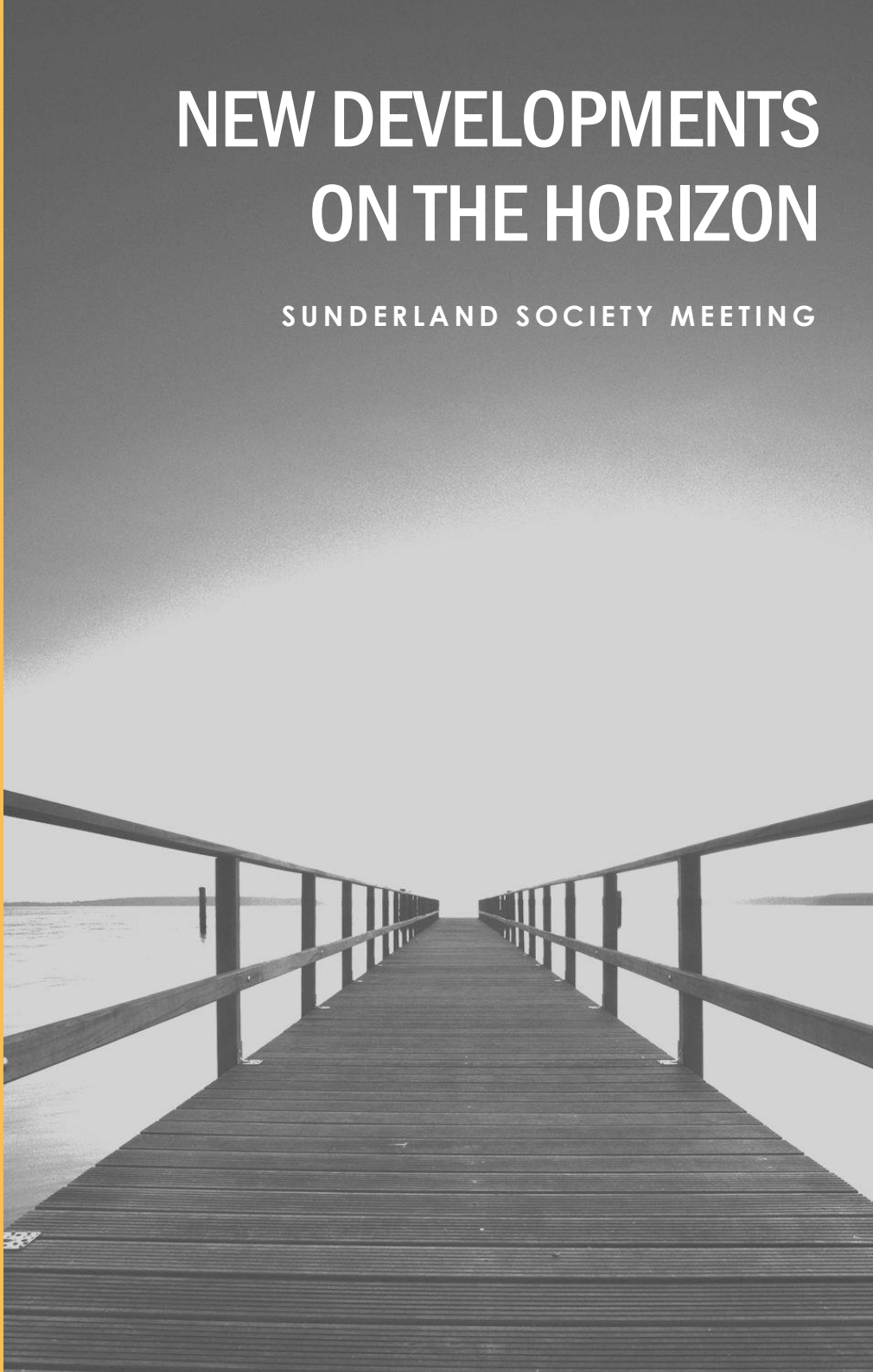
NEW DEVELOPMENTS ON THE HORIZON

SUNDERLAND SOCIETY MEETING



STANFORD, CALIFORNIA

MARCH 3-6, 2018

Welcome

23rd Annual Sunderland Society Meeting

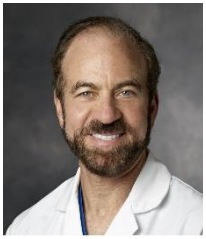
Dear Sunderland Members and Guests:

It is with great pleasure and gratitude that Dr. Gary Steinberg and I welcome you to Stanford for the 23rd meeting of the Sunderland Society. We want to honor its namesake, Sir Sydney Sunderland, and his commitment to pursuing excellence in the science, art, and clinical practice of peripheral nerve surgery. The theme of the scientific program, "new developments on the horizon", emphasizes and encourages the process of taking new ideas and techniques from the laboratory bench into the clinical arena. This theme epitomizes Stanford's mission: "research informs leading edge clinical care to promote the public welfare."

Stanford is not only an institution of academic excellence, but also houses numerous artistic treasures in the Cantor Arts Center, which contains one of the largest collections of Rodin sculptures, and the Anderson Museum that focuses on modern art. Stanford is also an athletic powerhouse as evidenced by its large number of Olympic and star athletes, as well as its world-class athletic facilities.

We look forward to sharing and enjoying these wonderful resources and experiences with you, and hope that you leave intellectually invigorated and emotionally charged.

Sincerely,



Gary K Steinberg, MD, PhD
Chairman
Department of Neurosurgery
Stanford University
California, USA

Michel Kliot, MD
President
Clinical Professor
Department of Neurosurgery
Stanford University
California, USA

Table of Contents

Scientific Program

Saturday, March 3 2018

5:00 pm Welcome Reception At Stanford Park Hotel

Sunday, March 4 2018

6:45 am Transportation To Stanford Medicine: Li Ka Shing Conference Center

7:15 am Breakfast

Business meeting for Sunderland Society Members

8:15 am Opening Ceremony: Dr. Gary Steinberg and Dr. Michel Kliot

Scientific Session I
8:45 am- 10:00 am
Chairs: Tessa Gordon and Martijn Malessy

8:45 am Electrical Stimulation For Long Nerve Grafts

Wilson "Zack" Ray

9:00 am Therapeutic Effect Of Laser Photobiomodulation For Peripheral Nerve Injuries And Muscle Preservation

Shimon Rochkind

9:15 am Phagocytic Capacity And Immunoregulatory Molecules Of Schwann Cells And Olfactory Ensheathing Cells To Enhance Axonal Regeneration After Peripheral Nerve Energy

Christine Radtke

9:30 am Pro-Regenerative Macrophages Regulate Schwann Cell Dynamics Following Nerve Injury

Rajiv Midha

9:45 am The Role Of Binding Proteins In Localized Fk506 Delivery To Enhance Nerve Regeneration

Gregory H Borschel

10:00 am Break

Scientific Session II
10:30 am -12:00 pm
Chairs: Lukas Rasulic and Robert Schmidhammer

10:30 am Development Of Peripheral Nerve Diffusion Tensor Imaging As A Measure Of Axonal Integrity

Neil G Simon

10:45 am Correlation Of Magnetic Resonance Imaging (MRI Neurography) And Electrodiagnostic Study Findings With Intra-Operative Findings In Post-Traumatic Brachial Plexus Palsy

Mukund R Thatte

Sunday, March 4 2018 *cont.*

11:00 am **Positive Impact Of Intraoperative Neurophysiological Monitoring For Lumbosacral Plexus Tumor Surgery**
José Fernando Guedes-Correa

11:15 am **Desmoid Fibromatosis In The Brachial Plexus Mimicking An Ulnar Nerve Entrapment**
Lars B Dahlin

11:30 am **Phrenic To Musculoctaneous Nerve Transfer In Traumatic Brachial Plexus Injury: How Independent Does Elbow Flexion Become From Respiration?**
Mariano Socolovsky

11:45 am **Joint Flexion And Nerve Suture Without Tension: An Old Technique Can Be Updated?**
Mariano Socolovsky

12:00 pm **Lunch**

1:00 pm **Synaptic Plasticity: The Brain's Response To Experience**
Robert Malenka

2:00 pm **24th Sunderland Society Meeting**
Shimon Rochkind

Iris & B. Gerald Cantor Arts Center For Visual Arts
2:15 pm – 4:15 pm
Transportation service provided

House Family Vineyards
5:15 pm – 9:00 pm
Transportation service provided

Monday, March 5 2018

7:00 am Transportation To Stanford Medicine: Li Ka Shing Conference Center

7:30 am Breakfast

Business Meeting For Sunderland Society Members

Scientific Session III
8:30 am- 10:00 am
Chairs: David Chiu and Mariano Socolovsky

8:30 am Targeted Muscle Reinnervation Treats Residual Limb Pain And Phantom Limb Pain In Major Amputees
Gregory A Dumanian

8:45 am Regenerative Peripheral Nerve Interfaces For The Treatment Of Painful Neuromas
Stephen W P Kemp

9:00 am Acellular Nerve Allografts Prevent Neuroma Formation In Both Rodent And Swine Nerve Transection Models
Amy M Moore

9:15 am Dermal Sensory Interfaces For Providing Feedback To Amputees
Paul S Cederna

