital damage in this condition.

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Israel CHAMBI, L Miller
Neurosurgery, Santa Ana (USA); drisraelchambi@yahoo.com

RECURRENT OF THORACIC OUTLET SYNDROME FOLLOWING A TRANS-AXILLARY FIRST RIB RESECTION

Aim: Surgical removal of the first rib has been the preferential approach by vascular and thoracic surgeons in patients presenting with clinical and radiological evidence of compression of the brachial plexus when the symptoms become refractory to conservative treatment. The purpose of this study was to determine the effectiveness of the trans-axillary method in decompressing the brachial plexus.

Materials & Methods: We performed a retrospective study in 18 patients (all females) that underwent first rib resection for decompression of the brachial plexus in between 2009 and 2015 using the trans-axillary method. These patients demonstrated marked improvement following surgery, however, within 3 to 12 months developed signs and symptoms of further compression of brachial plexus supported by ultrasound imaging, neurological examination and neurodiagnostic testing.
Results: The supraclavicular approach using the operative microscope was used to treat these patients with compression of the brachial plexus. At surgery, four patients had fibrosis in the scalenus minimus causing compression of the lower trunk of the brachial plexus; two patients had a fibrous intermediate scalenus muscle (a bridging muscle in between the scalenus anterior and the scalenus medius) going in between the middle and the lower trunk of the brachial plexus and causing compression of the middle and the lower trunk of the brachial plexus. In nine cases, a fibrous intermediate scalenus was found going in between the upper and the middle trunk with severe compression of the middle trunk of the brachial plexus and in three cases, there was fibrous scalenus minimus causing compression of the lower trunk of the brachial plexus and intermediate scalenus going in between the upper and the middle trunk of the brachial plexus causing compression of the middle trunk of the brachial plexus. Postoperative motor and sensory improvement was seen in all patients and two patients continued to complain of pain in distribution of the lower trunk of the brachial plexus. Pneumothorax in two cases was treated during surgery with the use of catheter and aspiration while applying a Valsalva maneuver by the anesthesiologist.

Conclusions: In patients with clinical, electrical and radiological evidence of compression of the brachial plexus, the supraclavicular approach with direct visualization appears to be the most effective or preferable method to identify the anatomical variations of the scalenus complex in order to maximize the decompression of the brachial plexus.

Howard M CLARKE, ES Ho, CG Curtis, K Davidge
The Hospital for Sick Children and the Department of Surgery, University of Toronto (CAN); howard.clarke@utoronto.ca

SENSORY OUTCOME IN CHILDREN WITH OBSTETRICAL BRACHIAL PLEXUS PALSY FOLLOWING MICROSURGICAL RECONSTRUCTION

Aim: Outcomes in motor recovery of children with obstetrical brachial plexus palsy (OBPP) with and without microsurgical intervention has been studied extensively. Sensory outcome has been evaluated in a few studies. The purpose of this research is to evaluate the sensory function of the hand in children with OBPP who had microsurgical reconstruction of the brachial plexus.

Materials & Methods: The sensory thresholds of children with upper and total plexus palsy were evaluated with the Weinstein Enhanced Sensory Test (WEST), and a test of stereognosis.

Results: Sixty-two children participated in this study with a mean age of 10.9 + 3.3 years (range, 6 – 10 years). Twenty-five (40%) of the children evaluated had abnormal sensory threshold in their affected hand. Only four children (3 upper plexus, 1 total plexus) had loss of protective sensation or higher threshold. The sensory thresholds of the children’s unaffected and affected hand were not significantly different in the median (medial and lateral cords), C7 (Long digital pulp) and C8/ulnar nerve (little digital pulp) distributions. Sensory thresholds in
the C6 (thenar eminence) and radial nerve/posterior cord (dorsal fist web) distributions were significantly higher in the affected hand. (Wilcoxon Signed Rank Test, P <0.01) Thirteen of the children with upper plexus (46%) and 12 (35%) of the children with total plexus palsy had abnormal sensory thresholds. The proportion of children with and without sensory threshold impairment was not significant between the two groups (Fisher’s Exact test = 0.44). Slightly more children with total plexus injuries, n=13 (38%), than upper plexus, n=5 (18%) had an impairment in stereognosis function, but this did not reach statistical significance (Fisher’s Exact test = 0.07).

Conclusions: Sensory recovery in OBPP after microsurgical reconstruction is good. A large portion of children achieve normal sensory outcome, and those who had deficits had mild impairments. Children with total plexus palsy who had reconstruction of the lower trunk had the potential to achieve good sensory recovery similar to their upper plexus counterparts.

Howard M CLARKE, K Davidge, WJ Lee, ES Ho, D Stevens
The Hospital for Sick Children and the Department of Surgery, University of Toronto (CAN); howard.clarke@utoronto.ca

PAIN IN INFANTS WITH OBSTETRICAL BRACHIAL PLEXUS PALSY FOLLOWING PRIMARY MICROSURGICAL RECONSTRUCTION

Aim: Pain in children with obstetrical brachial plexus palsy (OBPP) is under-appreciated and not well understood. Objective evaluation of pain in infants with OBPP is needed to better understand longitudinal trajectories of pain experienced by this population. The purpose of this study was to evaluate postoperative pain in infants with OBPP undergoing microsurgical reconstruction.

Materials & Methods: A retrospective cohort study was conducted of infants with OBPP undergoing microsurgical reconstruction of the brachial plexus between 2001 and 2015. Postoperative pain was evaluated using the well-validated Face, Legs, Activity, Cry, Consolability (FLACC) scale, as well as opioid requirements. FLACC scores and opioid requirements were compared in patients with upper plexus palsy versus total plexus palsy.

Results: 159 infants were evaluated: 60 (38%) with upper plexus and 99 (62%) with total plexus palsy. Mean age at the time of surgery was 6.8 ± 3.1 months. The overall mean and median of the FLACC scores were 0.8 ± 1.9 and 0 for all observations (n=3213 scores). Both the median and the distribution of FLACC scores did not statistically differ between postoperative days 1 through 8. The proportion of FLACC scores > 0 was not statistically different between infants with total versus upper plexus palsy. The overall mean and median of opioid requirements from the post-anaesthesia care unit to postoperative day 2 were 4.5 ± 1.9 mg and 4.2 mg, respectively. After adjusting for patient weight, there was no significant difference in opioid requirements between patients with total versus upper plexus palsy.

Conclusions: Objective assessment of infants with OBPP who had microsurgical reconstruction indicated that these infants have minimal to no pain in the immediate
postoperative period. There was no difference in pain experienced by infants with upper versus total plexus palsy.

Patrick DÖMER, U Janssen-Bienhold, B Kewitz, C Heinen, T Kretschmer
Department of Neurosurgery, Evangelisches Krankenhaus Oldenburg - Carl von Ossietzky University Oldenburg (GER), patrick.doemer@uni-oldenburg.de

ANALYSIS OF REGNERATION AND MYELINATION ASSOCIATED PROTEINS IN HUMAN NEUROMA IN CONTINUITY AND DISCONTINUITY (BIObol MOL)

Aim: Neuromas are a nerve’s response to massive trauma. After a traumatic lesion to a peripheral nerve, regenerating axons attempt to cross the injury site, as long as scar tissue or a gap do not counteract sprouting. If target-oriented sprouting is prevented by an exaggerated connective tissue response or gap, a spindle (in continuity) or bulb shaped stump neuroma (discontinuity) will form. It consists of disorganized axons intermingled within connective tissue. Diverse neuroma manifestations and segments (proximal, distal, central, proximal end-bulb) can be described. So far, rat models have shown that regeneration associated genes (RAGs) play an important role for axonal regeneration and for the establishment of a growth-supporting environment by Schwann cells. On a molecular scale, however the precise sequence has not been extensively resolved for human nerve. Therefore, human neuroma formation, its influencing factors and differences in neuroma composition are still of interest. Particularly so, if these findings can be correlated to clinical findings, lesion mechanism, latency between trauma and surgery and success of reconstruction. As such our approach to human neuroma analysis is embedded in a local multi-dimensional nerve data bank for further analysis (BIObol).

Materials & Methods: Axonal sprouting and status of myelination was analyzed in human neuromas (3x stump neuromas, 3x neuromas in-continuity). Unlesioned graft and neuroma tissue was obtained from nerve grafted patients during the operation. Tissue samples were prepared directly in the OR for fixation (2% PFA, over night) or frozen at -80°C immediately after resection. For immunochemistry, cryosections (20 µm) were blocked (10% NGS in 0.1M PB-Tx100, 1h) and incubated with antibodies (ABs) detecting NF (1:1000), Gap43 (1:500), MBP (1:500), NG2 (1:50) and S100 (1:500) over night (4°C). Corresponding fluochrome conjugated ABs (1:1000) were applied at RT for 2h. For Western-Blot analysis 30 µg protein of each sample was separated by SDS-PAGE on 10% gels and transferred on nitrocellulose membrane. After blocking (5% powdered milk in TBS-Tween), blots were incubated with primary ABs (1:1000, 4°C over night) and HRP conjugated secondary antibodies (1:1000, RT, 2h).

Results: NF-immunoreactivity patterns indicate a significant reduction of axons from the proximal to the distal segment of each neuroma. No axonal structures were present in the distal nerve stump. Gap43 positive axons and growth-cones were in close proximity to NF-positive nerve fibers. Growth-cones positive for Gap43 sprout alongside NF-positive fibers in a
piggyback-like manner, underlining the remaining axonal plasticity within neuroma tissue. Myelin sheath labeling revealed mature NF-expression as well as plasticity-associated Gap43-expression of axons, which become myelinated by Schwann cells. This was validated by the Schwann cell marker S100. Within the neuromatous tissue, regenerating nerve fibers were ensheathed by NG2-positive cells, forming endoneurial tube-like structures. The distribution of NF, Gap43 and MBP in the different segments of the neuromas was verified by Western-Blot analysis.

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Michael FOX, A Rashid, H Abdul-Jabar, M Sinisi, T Quick
The Royal National Orthopaedic Hospital, London (UK), drmikefox@aol.com

EFFECTS OF SURGICAL DECOMPRESSION ON NEUROPATHIC PAIN IN PATIENTS WITH INFRACLAVICULAR BRACHIAL PLEXUS INJURIES

Aim: Our aim was to study the effects of surgical decompression on neuropathic pain in patients with infraclavicular brachial plexus injuries.

Materials & Methods: Sixty-three patients underwent neurolysis of closed infraclavicular brachial plexus injuries at our institution between June 2008 and June 2012. The primary outcome measures were the change in Visual Analogue Pain Score and Neuropathic Pain Symptom Inventory Score before and after surgery. We also assessed the presence of a link between time to surgery and change in magnitude of pain score.

Results: 51 patients (84%) were included in the study. The majority of referrals were from regional orthopaedic units. The most common mechanism of injury was glenohumeral joint dislocation. The mean time to surgery was 123.9 days (range 3-748 days). The most common pattern of nerve injury was to the posterior and lateral cords or medial and lateral cords. 57% of patients experienced subjective improvement within the first 8 weeks of surgery. Follow-up was conducted at a mean of 37.3 months (range 13-65) post-operatively. The mean reduction in Visual Analogue Pain Score was 4.3 (p<0.05) and the mean reduction in Neuropathic Pain Symptom Inventory Score was 48.2 (p<0.05). The Pearson correlation coefficient for time to
surgery vs. changes in VAS score was -0.29 (p<0.05) whereas the Pearson correlation coefficient for time to surgery vs. change in NPSI score was 0.08 (p>0.05).

Conclusions: This study is retrospective and limited in number. It does however give some weight to argument that early decompression and decompression of neural elements reduces pain.

Debora GAROZZO, V Petralia
Santa Maria della Misericordia Hospital, Rovigo (Italy) & Neurospinal Hospital, Dubai (UAE);
Debora.garozzo@sem-brachialplexus.com

A CLINICAL STUDY ON DEAFFERENTATION PAIN FOLLOWING BRACHIAL PLEXUS INJURIES.

Aim: Brachial plexus injuries are associated in more than 70% of cases with root avulsions: unfortunately it is well known that avulsive injuries are almost systematically causing the onset of pain (so-called deafferentation pain) along the paralysed arm, often presenting with such intensity to completely disrupt the quality of life of these patients and thus becoming their main concern more than the disability itself. The present study aimed to assess the clinical presentation and the factors influencing the onset, intensity and duration of deafferentation pain.

Materials & Methods: We interviewed 89 patients (82 males and 7 females) that had brachial plexus reconstruction in the years 1983-2015 at the Santa Maria della Misericordia Hospital in Rovigo, Italy. All the patients included in this study presented avulsive injuries: 2 root avulsions in 10% of cases, 3 avulsions in 30%, 4 avulsions in 19% and 5 avulsions in 41%. The data were collected to investigate deafferentation pain, focusing on the time of its onset, intensity, clinical presentation and duration with respect to the traumatic event. We studied the factors influencing the intensity of pain, the therapies followed by the patients also in relation with their lifestyle as well as the outcome after surgical treatments (13 patients underwent Drezotomy).

Results: Only 2 patients (one with 2 avulsed roots and the other one with 5 root avulsions) out of 89 did not report on deaffentation pain. In the majority of cases, the onset of pain was reported to have occurred immediately after the traumatic event or within one month after it and its intensity remained stable ever since. Opioids and cannabinoids seem to be the most effective drugs although in the vast majority of cases, pharmacological treatment is largely ineffective. Surgical treatment for deafferentation pain has proved to have poor outcome as well, due to the recurrence of pain. The influence of lifestyle and psychological issues (given the role of central mechanism in the onset of deafferetation pain) was also assessed and clearly demonstrated that psychotherapy should be taken more in account than presently considered. More than 60% of these patients is not working (in spite of being in productive years) and deafferentation pain is one of the main reasons why they cannot be regularly employed. 82% of the patients in our study considered pain their main concern more that the invalidity consequent to the brachial plexus injury itself.

Conclusions: Deafferentation pain seems to be a major cause of invalidity in patients with
brachial plexus injuries, more than the functional impairment itself. There is also a dearth of medical information concerning this problem among the professional figures interacting with such patients that can partly explain the ineffective treatment they receive. In our study it was clearly demonstrated that, differently from what mostly reported in the literature, there is no subsidence of pain through the years: it is just the capacity of the patient to adapt to and live with it that results in an apparent decrease of pain intensity.

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Tessa GORDON, JE de Zepetnek
Department of Surgery, Division of Plastic Surgery, The Hospital for Sick Children, University of Toronto (CAN) and Division of Neuroscience, Faculty of Medicine and Dentistry, University of Alberta, Edmonton (CAN); tessa.gordon@gmail.com

THE SIGNIFICANCE OF MUSCLE FIBER TYPE GROUPING IN SKELETAL MUSCLES REINNERVATED AFTER NERVE INJURY AND SURGICAL REPAIR.

Aim: Motor unit (MU) muscle fibers innervated by one motoneuron, and the same muscle fiber types are normally distributed in a mosaic pattern in muscle cross-sections. Our previous findings demonstrated that this distribution is restored in large hindlimb muscles after transection of the nerve and coaptation of randomly aligned nerve stumps but that MU muscle fiber and muscle fiber types exhibit grouping when the nerve supply is reduced. Here, we asked whether 1) MU muscle fiber and muscle fiber type clumping, defined as a significant increase in numbers of the fibers that are adjacent to one another, occurs in a smaller reinnervated rat hindlimb muscle, and 2) slow and fast motoneurons preferentially regenerate their nerve fibers within their original endoneurial pathways.