9:30 am Nerve Transfers To Address Blindness In Neurotrophic Keratopathy: Clinical Outcomes
Gregory H Borschel

9:45 am The Intercostobrachial Nerve As A Sensory Donor For Hand Reinnervation In Brachial Plexus Reconstruction
Mario Siqueira

10:00 am Break

Scientific Session IV
10:15 am- 12:00 pm
Chairs: Howard Clarke and Robert Spinner

10:15 am Successful Control Of Virtual And Robotic Hands Using Neuroprosthetic Signals From Regenerative Peripheral Nerve Interfaces In Humans
Paul S Cederna

10:30 am Quantifying Real-World, Patient-Initiated Arm Movement Following Nerve Reconstruction For Upper Brachial Plexus Injury
Susan H Brown

10:45 am Nerve Transfer And Nerve Graft Repair Yield Similar Functional Shoulder Outcomes In Neonatal Brachial Plexus Palsy
Lynda J-S Yang

Monday, March 5 2018 *cont.*

11:00 am Primary Shoulder Surgery As A Possible Complete Treatment For Obstetrical Brachial Plexus Injury
Howard Clarke

11:15 am Knowledge Of Neonatal Brachial Plexus Palsy Among Medical Professionals In North America
John McGillicuddy

11:30 am Temporally Controlled GDNF Gene Therapy Promotes Regeneration Of Motor Axons In Spinal Ventral Root Repair
Joost Verhaagen

11:45 am Large-Gap Peripheral Nerve Repair Using Amniotic Fluid Derived Stem Cells Seeded Acellular Nerve Allografts
Zhongyu "John" Li

12:00 pm Lunch

Scientific Session V
1:00 pm - 2:00 pm
Chairs: David Kline and Alan Hudson

1:00 pm A Neuroscientist's Trek Along The Road To Functional Recovery After Nerve Injuries
Tessa Gordon

1:30 pm Mouse Rapid-Stretch Nerve Injury Model: Severity Can Be Defined Biomechanically
Mark A Mahan

1:45 pm Visualization Of Human Posterior Interosseous Nerves In Healthy Subjects And In Patients With Type 1 And 2 Diabetes By X-Ray Phase Contrast Zoom Tomography
Lars B Dahlin

2:00 pm Molecular Imaging At A Cellular Resolution In Vivo Using Optical Coherence Tomography
Adam De La Zerda

3:00 pm Break

3:15 pm Honored Members: Dr. Kline and Dr. Hudson

Anderson Collection At Stanford University
3:50 pm – 6:00 pm

Il Fornaio
6:15 pm – 10:00 pm
Transportation service provided

Tuesday, March 6 2018

6:45 am Transportation To Stanford Medicine: Li Ka Shing Conference Center

7:15 am Breakfast

Business meeting for Sunderland Society Members

Scientific Session VI
8:15 am - 10:00 am
Chairs: Lynda Yang and Eric Zager

8:15 am A Clinical Retrograde Study Of The Effectiveness And Safety Of Thread Carpal Tunnel Release (Tctr)
Danzhu Guo

8:30 am A Cadaveric Study Of Thread Cubital Tunnel Release
Danqing Guo

8:45 am Transposition Of The Lateral Femoral Cutaneous Nerve
Amgad S Hanna

9:00 am Changes In Electromyographic Patterns And Global Masticatory Force After Masseter Nerve Transfer In Patients With Unilateral Facial Paralysis
Alexander Cardenas-Mejia

9:15 am Facial Reanimation In The 7th And 8th Decades Of Life
Alexander Cardenas-Mejia

9:30 am Targeted Cutaneous Nerve Biopsy
Robert J Spinner

9:45 am Distal Peroneal Nerve Decompression After Sciatic Nerve Injury Secondary To Total Hip Arthroplasty
Thomas J Wilson

10:00 am Break

Scientific Session VII
10:30 am - 11:00 am
Chairs: John McGillicuddy and Mario Siqueira

10:30 am The Natural History Of Schwannomas
Allan J Belzberg

10:45 am Whole Exome Sequencing Of Growing And Non-Growing Cutaneous Neurofibromas From A Single Patient With Neurofibromatosis Type 1
Michel Kliot

11:00 am Brachial Plexus Tumors – A Personal Series
Eric L Zager

Tuesday, March 6 2018 *cont.*

11:15 am Tailored Approach To Retroperitoneal Lumbosacral Plexus And Nerve Associated Tumors
Thomas Kretschmer

11:30 am Persistent Sciatic Pain Following Back Surgery
Israel P Chambi

11:45 am To Use Or Not To Use Viable C5-C6 Stumps In Brachial Plexus Traction Injuries?
Lukas Rasulić

12:00 pm Closing Remarks

12:15 pm Lunch

1:15 pm Tour Of Hoover Tower and Stanford Dish
Alternate: Transportation service to Stanford Park Hotel provided

Guest Speaker

Synaptic Plasticity: The Brain's Response To Experience

Robert C Malenka, MD, PhD
Pritzker Professor of Psychiatry & Behavioral Sciences
Associate Chair, Department of Psychiatry & Behavioral Sciences
Deputy Director, Stanford Neurosciences Institute

Dr. Robert C. Malenka is the Pritzker Professor of Psychiatry and Behavioral Sciences, Director of the Nancy Pritzker Laboratory, and Deputy Director of the Stanford Neurosciences Institute. He is a world leader in elucidating the mechanisms underlying the actions of neurotransmitters and the molecular mechanisms by which neural circuits are reorganized by experience. His contributions over the last 30 years have laid the groundwork for a much more sophisticated understanding of the mechanisms by which neurons communicate and the adaptations in synaptic communication that underlie all forms of normal and pathological behavior. He was trained as both a clinical psychiatrist and cellular neurobiologist and has been at the forefront of helping to apply the knowledge gained from basic neuroscience research to the treatment and prevention of major neuropsychiatric disorders.

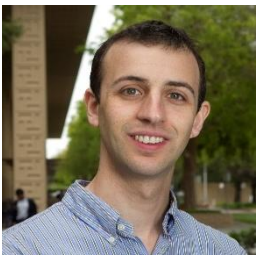
Dr. Malenka graduated from Harvard in 1978, summa cum laude and Phi Beta Kappa in biology. He received an M.D. and a Ph.D. in neuroscience in 1983 from Stanford University School of Medicine. Over the ensuing 6 years, he completed residency training in psychiatry at Stanford and 4 years of postdoctoral research at the University of California, San Francisco (UCSF). In 1989, he was appointed Assistant Professor of Psychiatry and Physiology at UCSF, ultimately reaching the rank of Professor in 1996. In addition to running an active research program at UCSF, he was the Director of the Center for the Neurobiology of Addiction and Associate Director of the Center for Neurobiology and Psychiatry. He returned to the Stanford School of Medicine in 1999.

He is an elected member of the National Academy of Sciences and the National Academy of Medicine as well as an elected fellow of the American Academy of Arts and Sciences, the American Association for the Advancement of Science, and the American College of Neuropsychopharmacology. He has served on the National Advisory Council on Drug Abuse and as a Cou1ncilor for the Society for Neuroscience and the American College of Neuropsychopharmacology. He is on the scientific advisory boards of numerous non-profit foundations including the Cure Alzheimer's Fund, the Brain and Behavior Research Foundation, the International Mental Health Research Organization and the Stanley Center for Psychiatric Research. He is also on the editorial boards of many prominent journals including *Neuron, Translational Neuroscience, and Biological Psychiatry*.

He has been the recipient of numerous awards including the Society for Neuroscience Young Investigator Award (1993), the Daniel Efron Award from the American College of Neuropsychopharmacolgoy (1998), the Kemali Foundation International Prize in Neuroscience (2000), the CINP-Lilly Neuroscience Basic Research Award (2002), the Perl/UNC Neuroscience Prize (2006), the NARSAD Goldman-Rakic Prize for Outstanding Neuroscience Research (2010), the Pasarow Foundation Award for Extraordinary Accomplishment in Neuropsychiatry Research (2011), and the Society for Neuroscience Julius Axelrod Prize (2016).

Dr. Malenka's findings have been published in over 260 research papers in leading science journals. He has also co-authored a textbook entitled Molecular Neuropharmacology: A Foundation for Clinical Neuroscience (McGraw Hill, 3rd edition, 2015). His many years of investigation have produced a number of hypotheses that provide the foundation for much of the research in many of the world's laboratories that study how neurons communicate with one another and how this communication is modified during learning and by experience. His laboratory continues to conduct cutting edge research on the molecular mechanisms of neural communication as well as the role of synaptic dysfunction in brain disorders, including addiction, autism, depression, and Alzheimer's disease.

Molecular Imaging At A Cellular Resolution *In Vivo* Using Optical Coherence Tomography



Adam de la Zerda, PhD
Assistant Professor
Departments of Structural Biology, and Electrical Engineering, by courtesy
School of Medicine, Stanford University

Dr. Adam de la Zerda is an Assistant Professor in the departments of Structural Biology and Electrical Engineering at Stanford University. He is working on the development of new medical imaging technologies to detect cancer at an early stage and guide physicians towards optimal treatment of the cancer. He has received numerous awards including *Forbes Magazine* 30-under-30 in Science and Healthcare (for years 2013 and 2014), the Chan-Zuckerberg Biohub Investigator, the Pew-Stewart Scholar of Cancer Research Award, the US Air Force Young Investigator Award, the Dale F. Frey Award, the NIH Director's Early Independence Award, the Damon Runyon Fellowship, and the Young Investigator Award at the World Molecular Imaging Congress. He has published over 20 papers in leading journals including Nature Nanotechnology, Nature Medicine, Nano Letters, and PNAS, some of which received significant press coverage from *Forbes*, *US News,* and *The Washington Post*. He is the founder of a medical diagnostics start-up called Click Diagnostics.

Honored Guests

Alan R Hudson, MD

Honored Scientific Speaker
Tessa Gordon, MD, PhD

David G Kline, MD

Electrical Stimulation For Long Nerve Grafts

Ying Yan, Manu Stephen, Matthew MacEwan, and **Wilson Ray**

Department of Neurosurgery, Washington University School of Medicine; St Louis, MO, USA; rayz@wustl.edu

Introduction: In clinical practice, long nerve grafts are often necessary to repair large nerve defects. The use of long nerve grafts is frequently met with suboptimal outcomes. Chronic denervation in target end organs is typically cited as the primary driver for incomplete functional recovery. Brief low-frequency electrical stimulation (ES) of the proximal nerve stump after primary repair has been clearly demonstrated to facilitate peripheral nerve regeneration in both freshly axotomized and chronically denervated peripheral nerve and has been applied successfully in clinical practice. In this study, we sought to evaluate the effect of electrical stimulation in a long nerve graft (4cm) rodent sciatic nerve model.

Methods: Rat sciatic nerves were transected and repaired with a 4cm nerve graft. The study was composed of six groups including isograft (Lewis as donor and recipient) and acellular nerve allografts (ANA) (Sprague Dawley as donor and Lewis as recipient). Treatment included either; 1 hour for 1 day, 1 hour a day for 3 days, or 1 hour a day for 6 days - ES was applied at the proximal nerve stump (proximal to nerve graft, 1 hour, 20Hz, 3V). At an endpoint of 14 weeks post-surgery, electromyogram test (EMG) in *tibialis anterior* (TA) and muscle contractile force measurement in extensor digitorum longus (EDL) were performed for functional recovery assessment. EDL muscle mass ratios were measured as well to evaluate muscle atrophy and its recovery. Nerve segments distal to nerve grafts were harvested for histomorphometric analysis.

Results: At the time point of 14 weeks post-surgery, EMG recordings in TA muscle showed significantly better muscle activation in all isograft groups compared to ANA groups. There was no significant difference among the isograft groups with or without ES. ANA with one hour stimulation showed a trend of higher evoked amplitude when compared with ANA/no stimulation group. For evoked EDL tetanic force, isograft with one time electrical stimulation showed a non-significant trend of higher force induction compared with other isograft groups (3 and 6 days). In contrast, all ANA groups failed to induce measurable muscle force production. All isograft groups demonstrated significantly more muscle mass as compared to ANA groups. Histomorphometric analysis results (Figure) demonstrate 3 days (201 ± 50) and 6 days (278 ± 52) of ES had higher total axon counts as compared to 1 day of ES (156 ± 69) or isografts without ES (158 ± 61). *See Figure 1 on page 52.*

Conclusions: Our results support the use of 1 hour of ES at the time of surgical repair in a long graft model. While these results are interesting, the authors recommend caution in the clinical interpretation of these results. Additional experiments with extended endpoints (20 weeks) to account for the long nerve grafts are underway, which may support additional days of ES as demonstrated in the higher total axon counts in the 3 and 6 day groups. We hypothesize the repeat surgical exposure of the nerve in the 3 and 6 day cohort may also have affected final outcomes. Additional work is underway with resorbable wireless stimulators that may minimize the observed inflammatory response. We expect the extended endpoints to provide additional insight on the potential benefits of electric stimulation in nerve repairs involving long nerve grafts.

Therapeutic Effect of Laser Photobiomodulation for Peripheral Nerve Injuries and Muscle Preservation

Shimon Rochkind

Tel Aviv Sourasky Medical Center, Tel Aviv University, Tel Aviv, Israel; rochkind@zahav.net.il

Introduction: Numerous attempts have been made to enhance and/or accelerate the recovery of peripheral nerve injuries (PNI) and decrease or prevent atrophy of the corresponding muscles. Among the various proposed methods, laser photobiomodulation has received increasing attention.

Methods: We previously investigated the effect of laser photobiomodulation (low power laser irradiation) with 632.8 nm and 780 nm wavelengths in incomplete and complete PNI models. Laser photobiomodulation was applied for accelerating and enhancing axonal growth and decrease muscle atrophy. We introduced a new methodology of triple treatment, applied simultaneously at three areas: injured area of the peripheral nerve, corresponding segments of the spinal cord, and corresponding denervated muscle, with the ultimate goal of achieving improved limb function.

Results: In an in-vitro model, we found that laser photobiomodulation induces nerve cell activation, affects nerve cell metabolism, and stimulates nerve processes sprouting.
In studies on injured peripheral nerves of rats, we found protective immediate effects which increase the functional activity of the injured peripheral nerve, maintains functional activity of the injured nerve over time, decreases or prevents scar tissue formation at the injured site, prevents or decreases degeneration in corresponding motor neurons of the spinal cord, and significantly increases axonal growth and myelination. Moreover, direct laser irradiation of the spinal cord improves recovery of the corresponding injured peripheral nerve. In the early stages of muscle atrophy, we found that laser photobiomodulation applied for treatment of rat denervated muscle may preserve the muscle by maintaining CK activity and the amount of AChR close to its initial level before injury.

Conclusions: The significance of the performed studies is in the provision of an innovative laser technology in the field of cell therapy and its therapeutic value for PNIs. Well-designed clinical studies are needed to evaluate the effectiveness and role of laser photobiomodulation treatment in a clinical setting.

Phagocytic Capacity And Immunoregulatory Molecules Of Schwann Cells And Olfactory Ensheathing Cells To Enhance Axonal Regeneration After Peripheral Nerve Injury

Tamara Weiss and **Christine Radtke**

Department of Plastic and Reconstructive Surgery, Medical University of Vienna, Vienna, Austria; christine.radtke@meduniwien.ac.at

Introduction: Schwann cell (SCs) and olfactory ensheathing cells (OECs) are the principal glia of the peripheral and olfactory nervous system, respectively. Although both ensure the integrity of nerve fibers, they exhibit additional functional competences that are adapted to the nature of the nerve they support. SCs gained attention as they possess the ability to facilitate axon regeneration by transforming into a dedicated repair phenotype after injury. In contrast, OECs are specialized to the needs of freshly generated neurons because mammalian olfactory receptor neurons are replaced throughout lifetime. In line with their physiological roles, several studies have highlighted beneficial effects of OECs and SCs in regenerative approaches not only for the spinal cord but also for peripheral nerves and they emerged as the leading candidates for autologous transplantation therapies. However, there is still a lot to learn about the neuroprotective and regenerative strategies of these two glial cell types and whether these can be exploited to improve therapeutic approaches. Moreover, accumulating evidence for an immunomodulatory potential of glia holds yet to be determined implications in regenerative medicine. Especially the reported up-regulation of MHCII and cytokines as well as the capacity of phagocytic debris clearance could cause various immunological effects that may influence the therapeutic outcome. Hence, understanding how OECs and SCs exert repair processes and affect the immune response after injury is of utmost interest to assess advantages and limitation of these cell types in transplantation therapies. Thus, we investigated immunoregulatory molecules and the phagocytic capacity of OECs in comparison to SCs to exploit the involved pathways and develop novel approaches or auxiliary therapies for peripheral nerve regeneration.

Methods & Preliminary Results: Highly pure human primary cultures of OECs were co-cultured with a human neuroblastoma tumor cell line that possesses a high spontaneous apoptosis rate. After 11 days of culture, multicolor immunofluorescence analysis by confocal microscopy was performed. In addition, the presence of several potent macrophage attracting factors in the medium of human primary repair OECs by using cytokine antibody arrays was determined

Conclusions: Our results suggest, to our knowledge for the first time, that repair OECs and SCs are able to phagocytize cellular debris in addition to the well known clearance of myelin. In a next step, the phagocytic capacities and pathways, cytokine production and regulation of immunomodulatory molecules will be compared between human primary SC and OEC cultures to expand the knowledge of their functional competences and to improve cell based therapies for peripheral nerve regeneration.

Pro-Regenerative Macrophages Regulate Schwann Cell Dynamics Following Nerve Injury

Jo Anne Stratton Alex Holmes, Nicole Rosin, **Rajiv Midha**, and Jeff Biernaskie

Department of Clinical Neurosciences, Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada Department of Comparative Biology and Experimental Medicine, Faculty of Veterinary Medicine, University of Calgary, Calgary, Alberta, Canada; rajmidha@ucalgary.ca

Introduction: Many individuals are affected by nerve injury, resulting in functional deficits and pain. Pro-regenerative macrophages are well known for their role in promoting tissue repair and remodeling – a process that is important for full functional recovery in many injury environments. However, the role of pro-regenerative macrophages in nerve injury is not as well defined. We aimed to decipher the role of macrophages during nerve regeneration.