Materials & Methods: MU contractile forces in rat tibialis anterior muscles were recorded four to six months after nerve transection and repair and in normally innervated muscles. The muscle fibers of isolated MUs were depleted of glycogen by exhaustive electrical stimulation for later visualization with periodic acid staining and enumeration. Muscle fiber types were identified with histochemical staining and counted.

Results: MU muscle fibers occupied defined territories in muscle cross-sections. These territories were smaller after reinnervation with significantly more MU muscle fibers lying adjacent to one another, in parallel with a corresponding increase in adjacencies of muscle fiber types. Whilst regenerating nerve fibers did not reinnervate their former muscle fibers, reinnervated slow muscle fibers were again located within the deep muscle compartment but there was a significant increase in their number and their location in more superficial muscle regions.

Conclusions: We conclude that 1) reinnervated MU muscle fibers in the relatively small muscles of the rat demonstrate ‘clumping’ within smaller muscle territory areas and 2) reinnervated slow muscle fibers are increased in numbers, tend to locate to the deep muscle regions but significant numbers are located abnormally in more superficial regions.

Significance: Fiber type clumping in reinnervated muscles is predictive of muscle
reinnervation in small but not large muscles. In the latter muscles, clumping is more indicative of sprouting resulting from partial nerve injury rather than reinnervation of denervated muscles after complete nerve injury.

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Fernando GUEDES, F Torrã£o, H Spener, D Barbosa
Division of Neurosurgery, Gaffree et Guinle University Hospital, Federal University of Rio de Janeiro State-UNIRIO (BR); neuroguedes@yahoo.com.br

MISDIAGNOSE IN BIOPSIED TUMORS OF PERIPHERAL NERVES – CONSEQUENCES AND LESSONS FROM A SURGICAL SERIES

Aim: Biopsies are routinely taken in the work-up and treatment planning for soft tissue tumors. Peripheral nerve tumors (PNT) comprises a heterogenic group of relatively rare masses with unspecific clinical presentation. Preoperative biopsy (POB), of any kind, in patients with PNT is controversial. There is no consensus regarding its indications and clinical consequences. Our study aims to evaluate the efficacy and consequences of POB in a series of patients who underwent surgical excision of PNT.

Material & Methods: We retrospectively reviewed the charts of 17 patients with PNT who were biopsied in non-specialized centers prior to referral to our service. All patients underwent complete clinical and neurological examination at our center. Information concerning clinical presentation, biopsy type and results, final histopathological diagnosis and outcome was recorded. Surgical implications related to the realization of POB were also assessed.

Results: The tumors were located as follow: six brachial plexus lesions (35.2%), three median nerve (17.6%), two peroneal nerve (11.8%), one ulnar nerve (5.8%), one radial nerve (5.8%), one medial brachial cutaneous nerve (5.8%), one femoral nerve (5.8%) and one in right arm (5.8%). Twelve patients (70%) had slight to moderate pain and no patients reported functional deficit before biopsy. Eleven patients (64%) were evaluated by magnetic resonance imaging (MRI) before POB. Six (35.2%) underwent biopsy without any imaging procedure. Two patients (11.7%) had open biopsy interrupted due to excruciating pain. Ten (58.8%) biopsies had inconclusive results. Eight patients (47%) had POB initial diagnosis proved wrong after final histopathological analysis. All patients presented severe pain after biopsy. Nine patients (53%) developed a new motor deficit. Tumor resection was hampered by scar formation in all cases.

Conclusions: POB were shown either inconclusive or inaccurate in our series of patients with PNT. After POB patients have a high probability of developing or worsening neuropathic pain or even motor/sensory deficit. Whenever a benign PNT is highly likely, we should be reluctant regarding the performance of such invasive procedure due to the possibly harmful consequences. Surgical excision of PNT may become more technically demanding after POB.
A NEW TECHNIQUE FOR ULTRA-MINIMALLY INVASIVE SURGERY

**Aim:** The aim was to introduce a non-scalpel ultra-minimally invasive technique with a precise manipulating accuracy for peripheral nerve decompressive surgery.

**Material & Methods:** A piece of flexible smooth thread was utilized as cutting tool to transect the targeted soft tissue to decompress the entrapped peripheral nerve. The dissecting thread was looped around the target tissues percutaneously with the help of spinal needle under the ultrasound guidance. The transection was done through the frictional shear force generated in the pressure concentrated location on the target tissues by pulling both ends of the thread with back and forth sliding motion. There were only two needle punctures at the entry and exit points with no surgical incision. The technique was verified in the cadavric study and clinical trial through the thread carpal tunnel release (TCTR) and the thread trigger finger release (TTFR) procedures.

**Results:** The cadaveric study revealed complete transection of the transverse carpal ligament. The superficial palmar arterial arch, superficial palmar aponeurosis, Berrettini branch between median and ulnar nerve, common digital nerves, and median nerve with recurrent branch and palmar cutaneous branch were protected. The outcomes of 180 TCTR cases revealed significant improvement in the short-term results, and better in long-term results than that with the open or endoscopic release. There was no neurovascular complication for any cases. Significant relief of symptoms was observed 3 to 5 hours post procedure. Most patients used their hands the day of the procedure for simple daily activity. Patients reported their sleep quality was improved on the surgical day. Most patients with office jobs were able to return to work within 24 hours, and those with repetitive jobs returned to work in about two weeks. The preliminary result from 10 clinical cases of TTFR revealed early symptoms relief and function recovery with no complications.

**Conclusions:** The thread technique has been shown to be safe and effective. The advantage of this technique is complete transection of the target tissues with no collateral injury. The thread technique provides a new ultra-minimally invasive method to the future peripheral nerve decompression.

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**Danqing GUO, Danzhu Guo, Joseph Guo**
BayCare Clinic, Green Bay, Wisconsin (USA); danqingg@gmail.com

THE NEEDLE-TO-NEEDLE INSERTING APPROACH FOR THREAD TRIGGER FINGER RELEASE (TTFR)

**Aim:** The thread trigger finger release (TTFR) showed safe and effective in a cadaveric study, but during a clinical trial it was found difficulty for an operator to manipulate the routing needle exiting at the designed point, raising a risk of iatrogenic neurovascular or other injuries. The
aim of the study was to improve accuracy for needle routing process to ensure a complete trigger finger release without iatrogenic injuries.

**Material & Methods:** In the clinical trial, the ultrasound guided routing process of TTFR was modified with the needle–to-needle inserting approach. A needle was inserted into the skin at the entry point, while a fine needle inserted into the skin at the designed exit point. Then the fine needle was inserted into the tip of the other needle and guided out of the skin at the exit. Up to now the performance was done on four patients for a total of 9 finger/thumbs (1 thumb, 1 little finger, 2 index fingers, 2 middle fingers, and 3 ring fingers).

**Results:** Each performance resulted in an immediate symptom release and an outcome without complication. The recover period for patients was relatively short and there was no scar. The needle routing accuracy was within 0.2 mm, and the average time for a procedure was 10 to 15 min.

**Conclusions:** The preliminary clinical study showed the TTFR with needle-to-needle inserting approach was safe and effective. We continue the clinical study to further verify the findings.

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Amgad HANNA  
University of Wisconsin, Madison, WI (USA); ah2904@yahoo.com

**THE LATERAL FEMORAL CUTANEOUS NERVE CANAL**

**Aim:** Meralgia paresthetica causes dysesthesias and burning in the anterolateral thigh. Surgical treatment includes nerve transection or decompression. Finding the nerve in surgery is very challenging. We conducted a cadaveric study to better understand the variabilities in the anatomy of the lateral femoral cutaneous nerve (LFCN).

**Materials & Methods:** Twenty embalmed cadavers were used for this study. We studied the LFCN relationship to different fascial planes, and the distance from the anterior superior iliac spine (ASIS).

**Results:** A complete fascial canal was found to surround the nerve completely in all the specimens. The canal starts at the inguinal ligament proximally and follows the nerve beyond its terminal branches. The nerve could be anywhere from 6•5 cm medial to the ASIS to 6 cm lateral to the ASIS. In the latter case, the nerve may lodge in a groove in the iliac crest. Other anatomical variations found were the LFCN arising from the femoral nerve, and a duplicated nerve. A thick nerve was found in one case where it was riding over the ASIS.

**Conclusion:** The variability in the course of the LFCN can create difficulty in surgical exposure. The newly defined LFCN canal renders exposure even more challenging. This calls for high-resolution pre- or intra-operative imaging for better localization of the nerve.

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Amgad HANNA, K Lee, M Ehlers
University of Wisconsin, Madison, WI (USA); ah2904@yahoo.com

PREOPERATIVE ULTRASOUND-GUIDED WIRE LOCALIZATION OF THE LATERAL FEMORAL CUTANEOUS NERVE

Aim: Difficulty and sometimes inability to find the lateral femoral cutaneous nerve (LFCN) intraoperatively is well known. Variabilities in the course of the nerve are well documented in the literature. In a previous paper, we have defined a tight fascial canal that completely surrounds the LFCN in the proximal thigh. These two factors render finding the nerve intraoperatively, to treat meralgia paresthetica, sometimes very challenging. We explored the use of preoperative ultrasound to minimize operative time and eliminate situations where the nerve is not found.

Materials & Methods: Since 2011, we have used pre-operative ultrasound-guided wire localization (USWL) in 19 cases to facilitate finding the nerve intraoperatively. Data was collected prospectively with recording of the timing from skin incision to identifying the LFCN; this will be referred to as the skin-to-nerve time.

Results: In 2 cases, the localization was incorrect. In the 17 cases where the LFCN was correctly localized, the skin-to-nerve time ranged from 3 minutes to 19 minutes. The mean was 8.5 minutes, and the median was 8 minutes.

Conclusions: Preoperative USWL is a useful technique that minimizes the time needed to find the LFCN. For the less experienced surgeon, it is extremely valuable. For the experienced surgeon, it can identify anatomical abnormalities such as duplicate nerves, which may not be readily recognizable without ultrasound. Collaboration between the surgeon and the radiologist is very important especially in the early cases.

Andrew HART, T Reekie, J Roberts, G Miles, M Riehle
University of Glasgow / Canniesburn Plastic Surgery Unit (UK); Andrew.Hart@glasgow.ac.uk

ESTABLISHING AN ETHICAL AND FINANCIALLY SELF-SUPPORTING SYSTEM TO PROVIDE Viable HUMAN DORSAL ROOT GANGLION NEURONS FOR IN VITRO PAIN RESEARCH

Aim: Despite widespread recognition that murine models (in vivo & in vitro) inadequately reflect clinical findings, the fields of peripheral nerve injury and pain research remain reliant upon lower-order species. Translational research is stalled and its reliance upon murine models becomes increasingly ethically untenable. Therefore a critical need exists for earlier pipeline introduction of human-derived data. This project sought to establish an ethically defensible, not-for-profit, reproducible system to provide human primary sensory neurons and protocol support for in vitro research, with initial focus upon pain therapy.

Materials & Methods: With NC3Rs grant funding and industry support (CrackIt DRGNet Challenge 9) ethical and pragmatic scoping exercises identified solid organ transplant donors
as the optimal tissue source. Donor identification and authorisation processes were established with NHS Blood & Transplant (Scotland). Over a 3-year period surgical retrieval protocols were iterated and optimised, and DRG dissociation / neuron extraction / culture protocols developed in parallel with porcine modelling work. Cellular yield was quantified, and output characterised with histochemical and electrophysiology (single-cell patch-clamping) markers.

**Results:** Ethical / legal assessments and specialist nurse feedback has been favourable. A mean 82% of donors families authorise DRG retrieval for research; solid organ donation/retrieval has not been affected. Surgical retrieval times have plateaued, with a median 22 DRG/donor retrieved during the hour that follows solid organ retrieval (median pre-retrieval ischaemia time 133min, range 67-257). DRG are placed into a plegic transport system and dissociation commenced within a median 118 minutes (range 55-175min). Yield is highly variable, subject to numerous individual patient factors, and to a profound learning curve, yet a median 20,966 DRG neurons are delivered (range 5670-44,400). Further cell loss occurs during initial rescue culture, but cells that survive to day 4 thereafter remain robust (viable in culture >4 weeks), and demonstrate morphologically, histochemically (e.g. NF200, CGRP, PV positive) and electrophysiologically (e.g. spontaneous, voltage-change and pharmacologically induced action potential generation) neuronal phenotypes. Systems for cryopreservation and for transport were developed and tested. Cryopreserved transported and thawed neurons remain morphologically and histochemically neuronal but viability is improved during shipping (50-750 miles) in suspension or plated. Porcine cervical DRG neurons (~150kg Landrace) have been found to match human cells well, with greater homology than found with murine cells/tissues (Sprague-Dawley rat, ~200g).

**Conclusions:** Numerous and considerable ethical, practical, and biological barriers have been overcome to deliver a system of protocols and procedures that can soon be rolled out internationally to support translational peripheral nerve regeneration / pain research by the cost-effective provision of human primary sensory neurons for in vitro models. Persisting problems relating to ethical sensitivities, low yield, and unpredictable scheduling will limit broad conversion from animal to human cell lines for high-volume translational research work which abattoir derived porcine DRG may provide a better source of cells until iPSC cell lines are better available, characterised, and costed. Mechanistic research will likely remain with the murine model.

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Andrew HART, S Thomson, P Kingham, M Riehle
University of Glasgow / Canniesburn Plastic Surgery Unit (UK); Andrew.Hart@glasgow.ac.uk

**SURFACE LINEAR MICROPATTERNING TO ENHANCE NEURITE OUTGROWTH IS A TRANSLATIONALLY RELEVANT TOOL, AND INFORMS ON DRUG DISCORY PIPELINES**

**Aim:** In order to improve the outcome of nerve repair, or reconstruction, it is necessary to better understand and control the cell-scale events during axonal outgrowth into the distal
nerve. Many approaches have been investigated (e.g. neurotrophic factors, acellular conduits/wraparounds, cell therapy) but a major advance has eluded the application of single technologies and a so combinatorial approach is likely needed. Surface microtopography is a powerful, highly translatable, determinant of axonal growth and phentypic behaviour. This study examines its effect upon molecular pathways relevant to directional growth and to neuroprotective pharmacotherapy, and informs upon future pharmacological targets and translational progression.

**Materials & Methods:** Using the neonatal rat DRG explant model, the effect of growth over smooth vs. patterned (12um x 5um channelling) substrates was used to assess the impact of patterning upon axonal growth, and upon differential regulation of key molecular pathways. Substrate fabrication involved UV-photolithography to create silicone masters, spin coating with PDMS (10:1 base:curing agent), and plasma deposition of poly-L-lysine. After screening experiments, mTOR, CrAT and MAP3K12 merited further investigation using a combination of quantitative immunohistochemistry (neurite outgrowth / morphology / cell migration / gene product intracellular localisation), quantification of gene expression (organotypic PCR; ELISA/in-cell Western), and 4-D co-localisation. The mTOR pathway was further interrogated using rapamycin (antagonist) and mTORC1 / mTORC2 activation markers. Preservation of the impact of patterning in 3-D was investigated using novel radiopaque PCL conduits and micro-CT.