Methods: First, we performed RNAseq on macrophages from day 3 and 8 post-injury, discovering that these cells expressed an array of factors including Growth Arrest Specific 6 (Gas6), HBEGF, and IL6. Following the addition of these factors to immature Schwann cell cultures, we found that Schwann cells were responsive to Gas6 and IL6, namely Schwann cells exited cell cycle, suggestive of a role for macrophages during the process of Schwann cell maturation. We performed nerve injury in Thy1-GFP reporter rats, and eight days later treated them with mannosylated clodronate liposomes to ablate macrophages, or control liposomes.

Results: Using compound muscle action potential analysis, we found that macrophage ablation resulted in long-term deficits in conduction velocity, suggesting poorer myelination, but no effect on conduction amplitude. In addition, we found that there was an increase in Schwann cell density, specifically immature Schwann cells, as well as a decrease in the percentage of remyelinated axons in the ablation group. Finally, macrophage targeted knock out of Gas6 in nerve injury results in an increase in Schwann cell density as well as a reduction of remyelinated internode length demonstrating that macrophage-derived Gas6 independently regulates Schwann cell dynamics in peripheral nerve injury.

Conclusions: Taken together, this dataset has enhanced our understanding of the mechanisms driving recovery following nerve injury – an important step towards developing more targeted treatment options.

The Role Of Binding Proteins In Localized FK506 Delivery To Enhance Nerve Regeneration

Gregory H Borschel, Kasra Tajdaran, and Tessa Gordon

The Hospital for Sick Children and University of Toronto, Canada; gregory.borschel@sickkids.ca

Introduction: Despite the growing interest in local FK506 delivery for enhancing axon regeneration, the exact mechanism of FK506's action within the peripheral nerve is still unknown. In this study, we analyzed the expression of FK506-binding proteins (FKBP), a family of immunophilins that act as receptors for FK506, within the injured peripheral nerve and following local FK506 administration. We investigated the expression of FKBP-12 and FKBP-52, which have been shown to drive immunosuppressive and neurotrophic properties of FK506 within the central nervous system, respectively.

Methods: A sciatic nerve transection model was used in transgenic *Thy1*-GFP+ rats expressing green fluorescent protein (GFP) in axons. The rats underwent nerve transection and repair either with or without local FK506 delivery using a particulated FK506 delivery system. In the sham group, rats did not sustain any nerve injury. Seven days post repair, FKBP-12 and FKBP-52 expression within the sciatic nerve was analyzed using immunohistochemistry. S100 and ED-1 staining was used to determine whether Schwann cells (stained with S100 antibody) or macrophages (ED-1) co-expressed binding proteins within of the peripheral nerve.

Results: Seven days post-repair, with and without FK506 delivery, FKBP-52 was specifically expressed within the Schwann cells in both the proximal and distal stumps adjacent to the site of sciatic nerve injury. Following FK506 local administration, we observed significantly elevated Schwann cell proliferation within the distal nerve stump compared to the nerve samples without any FK506 delivery. FKBP-52 expression was minimal in the regions of the proximal and distal nerve stumps not adjacent to the injury. FKBP-12 was mainly expressed in the vacuoles of the degenerated nerve fibers in the distal nerve stump, with minimal expression in the proximal nerve and at the site of nerve injury.

Conclusions: The mechanism of action of FK506 on nerve regeneration has not been completely characterized. Our findings suggest that FK506 acts on the Schwann cells at the site of injury, accounting, at least in part, for the profound enhancement of nerve regeneration when applied locally.

Development Of Peripheral Nerve Diffusion Tensor Imaging As A Measure Of Axonal Integrity

Neil G Simon, Michel Kliot, Thomas Gallagher, Jim Lagopoulos, and Matthew C Kiernan

St Vincent's Clinical School, University of New South Wales, Darlinghurst, NSW, Australia; n.simon@unsw.edu.au

Introduction: Diffusion tensor imaging (DTI) of brain is established as a method of measuring the integrity of axons in white matter tracts. However, the tools with which to assess peripheral nerve axonal integrity *in vivo* are limited.

Methods: DTI protocols were developed to assess the integrity of peripheral nerves. A total of 25 control subjects and 24 patients with amyotrophic lateral sclerosis (ALS), peripheral nerve injury or peripheral nerve tumors were studies using peripheral nerve DTI techniques and compared with clinical and electrophysilogical assessments in multiple studies. Initially, the feasibility of DTI for delineating normal nerve tissue was determined in patients with peripheral nerve sheath tumors (PNSTs). Subsequently, the feasibility of detecting changes in axonal density was assessed in examples of peripheral nerve injury and recovery. The test-retest reliability of peripheral nerve DTI was assessed in a cohort of healthy controls. The protocol was then applied in a cohort of amyotrophic lateral sclerosis patients with serial clinical, electrophysiological and MRI measurements performed at 0, 3 and 6 months.

Results: DTI was able to delineate normal nerve fascicles from PNST tissue. Loss of axonal integrity followed by axonal regeneration was demonstrated in a patient with peroneal nerve transection. In control studies peripheral nerve DTI was shown to be reproducible with excellent reproducibility (intraclass correlation coefficient 0.89-0.96 for fractional anisotropy). In ALS patients, there where significant changes in DTI metrics were seen over time that correlated with clinical and electrophysiological measures, and indicated axonal degeneration with advancing disease.

Conclusions: In total, this collection of studies has demonstrated the utility of peripheral nerve DTI as a potential clinical and research tool for the measurement of axonal degeneration and regeneration.

Correlation of Magnetic Resonance Imaging (MRI Neurography) And Electrodiagnostic Study Findings With Intra-operative Findings In Post-Traumatic Brachial Plexus Palsy

Mukund R Thatte and Neehar R Patel; mthatte@gmail.com

Bombay Hospital Institute of Medical Sciences, Mumbai, India.

Introduction: The typical patient of post traumatic Brachial Plexus Injury (BPI) is a young male who has had an accident while riding a two-wheeler. It is important to determine whether the lesion in question is Pre-ganglionic (PRE-G) or Post-ganglionic (POST-G) for purposes of surgical planning. Tools such as Magnetic Resonance Imaging (MRI) and Electrodiagnostic studies (EDx) have been used to provide details regarding the injury pattern. However, neither of the two is considered the reference standard yet. In this study we have corelated these two versus actual surgical findings.

Methods: 48 Patients of BPI fitting the inclusion criteria were seen on an out-patient basis, where they all underwent a complete neurological examination of the upper limb. Following this workup, they underwent a detailed Electro Diagnostic Study (EDx). After interpreting the data, the conditions of all spinal roots from C5 to T1 (i.e. their level of injury, whether Pre-Ganglionic, PRE-G, or Post-Ganglionic, POST-G) were noted. Magnetic Resonance Imaging (MRI) of the affected brachial plexus was documented for each root from C5-T1. Intra Operative findings were then noted. All roots were traced right up to the foramen. Comparison of intra-op findings with the pre-operative MRI and Edx reports were tabulated.

Results: MRI accurately diagnosed 138 roots as injured of the 147 injured roots and MRI Sensitivity for the detection of BPI was 93.88%; however, it lacked Specificity. EDx correctly identified 146 out of 147 injured roots and thus Sensitivity of Edx for detection of BPI was 99.32%; however, 74 of the 93 normal roots were erroneously diagnosed as injured which meant that the EDx lacked Specificity. With Edx and MRI in unison, Sensitivity was 100% which meant that if a given patient with a BPI is subjected to both tests, not a single patient's trauma will go unnoticed.

Conclusions: Edx and MRI are two highly Sensitive investigation modalities whose combined Sensitivity is 100% for detection of a brachial plexus injury. Therefore, both should be done as they are excellent Screening Tests. Some weaknesses of our study must be mentioned: 1) The inaccuracy inherent in using surgery as the reference standard (because an intact root may be centrally avulsed and may not get detected on MRI too). 2) Approximately 20% of roots incorporated in the intact category were probably centrally avulsed. This too could have generated fallacies in our analysis.

Positive Impact Of Intraoperative Neurophysiological Monitoring For Lumbosacral Plexus Tumor Surgery

José Fernando Guedes-Correa, Francisco Torrao-Junior, Carlos Alberto De Souza Moreira, Hebert Spener Junqueira, and Rogério Martins Pires Amorim

Neurosurgery Division. Gaffrée e Guinle University Hospital, Federal University of Rio de Janeiro State, Rio de Janeiro, Brazil; neuroguedes@yahoo.com.br

Introduction: Lumbosacral plexus tumors (LSPT) form a group of rare neoplastic lesions with an extremely difficult management, due to the noble structures that can be anatomically related, like bladder, rectum and lumbar spine. They usually present nonspecifically, with vague complaints of abdominal or pelvic pain, constipation, and sciatica. Ultrasound, CT, and MRI are all capable of identifying these tumors. In order to make it easier to completely resect this kind of lesion and minimize the possibility of a persistent neurological deficit at once, the so called Multimodal Intraoperative Neurophysiological Monitoring (MINM) has been employed in some centers, regardless of the fact that evidence in the literature is still scarce and non-systematic.