**Results:** Microtopography considerably potentiated neurite outgrowth by Day 3, and enabled high fidelity directional control. mTOR and CrAT gene expression peaked at 72 hours, thereafter falling (CrAT) to baseline (mTOR). MAP3K expression was not temporally controlled. Substrate patterning potentiated mTOR (p<0.005), inhibited MAP3K, and did not affect CrAT gene expression. mTOR gene expression peaked between 48-72 hours, coincident with the first period of rapid neurite outgrowth and glial migration, and correlates with neurite length at 48 hours (Spearman correlation r=0.7920, P<0.005). mTOR protein was located to glia and in a punctate distribution along neurites, protein levels peaked at 72 hours and were significantly increased by patterned substrate. Rapamicin inhibited neurite growth only on flat substrate, and differential effects upon mTORC1 & mTORC2 were found. Surface patterning protected against rapamicin and enhanced neurite growth by signalling via mTORC2 (phAKT), upstream of PI3K. Patterning also directs nerve growth in 3-D, and can be assessed by micro-CT.

**Conclusions:** Micropatterned guidance channels powerfully elongate and direct early neurite outgrowth via mechanisms signalled through the mTORC2, raising the potential to enhance neurite growth from the proximal stump into a nerve repair / reconstruction by pharmacological manipulation (e.g. PTEN inhibitors or specific small molecule targets), and by micropatterned repair constructs. Existing putative neuroprotective pharmacotherapeutics will support outgrowth, acting via CrAT. Micro-CT offers a promising tool to assess nerve growth in 3D, in intact PCL conduits.
Christian HEINEN, T Schmidt, T Kretschmer  
Department of Neurosurgery, Evangelisches Krankenhaus Oldenburg - Carl von Ossietzky University Oldenburg (GER); christian.heinen@uni-oldenburg.de  

HIGH-FREQUENCY ULTRASOUND IMAGING OF GRAFTED PATIENTS - MORPHOLOGICAL CHANGES OVER TIME (BIOBOL-NERVE; INTERIM RESULTS)  

**Aim:** The capability of imaging methods to detect nerve regeneration in a clinical setting still needs to be proven. Until now, there are limited reports on high-resolution MRI depicting axonal recovery and outgrowth in animal models. Little is known about the potential usefulness of ultrasound to detect fascicular reorganisation after nerve trauma in humans. In an ongoing trial, registered by our local ethics committee, we evaluate the capability of high-frequency neurosonography (HFNS) to detect anatomical reorganisation after graft reconstruction. Functional results will be correlated to depicted ultrasound morphology.  

**Materials & Methods:** To date, n=9 patients with traumatic nerve lesions requiring graft reconstruction were prospectively included. Assessment encompassed physical and electrophysiological examinations (motor and sensory function, pain, EMG, nerve conduction studies). In addition, pre-, intra- and postoperative high-frequency ultrasound imaging was performed using a 15-6 (pre- and postoperatively) and 13-6 MHz (intraoperatively) probe.  

**Results:** Of the n=9 patients, n=7 were male, n=2 were female. Follow-up of at least 6 months was available for n=8 patients. Longest follow-up was 24 months. The following nerves were affected: n=2 radial nerves, n=1 posterior interosseus nerve, n=1 ulnar nerve, n=2 peroneal nerves, n=2 infraclavicular brachial plexus/ musculocutaneous nerve and n=1 accessory nerve. In all patients early caliber enlargement at the suturing sites was detected. At first the suture sites were clearly visible and pronounced, followed by appearance of rather chaotic hypoechogenic nerve echotexture. In the further course, a hint of fascicular rearrangement was observable. In deeply situated nerves such as infraclavicular plexus/ axillary nerve or very obese patients, impaired tissue penetration of the high-frequency neurosonography hampered detailed assessment of morphological changes. So far, in n=7/8, with follow-up of at least 6 months successful reinnervation took place. All of these patients showed the above mentioned morphological changes aside from n=2 patients. In these neurosonography was restricted due to deep location and obesity.  

**Conclusions:** In our experience high-frequency neurosonography may be a promising tool for imaging of nerve regeneration. In a preliminary evaluation of this ongoing series, there seemed to be a positive correlation between clinical improvement and morphological changes in terms of fascicular reorganisation. A larger series is warranted to verify results and confirm usefulness of HFNS in this regard. We are eagerly awaiting results of further evaluation as patient numbers and follow-up periods grow.
Variations in lumbar plexus anatomy – a cadaver study

Aim: If compared to the brachial plexus, the lumbosacral plexus literature and anatomical database is limited. Yet, we see a clinical need to increase detailed knowledge for reconstructive procedures and tumor surgery. In this ongoing project, we strive to describe variants in lumbosacral plexus anatomy with regard to contributing roots, root pattern, nerve formation and measures. Extra-attention will be devoted to the pudendal nerve.

Materials & Methods: So far, n=8 lumbosacral plexus (n=1 Thiel fixated and n=3 fresh frozen specimen, all male) were dissected in supine position. Spinal nerve contribution to the major nerves, horizontal distance from the midline at promontory level to each nerve and range of motion in cm during Lasègue maneuver were assessed via a transabdominal approach without removal of the inner organs. Psoas major muscle was desinserted at its distal portion. For pudendal nerve inspection, the sacrospinal ligament was cut.

Results: Spinal nerve contribution to femoral nerve ranged from L1 to L4, to sciatic nerve from L4 to S3, to obturator nerve from L1 to L4, to genitofemoral nerve from TH 12 to L3, to lateral femoral cutaneous nerve from L1 to L3 and to pudendal nerve from S1 to S4. There were clear intrapatient differences in distribution pattern. In one specimen, we found a complete separation of the obturator-femoral complex from the sciatic plexus. In n=3 plexus obturator and femoral nerve, in n=1 plexus pudendal nerve and sciatic nerve exchanged fibres. Average distance from midline at promontory level to femoral nerve was 8 cm, to obturator nerve 5.8 cm, to genitofemoral nerve 8 cm, to lateral femoral cutaneous nerve 10 cm. When performing a 90° Lasègue maneuver, the femoral nerve did not show any relevant movement, whereas the sciatic nerve could be extended with a mean of 5 mm.

Conclusions: Even in a very limited number of specimen, the anatomy of the lumbosacral plexus seems to harbour a large variety both intra- and interindividually. When clinically assessing lumbosacral plexus lesions, these should be taken into account. Measures related to the promontory have the potential to help in intraoperative identification. However, further studies with larger numbers of specimen are required.

Fascicular neuritis: a novel imaging diagnosis as a cause of AINS and PINS

Aim: It has been difficult to prove the existence of fascicular/partial nerve lesions in spontaneous neuropathies using clinical and electrophysiological findings. We sought to
Percutaneous Endoscopic Lumbar Discectomy VI:
A Meta-Analysis of the Literature

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determine lesion sites and spatial lesion patterns in nontraumatic anterior interosseous nerve syndrome (AINS) and posterior interosseous nerve syndrome with high-resolution sonography (US) and magnetic resonance neurography (MRN).

Materials & Methods: In 20 patients with a nontraumatic AINS and 19 patients with PINS, and 20 healthy controls, a large coverage MRN of the upper arm, elbow and proximal forearm as well as US of the median and radial nerves were performed. Lesion classification was performed by visual rating, on MRN with additional quantitative analysis of normalized T2 signal nerve voxels.

Results: In AINS, all patients and no controls, had T2 lesions of individual fascicles within upper arm median nerve trunk that strictly followed a somatotopic topography. The affected fascicles were identified as those that will form the anterior interosseous nerve further distally. Of 19 patients with PINS, only 3 (16%) had a focal neuropathy at the entry of the radial nerve deep branch into the supinator muscle at forearm level. The other 16 (84%) had proximal radial nerve lesions at the upper arm level with a predominant lesion focus 8.3 ± 4.6 cm proximal to the humeroradial joint. Most of these lesions (75%) followed a specific somatotopic pattern, involving only fascicles that would form the posterior interosseous nerve. On US the lesions appeared as hypoechoic thickenings of isolated fascicles.

Conclusions: Neuroimaging reveals fascicular lesions with strict somatotopic organization in upper arm median nerve trunks of AINS patients. The data strongly support that AINS in the majority of cases is a multifocal mononeuropathy selectively involving, within the main trunk of the median nerve, the motor fascicles that continue distally to form the anterior interosseous nerve. PINS is not necessarily caused by focal compression at the supinator muscle but is instead frequently a consequence of partial fascicular lesions of the radial nerve trunk at the upper arm. Based on neuroimaging, these entities are of inflammatory autoimmune origin and can be described as a fascicular neuritis that can affect several major nerves and is not treatable by surgery.

Henrich KELE, M Pham, M Bendszus, P Bäumer
Center for Neurology and Clinical Neurophysiology Neuer Wall, Hamburg (GER);
kele@neurologie-neuer-wall.de

PERIPHERAL NERVE IMAGING IS INDISPENSABLE FOR CORRECT DIAGNOSIS AND THERAPY IN CERTAIN PERIPHERAL NEUROPATHIES

Aim: Recent research showed that partial neuropathies as well as the AINS and PINS, are predominantly inflammatory conditions described on imaging as a fascicular neuritis. It is to demonstrate the cases requiring prompt surgery in these neuropathies that can be identified only with neuroimaging.

Materials & Methods: We present a series of patients with acute and subacute neuropathies, 3 with AINS, 1 with PINS and 1 partial radial neuropathy. The history and symptoms reminded in all but 1 case (partial radial neuropathy) of a neuralgic amyotrophy. All patients underwent a
thorough electrophysiological examination and neuroimaging, high-resolution ultrasound (US) and magnetic resonance neurography (MRN).

**Results:** There were 2 cases of a fascicular torsion of median nerve fascicles (one in the main trunk in a thickened nerve, another of the AIN just distal to the branching site) and a AIN-compression by a fascia. The PINS was caused by 2 fascicular torsions of radial nerve fascicles in the main trunk that would represent more distally the PIN. The partial radial nerve lesion was spectacular: it was caused by 2 radial nerve torsions in a distance of 9 centimeters on the basis of a multifocal swelling of several peripheral nerves. Postoperatively, further diagnostics revealed a neuroborreliosis that required a high-dose therapy with antibiotics. All conditions were preoperatively identified by US. MRN showed a monofascicular lesion pattern in all but the radial nerve torsion. All operated patients showed a good outcome. The median trunk AIN was considered as a secondary torsion in an inflammatory neuropathy and did not undergo surgery.

**Conclusions:** Despite the evidence that favors an inflammatory origin of partial neuropathies there are still conditions requiring prompt surgical interventions. The cases show that it is not possible to make a correct diagnosis and adequate therapy based on clinical and electrophysiological data. Neuroimaging is vital for quick and correct decision making.

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**Michel KLIOT, J Rogers, H Liu, M Cotton, N Dahdaleh**
Stanford & Northwestern University Feinberg School of Medicine Departments of Neurosurgery, Stanford (USA) michelkliot@gmail.com

**TESTING FLEXIBLE INTEGRATED CHIPS (BIOSTAMP) PLACED ON THE SKIN TO MONITOR NERVE-MUSCLE FUNCTION DURING PERIPHERAL NERVE, SPINE, AND CRANIAL NERVE SURGERY**

**Aim:** To test the clinical ease of use and reliability of employing newly developed and proprietary surface skin sensors, consisting of flexible integrated computer chips, to measure both movement and electrophysiological activity and responses in muscle in response to nerve stimulation. We compare the performance of these new skin surface devices with traditional needle EMG monitoring techniques during peripheral nerve, spine, and cranial nerve surgery.

**Material & Methods:** We present intraoperative patient data investigating the clinical ease of use and reliability of applying newly developed and proprietary surface skin sensors (Biostamp), consisting of flexible integrated computer chips with blue tooth technology, to measure electrophysiological activity and responses in targeted muscles in response to nerve stimulation in the surgical settings of peripheral nerve, spine, and cranial nerve surgery. The threshold of peripheral, spinal, and cranial nerves to monopolar electrical stimulation in eliciting a response from a target muscles was compared using standard percutaneous needle electromyography (EMG) techniques, conventional surface EMG in some cases, and Biostamp applied on the skin overlying the muscle being tested.
**Results:** Our preliminary data demonstrates that the performance of these new Biostamp devices compares favorably with traditional needle EMG and skin surface recording techniques.

**Conclusions:** Biostamp offers sureons a relatively easy way to monitor and protect peripheral nerve, spinal, and cranial nerves during surgery that does not rely on having a trained team of electrophysiologists to perform intraoperative monitoring.

**Disclosures:** MC10, Axogen.

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**Kartik G KRISHNAN, C Wittekindt, PM Richardson**

Justus Liebig University of Giessen (GER); Kartik.Krishnan@neuro.med.uni-giessen.de

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**A COMPARATIVE EVALUATION OF THE METHOD OF INNERRATION IN MICRONEUROVASCULAR REANIMATION (FMT) IN UNILATERAL FACIAL PALSY**

**Aim:** Free muscle transfer (FMT) is one salient option for mimic reanimation in long standing facial palsies. Motor nerves that serve as axon donors for the FMT are either the contralateral facial nerve or the ipsilateral neighbouring nerves (masseteric/hypoglossal/accessory). This paper aims to compare two methods of innervation of the FMT used in facial reanimation: contralateral facial nerve and ipsilateral masseteric nerve. This is a retrospective study.

**Materials & Methods:** We evaluated 49 patients with irreparable unilateral facial palsy treated with FMT between 2000 and 2014 (18 females and 31 males; mean age 36.3 years, age range 19–71 yrs). All surgeries were one-stage procedures. 11 patients (Group FN) had their FM-flaps innervated through the buccal end-branches of the facial nerve at the contralateral nasolabial fold, whereas the rest 38 FM-flaps (Group MN) underwent ipsilateral masseteric innervation. For evaluation of results we used: (a) qualitative electromyography (EMG) in the FMT at 3 and 6 months postop, (b) the absolute commissural excursion and the commissural excursion index (CEI) / synkinesis and (c) patient self-evaluation. The Mann-Whitney-U-test and the Wilcoxon-signed-rank test were used to calculate the statistical significance using a level of 0.05 in a 2-tailed hypothesis (for CEI).

**Results:** The mean follow-up was 25.3 months (range: 14 – 56 months). In Group FN, 10 patients (90.1%) showed reinnervation potentials in the FMT in EMG at 6 months (3 patients at 3 months- 27.3%). Clinical muscle contraction with positive effects on the CEI was seen in 4 of 11 patients (36.4%). One patient in this group had FMT failure. In Group MN, 36 patients (94.7%) had volitional innervation with EMG potentials at three months follow-up. In 32 patients (84.2%), clinical contractions of the FMT began already at 4 months and a significant improvement of the CEI was seen in 36 patients at their latest follow-up (94.7%). Two patients had FMT failures resulting only in restoration of static symmetry. Synkinesis was a significant issue in the Group MN. However, only 11 patients (28.9%) were able to overcome this phenomenon. Improvement of CEI in the Group FN was statistically insignificant (p=0.985), whereas in Group MN it was (p<0.005). Comparison of the FN and MN groups favoured the results obtained in the MN group. (p<0.005).
Conclusions: Our results denote that the ipsilateral MN innervation of FMT might be a better option than via contralateral FN. However, our study is retrospective and is of disparate cohorts, thus afflicted with bias.

Thomask Kretschmer, U Janssen-Bienhold, P Doemer, B Kewitz, C Heinen
Department of Neurosurgery, Evangelisches Krankenhaus Oldenburg - Carl von Ossietzky University Oldenburg (GER), thomas.kretschmer@uni-oldenburg.de

BIOBOL – A MULTILAYERED NERVE DATA BANK OF Grafted Patients

Aim: We introduce an ongoing project (BIOBol – Biobank Oldenburg), that prospectively samples and registers clinical-, tissue-and outcome data of nerve grafted patients. The objective is to identify factors that essentially affect functional reconstitution by correlating multidimensional descriptive data about clinical status, tissue -compound and obtained results after nerve grafting. Some hypotheses we are interested in: expression profiles of regeneration associated genes and proteins (RAG, RAP) are time sensitive, differ in neuroma segments, do not differ in grafts, do not differ in dependence of distance to spinal cord.

Materials & Methods: Besides all clinically relevant data the corresponding tissue “make-up” of the traumatized nerve on a molecular level and the changing neurosonographic image morphology of the grafted segment are captured prospectively from pre-op to postop in regular intervals (preop, intraop, 6, 12, 18, 24, 30, and 36 months postop). For molecular biology mRNA, RT-PCR, gel-electrophoresis and sequencing are used; proteinbiochemistry is done by SDS-PAGE, Western Blot and densitometry; immunohistochemistry is by confocal microscopy and image analysis. So far, markers for Schwann cell proliferation (MBP, PMP22, NG2, CNPase), fibroblasts (Thy1/CD90), axon growth and stabilization (GAP43, MAP1B, NCAM, NF-200) were used. The obtained data is fed into a custom-made web-data-base, that allows for later correlation analysis by different evaluation algorithms.

Results: To date 42 grafted patients were included in the biobank. Apart from a continuous feed of clinical data (BIOBol clinic), first results of molecular biology, proteinbiochemistry and immunocytochemistry (BIOBol Mol) are available in parallel with neuroimaging (BIOBol-image) of grafted segments. Patient data are fed separately from blinded tissue data. Overall data will not be correlated until final functional results, complete follow-up of image morphology and tissue results are available. In the further course we want to be able to start comparative analysis that ultimately allows identifying prognostic parameters of functional reconstitution for patients in need of nerve reconstruction. Examples of BIOBol-image (CHeinen) and BIOBol-Mol (PDOemer) will be presented separately.

Conclusions: It is feasible to collect multidimensional human data including results of tissue analysis. So far the approach seems worthwhile, even if effort is quite substantial. We are confident to be able to extract clinically relevant data that will support or decline some of our hypotheses.
Zhongyu Li, T Liu, TL Smith, JF Plate, J Cai
Wake Forest School of Medicine. Winston-Salem (USA); zli@wakehealth.edu

AGING INFLUENCES THE EXPRESSION OF ENERGY SENSOR SIRT1 DURING WALLERIAN DEGENERATION

Aim: The underlining molecular mechanisms of poor neurologic recovery after peripheral nerve injury in adults remain unclear. Cellular energy NAD+-dependent SIRT1 deacetylase coordinates Wallerian degeneration (WD) after peripheral nerve injury by reprogramming immunometabolic genes and posttranslational modifications of signal proteins and metabolic key enzymes. Age-associated alterations of inflammatory response during WD may contribute to the decline of axonal regeneration potential.

Materials & Methods: Sciatic nerve crush model was produced in young (2-month old) and adult (12-month old) Lewis rats. Animals receiving surgery without axon crushing were set for sham control. Sciatic nerve samples were harvested at 1, 3 or 10 days after axonal crush and continuous sections distal to the marked injury site were made for histology and immunohistochemistry studies. Modulation of inflammatory gene expression by sciatic nerve tissues were analyzed using qRT-PCR. The effect of NAD+ downstream effector SIRT1 on WD generation was studied by administering SIRT1 specific inhibitor EX-527 or vehicle after nerve crush injury.

Results: In contrast to young animals, adult animals displayed an initial immune suppressive response after axonal crush with attenuated expression of pro-inflammatory genes (TNF-α, MCP-1) and delayed recruitment and activation of hematogenous macrophages. These modifications of WD in adult animals were positively correlated with basal axonal expression of SIRT1. Pharmacological inhibition of SIRT1 by EX-527 restores pro-inflammatory MCP-1 gene expression.

Conclusions: Aging alters the process of WD after peripheral nerve injury. Rejuvenation of WD by modulating SIRT1 activity could be a potential adjunct therapeutic strategy for the treatment of peripheral nerve injury in adult patients.

Mark A MAHAN, S Yeoh
University of Utah, Salt Lake City (USA); mark.mahan@hsc.utah.edu

BIOMECHANICAL DYNAMICS OF RAPID-STRETCH NERVE INJURY ANIMAL MODEL

Aim: While the majority of adult brachial plexus injuries result from high speed mechanisms, no laboratory model has been created to model rapid-stretch nerve injuries. Furthermore, prior research on nerve biomechanics is conflicted. Understanding the biomechanical response of nerves to rapid stretch, including failure location, is essential to developing models that mimic the clinical scenario.

Materials & Methods: The sciatic nerves of 103 freshly euthanized Sprague-Dawley rats were dissected and subjected to rapid- and slow-stretch methods. Rapid-stretch injury
involved fixed direction strain produced via constrained weight drop applied to an intact nerve. Slow-stretch techniques included fixed direction strain produced by slowly progressive force and formal material testing instrumentation, both to an intact nerve. Maximal nerve strain, persistent length deformation, regional strain variation and location of nerve failure were recorded.

**Results:** Both rapidly- and slowly-stretch sciatic nerves failed at similar strain deformation values, which depended upon the vector of force (antero-posterior vector: rapid = 61.6%, slow = 56.6%; longitudinal vector: rapid = 14.4%, slow = 20.1%). The regional strain variation varied in association with periarticular regions, with maximal compliance at the knee (69.1%), and at the hip (64.6%), and least at the mid portion of the sciatic nerve (10.1%). Rupture location of stretched sciatic nerves was dependent upon vector more than the rate of stretch and was associated with the differing regional compliance or branch location (antero-posterior vector associated with rupture at the hip/hamstrings branch in 70.1%; longitudinal vector associated with rupture at spinal (17%), middle (43%) and at trifurcation (30%). Velocity of stretch was positively associated with maximal strain and odds of rupture increased when sciatic nerves were stretched above 6 m/s. Elastic deformation (with return to within 15% of baseline value) occurred below 50% maximal strain (37% ±12% stdev), whereas plastic deformation (persistent length change) occurred above 50% maximal strain (59% ±17% stdev).

**Conclusions:** Effects of rapid-stretch nerve injury can reliably be predicted upon the vector and the rate of injury. Rupture of the sciatic nerve was predominantly predicted by rate of stretch. The location of nerve rupture was correlated with loading, with longitudinal tension on the nerve associated with avulsions and strain accumulation at non-compliant regions. In contrast, antero-posterior tension led to rupture at proximal branch points. Elastic-to-plastic deformation predictably followed the maximal strain occurred during stretching.

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**Mark A MAHAN, W Warner, J Zhang**  
University of Utah, Salt Lake City (USA); mark.mahan@hsc.utah.edu

**HISTOLOGIC EVALUATION OF RAPID-STRETCH NERVE INJURY ANIMAL MODEL**

**Aim:** While the majority of adult brachial plexus injuries result from high speed mechanisms, no laboratory model has been created to model rapid-stretch nerve injuries. Importantly, the microanatomical injury of rapid-stretch has not be qualitatively nor quantitatively described. Elucidating the patterns of injury is essential to developing models that mimic the clinical scenario.

**Materials & Methods:** The sciatic nerves of 28 freshly euthanized Sprague-Dawley rats were dissected and subjected to rapid-stretch nerve injury, utilizing fixed direction strain produced via constrained weight drop applied to an intact nerve. Biomechanical parameters, including maximal nerve strain, persistent length deformation, regional strain variation and location of nerve failure were recorded to categorize nerve injury patterns. Sciatic nerves were then histologically evaluated with modified Lillie's trichrome staining, osmium tetroxide, and
immunofluorescent techniques. Serial longitudinal sectioning was performed to volumetrically quantify nerve injury patterns.

Results: Five injury grades were produced: control, sham, elastic (stretch with return to within 15% of pre-stretch length), plastic (persistent length change) and rupture. Two patterns of injury were noted on histologic examination of all injury grades: loss of fiber undulation (straight fibers) and microruptures of fibers. Epineurial tissue appeared torn or dehisced in all ruptured and plastic-phase stretches, while in elastic-phase stretch the epineurium was thinned and variably torn. No cases of intact epineurium and complete internal disruption were found (Sunderland grade 4). Serial longitudinal sectioning demonstrated a predilection for microruptures at the hamstring branch in elastic and plastic grade injuries, and incidence of microruptures demonstrated distinct levels based upon injury grade (p<0.05, Two-way ANOVA with posthoc tests). Loss of fiber undulation, similarly, was found to correlate with progressively severe injury (p<0.05, Two-way ANOVA with posthoc tests). Laminin immunofluorescence demonstrated that endoneurial tubes were intact in sciatic nerves stretched within elastic limits, but ruptured in plastic grade injuries.

Conclusions: The microarchitecture of peripheral nerves is altered in predictable patterns that primarily affect the fibers of the nerve, not external structural elements. The internal architecture is injured in graded fashion that reflects the tissue biomechanics. Nerve fibers are more resistant to rapid stretch than epineurium. This study suggests a new consideration for producing graded nerve injuries with a rapid-stretch nerve injury model.

Rajiv MIDHA, JA Stratton, R Kumar, J Biernaskie
University of Calgary (CA), Rajiv.midha@ahs.ca

ISOLATION AND CHARACTERIZATION OF MYELINATING SCHWANN CELLS FROM ADULT HUMAN SKIN

Aim: Supplementing the injured nerve with autologous Schwann cells (SCs) has the potential to rejuvenate the injury environment and may improve functional outcomes. Although promising, SC harvesting from nerve for autologous transplantation, require invasive surgery for collection, causing additional discomfort and neurological loss. As such, several laboratories have been developing protocols to derive SCs from the easily accessible skin. Using rodent skin-derived SCs (SkSCs), it has been shown that SkSCs can improve anatomical measures and behavioral outcomes following CNS and PNS injury. Because most of the convincing research pertaining to SkSC has been demonstrated using neonatal rodent cells, it is paramount that similar experiments are performed using adult human SkSCs. We hypothesized that adult human skin SCs (hSk-SCs) would be comparable to adult human nerve derived SCs (hN-SCs) in their phenotypic and myelination capacity.

Materials & Methods: SCs from adult human skin (hSk-SCs) and sciatic nerve SCs were isolated (soon after death) from 4 adult male cadaveric donors (ages 27-46 years). Both cell types were cultured in identical SC media conditions, and expanded until purification. Cells were characterized and compared for transcription profiling and cell surface markers for in
vitro phenotype, compared for axon support in a DRG explant assay and their myelination capacity following in vivo transplantation.

**Results:** Within 2 weeks of isolating and culturing adherent mixed skin cells in serum-free SC media, colonies of bipolar shaped cells were sporadically detectable. Within 2-4 weeks of growth, we selected these colonies using cloning cylinders, and re-plated these colonies. By 5 weeks (without going through an intervening sphere stage), we obtained 3-5 million purified SCs, a cell number appropriate for clinical transplantation. We found that hSk-SCs appeared transcriptionally indistinguishable from hN-SCs with both populations exhibiting expression of Schwann cell-specific lineage-specific genes including: SOX10, SOX9, AP2A1, CDH19, EGR1, ETV5, PAX3, SOX2, CX32, DHH, NECL4, NFATC4, POU3F1, S100B, and YY1. Phenotypic analysis of hSk-SCs and hN-SCs cultures revealed highly enriched populations of SCs indicated by the percentage of SOX10+ve cells (89% and 77%, respectively) and a battery of other SC-associated proteins (PAX3, CDH19, ETV5, SOX2, POU3F1, S100B, EGR2, and YY1). We also show that both hSk-SCs and hN-SCs are capable of promoting axonal growth to similar degrees; and that a subset of both associate with regenerating axons and form myelin (MBP, P0 or fluoromyelin+; confirmed by immunogold EM), following transplantation into the injured mouse sciatic nerve.

**Conclusions:** This work demonstrates for the first time that myelin-producing Schwann cells can be isolated from adult human skin. Skin-derived Schwann cells maintain their growth promoting properties and closely resemble Schwann cells derived from the sciatic nerve, thus representing a highly accessible source of autologous Schwann cells for nervous system repair.

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Willem JR van OUWERKERK, A Hillebrand, B van Dijk
Neurosurgery VUmc Amsterdam (NL) w.vouwerkerk@vumc.nl

**CHANGE OF CORTICAL MOTOR PROGRAM IN MAGNETENCEPHALOGRAPHY (MEG) STUDIES IN LATE ACCESSORY TO SUPRASCAPULAR NERVE TRANSFER IN OBSTETRIC BRACHIAL PLEXUS LESIONS**

**Aim:** Test and discuss hypothesis of developmental apraxia as cause of failing external rotation in obstetric brachial plexus lesions with otherwise spontaneous recovery. It is not uncommon that children suffering an obstetric brachial plexus lesion (OBPL) may recover spontaneously except for active glenohumeral exorotation. In general, these are Group I lesions of spinal roots C5 and C6 or the Superior Trunk. All functions recovered except for the function of the Suprascapular Nerve, which surprisingly is a branch of the otherwise recovered and functioning Superior Trunk. Contradictory observations are made in these children not fitting peripheral nerve lesions.

**Material & Methods:** In over 80 patients where only active exorotation did not recover an Accessory to Suprascapular Nerve Transfer was performed at varying ages, the majority over 12 months and even in much older children from 3 to 15 years of age. To investigate possible changes in central cortical representation a pilot study was performed in a case of a boy aged
15 years with the classical picture of lack of active exorotation. An accessory to suprascapular nerve transfer was performed with excellent results as will be shown in video’s. Before operation and during follow up MEG studies were performed for different tasks, especially exorotation. Shift of cortical motor representation could be demonstrated in follow up studies.

**Results:** Over 90% of children reached functional exorotation over 0° (more than neutral position) and were able to reach their mouth without or a minimal Trumpet sign. Electromyography showed voluntary muscle activity and MRI showed hardly any muscle atrophy or fatty degeneration of spinatus muscles. During operations the Suprascapular Nerve was intact and reactive. In case of a 15-year old male lacking exorotation before operation and during follow up MEG studies were performed for different tasks, especially exorotation. Shift of cortical motor representation could be demonstrated in follow up studies after a late Accessory to Suprascapular nerve transfer.

**Conclusion:** In children with OBPL showing spontaneous recovery of arm function except for exorotation an Accessory to Suprascapular Nerve Transfer is a very good option to restore active external rotation. Timing of the procedure is not proven to be strictly age dependent. Central nervous system plasticity plays an as yet to be investigated role in recovery or suppression of recovery.