Methods - Clinical Material: From 2005 to 2017, at the Division of Neurosurgery of Gaffrée e Guinle University Hospital, Federal University of Rio de Janeiro State, a total of 18 patients affected by LPST were surgically treated, but only in the last 6 cases, 4 women and 2 men, with ages from 32 to 49 years old, were we able to employ the MINM. All of our patients were submitted to careful anamnesis and complete physical exam, and then underwent complementary investigations, with magnetic resonance imaging (MRI) of the lumbar spine and pelvis, and electroneuromyography (ENMG) exams. None of them had any syndrome associated with peripheral nerve tumors. Both pre- and post- operatively these patients had their motor function assessed using the MRC (Medical Research Council) scale, their pain evaluated based on VAS (Visual Analogue Scale), their sensation assessed, along with other symptoms checked, all with anamnesis and physical exam. The neurophysiologic parameters analysed were multimodal motor evoked potential (MEP), somatosensory evoked potential (SSEP), and electromyography (EMG) with and without stimuli. The answers were summarized as individualized reports.

Results: No patient developed a motor or sensory deficit in the postoperative period. Actually, one of them showed a preoperative paresis of thigh flexion and leg extension, graded M2, that recovered completely after surgery. The VAS pain assessment, demonstrated that every patient had severe pain, ranging from 6 to 9, and all ameliorated significantly during the post-operative period, with scores from 0 to 2. Only one tumor could not be completely removed, since the hardness of the lesion demanded extensive manipulation, that was affecting electrophysiologic parameters, leading to a decision to perform a partial resection to avoid definitive neurologic damage, though about eighty percent of the tumor could be safely removed. Electrophysiologic responses in patients were similar both in pre- and post- operative analysis.

Conclusions: The neurophysiological monitoring for LSPT was available recently for us, and the real-time information provided during surgery allowed us to have total or near total resection with control of traction and manipulation impact, lessening the degree of impairment of nerve fibers, that culminated with function-sparing surgeries.

Desmoid Fibromatosis In The Brachial Plexus Mimicking An Ulnar Nerve Entrapment

Emelie Styring, Marie Ahlström, Pehr Rissler, Fredrik Mertens, Kasim Abul-Kasim, and **Lars B Dahlin**

Departments of Orthopedics, Oncology, Clinical Genetics and Pathology, Radiology, and Hand Surgery, Lund University and Skåne University Hospital, Malmö, Sweden; lars.dahlin@med.lu.se

Introduction: Ulnar nerve entrapment is a common cause of sensory disturbance and weakness in the upper extremity, especially in patients with diabetes mellitus. Deep-seated soft tissue tumors are rare, but should be considered in the differential diagnosis when the symptomatology is atypical and severe pain is present.

Case Report: A 37-year-old man with type 1 diabetes mellitus was referred from a local GP due increasing pain, numbness and weakness in his right arm corresponding to the ulnar nerve and developing over more than one year. He had been treated for a frozen shoulder on the right side with physiotherapy and several cortisone injections. MR neurography was inconclusive without any signs of a local ulnar nerve compression at elbow level. The patient had also been treated with high doses of opioids due to pain.
At examination, the symptoms and clinical signs did not specifically correspond to an ulnar nerve entrapment. No local Tinel's sign was present along the brachial plexus or the major nerve trunks when other causes than entrapment were considered. An x-ray of the chest revealed a suspected lesion in the apical part of the lung. A CT-scan and a MRI showed an 8 x 4.5 x 5 cm large mass located in right supraclavicular fossa with extension into the thoracic aperture, upper mediastinum, and into the lateral parts of neural foramenae C6-C7 and C7-Th1. On MRI, the mass showed low signal intensity on T1W-images and high signal intensity on T2W-images and exhibited strong homogeneous contrast enhancement. After a non-diagnostic fine needle biopsy, a repeated ultrasound-guided fine and core needle biopsy was made, which showed a desmoid tumor. Due to the severe symptomatology, the diagnosis of a desmoid tumor, and the tumor location, surgery was deemed to be associated with too severe a functional impairment risk. Treatment was initiated with doxorubicin.

Conclusions: Nerve entrapment is a common cause of discomfort and impaired function in the upper extremities. However, if the symptomatology is atypical and particularly when severe pain is present, different etiologies, including various tumors, have to be considered and the diagnostic work-up broadened.

Phrenic To Musculoctaneous Nerve Transfer In Traumatic Brachial Plexus Injury: How Independent Does Elbow Flexion Become From Respiration?

Mariano Socolovsky, Martijn Malessy, Gonzalo Bonilla, Gilda di Masi, Conti María Eugenia, and Lovaglio Ana

Peripheral Nerve & Brachial Plexus Surgery Program, Department of Neurosurgery, University of Buenos Aires School of Medicine, Buenos Aires, Argentina; marianosocolovsky@gmail.com

Introduction: The main objective of the present study was to determine the relationship between breathing movements and elbow flexion in patients with a traumatic brachial plexus injury undergoing a phrenic nerve transfer to restore biceps flexion. More specifically, we studied whether or not biceps strength and the range of elbow flexion differ between full inspiration and expiration, and whether EMG activity of the biceps muscle differs between maximum forced breathing and normal breathing.

Methods: We retrospectively reviewed patients with a severe brachial plexus palsy in which a phrenic nerve (PN) to musculocutaneous nerve (MCN) transfer was performed to restore biceps muscle function. BMRC muscle strength grading system and a dynamometer were used to measure biceps strength. This was measured during a maximal inspiratory effort followed by a measurement during a respiratory repose and after a maximal expiratory effort. In addition, the maximum degree of elbow flexion was obtained for each patient, in the following situations: (1) after a maximal inspiration, (2) during normal breathing, and (3) after maximal expiration. Postoperative EMG testing of the biceps was also performed at the final follow-up visit. The number of MUPs was measured in three different situations: (1) during normal breathing with the arm in rest, (2) during sustained maximal inspiration with the arm in rest, and (3) during maximal voluntary biceps contraction. Triceps EMG testing was also used as a control employing the same protocol. Statistical analysis was performed for the obtained data.

Results: Twenty-one patients fit the inclusion criteria and were deemed eligible for the study. The mean interval from trauma to surgery was 5.5 months. The mean duration of follow-up was 2.6 years. Across the entire sample, mean biceps strength was 0.21 after maximal expiration versus 0.29 upon maximal inspiration, a difference of 0.08 ($t = 4.97$, $p < 0.001$). Similarly, there was almost a 21º difference in maximum elbow flexion, from 88.8º after expiration to 109.5º during maximal inspiration ($t = 5.05$, $p < 0.001$). Mean involuntary elbow flexion movement during normal breathing was almost 20º. With respect to EMG activity, measuring involuntary activity during biceps muscle at rest and EMG activity during biceps muscle contraction, there were statistically-significant direct correlations between readings taken during normal breathing and during deep breathing, which were moderate ($r = 0.66$, $p < 0.001$) and extremely strong ($r = 0.94$, $p < 0.001$), respectively. Also, involuntary activity differed significantly between normal and deep breathing (2.14 vs. 3,14; $t = 4.58$, $p < 0.001$). The degrees of flexion were significantly larger after a follow-up of 2.6 years or less, than if this follow-up was longer. Breathing had a larger effect on biceps contraction in patients with a short time of regeneration after the PN-MCN transfer than with a longer one.

Conclusions: In summary, our results clearly suggest that the impact of breathing on elbow function does wane over time post phrenic nerve transfer for elbow function reconstruction after a brachial plexus injury, and that this waning might impact elbow range of motion more than biceps muscle strength. Brain plasticity occurring after the PN-MCN nerve transfer probably is linked to these changes. Further research is necessary to corroborate these conjectures.

Joint Flexion And Nerve Suture Without Tension: An Old Technique Can be Updated?

Mariano Socolovsky, Danilo Battaglia, Rafael Barousse, and Javier Robla

Peripheral Nerve & Plexus Program, Department of Neurosurgery, University of Buenos Aires School of Medicine, Buenos Aires, Argentina; marianosocolovsky@gmail.com

Introduction: When Delorme described in 1915 three basic principles required for a successful nerve repair: (1) resection of scar until healthy bed is secured, (2) excision of damaged nerve until healthy stumps are reached, and (3) tension-free suture by adequate mobilization of adjacent joints or nerve grafting, his work was heavily criticized. One century after, the history gave reason to all his statements except for one: joint flexion to avoid the use of nerve grafts, still remains controversial.

Methods: In the present paper, we describe a case where ultrasound, MRI neurography and an intense and careful physiotherapy program were employed to determine the progression of the immobilization of a flexed knee joint, in order to avoid damage to a traumatically injured peroneal nerve that was directly suture repaired in a young patient. The results were so good, that the patient started to show clear signs of motor peroneal function recovery less than three months after the surgical repair.

Conclusions: The use of ultrasound and MRI could keep the old joint flexion technique valid at present, in selected lower-limb nerve injured patients.