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**Tom QUICK, K Johnson, H Brown**
Royal National Orthopaedic Centre & University College London (UK); t.quick@ucl.ac.uk

**Reanimated elbow flexion – when is good enough? And how much better than better is better?**

**Aim:** When assessing motor recovery following nerve and muscle transfers (aimed at restoring elbow flexion) the vast majority of patients achieve a muscle power grade IV (MRC IV). However, it cannot be forgotten that each individual patient has their own specific needs, which may lead to huge variations in patient experience (Tung & Mackinnon 2010). Our aim is to explore the lived experience of motor recovery in detail from a subjective view point. This study is designed to both illustrate the experiences and quantify a Minimal Clinical Important Difference (MCID) for elbow flexion. MCID is defined as how much outcome improvement would be necessary before the patient cohort noticed a benefit (Gatchel & Mayer 2010; Kvien et al. 2007). This data will allow a power analysis to be performed will inform future studies.

**Materials & Methods:** An electronic questionnaire has been designed and administered to a cohort of patients who have undergone surgery to restore elbow flexion at the RNOH prior to 2014. The questionnaire is deemed to be a subjective quantitative assessment of outcome and relates to the patient’s functional ability, self assessed risk profile, goal attainment and outcome satisfaction. Ethical approval was achieved prior to the start of the study. Recruitment began in July 2016 and will continue for 1 year.

**Results:** The most striking element of this data is the narrative of patient experience which in itself is informative for clinicians. We have shown there is widespread satisfaction with
reanimation procedures for the elbow. There is however a wide spread of preoperative expectation of function. Those with chronic disability have lower expectations of attainment but similar motor recoveries and satisfaction ratings. The patient’s Likert rating of risk adversity does not appear to inform their decision to recommend the procedure to others.

**Conclusions:** This early report from a project that still has 12 months to run suggests that managing pre operative expectation of functional outcome is likely to improve satisfaction. Providing narrative to patients is likely to add to the experience of nerve recovery which is understandably very varied. Presently, it is too early to interpret the results to provide a MCID for elbow flexion power. Our assessment of MCID will be continued as part of a mixed methods approached utilising a systematic statistical review, a review of combined error and a Delphi exercise.

Tom QUICK, K Johnson, H Brown, M Fox, M Sinisi, A MacQuillan
Royal National Orthopaedic Centre & University College London (UK); t.quick@ucl.ac.uk

**A STUDY OF HAND HELD DYNAMOMETRY ASSESSMENTS OF PEAK FORCE GENERATED FATIGABILITY AND RELATED SURFACE EMG ASSESSED CO-CONTRACTION [INTERIM RESULTS]**

**Aim:** The traditional assessment of muscle renervation outcome has been the discrete MRC scale. This scale is non-linear with over 95% of the potential force generation and 90% of most reported outcomes contained within one grade (MRC IV). A previous study within a cohort of nerve transfers to elbow flexion (n =21) demonstrated that the distribution of continuously measured peak force outcomes from nerve transfer is Gaussian (Quick et al 2016). In order to develop and deepen assessment of outcomes in the nerve transfer model renervated muscle, the impact of fatigability (Maricq et al 2014) and the impact of co-contraction (Hautier et al. 2000) (between agonist and antagonist groups) need to be quantified Thus we aim to establish the prevalence, severity and impact of these aspects of motor function in a a cohort of nerve transfer patients.

**Materials & Methods:** An ethically approved, prospective study is currently enrolling post operative patients from our institution. Non-invasive, sEMG (agonist and antagonist), electronic goniometry and hand held dynamometry are applied to reanimated elbow flexor force generation and compared to the unaffected side. This technique has been developed to provide holistic information regarding force outcomes, fatigability and the presence and variance of co-contraction. The participants are examined by two researchers to ensure inter-rater reliability. We present our early data.

**Results:** Our study is too at too early a stage to reach conclusions. We show methodology and early results from sEMG and hand held dynamometry real time fatigability studies. Co contraction is a widely evident occurrence it is unclear if this is always pathologic and detrimental to force generation and or global function. It is also unclear if the increased fatigability is linked with co-contraction. These questions will be addressed as we continue to recruit.
**Conclusions:** Fatigability and co-contraction are important considerations when assessing movement patterns and muscular function especially within renervated muscles. Early results suggest how prevalent these impairments are. These insights will inform designs of new PROMs and will allow us to more accurately assess outcomes and thus drive improvement in muscle renervation treatment and rehabilitation. Further studies are needed to focus on the many facets of motor recovery and the important drivers of patient related outcomes and satisfaction.

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Tom QUICK, M Wilcox, V Mudera, J Philips
Royal National Orthopaedic Centre & University College London (UK); t.quick@ucl.ac.uk

**HUMAN IN VIVO SCHWANN CELL CHANGE. AN IMMUNOHISTOCHEMICAL ASSESSMENT COMPARING INNERVATED AND DENERVATED HUMAN NERVE. [INTERIM RESULTS]**

**Aim:** The regenerative capacity of human nerves is less than that in rodents but the reasons for this remains unknown. A great deal is known about peripheral nerve regeneration through animal models but much less is known about regeneration in humans. The current knowledge base of human peripheral nerve regeneration has been developed from single cases or tissue culture away from the complex interactions of in vivo injury (Morrissey 1991). Recent findings have shown the plasticity of Schwann cells (SCs) and their ability to switch differentiation states through the process of Wallerian degeneration are largely responsible for the regenerative capacity observed in the PNS (Jessen & Mirsky 2008; Jessen & Mirsky 2005; Jopling et al. 2011) There are many potential targets in this complex and unique phenotypic shift seen in the model of SC phenotypic change after denervation but one that has attracted attention for coordinating or initiating this change is c-jun (Arthur-Farraj et al. 2012; Fontana et al. 2012; Parkinson et al. 2008). The transcription factor c-jun is found in SCs and is thought to be the principle regulator of peripheral nerve regeneration in rodents. The ability of Schwann cells to change from their normal myelinating phenotype (associated with the marker S100 in murine tissue (Mata et al. 1990) to a growth supportive phenotype, when axon contact is lost, is thought to be governed (at least in part) by c-jun. We have designed a study to compare the human in vivo SC phenotypic change with what is known from mammalian models regarding the expression of c-jun.

**Materials & Methods:** Through an ethically approval prospective study enrolled patients from the RNOH undergoing nerve surgery. We have utilised excess denervated human tissue from these subjects for study. The tissue has been prepared and stains with antibodies for c-jun, S100 and Neurofilament. The cases have differing times from original injury and thus taken together will model the differences that occur over time following denervation. We have utilised fluorescent immunostaining and quantification was achieved using the "velocity software and cell count.

**Results:** We demonstrate early results of a small number of cases to suggest that c-jun is not present in innervated nerve and its expression peaks before one month and decreases after
this period. Similarly, expression of S100 progressively declined as denervation period increased. This is an early report of a project that will run for another 12 months and through this period expects to acquire enough data to build a full picture of longitudinal change in expression of c-jun in a human model of nerve injury.

Conclusions: Much is known about the changes that Schwann Cells (SCs) undergo from animal models and human cell culture experiments when denervated. We continue to study the human in vivo case for comparison to see if these changes are applicable in human nerve injury.

Christine RADTKE, T Kornfeld, K Reimers, PM Vogt
Medical University of Vienna, (AT), Yale University School of Medicine (USA); Christine.radtke@gmx.net

ENHANCED NERVE REGENERATION OF CRITICAL SIZE NERVE DEFECTS FOLLOWING IMPLANTATION OF A BIOMIMETIC NERVE CONDUIT BASED ON SPIDER SILK

Aim: The clinical outcome in long length nerve defects is disappointing and research continues to develop approaches to optimize functional recovery. The usage of spider silk fibers as guidance material for nerve regeneration is a novel and unique idea and was investigated successfully as biomimetic guidance material for nerve regeneration. The spider dragline silk from the spider Nephila clavipes has crucial unique characteristics regarding nerve regeneration guidance. Acellularized veins filled with these spider silk fibers a linear array as guidance material for outgrowing axons were used for implantation as an artificial nerve conduit. Axonal regeneration and functional outcome was determined after implantation of the nerve conduit in a large animal model as preclinical application evaluating proof of concept. Moreover, the growth rate of regenerating peripheral axons through the construct was explored.

Materials & Methods: Nerve conduit implantation was performed on 28 sheep with survival times ranging from 20 days to 180 days to determine the rate of nerve regeneration through the construct. In all sheep, a critical size tibial nerve defect (6.0 cm) was induced followed by surgical engraftment of spider silk nerve conduits or autologous nerve transplant respectively as control group. Electrophysiological recordings including measurements of nerve conduction velocity and amplitude were performed in nerves after spider silk nerve conduit transplantation and compared to autologous nerve transplantation followed by behavioral and histological analysis.

Results: No adverse effects were observed; there were no signs of foreign body reaction or any immune response. Data indicated that nerve conduction velocity was restored after nerve conduit implantation. Axonal regeneration could be demonstrated by positive neurofilament staining throughout the regenerated nerve while positive S-100 staining demonstrated endogenous Schwann cells migration into the nerve construct. No significant difference to the autologous tissue grafts could be observed as current gold standard in reconstructive nerve
surgery. The normal rate of nerve regeneration is generally considered to be about 1 mm per day, after implantation of the described nerve conduit, this rate could be significantly increased. This study demonstrates successful nerve regeneration by an artificial conduit over a critical size defect in a preclinical model bringing nerve conduit implantation a remarkable step beyond the state of the art.

**Conclusions:** Thus, the nerve stent could lead to a paradigm shift in the treatment of peripheral nerve lesions by enhancing and enabling nerve regenerating in extended nerve defect injuries by an artificial nerve implant. Therefore, the nerve conduit based on spider silk can improve functional outcome, reduce morbidity and possibly allow patients in near future to receive treatment that are currently difficult to obtain due to limitation of autologous donor grafts and absence of effective alternatives for extended nerve defect injuries. These data demonstrated that the nerve conduit based on spider silk can significantly enhance and improve reconstructive nerve surgery.

Christine RADTKE, S Masanori, KL Lankford, V Gallo, J Kocsis
Medical University of Vienna (AT), Hannover Medical School (GER);
Christine.radtko@gmx.net

**CNPase expression in olfactory ensheathing cells**

**Aim:** A large body of work supports the proposal that transplantation of OECs into various nerve injuries can promote axonal regeneration and restore functional recovery. Yet, there is an important controversy as to whether the transplanted OECs associate with axons and form peripheral myelin, or if they recruit endogenous SCs that form myelin.

**Materials & Methods:** Olfactory bulbs from transgenic mice expressing the enhanced green fluorescent protein (eGFP) under the control of the 2-3-cyclic nucleotide 3-phosphodiesterase (CNPase) promoter were studied. Here, we examined CNPase expression in OECs from adult CNPase transgenic mice both in situ and in vitro in order to determine if OECs express CNPase commensurate with their myelination potential.

**Results:** eGFP was observed in the nuclei and cytoplasm of glial cells in the outer nerve layer (ONL) of the olfactory bulb where olfactory ensheathing cells (OECs) reside, and in oligodendrocytes in the interior of the olfactory bulb. Immunohistochemical analysis for CNPase in the olfactory bulb demonstrated weak expression of CNPase in the ONL, but intense expression in oligodendrocytes. However, dissociated OECs derived from the olfactory bulb and maintained in culture for 4 days had both intense eGFP expression and CNPase immunostaining. Transplanted eGFP cells survived in peripheral nerve. These data indicate that CNPase expression of OECs in vivo is present as evidenced by accumulated intracellular eGFP in OECs of the ONL in CNPase transgenic mice. Moreover, in culture the OECs maintain strong eGFP expression, but also increase their expression CNPase. Thus, while OECs do not normally form myelin on the fine calibre olfactory nerve axons, their upregulation of CNPase in culture is commensurate with the observation that transplantation of cultured
eGFP-OECs from can form myelin when transplanted into injured peripheral nerve.

**Conclusions:** OECs share the molecular machinery of CNPase expression with oligodendrocytes and Schwann cells indicating a third dominant myelinating cell type within the nervous system. These results encourage ongoing work with OECs as a therapeutic tool to enhance peripheral nerve repair, in CNS trauma and demyelinating diseases.

Christine RADTKE, K Reimers, PM Vogt, JD Kocsis
Medical University of Vienna (AT)/ Hannover Medical School (GER)/ Yale University School of Medicine (USA); Christine.radtke@gmx.net

**ANALYSIS OF MOTOR HAND RECOVERY IN A NONHUMAN PRIMATE FOLLOWING MEDIAN NERVE REPAIR AS A PRECLINICAL MODEL FOR NERVE CONDUIT IMPLANTATION**

**Aim:** Peripheral nerve injury is a common and debilitating consequence of traumatic injury. Surgical repair of peripheral nerve transection can result in nerve regeneration and functional recovery. However, the clinical outcome, particularly in nerve defect injuries, is disappointing and research continues to develop approaches to improve functional outcome including the development of nerve conduits for optimal enhancement of axonal regeneration. Model systems to evaluate nerve conduit implantation as a preclinical model are limited. Therefore, a median nerve defect injury in the non-human primate was established. Here, we describe the sequence of functional recovery of fine hand movements in combination with electrophysiological recordings following repair of a critical size median nerve defect as a preclinical model system for the evaluation of nerve conduit implantation.

**Materials & Methods:** In the nonhuman primate, a 2.0 cm defect injury of the median nerve was induced and reconstructed either by nerve conduit implantation or autologous nerve transplantation respectively. All animals were familiarized and fully trained on each behavior task preoperatively. Postoperatively, animals were tested and scored on fine motor dexterity including precision grip (thumb forefinger apposition), well-reach test and the staircase test at monthly intervals. Moreover, noninvasive electrophysiological studies were carried out to determine of median nerve conduction velocity and to the innervation of thenar muscles.

**Results:** Immediately after injury and nerve reconstruction, significant loss of fine hand movements was observed; the animals had difficulty picking up small objections with the thumb and forefinger. No adverse effects could be observed after conduit implantation and the sequence of functional recovery following was characterized in comparison to autologous nerve transplantation and showed comparable results in both experimental groups. With increasing regeneration of the median nerve, recovery of fine motor dexterity of the hand could be observed. 12 months after median nerve repair, the behavioral outcome and thenar muscle innervation indicated almost complete functional restoration.

**Conclusions:** This model of nerve defect repair of the median nerve in the NHP provides for a model system that allows testing of nerve conduction and fine hand movements. This detailed analysis in a nonhuman primate following nerve defect nerve repair could serve as an
important preclinical model for system for conduit implantation providing data on the safety and efficacy.

Lukas RASULIC, A Savic, F Vitosevic, I Cinara, M Samardzic
Clinic of Neurosurgery, Clinical Center of Serbia, University of Belgrade, Faculty of Medicine (SER); lukas.rasulic@gmail.com

IMPACT ON QUALITY OF LIFE, DISABILITY AND PATIENT SATISFACTION AFTER SEVERE BRACHIAL PLEXUS INJURY FOLLOWED BY SURGICAL REPAIR

Aim: The aim of this paper is to present current concept of brachial plexus injury treatment and brain plasticity after surgical repair of brachial plexus injury. We present the results of treatment, with special attention towards the results of surgical treatment – not just the motor deficit, but also the quality of life and associated disorders after brachial plexus injury.

Materials & Methods: Between 1999 and 2012 we operated on 138 patients with brachial plexus injury. We documented the data: localization of the injury, the type of treatment that was used, timing of the surgery, patient age, preoperative and postoperative motor deficit, functionality, pain, quality of life, patient satisfaction, psychosocial health. In our quality of life investigation we used new plexus-specific outcome questionnaire (Ulm Questionnaire) with categories of satisfaction, functionality, pain, comorbidities, and work; and the disability of the arm, shoulder, and hand questionnaire (DASH).

Results: Patient age, type of lesion and timing of the surgical treatment are the most important factors in the recovery after BPI. The majority of papers in literature present only the motor deficit results after surgical treatment. Only small percentage of the reported data concerns pain after BPI (17%), quality of life (5%), function or disability (6%), patient satisfaction and psychosocial health (3%). In our study, satisfactory recovery (>M3) was found in 92.7% of cases where neurolysis was performed, in 90.4% of cases where direct suture was performed, 92.8% of cases where split repair was performed and 88.7% of nerve grafting. In our quality of life investigation 69 patients agreed to participate. There were 62 males, and 7 females. Mean age was 32.7 years. The DASH score normalized mean for the study group was 70.15 (SD 15.01). Comparing that with the general population normalized mean of 50 (SD, 10.00) showed more disability in the brachial plexus injury group (p<0.001). Also, patients who had early surgery scored consistently better in the DASH than their counterparts. According to the Ulm Questionnaire, in patients with C5–C6 lesions 90%, with C5-C7 lesions 50% and in C5-T1 lesions 67% were satisfied and would undergo surgery again. Overall of 87% gave positive answer for this question. The majority of patients (83%) were satisfied with the results of surgery (C5-C6 group: 95%, C5-C7 group 50% and C5-T1 group 81% were satisfied). Eighty-six percent of patients had complained to pain and 21% to depression/anxiety. Fifty-two percent of those who worked before their injury remained unemployed or incapacitated for work. Forty-five percent of previous workers returned to their former occupation.
Conclusions: Outcome reporting for brachial plexus surgery is usually focused on motor recovery. The minority of studies show quality of life, function, pain, and satisfaction of treated patients. It may be useful to include these parameters in more studies since it will help us to better understand the effect of brachial plexus reconstruction surgery.

Wilson Z RAY, M MacEwan
Washington University, Saint Louis (USA); rayz@wudosis.wustl.edu

Resorbable electronics for peripheral nerve interfacing

Aim: Functional electrical stimulation of peripheral nerve tissue has been demonstrated to restore sensorimotor function and accelerate axonal regeneration in vivo. Yet, existing methods of applying electrical stimulation to peripheral nerve tissue have presented significant barriers to clinical translation. The present study describes the implementation of a fully resorbable wireless nerve stimulator capable of delivering functional, therapeutic, and diagnostic electrical stimulation of injured and uninjured peripheral nerve tissue.

Material & Methods: Fully resorbable electronic implants were fabricated and subcutaneously implanted into Lewis rats. Implanted devices were utilized to deliver functional and brief electrical stimulation (0.20Hz) to sciatic nerves following nerve crush, nerve transection/repair, and sham surgery. Following initial electrical stimulation, implanted wireless devices were utilized to serially assess functional recovery over 3 months postoperatively.

Results: Fully resorbable wireless nerve stimulators were shown to successfully stimulate peripheral nerve tissue in vivo for over 2 weeks prior to dissolution. Brief electrical stimulation delivered by the implants was observed to increase both the rate of functional recovery and maximal capacity for functional recovery following nerve transection and repair. Fully resorbable stimulators successfully facilitated both therapeutic stimulation of peripheral nerve tissue as well as serial assessment of nerve and muscle function following nerve crush and nerve transection injury.

Conclusions: The present study highlights the ability of a new class of fully resorbable implantable electronics to successfully interface and therapeutically stimulate peripheral nerve tissue. Fully resorbable wireless nerve stimulators may therefore serve as a novel means of facilitating therapeutic electrical stimulation and neuromodulation in a variety of clinical settings.

Disclosures: Globus-Consulting, Depuy-Consulting, Ulrich-Consulting
SHIMON ROCHKIND, M LIVNAT, M ALMONG, Z NEVO
Division of Peripheral Nerve Reconstruction, Department of Neurosurgery, Tel Aviv Sourasky Medical Center, Tel Aviv University (ISRAEL); shimonr@tlvmc.gov.il

GUIDING REGENERATIVE GEL (GRG) AND ANTI-GLIOTIC GRG (AGRG) FOR RECONSTRUCTION OF SEVERELY INJURED PERIPHERAL NERVE AND SPINAL CORD

Aim: GRG and AGRG were developed to simulate the extracellular milieu, support growth and activity of axons and cells upon implantation, overcome the astro-glial scar barrier and serve as a regenerative and repair source for nerve tissue reconstruction.

Materials & Methods: The GRG is composed of: 1) Sodium dismutase - anti-oxidant, found to exhibit high anti-inflammatory activity; 2) Proprietary peptide (16 amino acids) based on the active sites of laminin peptide and containing two penta-peptides, which acts as a scaffold for the nerve fibers to grow along; and 3) hyaluronic acid, which is highly hydrated and contributes to the success of survival, growth and regeneration of nerve fibers. The GRG resembles the extracellular matrix. AGRG is a combination of GRG and anti-gliotic agents, promoting axonal penetration through the glial scar barrier and preventing formation of newly formed scars. Efficacy of GRG and AGRG was evaluated on experimental peripheral nerve and spinal cord injury rat models.

Results: Peripheral nerve reconstruction - In vivo study (3 months) on peripheral nerves with massive nerve loss showed that GRG loaded into a commercial-collagen tube enabled massive growth of myelinated axons and continuation of axonal sprouting through the tube to the distal part of the nerve in a 15mm long gap nerve in rats, which is not possible when bridging with an empty tube. No significant difference was found between GRG and ‘gold standard’ treatment (nerve autograft) study groups, emphasizing that the GRG enables optimal axonal regeneration. In a long-term (7 months) in-vivo study, evaluating the GRG's ability to promote regaining of function to the formerly paralyzed limb, the GRG was shown to exhibit regaining of function to the paralyzed limb following massive nerve loss of 15 mm, while the ‘gold standard’ treatment only supported limited movement, and an empty tube was unable to support any movement. Spinal cord reconstruction - In a preliminary conducted and ongoing in-vivo study evaluating the efficacy of AGRG in promoting nerve regeneration following complete SCI (2 mm removal of spinal cord), AGRG: 1) Improved movement in previously paralyzed limbs – BBB score at the AGRG group reached 8 after 60 days. The rat was able to move extensively at least one or two joints and slight of the third joint, while in control group stayed completely paralyzed. 2) Promoted regaining of conductivity in the previously paralyzed limbs – while regained conductivity (SSEP) is evident in the AGRG group beginning from 60 days after the SCI, no conductivity is found at the control group. 3) Promoted axonal penetration through the glial scar barrier – neuronal fibers were found in lesion area of the spinal cord treated with AGRG: whereas in a control rat no sprouting of neuronal fibers were found.

Conclusion: These results highlight GRG and AGRG potential to promote regeneration of nerve tissue.
R Rosenauer, M Schmidhammer, S Tsolakidis, N Janjic, H Millesi,
Robert SCHMIDHAMMER
Millesi Center at the Vienna Private Clinic, Vienna (Au); schmidhammer@wpk.at

THE CORRELATION OF REDUCED CLAVICLE GROWTH TO PATHOLOGICAL SCAPULA POSITIONING AND ROTATION IN BRACHIAL PLEXUS BIRTH PALSY: A RETROSPECTIVE STUDY

Aim: Although most brachial plexus birth palsies show sufficient spontaneous recovery, altered development with the tendency to secondary operations is likely. Furthermore, growth of the affected limb and the whole shoulder girdle is decreased. This is amongst other things associated with pathological scapula positioning and rotation of the scapula, which was described as scapular dyskinesia by Chung et al. The objective of this present investigation was to clarify the relationship of increasing length differences of the clavicle to different types (static or dynamic) of scapular dyskinesia.

Materials & Methods: Twenty-five patients out of 147 suffering from obstetric brachial plexus palsy were included in this retrospective study. CT scans of the thoracic cage including both shoulder joints and both clavicles were obtained preoperatively between 2010 and 2012. In total there were 18 female and 7 male patients with a mean age of 10 years (ranging from 2 to 23). The right side was affected in 21 patients, and the left in 4 patients. Radiographic measurements were performed in axial plane and three dimensional reconstructions using Osirix MD®. In addition, functional evaluation regarding possible movement and scapular dyskinesia was performed. Statistical analysis (t-test paired and unpaired, Pearson correlation) were performed using IBM® SPSS® Statistics.

Results: We found an increasing difference of the length of the clavicle (absolute and percentage) in children with a more pronounced scapular dyskinesia. Additionally, there was a significant difference of the difference of the angle of the scapula to the sagittal plane between Group 1 and Group 3. Significant positive correlations were found for the age and the absolute difference of the clavicle length and the length and the width of the scapula on the affected side. Furthermore, there was a significant positive correlation for the percentage of the difference of the clavicle length and the difference of the angle of the scapula to the sagittal plane. There were no differences of the functional scorings between the three Groups (Mallet, gleno-humeral range of motion and global abduction).

Conclusions: Scapular dyskinesia, as a frequent finding in brachial plexus birth palsy, shows a strong relationship to reduced clavicle growth. The clavicle length, as a relatively easy examinable parameter, compared to the healthy side can be used to estimate the grade of scapular malposition at the thoracic cage. With increasing difference of the length of the clavicles the grade and severity of scapular dyskinesia increases as well.
APPROACHES TO POWERED HAND ARM ORTHOTICS AS A SYNERGETIC TREATMENT TO NEUROSURGERY

Aim: The level of regained hand arm function after central or peripheral nervous system injuries is critical to independent living and quality of life. In cases of peripheral (e.g. brachial plexus) injuries where neurosurgeons see limited success chances through reconstructive interventions or find limited output postoperatively new ways of external power assist orthotics may help to fulfill hand arm functional needs. Early stages of exoskeletal approaches to shoulder, elbow and long finger functional assist are presented and discussed. A future of hybrid approaches for mixed operative and exoskeletal treatment strategies as primary or secondary therapeutic decision paths is discussed.

Materials & Methods: Three paths to orthotic powered assist are presented. A motorized dorsal hand long finger orthosis module was designed and developed to open and close the long fingers of an individual hand based on a single motor gear box unit. The device is intended to assist in EEG based learning with a motor control interface to BCI controls. It may also be actuated based on neural or muscular activity and may work as a functional finger force and grip enhancer. Preliminary results generated with Tuebingen University in EC project EU-WAY are presented in stroke patients. A motorized elbow joint orthosis module was designed and developed to flex and extend the elbow joint in sagittal plain movements based on a flat motor and Harmonic Drive gear box unit. This device is intended to assist in EMG signal plus physiotherapist based assist or resist training modes and was developed in IGF project with University Geel, Belgium. A third version is a wearable trunk shoulder elbow exoskeleton for power assist of elbow and shoulder. The first generation is designed to assist in manual lifting and above head manipulations of healthy subjects to prevent from occupational illnesses from chronic joint overload.

Results: Powered exoskeletal devices can show actuation of deficient limbs. Smart combinations of sensory, actuators controls and mechanical human interfaces can help support daily gripping and lifting functions. But additional weight of a exoskeletal system on a functionally deficient hand arm system is a true problem. Therefore miniaturized approaches and trunk fixated hand arm helpers are key.

Conclusions: Powered exoskeletal modules may support joint functions in future therapies. New peripheral nervous stimulation implants may even improve signal specificity and signal robustness to motor actuations. Hybrids of surgical approaches and powered joint actuation may assist in future rehabilitation of reduced limb functions.
Mario SIQUEIRA, R Martins, L Foroni, CO Heise
Department of Neurosurgery University of São Paulo Medical School (BR); mgsiqueira@uol.com.br

**FUNCTIONAL OUTCOME OF ACCESSORY-SUPRASCAPULAR NERVE TRANSFER FOR RESTORATION OF SHOULDER FUNCTION IN TRAUMATIC BRACHIAL PLEXUS PALSY IN ADULTS**

**Aim:** Paralysis of the shoulder related to injury to the upper elements of the brachial plexus make the use of the upper extremity difficult even when distal functions are preserved. The purpose of this study was to evaluate the functional outcome of spinal accessory to suprascapular nerve transfer (XI-SSN) performed for restoration of shoulder function in traumatic brachial plexus injuries.

**Materials & Methods:** This is a retrospective study involving 105 cases of partial (52 cases) and total (53 cases) brachial plexus injuries operated upon at the Peripheral Nerve Surgery Unit of the University of São Paulo Medical School between 2006 and 2012. The inclusion criteria were: adult patients, interval between trauma and surgery lesser than ≤ 12 months and follow-up of at least 24 months. The average age of patients was 28.6 years (range 18-81yrs). The average interval between injury and surgery was 7.4 months (range 1-12 months). The partial injuries were treated through XI-SSN transfer (23 cases), XI-SSN transfer plus triceps branch to axillary nerve transfer (14 cases) and XI-SSN transfer plus pectoralis minor to axillary nerve transfer (15 cases). The total injuries underwent XI-SSN transfer alone (53 cases). The functional outcome for shoulder abduction and humerus external rotation was assessed by measuring range of movements through goniometry. A good result was considered when an active movement of 30 degrees or more for shoulder abduction and 55 degrees or more for shoulder external rotation was achieved.

**Results:** Good results for shoulder abduction were seen in 67 cases (63.8%), 32 cases (61.5%) of partial lesions and 35 cases (66%) of total lesions. In relation to shoulder external rotation only 14 patients, 11 cases (21%) of partial lesions and 3 cases (5.6%) of total lesions achieved good results. When analyzing the different techniques applied to partial lesions we found out that the XI-SSN transfer alone resulted in 65.2% (15 cases) of good results for abduction and 21.7% (5 cases) of good results for external rotation. The association of XI-SSN and triceps-axillary nerve transfers resulted in good results for abduction in 57% (8 cases) and for external rotation in 35% (5 cases). The XI-SSN complemented by the pectoralis minor-axillary nerve transfer achieved good abduction in 60% (9 cases) and good external rotation in 6.6% (1 case). Statistical analysis demonstrated no significant difference among the results of the techniques for shoulder abduction. In relation to the external rotation there was a significance only in the comparison of the results of the XI-SSN plus triceps branch-axillary nerve transfer with the XI-SSN transfer in total lesions.

**Conclusions:** Overall the XI-SSN transfer, alone or together with a transfer for the axillary nerve, resulted in modest but useful recovery of shoulder abduction in our series. However, the results concerning shoulder external rotation are far from being acceptable.
Mario SIQUEIRA, R Martins, L Foroni, CO Heise
Department of Neurosurgery University of São Paulo Medical School (BR); mgsiqueira@uol.com.br

RESTORATION OF ELBOW FLEXION IN ADULT TRAUMATIC BRACHIAL Plexus PALSY: COMPARISON OF OUTCOMES WITH NERVE GRAFTING AND NERVE TRANSFER TECHNIQUES IN 169 PATIENTS

Aim: To present a retrospective analysis of the functional outcomes of primary grafting and of different transfer techniques for restoration of elbow flexion in 169 adult patients with traumatic brachial plexus injury.