Targeted Muscle Reinnervation Treats Residual Limb Pain And Phantom Limb Pain In Major Amputees

Gregory A Dumanian, Lauren M Mioton, Jason H Ko, Sumanas W Jordan, J Byers Bowen, Jason M Souza, Benjamin K Potter, Scott M Tintle, George P Nanos, Mickey S Cho, William J Ertl, and Ian L Valerio

Division of Plastic Surgery, Northwestern Feinberg School of Medicine; the Department of Plastic Surgery, Chicago, IL, USA; dumanian1@gmail.com

Introduction: Upper and lower extremity amputees suffer from unpredictable amounts of neuroma-related residual limb pain and phantom limb pain. Despite a myriad of proposed therapies, there are to date no reliable treatment or prevention strategies for these conditions that can profoundly decrease patient function and quality of life. Targeted muscle reinnervation (TMR) is a surgical nerve transfer procedure that reroutes cut nerve endings to redundant motor nerve branches. The surgical procedure was originally designed for intuitive control of myoelectric prostheses, but was used in this study for the treatment and control of amputee-related pain.

Methods: TMR was performed in 33 established amputees for chronic pain as well as concurrently in 40 patients undergoing major limb amputation as a preemptive measure for symptomatic neuromas and phantom limb phenomena. Outcomes were assessed using the Patient Outcomes Measurement Information System (PROMIS) and a Numerical Rating Scale (NRS), and were compared to a cross-section of over 700 untreated amputee controls.

Results: With over one year mean follow-up, patients undergoing TMR at the time of major limb amputation had a dramatic improvement in postoperative residual limb pain and phantom limb pain in comparison to the untreated amputee control group. Established amputees treated with TMR had a modest improvement in their symptoms in comparison to their preoperative state, but not to the level achieved by the acutely treated patients.

Conclusions: Preemptive surgical handling of amputated nerves at the time of limb loss, rather than post-operative medical management, will become the new standard of care for amputee-related pain syndrome.

Regenerative Peripheral Nerve Interfaces for the Treatment of Painful Neuromas

Stephen W P Kemp, Theodore A Kung, Carrie A Kubiak, Jason L Kessler, and Paul S Cederna

Department of Surgery, Section of Plastic Surgery, The University of Michigan, Ann Arbor, MI, USA; swpkemp@med.umich.edu

Introduction: Approximately 185,000 amputations are performed each year in the United States. Symptomatic neuromas occur in approximately 30-40% of individuals after limb loss, and phantom limb pain affects 70-95% of these patients. We have previously shown that Regenerative Peripheral Nerve Interfaces (RPNIs) can be used to treat symptomatic end neuromas that develop after major limb amputation. Here, we will highlight recent clinical and pre-clinical animal studies which have investigated the potential of RPNIs to prevent neuroma formation and to mitigate the experience of phantom limb pain.

Methods: Clinically, RPNIs were performed during the time of amputation by implanting transected peripheral nerves into free muscle grafts harvested from the amputated limb. Patients who underwent major limb amputation with simultaneous prophylactic RPNI implantation were identified. At follow up, all patients were evaluated for symptomatic neuromas, residual limb pain, phantom limb pain, and quality of life measurements. Our rodent studies evaluated: (1) mixed nerve (tibial) neuromas; (2) sensory nerve (sural) neuromas, and; (3) motor nerve (femoral) neuromas. Functional pain outcome measures assessed mechanical allodynia (von Frey test), heat allodynia (Hargreaves test), and cold allodynia (acetone test).

Results: RPNIs were prophylactically implanted in 38 patients who underwent 44 major limb amputations. Zero of the 142 surgical sites (0%) demonstrated any clinical evidence of symptomatic neuroma postoperatively. Fourteen patients (37%) reported symptoms of phantom limb pain, although to a much lesser degree than pre-operatively. Our rodent studies demonstrated that only tibial nerve neuromas displayed mechanical, heat, and cold allodynia.

Conclusions: Prophylactic RPNIs in major limb amputees resulted in a considerably lower incidence of both symptomatic neuromas and phantom limb pain. Furthermore, prophylactic RPNIs did not contribute to increased morbidity compared to standard amputation techniques. Pre-clinical animal work established the tibial neuroma model as the standard for assessing the ability of RPNIs to diminish peripheral neuroma pain and the central mechanisms leading to phantom limb pain.

Acellular Nerve Allografts Prevent Neuroma Formation in Both Rodent and Swine Nerve Transection Models

Amy M Moore, Miles Bichanich, Daniel A Hunter, Xueping Ee, Lauren Schellhardt,Thomas Davis, Scott M Tintle, and Matthew D Wood

Department of Surgery, Washington University School of Medicine, St Louis, MO, USA; mooream@wustl.edu

Introduction: Painful neuromas are a common reason for reoperation after limb amputation. Previous research using acellular nerve allografts (ANAs) has shown an unintentional, controlled termination of axonal regrowth with long graft length. The purpose of this study was to evaluate the effectiveness of using the ANAs to "cap" injured nerves at the time of amputation and dwindle regeneration to prevent neuroma formation.

Methods: Thy1-GFP and Lewis rats were randomized to three groups: 1) nerve transection alone, 2) traction neurectomy, and 3) 5cm ANA attached to the proximal nerve end. The Thy1-GFP rat nerves were serially imaged with fluorescence microscopy for 20 weeks. Lewis rats were sacrificed at 20 weeks for quantitative nerve histology and immunohistochemistry. Quantitative RT-PCR of the dorsal root ganglia (DRG) assessed a panel of pain-associated genes. Twenty Yucatan swine were randomized into two groups: 1) ulnar nerve transection and 2) ulnar nerve transection with the coaptation of a 5 cm ANA. Swine were harvested at 20 weeks at which time quantitative nerve histology and electron microscopy was performed. ANOVA with post hoc analysis were performed to evaluate significance ($p<0.05$).

Results: Aberrant axonal growth was seen in the transection alone and traction neurectomy groups in the rodents and the swine ulnar transection group. Immunohistochemisty and histomorphometric data demonstrated axonal regeneration into the proximal portions of the 5cm ANAs with a gradual distal tapering in the small or large animal models. Gene expression of the rat DRG at 5 weeks demonstrated increased pain-associated genes (BDNF, GAL, VGF and CCK) in the transection and traction neurectomy groups compared to the 5cm ANA group.

Conclusions: Aberrant axonal growth is controlled to termination with 5cm ANA "caps" in both rodent and swine models. Gene expression data in the rodent supports pain mediation, but rodent behavior testing is ongoing to confirm these findings.

Dermal Sensory Interfaces For Providing Feedback To Amputees

Paul S Cederna, Alixandra L VanBelkum, Ian C Sando, Gregory R Gerling, Daniel C Ursu, Yaxi Hu, Elizabeth A Mays, Jana D Moon, Melanie G Urbanchek, and Steve Kemp

University of Michigan, Department of Surgery, Section of Plastic Surgery, Ann Arbor, MI, USA; cederna@med.umich.edu

Introduction: We developed a Dermal Sensory Interface (DSI) with the ultimate goal of providing amputees with meaningful sensory feedback through the residual nerve. Our purpose was to: a) determine predictability of afferent nerve action potentials evoked by electrical stimuli delivered to DSIs; and b) verify that sensory peripheral nerves neurotize DSIs implanted subcutaneously without forming neuromas.

Methods: Rat hind limbs were assigned into one group: a) control full-thickness skin (n=10), b) control de-epithelialized skin (n=10), c) control sural nerve (n=10), and d) DSI (n=10). Each DSI was constructed by surrounding the residual sural (sensory) nerve with an autologous de-epithelialized glabrous skin graft. Following two months' convalescence, patterned electrical stimuli were applied, and evoked responses were recorded at the sural nerve.

Results: All DSIs showed healthy revascularization. Over 96% of pulses delivered to DSIs at 100 A above absolute current threshold elicited graded compound sensory nerve action potentials (CSNAPs) at frequencies ≤100Hz. Three-dimensional microscopy visualized robust reinnervation of DSIs originating from transected sural nerve fibers without formation of neuroma.

Conclusions: Electrical stimuli of varying frequency and amplitude reliably evoke graded sensory nerve feedback from DSIs and sensory fibers regenerate throughout DSI constructs without signs of neuroma.

Nerve Transfers To Address Blindness In Neurotrophic Keratopathy: Clinical Outcomes

Gregory H Borschel, Joseph Catapano, Ronald Zuker, and Asim Ali

The Hospital for Sick Children and University of Toronto, Toronto, Canada; gregory.borschel@sickkids.ca

Introduction: Neurotrophic keratopathy (NK) is caused by loss of sensory innervation to the cornea. Patients with NK are susceptible to occult corneal injury and poor corneal healing, which causes scarring of the cornea and inevitable vision loss. Surgical reinnervation of the cornea using sensory nerve transfers restores corneal sensation, prevents vision loss in patients with NK, and enables cornea transplant.

Methods: In this single-center prospective cohort study, we included patients with advanced neurotrophic keratopathy. Pre- and post- operatively we measured corneal sensation, best spectacle corrected visual acuity (BSCVA), and metrics of ocular surface health. Immunohistochemistry and magnetoencephalography (MEG) were used to document corneal reinnervation.