Materials & Methods: The surgical procedures were divided in three groups: (1) Grafts from C5 and/or C6 to the upper trunk, anterior division of the upper trunk, lateral cord and musculocutaneous nerve - 38 patients; (2) Intraplexus nerve transfers (ulnar nerve fascicle, median nerve fascicle and ulnar/median nerves fascicles) - 78 patients and (3) Extraplexus nerve transfers (phrenic nerve, spinal accessory nerve and intercostal nerves) – 53 patients. C5 and C6 roots avulsions and late referral were the indications for nerve transfers. After surgery the patients were evaluated every six months for at least 18 months. M3 or more was considered a good result.

Results: Twenty three patients (60.5%) submitted to grafting achieved M3 or more. Long grafts (more than 10cm) tend to present worse results. Among the intraplexus nerve transfers 86% of the ulnar fascicle technique, 56.2% of the median fascicle technique and 100% of the ulnar/median fascicles technique achieved M3 or more. The utilization of the spinal accessory nerve, the phrenic nerve and the intercostal nerves in the extraplexus nerve transfers lead to good results in 38.5%, 61.1% and 36.3%, respectively. The incidence of good/excellent outcomes was 60.5% for nerve grafting, 80.7% for intraplexus nerve transfers and 45.2% for extraplexus nerve transfers.

Conclusions: A functional restoration of elbow flexion was achieved in 62.1% of the patients in our series. In most of the techniques applied the results were acceptable according to the literature data. Our worse results were with the spinal accessory and intercostal nerve transfers and nowadays we use these donors for transfers only when there is no other option available. Nerve grafts are certainly a possibility for restoration of elbow flexion, but according to our results and to the reports in the literature intraplexus nerve transfers achieve better results. Extraplexus nerve transfers are used in complete brachial plexus lesions and present the worse outcomes.
Mariano SOCOLOVSKY, G di Masi, G Bonilla, A Lovagl
Peripheral Nerve & Brachial Plexus Program, Department of Neurosurgery, University of Buenos Aires School of Medicine, Buenos Aires (AR); marianosocolovsky@gmail.com

TRANSGLUTEAL APPROACH TO THE SCIATIC NERVE: AN ANATOMICAL AND CLINICAL STUDY

Aim: Complete section of the gluteus maximus muscle when approaching the sciatic nerve in the buttock can result in significative aesthetic & functional morbidity, and in a prolonged postoperative recovery period. By contrast, dissecting through the muscle splitting ist fibers is faster, less invasive, and diminishes recovery time. The aim of this presentation ist to expose the results obtained both in an anatomical study and in a clinical series where we used the transmuscular approach to expose the sciatic nerve distal to the sciatic notch.

Materials & Methods: Both gluteal regions from each of ten fresh cadavers were dissected via a transgluteal approach, after exposure of the sciatic nerve, the maximum length of exposed nerve was measured. Also we retrospectively selected 33 traumatic sciatic nerve lesions within the buttock, operated upon from January 2005 to November 2014, with a minimum follow-up of 2 years. In all patients, a transgluteal approach was employed to explore and –when necessary- reconstruct the nerve.

Results: The mean sciatic nerve exposure obtained was 115.4+/-17.9 mm, ranging from a maximum of 185 mm to a minimum of 79 mm. In all 20 cases, it was possible to perform microsurgical reconstruction under the microscope. Nineteen males and fourteen females, with a mean age of 36.5 years, were studied. The etiology of the nerve lesion was previous hip surgery (n = 8), trauma (n = 6), injection (n = 6), traumatic hip dislocation (n = 6), stab wound (n = 3), gunshot wound (n = 2), and tumor (n = 2). In 28 (84.8%) cases, a motor deficit was present; in 22 (66.6%) cases neuropathic pain and in 24 (72.7%) cases sensory alterations were present. In all cases, the transgluteal approach was adequate to expose the injury and treat it by neurolysis alone (21 cases), neurolysis and neurorrhaphy (7 cases), and reconstruction with grafts (5 cases; three of these paired with neurolysis). The mean pre- and postoperative grades for the tibial nerve (LSUHSC scale) were 1.6 and 3.6, respectively; meanwhile, for the peroneal division, preoperative grade was 1.2 and postoperative grade was 2.2.

Conclusion: The transgluteal approach is useful in the operative repair of lesions of the proximal sciatic nerve. Complex lesions, like nerve trauma requiring grafts and nerve tumours, can be treated with minimal risk. Nevertheless, it is less comfortable for the surgeon, and the entire extent of the exposed nerve might not be visualized simultaneously during surgery.
Mukund R THATTE, B Gangurde, B Raut, K Ladkat, R Mehta
Plastic Surgery, Bombay Hospital Mumbai (IN); mthatte@gmail.com

DISTAL TRANSFERS AS A PRIMARY TREATMENT IN OBSTETRIC BRACHIAL PLEXUS PALSY - A SERIES OF 20 CASES

Aim: The purpose of this study was to examine the results of Oberlin’s transfer and spinal accessory nerve (SAN) to suprascapular nerve (SSN) (with or without axillary nerve neurotization as primary treatment in children with Narakas type I obstetric brachial plexus injuries (OBPI), in cases when parents refuse consent for conventional root level reconstruction. A problem which is very common in South Asia, and probably many other parts of the world.

Materials & Methods: Twenty children, all of who were Narakas Grade I with poor shoulder abduction and no antigravity biceps function but with good hand function were treated with SAN to SSN and Oberlin’s transfer at an average age of 5.75 months; (SD 3.27). All the patients were postoperatively evaluated with the Modified Medical Research Council (MMRC) grading for power and Mallet score for shoulder till an average of 2.75; (SD 0.8) years postoperatively.

Results: Three patients were lost to follow up. Of the remainder 11 had grade 4+ power of elbow flexion and six patients had grade 4 power at one year and all had 4+ power at final follow up. At final follow up the mallet score was an average of 15.05; (SD 4.22, (range 9 to 20). Shoulder abduction and external rotation were only grade 3 each.

Conclusions: From the current series it can be concluded that Oberlin’s transfer combined with other transfers, used as primary surgery in Narakas Gr. I Obstetric brachial plexus palsy gives a reasonable outcome and deserves consideration under these circumstances.

Disclosures: This paper is now published in JHS European as epub and will soon be in print, this was presented in the WCNS meeting in Delhi in Feb 2016 as well as in Club Narakas in Barcelona in Feb 2016

Mukund R THATTE, N Nayak,
Plastic Surgery, Bombay Hospital Mumbai (IN); mthatte@gmail.com

A PROSPECTIVE STUDY COMPARING CLASSICAL INTRAPLEXAL REPAIR V/S PRIMARY DISTAL TRANSFER IN NARAKAS GROUP I BABIES WITH A FOUR YEAR FOLLOW UP

Aim: The current international standard in the surgical management of Obstetrical Brachial plexus palsy (OBPP) is Neuroma excision and Intraplexal repair with nerve grafts. However a newer technique is distal nerve transfers. Despite voluminous literature about individual merits of each method, a prospective study has not been done till now in OBPP. This study attempts to compare the results of primary intraplexal repair with distal nerve transfers in Obstetrical Brachial plexus palsy.
Materials & Methods: A prospective study of 32 children less than 9 months of age with clinical Narakas group I OBPP was conducted from 2012 to 2015. Due to ethical consideration true randomisation was not possible. Depending on parental choice and consent for neuroma excision after being fully counselled regarding current standard of care, the children were divided into classical intraplexal repair (group A) and distal nerve transfer groups (group B) with 16 in each group. Follow up at 3, 6, 9, 12, 15, 18 and 24 months was done with serial MRC grades and Gilbert’s shoulder score and the results were analysed. After the four year mark in the study in July 2016 the children were evaluated using Mallet score and strength determination of elbow flexion using a small weight of 500 gms. Co contraction, use of Botox and secondary shoulder surgery if any has been documented.

Results: 25% of children in Group B achieved MRC grade 3 or higher at 3 months while none had in group A. At 6 months, 100% in group B had achieved MRC Grade 3 with only 50% in group A which was statistically significant. Shoulder abduction analysis showed 53% in group B had achieved MRC grade 3 or higher at 3 months while none had achieved the same in group A. At 6 months 100% had achieved MRC grade 3 and higher in Group B while only 50% had done so in group A which was statistically significant. After about a year no significant differences were noticed.

Conclusions: Distal nerve transfers have a distinct statistically significant advantage of early recovery in elbow flexion at 6 months and shoulder abduction 3 and 6 months postoperatively over intraplexal repairs.

Joost VERHAAGEN, R Eggers, F de Winter, M Malessy, M Tannemaat
Laboratory for Neuroregeneration, Netherlands Institute for Neuroscience, Amsterdam, the Netherlands (NL); j.verhaagen@nin.knaw.nl

GENE THERAPY FOR GDNF WITH A STEALTH GENE SWITCH PROMOTES LONG-DISTANCE AXON REGENERATION AND FUNCTIONAL RECOVERY

Aim: Persistent lentiviral vector-mediated expression of glial cell line-derived neurotrophic factor (GDNF) to an injured peripheral nerve promotes axon regeneration but also results in trapping of regenerating axons at sites of high levels of GDNF expression thereby preventing target cell reinnervation. The aim of the current study was to test whether temporally controlled GDNF expression is effective and prevents the adverse effects of uncontrolled growth factor expression. We used a novel immune-evasive (“stealth“) gene switch to deliver GDNF to the injured nerve.

Materials & Methods: Rat ventral roots (L3-L6) were surgically avulsed, injected with the appropriate lentiviral vector, and reimplanted in the spinal cord. A doxycycline-inducible lentiviral vector-based „stealth“ gene switch was used to direct GDNF expression in ventral nerve roots. The current experiment consisted or 4 treatment groups of 15 rats each. Group 1: control group in which the ventral roots were avulsed and not reimplanted. Group 2: control group in which the avulsed roots were injected with a lentiviral vector encoding the reporter
gene GFP and reimplanted. Group 3: experimental group injected with the lentiviral vector-based gene switch encoding GDNF treated with doxycycline for 4 weeks. Group 4: experimental group injected with the gene switch encoding GDNF treated with doxycycline for 24 weeks. Regeneration was evaluated by histological and electrophysiological methods.

**Results:** Significantly increased motoneuron survival was observed in all GDNF treated groups irrespective of the doxycycline treatment period. At the reimplantation site, robust regrowth of regenerating motor fibers into the root occurs in both GDNF groups compared to GFP control. However, persistent GDNF expression resulted in coiled fiber growth and disrupted myelination, whereas in rats with 4 week GDNF expression fiber coiling was significantly reduced. The diameter of the ventral roots exposed to persistent GDNF expression is significantly increased in comparison to GFP controls. In contrast, in the 4 week GDNF treatment group, the large numbers of axons in the ventral root display a longitudinally organized growth pattern and the roots are less enlarged. Biweekly compound muscle action potentials (CMAP) measurements revealed that 4 wk GDNF expression led to an earlier recovery of a CMAP and a significant increase in amplitude compared to animals with persistent GDNF expression and GFP controls. Further histological analysis of axon regeneration and muscle reinnervation is currently ongoing.

**Conclusions:** This is the first report that shows that direct temporally controlled lentiviral vector-mediated delivery of GDNF to avulsed reimplanted ventral roots exerts a beneficial effect on axon regeneration and reduces, but not entirely prevents, axon trapping.

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Huan WANG, S Guo, C Charlesworth, RM Moore, RJ Spinner
Mayo Clinic, Rochester Minnesota (USA); wang.huan@mayo.edu

**PROTEOME OF THE DISTAL NERVE: ITS IMPLICATION IN DELAYED REPAIR AND POOR FUNCTIONAL RECOVERY**

**Aim:** Nerve regeneration and functional recovery is poorer when nerve repair is delayed. Among the many contributing factors, chronic denervation mainly affects Schwann cell function and axon outgrowth. After losing axonal contact, Schwann cells proliferate and secrete neurotrophic factors to provide a growth-supportive environment. With chronic denervation the permissive factors progressively decline. To better understand the global protein expression profiles, proteomics analysis of chronically denervated nerves was carried out in this study to delineate proteins that were contributory to this detrimental effect.

**Materials & Methods:** Rat sciatic nerve repair model was used. In 4 rats nerve repair was done immediately after transection, while in the other 4 rats repair was done after a 12 week delay. After 16 weeks, nerve samples distal to the repair site were harvested. Proteins were individually extracted using bead mill homogenizer containing SDS lysis buffer. 25 ug of protein from each sample was fractionated by SDS-PAGE gels. Gels were stained, excised, digested, and peptides extracted for analysis by nanoLC-MS/MS. Individual protein expression level of the surgery side was compared to that of the control side using label-free analysis.
(MaxQuant software). Any protein with a P value less than 0.05 and a fold change of ≥4 was considered as differentially expressed. Ingenuity Pathway Analysis (IPA) and Cytoscape softwares were used for pathway/network analysis.

**Results:** The distal nerve stump proteome contained 5754 detectable proteins. Differential expression analysis showed significant increase of immune and inflammatory response related proteins and decrease of proteins related to axon regeneration and lipid metabolism process in the delayed repair model. Proteins related to Schwann cell function and axonal outgrowth that were down-regulated included CBL, MPZ, PTGDS, MADD, IGDF1R, DHH, HSPB8, GJB1, SHH, MAPK11, ADGRG6, LGALS8, PAK3, CNTF, CAMKK1, TNPV1 and ARPP19. Proteins associated with inflammatory response and apoptosis that were up-regulated were S100A8, S100A9, PLA2G4A, CASP6, CASP3, IGFBP5 and C6. IPA revealed that protective pathways involved in LXR/RXR activation, RAC signaling, ERK/MAPK signaling, CNTF signaling, IL-6 signaling, and FGF signaling were inhibited in the delayed repair group, while 3 detrimental pathways including complement system, PTEN signaling and apoptosis signaling were activated.

**Conclusions:** The poorer regeneration in delayed repair may be attributed to down-regulation of beneficial proteins and up-regulation of detrimental proteins. The proteins and pathways identified in this study can be potential therapeutic targets.

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Mikael WIBERG, DSchaakxs, W Raffoul, DF Kalbermatten, PJ Kingham
Department of Surgical and Perioperative Sciences & Department of Integrative Medical Biology, Umeå University, Sweden (SE); mikael.pj.wiberg@umu.se

A COMPARISON OF AN ARTIFICIAL NERVE REPAIR CONSTRUCT AND NERVE GRAFTING WHEN USED IN COMBINATION WITH INTRAMUSCULAR INJECTIONS OF STEM CELLS FOR REDUCTION OF MUSCLE ATROPHY

**Aim:** Peripheral nerve injuries are often associated with loss of nerve tissue and require a graft to bridge the gap. Autologous nerve grafts are still the gold standard in reconstructive surgery but have several disadvantages such as sacrifice of a functional nerve, neuroma formation and loss of sensation at the donor site. Bioengineered grafts represent a promising approach to overcome these problems. Furthermore, functional muscle recovery after a peripheral nerve injury is far from optimal, in large part due to atrophy of the muscle arising from prolonged denervation. In this experimental study, we aimed to attain a better outcome after a peripheral nerve injury (in a rat sciatic nerve model) by both repairing the nerve lesion and treating the denervated muscle at the same time. We hypothesised that injecting regenerative stem cells in the denervated muscle would reduce the atrophy.

**Materials & Methods:** We compared artificial nerve constructs made from strips of poly-3-hydroxybutyrate (PHB), seeded with or without Schwann cell-like differentiated adipose stem cells, and autografts (reverse sciatic nerve grafts) in combination with stem cell injections in the gastrocnemius muscle. Six weeks after nerve injury, the effects of the stem cells on nerve
Sunderland Society Meeting  •  Frankfurt  •  Germany

regeneration and reduction of muscle atrophy were assessed. 

**Results:** PHB strips showed a high number of βIII-tubulin positive axons entering the distal stump and abundant endothelial cells. Animals treated with PHB strips without cells in combination with control growth medium intramuscular injections showed significantly more muscle atrophy than the other groups. Best results were obtained in the autograft group combined with intramuscular stem cell injections.

**Conclusion:** Bioengineering nerve repair in combination with stem cells is a promising technique to treat nerve lesions and associated muscle atrophy.

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Lynda YANG, K Chang, M Popadich, D Justice, L Rasmussen, TJ Wilson
Brachial Plexus Service, University of Michigan (USA); ljsyang@med.umich.edu

**NERVE TRANSFER OF ULNAR FASCICLE TO MUSCULOCUTANEOUS NERVE (OBERLIN TRANSFER) SIGNIFICANTLY IMPROVES FOREARM SUPINATION AS COMPARED TO NERVE GRAFT REPAIR IN NEONATAL BRACHIAL PLEXUS PALSY**

**Aim:** The use of nerve transfers vs nerve graft repair for Neonatal Brachial Plexus Palsy (NBPP) remains controversial. In adults, transfer of an ulnar fascicle to the biceps branch of the musculocutaneous nerve (Oberlin transfer) is reportedly superior to nerve graft repair for restoration of function after brachial plexus injury, especially in cases of isolated elbow flexion weakness. In pediatric patients with NBPP, less evidence exists to demonstrate whether nerve transfer yields better functional outcomes than nerve graft repair – with regard to elbow flexion and supination. Therefore, we report the comparative outcomes for infants with NBPP who have undergone the Oberlin transfer vs nerve graft repair.

**Materials & Methods:** This case series reviewed 19 patients (mean age at operation of 7 months) with Oberlin transfer and 31 patients (mean age at operation of 6 months) with nerve graft repair in a single institution from 2005-2016. Active range of motion in elbow flexion, forearm supination, and pronation were evaluated by certified occupational therapists pre- and post-operatively at 1-year. Biceps muscle power was evaluated via Medical Research Council (MRC) muscle grading scale. Additionally, the time to nerve transfer was compared to outcome. Standard statistical methods were used.

**Results:** Elbow flexion (in adduction: 54° vs 37°, P=0.27; in abduction: 58° vs 62°, P=0.74) and MRC strength of biceps (1 vs 2, P=0.89) showed similar improvements between Oberlin transfer and graft repair groups. However, regarding forearm supination, the Oberlin transfer group had significantly more function as compared to the nerve graft repair group (100° vs 19°, P<0.0001). Forearm pronation was maintained at 90° in Oberlin group while slightly improved in graft group (0° vs 32°, P=0.02). Additionally, no significant difference in outcome existed with earlier time to nerve transfer (p>0.5).

**Conclusions:** Our data demonstrates that the Oberlin transfer confers an advantageous recovery of forearm supination over graft repair while equivalent in elbow flexion recovery. Given that both functions comprise quality of movement, anecdotal evidence exists to support
the use of Oberlin transfer over nerve graft repair for function in the WHO-ICF Activity and Participation modalities. Further studies that remotely monitor real-world arm using body-worn movement capture technology will provide more insight into the most appropriate surgical strategy for NBPP.

Eric ZAGER, J Hong, J Pisapia, ZS Ali, GG Heuer
Perelman School of Medicine at the University of Pennsylvania (USA); zagere@uphs.upenn.edu

OUTCOMES AFTER SURGICAL TREATMENT OF PEDIATRIC NEUROGENIC THORACIC OUTLET SYNDROME

Aim: Neurogenic thoracic outlet syndrome (nTOS) is a rare compression syndrome of the brachial plexus that presents with pain in the affected limb and often sensory changes and motor weakness. There is very little published literature about the outcomes following treatment of nTOS in children.

Materials & Methods: After IRB approval, a prospectively collected database of peripheral nerve operations was reviewed from April 2010 to July 2016 and cases of neurogenic thoracic outlet syndrome in patients age 18 years or younger were extracted for analysis. Baseline patient characteristics, imaging and neurophysiologic data, operative findings, and outcomes and complications were assessed.

Results: Eight patients with ten cases of nTOS who underwent supraclavicular exploration, anterior scalenectomy and neurolysis were identified. Half of the patients were male. Disabling pain (both local and radiating) was the most common presenting symptom (100%), followed by numbness (50%), then tingling (20%). Average duration of symptoms prior to surgery was 16.4 months (+/-6.4). Sports-related onset of symptoms was seen in 70% of cases. Imaging revealed three cervical ribs, three prominent C7 transverse processes, two abnormal first thoracic ribs, and two normal patients. Neurophysiologic testing was normal in 80% of cases. All patients failed conservative management with 3 patients reporting minimal improvement in symptoms with physical therapy. With a mean follow-up of 8.9 months (+/-11.7), pain was completely resolved in 70% of cases, improved greater than 50% in one case, stable in one case, and worsened in one case. The patient who worsened described pain relief immediately following surgery, but developed increased numbness of the hand after falling at home on the affected limb that had not resolved at 22-month follow-up. There were three minor complications within 30 days of surgery; one patient developed a small pneumothorax that resolved spontaneously, one patient suffered hiccups for a period of three hours that resolved spontaneously, and one patient fell at home without injury. There were no new neurological deficits, wound infections, DVTs or readmissions.

Conclusions: Pediatric nTOS commonly presents with disabling pain and, unlike adult nTOS, is frequently associated with bony anomalies. Surgical decompression of the brachial plexus results in good response rates. Complications from supraclavicular exploration and neurolysis are rare but potentially serious, including pneumothorax.
Notes
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David KLINE
Professor emeritus, Lousiana State University Health Sciences Center, New Orleans; DKLINE@lsuhsc.edu

In the beginning, management of surgical nerve lesions were a part, albeit small, of broader meetings of general surgical, orthopedic, plastic, sometimes neurosurgical and even less frequently neurology meetings. The inception of what is now known as the Sunderland Society dedicated to the study and promulgation of the basic and clinical science of surgical nerve lesions can fairly, I believe be laid at the feet and more importantly the intellects of two men,—Morton Spinner MD and George Omer MD, MSc., both orthopedic surgeons, who also had interest and background in Hand Surgery. Both men had experience with nerve injuries in the Army Medical Corps during the Korean conflict and Omer had remained in the Army Medical Corps for a number of years thereafter. In the late 70’s, they envisioned a Study Club for Surgical Nerve Lesions, Spinner had a vibrant practice in Hand Surgery in Brooklyn, New York, and was a Clinical Professor of Orthopedic Surgery at the Albert Einstein College of Medicine also in New York, whereas Omer was Professor and Chair of Orthopedics and Chief of Hand Surgery at the University of New Mexico School of Medicine in Albuquerque.


In 1978, a group of surgeons interested in peripheral nerve pathology met at Duke University with J. Leonard Goldner as host. During this meeting a biannual program was discussed. A preliminary society was formed, with Raymond Curtis, J. Leonard Goldner, David Kline, George Omer, and Morton Spinner as the founding senior members of this society (Goldner letter, 1995).

The concept was crystallized at the mid-year meeting of the American Society for Surgery of the Hand (ASSH) in 1979, and The Peripheral Nerve Study Group was founded, with the purpose “to study in depth difficult problems and advances in peripheral nerve anatomy, physiology, and surgery”. Present at that meeting were Ray Curtis, Mike Jabaley, Joseph Kutz, George Omer, Morton Spinner, Jack Tupper, Jim Urbaniak and Shaw Wilgis. Leonard
Goldner was absent but aware of the meeting. Morton Spinner was elected president and Shaw Wilgis served as secretary-treasurer.

The first formal program of “the Peripheral Nerve Study Group” was held in New York City, in July 1980 with Morton Spinner as president. Sir Sydney Sunderland was a guest speaker. (More on the scientific content of the program will follow) At this meeting David Kline was elected president and George Omer was president-elect; Morton Spinner became past-president and Shaw Wilgis continued as secretary-treasurer. This was the first executive committee. It was determined that the “annual meetings” would be held approximately 18 months apart. The membership quickly expanded to include several more members from the United States as well as members from Australia, Austria, Canada, France, Italy, Sweden, Switzerland, and West Germany. Also at this meeting it was decided that the host of each subsequent meeting would also serve as president of the Nerve Study Club (subsequently The Sunderland Society). The meeting became a forum for informal exchange of ideas and experiences in peripheral nerve problems.

In September 1980, David Kline proposed that the name of the group be changed because it was similar to The Neurologic (Neurology) Nerve Study Group, which had met for a number of years. (Kline had attended several of their meetings both in New Orleans and at the Carville Hanson’s Disease Center outside Baton Rouge as a guest of Professor Richard Paddison. The meetings were interesting but not surgically oriented). The proposal was discussed by the executive committee. As president of the ASSH from 1978 to 1979, George Omer had invited Sir Sydney Sunderland to be the Founder’s Lecturer at the annual meeting; members of the ASSH were well aware of Sir Sydney’s professional contributions. In January 1981 David Kline wrote to all members: “Morton Spinner and the executive committee have suggested Sunderland Club as our new name.”

The second formal meeting was held in New Orleans in November 1981 with David Kline as president. At the business meeting, the name of the group was changed from The Peripheral Nerve Study Group to the Sunderland Society.

The third meeting was held in Santa Fe in May 1983, with George Omer as president. There were 22 members from six countries as well as several guests in attendance. Sir Sydney was in attendance, with his wife Lady Gwen, and he subsequently attended every meeting until his death in 1993 (as did his wife for most but not all meetings).

Since the founding of the Sunderland Society in 1980, there have been many memorable meetings:

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Members deceased and known by myself at this date are: William Bora, Raymond Curtis, J. Leonard Goldner, Robert Leffert, Algimentas Narakas, Morton Spinner, Sir Sydney Sunderland and Lady Gwen, Robert Tiel, and Jack Tupper.

Several have served as Secretary-Treasurer such as Shaw Wilgis, Michael Jabaley, Leo Happel, Tom Brushart, and more recently Rob Spinner.

L – R: Hanno Millesi, Yudong Gu & David Kline during the Shanghai Meeting in 2009
SOCIAL PROGRAMME

Bus pick-up venue: Grandhotel Hessischer Hof
Friedrich-Ebert-Anlage 40, 60325 Frankfurt am Main

Saturday, 3rd Dec. 2016
18:00 – 22:00 Reception at Grandhotel Hessischer Hof

Sunday, 4th Dec. 2016
10:00 – 13:00 Visit the Senckenberg Museum of Natural History
(Social programme for accompanying persons)
15:00 Bus transfer from Grandhotel to Städel Arts Museum
15:30 Guided Visit of the Städel Arts Museum
18:00 – 21:00 Dinner at Holbein Gourmet Restaurant
21:00 Bus transfer back to Grandhotel

Monday, 5th Dec. 2016
15:00 Bus transfer from Grandhotel to Christkindl Markt
15:30 – 16:30 Visit to Christmas Arts Market
16:30 Bus transfer from Christkindl Markt to Orangerie Bad Homburg
17:10 – 18:30 Classic Concert at Orangerie Bad Homburg
   Nina Vitol (soprano) and Bernhard Zosel (piano)
18:30 – 21:00 Dinner at Orangerie Bad Homburg
   After Dinner Lecture David Kline
21:30 Bus transfer back to Grandhotel

Tuesday, the 6th Dec. 2016
10:00 – 13:00 Frankfurt City Tour Hop-on / Hop-off bus ride
(Social programme for accompanying persons)
15:00 Bus transfer to Idstein
15:45 – 17:00 Guided tour of Idstein
17:00 Bus transfer from Idstein to Apfelwein Wagner
18:00 Dinner at Apfelwein Wagner, Frankfurt
21:00 Bus transfer back to Grandhotel
Concert
Monday, 5th December 2016
17:10 – 18:30
Klassik im Taunus

Bernhard Zosel (piano)  Nina Vitol (soprano)

Charles Gounod (1818 – 1893)
“O Dieu! Que de bijoux... Ah, ... je ris...”
Juwel Song of Marguerite from “Faust”

Giuseppe Verdi (1813 - 1901)
“Pace, pace...”
Leonoras aria from “La forza del destino”

Pyotr Ilyich Tchaikovsky (1840 - 1893)
Tatyana – “Letters Scene” from “Eugene Onegin”

Franz Lehar (1870 – 1948)
Vilja Song from “Merry Widow”

Giacomo Puccini (1858 – 1924)
“Sì, mi chiamano Mimì...” Aria of Mimi from “La Bohème”

Giuseppe Verdi (1813 – 1901)
“Ritorna vincitor...” Aria of Aida from “Aida”

Franz Lehar (1870 – 1948)
Giudittas Song from “Giuditta”
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WHERE ARE WE HEADING?

Formed in the late 1970’s as a small club with a handful of select members, who dedicated their lives to the study of the peripheral nerve, the Sunderland Society has continued to grow both in membership and profundity of insight. Over the years the Sunderland Society has transformed itself to a magnet that attracts the best minds from around the world. We speak different languages, yet in a common tongue that reflects our cogitation; we come from disparate scientific backgrounds, yet complement each other’s reasoning, enabling us to see the whole – we are indeed intensely diverse, yet we share our common love for the nerve.

I will not indulge in the history of the Sunderland Society here, which David Kline, one of the founding fathers of the society has done quite eloquently in this book. However, the significance of our meetings is worth mention: without doubt, a given Sunderland Society Meeting represents the best scientific thoughts on nerve of its time on the planet; in this, the meetings are rendered timeless! Over the decades one can see a slow, but steady shift of thought from regeneration to induction of neoteny, from biomechanical reconstruction to mechatronic reanimation– essentially hugging the serpentine road of ongoing developments in technology. The abstracts you see in these pages and in those of previous meetings need no introductions whatsoever - they speak for themselves.

Twenty-Sixteen was a unique year for Germany that will be etched in history: this year, disasters were transformed to opportunities for benevolence and goodwill, happenings that will completely change the outlook of an emerging modern society. The present meeting in Frankfurt, thus, has a special significance. Personally, for Thomas and myself, and for our respective alma maters (Carl von Ossietzky University of Oldenburg and Justus von Liebig University of Giessen), what better event can be a pinnacle of this historical year, than the conduct of the Sunderland Society Meeting? – the first time in its 36-year existence, Sunderland visits Germany...

And, we hope this will not be the last.

Kartik Krishnan
Frankfurt