Results: Sixteen patients (19 eyes) with NK underwent surgical reinnervation of the cornea. Median central corneal sensation improved from 0 mm pre-operatively (range, 0 to 10) to 60 mm (range, 0 to 60) post-operatively ($p < 0.001$). With a mean follow-up of 24 months (range, 6 – 53), vision was either stable or improved in 16 eyes. Vision further improved in five eyes that underwent successful corneal transplantation after corneal neurotization to correct preexisting corneal scarring. Corneal reinnervation after surgery was confirmed with immunohistochemical analysis of explanted corneal tissue and magnetoencephalography (MEG), which demonstrated the regions of the somatosensory cortex responsible for establishment of corneal sensation postoperatively.

Conclusions: Sensory nerve transfers restore corneal sensation, improve ocular surface health, and preserves vision in patients with NK. Early nerve transfer may change the treatment paradigm for these patients by restoring corneal innervation and preventing the complications of NK.

The Intercostobrachial Nerve As A Sensory Donor For Hand Reinnervation In Brachial Plexus Reconstruction

Mario Siqueira, Luciano Foroni, Roberto Martins, and Adriana Imamura

Peripheral Nerve Surgery Unit, Department of Neurosurgery, University of São Paulo Medical School, São Paulo, Brazil; mario.siqueira@hc.fm.usp.br

Introduction: Sensory reinnervation of the hand should always be one of the priorities in the management of severe traumatic brachial plexus injuries. We evaluated the anatomical feasibility of using the intercostobrachial nerve (ICBN) as a sensory donor for the sensory restoration of the hand and its functional outcome in traumatic severe brachial plexus injuries cases.

Methods:
Anatomic study – The ICBN was dissected in the lateral chest of 30 non-fixed cadavers, sectioned distally, and reflected towards the infraclavicular space. The lateral contribution to the median nerve (LCMN) was isolated and divided at its origin in the lateral cord and turned down towards the axilla for coaptation with the ICBN.
Clinical study – Eleven patients with mean age of 25 years old were submitted to the proposed transfer an average of 6.7 months after the injury to the brachial plexus. The patients were followed postoperatively for at least 36 months.

Results:
Anatomic study – The ICBN was present and had enough extension for a direct coaptation with the LCMN in all cadavers. The mean diameter of the ICBN at its origin and at the point of coaptation was 2.08 ± 0.67 mm and 2.74 ± 0.87 mm, respectively. The mean diameter of the LCMN was 3.69 ± 1.07 mm. The mean number of fibers in the ICBN was 984 ± 517 and 5273 ± 1134 in the LCMN.
Clinical study – Ten patients received at least the 4-red filament at the territory of the median nerve. Six patients felt sensation only in the cutaneous distribution of the median nerve, one patient had double sensation in the cutaneous distribution of both median and intercostobrachial nerves. and three patients referred sensitivity only in IBCN territory. Vibration was perceived in seven patients. Ten had perception of both warmth and cold. None of the patients had two-point discrimination. One patient experienced no sensory recovery at all.

Conclusions: Sensory hand reinnervation is possible with ICBN transfer and should be included in the surgical strategy for the treatment of complete brachial plexus injuries.

Successful Control of Virtual and Robotic Hands using Neuroprosthetic Signals From Regenerative Peripheral Nerve Interfaces in Humans

Paul S Cederna, Philip P Vu, Zachary T Irwin, Ian C Sando, Philip T Henning, Theodore A Kung, Melanie G Urbanchek, Cynthia A Chestek, and Steve Kemp

Section of Plastic Surgery and Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI, USA; cederna@med.umich.edu

Introduction: Regenerative Peripheral Nerve Interfaces (RPNIs) show promise in controlling neuroprosthetic devices. We have implanted and recorded from RPNIs in 3 subjects. Here, we present the results from our longest implanted subject with a distal transradial amputation.

Methods: An RPNI consists of a muscle graft that is neurotized by the distal end of a transected peripheral nerve. Once revasularized and reinnervated, the RPNI muscle graft serves as a stable bioelectric amplifier for efferent nerve action potentials and produces recordable electromyography (EMG) signals. The subject was implanted with RPNIs on the residual median, ulnar, and dorsal radial nerves. Using ultrasound, RPNIs were located, and percutaneous fine-wire bipolar electrodes were inserted for acute EMG recordings. Temporal features of the EMG waveforms (100-500Hz) were used for decoding algorithms.

Results: Eight months post-surgery, we recorded 300-400μV EMG signals from the median RPNI with signal-to-noise ratio (SNR) of 24.2 and 100-120μV EMG signal from the ulnar RPNI with SNR of 5.84. Additionally, EMG from residual muscles was obtained including the flexor digitorum superficialis with 100-120μV signals, SNR of 6.30, and flexor pollicis longus with ~1mV signals, SNR of 47.8. With these signals, the subject controlled a virtual robotic hand in real time with 96% accuracy, choosing 1 of 4 movements within 212 trials. Importantly, the subject controlled a physical Touch Bionics iLimb neuroprosthetic hand with 100% accuracy, choosing 1 of 3 movements within 100 trials.

Conclusions: RPNIs harness neural signals from transected peripheral nerves with sufficient amplitude and fidelity to control an advanced neuroprosthetic limb.

Quantifying Real-World, Patient-Initiated Arm Movement Following Nerve Reconstruction for Upper Brachial Plexus Injury

Susan H Brown, S J Saake, B W Smith, K W C Chang, K C Chung, and L J-S Yang

School of Kinesiology, University of Michigan, Ann Arbor, MI, USA; shcb@umich.edu

Introduction: Clinical assessment of function following nerve reconstruction for brachial plexus injury is based on clinician-elicited measures including muscle strength, active range of motion (ROM), and subjective feedback regarding perception of surgical outcomes such as the Disabilities of the Arm, Shoulder and Hand (DASH) instrument. However, to what extent current outcome measures capture actual arm use in everyday activities is unknown. Recent advances in body-worn sensor technology now make it possible to objectively quantify movement in remote settings. This pilot study focused on the application of accelerometry-based activity monitors to quantify arm use in patients following reconstructive surgery.

Methods: Clinical assessment of arm function (AROM, DASH) was performed in a clinic setting on five adults with upper brachial plexopathy (mean age 41 +/- 17 y). Patients then wore three-dimensional accelerometers (GT9X Link ActiGraph) on each wrist during waking hours for seven consecutive days. Commercial software was used to quantify arm acceleration magnitude that was then expressed as a ratio of affected to unaffected arm use.

Results: The mean acceleration magnitude ratio was 0.63 compared to typical control values of approximately 1.0. Magnitude values were positively correlated with both shoulder flexion ($p=0.02$) and abduction ($p=0.01$) AROM. In contrast, no correlation between magnitude and either elbow flexion or forearm supination was observed. Patient-reported perceptions of function based on DASH scores were not significantly correlated with arm use ($p=0.06$).

Conclusions: The results presented here demonstrate the value of accelerometry to objectively evaluate patient-initiated arm use in naturalistic settings, thereby overcoming some of the limitations associated with current evaluation methods.

Nerve Transfer and Nerve Graft Repair Yield Similar Functional Shoulder Outcomes in Neonatal Brachial Plexus Palsy

Lynda J-S Yang, Lynnette Rasmussen, Kate WC Chang, Denise Justice

Department of Neurological Surgery, University of Michigan, Ann Arbor, MI, USA;
ljsyang@med.umich.edu

Introduction: The use of nerve transfers versus nerve grafting for neonatal brachial plexus palsy (NBPP) has shown some encouraging results but remains controversial. In adult brachial plexus injury, nerve transfer for recovery of shoulder function yields similar functional outcomes as nerve graft repair. In NBPP, little evidence exists comparing outcomes of shoulder function after nerve transfer versus nerve grafting. Therefore, we compared 1-year post-operative outcomes for infants with NBPP who underwent nerve transfer versus nerve graft repair.

Methods: This retrospective cohort study reviewed patients with NBPP who underwent nerve transfer for shoulder function, spinal accessory nerve to suprascapular and radial nerve branch to axillary nerve (N=19) and nerve graft repair (N=26) at a single institution from 2005-2015. A single surgeon conducted intraoperative exploration of the brachial plexus and determined the surgical nerve reconstruction strategy undertaken. Active range of motion were evaluated pre- and post-operatively at 1-year.

Results: No significant difference between treatment groups was observed with respect to the mean change (pre- to post-operatively) in shoulder flexion and abduction (P>02). Shoulder exorotation demonstrated a trend in favor of nerve transfer (P=0.07). Demographic data, including age at operation, gender, race, side of NBPP, Narakas grade, lesion type/site, and atrophy of rhomboid were not significantly different between the nerve transfer and nerve graft repair groups.

Conclusions: Our preliminary data demonstrate that nerve transfer and nerve graft repair yield similar outcomes with regard to shoulder function. However, a slight advantage in exorotation may result after nerve transfer. Further studies that monitor real-world arm usage will provide more insight into the most appropriate surgical strategy for NBPP.

Primary Shoulder Surgery As A Possible Complete Treatment For Obstetrical Brachial Plexus Injury

Leahthan Domeshek, Kristen Davidge, Karen Klar, Alison Anthony, Sevan Hopyan, and **Howard Clarke**

Division of Plastic and Reconstructive Surgery, Division of Orthopaedic Surgery, and the Department of Rehabilitation Medicine, Hospital for Sick Children and the Department of Surgery, University of Toronto, Toronto, Canada; howard.clarke@utoronto.ca

Introduction: Treatment algorithms for the management of obstetrical brachial plexus palsy continue to evolve to deal with heterogeneous and complex lesions. Recently, we have undertaken secondary shoulder reconstruction within the first year of life as the complete treatment for the brachial plexus injury in a highly selected subset of this patient population.

Methods: Between 2015 and 2017 (out of 190 new patients seen), ten patients with obstetrical brachial plexus palsy were identified within the first year of life as having clinically apparent posterior subluxation of the glenohumeral joint on internal roation producing a mechanical limitation to elbow flexion where the forearm movement was blocked by impact with the torso. These patients underwent early shoulder reconstruction involving a subscapularis slide, teres major tendon transfer, and latissimus dorsi tendon transfer. In one patient, a more complex reconstruction was required.

Results: Results are reported for eight patients (one patient had insufficient follow-up and one family refused research consent). Four patients underwent shoulder surgery before the nine month cookie test (mean age at surgery 7.2 months) and four patients had shoulder surgery following a failed cookie test (mean age at surgery 10.1 months). Seven patients went on to pass the cookie test and avoid primary nerve reconstruction based on our published treatment algorithm. One patient continued to demonstrate poor elbow flexion and underwent a selective nerve transfer at 11.7 months of age producing successful restoration of elbow flexion.

Conclusions: Early shoulder subluxation in patients with obstetrical brachial plexus palsy may mask adequate neural recovery. In highly selected patients, early intervention at the level of the shoulder joint may obviate the need for primary nerve reconstruction. Clearly, further data will be required in order to better define this patient cohort and to follow these results over time.

Knowledge of Neonatal Brachial Plexus Palsy Among Medical Professionals in North America

John McGillicuddy, Alecia Daunter, and Kate Chang

The University of Michigan, Ann Arbor, MI, USA; jemc@med.umich.edu

Introduction: Neonatal brachial plexus palsy (NBPP) affects about 1 in 4 live births. Early referral of NBPP to an interdisciplinary clinic can provide timely diagnosis and treatment to infants with NBPP and can optimize recovery. A previous study from Saudi Arabia shows inadequate knowledge of NBPP among medical professionals is likely the reason for delayed referral.[1] We aim to compare the knowledge of NBPP among providers in North America with published Saudi Arabian data. In addition, we wished to compare the NBPP knowledge of pediatricians and general/family medicine providers versus other specialties in North America.

Methods: A modified 12 question survey regarding NBPP knowledge, diagnosis, and referral (6 multiple-choice from the Saudi Arabian study and 6 true-false questions of ours) was distributed in our hospital and via Qualtrics. Participants included providers from pediatrics, general medicine, neurology, neurosurgery, physiatry, plastic surgery, orthopedics, obstetrics, and physical/occupational therapy. Chi-square was applied for comparisons.

Results: Of 257 surveys collected so far, 40% were from pediatricians/general medicine and 60% from other specialties. Comparing only the first six questions, Saudi Arabian and North American providers reported similar NBPP knowledge except for the types of palsy and the timing of referrals. Saudi Arabian providers chose later referrals for both PT/OT and for nerve surgery (p-value<0.0001). We evaluated North American data using all 12 questions. There was little difference in the accuracy of the answers to each question between the two groups. We categorized North American data into three categories of NBPP knowledge (good: 9-12 correct answers; adequate: 6-8 correct; inadequate: 1-5 correct). Eighty-seven percent of North American providers showed good to adequate knowledge. Nevertheless, over 80% wrongly believed that 90% of NBPP babies recover normal movement. Pediatricians tended to refer earlier but did not recognize Horner's syndrome or lack of finger flexion at one month as signs of severe NBPP.

Conclusions: Overall North American providers demonstrated adequate knowledge about NBPP but remain overly optimistic about spontaneous recovery. Up to 40% of infants fail to achieve full functional recovery. Thus, continuous efforts to increase NBPP knowledge are indicated.

Reference: El-Essa RS, Al-Khilaiwi RM, et al. Obstetric Brachial Plexus Injury. Knowledge among health care providers in Saudi Arabia. Saudi Med J 2017 Jul; 38(7)721-726.

Temporally Controlled GDNF Gene Therapy Promotes Regeneration Of Motor Axons In Spinal Ventral Root Repair

Ruben Eggers, Fred de Winter, Stefan A. Hoyng, Martijn J.A. Malessy, Martijn R. Tannemaat, and **Joost Verhaagen**

Netherlands Institute for Neuroscience, Amsterdam, the Netherlands; j.verhaagen@nin.knaw.nl

Introduction: Glial cell line-derived growth factor (GDNF) promotes motor neuron survival and axon regeneration. Gene therapy for GDNF has shown promise as a strategy to promote repair following ventral root avulsion and reimplantation. Here we test whether temporally controlled expression of GDNF in reimplanted ventral roots promotes motor neuron survival, long-distance axon regeneration, and functional recovery.

Methods: Rat ventral roots (L3-L6) were avulsed, injected with the appropriate lentiviral vector, and reimplanted in the spinal cord. A doxycycline (dox)-inducible lentiviral vector-based "stealth" gene switch was used to direct GDNF expression. Four groups of 15 rats were used. Group 1: control group, the ventral roots were avulsed and not reimplanteded. Group 2: control group, the roots were avulsed, injected with a lentiviral vector encoding GFP and reimplanted. Group 3: avulsed and reimplanted roots were injected with the lentiviral vector-based gene switch encoding GDNF treated with dox for 4 weeks. Group 4: same as group 3 but treated with dox for 24 weeks. Regeneration was evaluated by histology and electrophysiology.

Results: Motor neuron survival was increased in both GDNF treatment groups. Persistent GDNF expression (24 weeks) results in misdirected fiber growth in the ventral root. In contrast, in the 4 week GDNF treatment group, large numbers of axons in the ventral root display a longitudinally organized growth pattern, whereas the roots are less enlarged compared to the 24 weeks group. Compound muscle action potentials revealed that 4 weeks of GDNF speeded up recovery by 6 to 8 weeks compared to the GFP control and 24 weeks of GDNF treatment group.

Conclusions: Temporally controlled delivery of GDNF to avulsed reimplanted ventral roots exerts a beneficial effect on axon regeneration.

Large-Gap Peripheral Nerve Repair Using Amniotic Fluid Derived Stem Cells Seeded Acellular Nerve Allografts

Xue Ma, Alejandro Jose Marquez-Lara, Tianyi David Luo, Eileen Martin, Thomas L Smith, and **Zhongyu Li**

Department of Orthopaedics, Wake Forest School of Medicine, Winston-Salem, NC, USA; zli@wakehealth.edu

Introduction: Lack of Schwann cells and permissive environment is a major concern for the usage of acellular nerve allograft (ANA). We hypothesized that ANAs can be seeded with amniotic fluid-derived stem cells (AFS) to promote and accelerate nerve regeneration.

Methods: A 15mm sciatic nerve gap was created surgically on Lewis rats (12 per group), the nerve gap was repaired immediately with ANA alone (Group 1), ANA seeded with micron sized iron oxide labeled AFS cells (Group 2), or autograft (Group 3). Walking track analysis and Electromyography were performed 4 months post- injury. The fate of AFS cells was tracked by MRI longitudinally for 4 weeks and by Prussian blue staining over times. Axon count and nerve morphology were documented. Analysis of neuromuscular junction (NMJ) was determined using immunohistochemistry.

Results: DAPI staining on longitudinal and cross sections of ANAs showed AFS cells spread evenly through the nerve fibers. Comparing to Group 1, Group 2 has significantly better recoveries in gait analysis ($P<0.05$), gastrocnemius CAMP ratio, axon diameter, myelin thickness, G-ratio and NMJ numbers ($P<0.01$ in all indices). There was no significant difference in motor recovery between Groups 2 and 3. MRI demonstrated the viability of AFS cells which appeared as fuzzy dark spots 4 weeks post-surgery. Iron staining further confirmed the localization of the AFS cells within the ANA.

Conclusions: 1) AFS cells can be seeded directly into ANA and remain viable *in vivo*. 2) Functional and histological outcomes after nerve repair with ANA are significantly improved after seeding with AFS cells and are comparable to the results after nerve autograft. Thus, AFS cells may be a suitable cell source to support and accelerate peripheral nerve regeneration following large gap nerve injury.

A Neuroscientist's Trek Along The Road To Functional Recovery After Nerve Injuries

Tessa Gordon

Department of Surgery, The Hospital for Sick Children, Toronto, Ontario, Canada;
tessat.gordon@gmail.com

Introduction: It is well known that Schwann cells in the peripheral nervous system support nerve regeneration after injury in contrast to the inability of the oligodendrocytes in the central nervous system to do so. Yet, it is also well recognized by clinicians but not by neuroscientists in general, that functional recovery is often poor after peripheral nerve injuries despite nerve repair. My interest in this problem dates back to the 1970's and continues to this day.

Methods: In animal models, including rats and cats, we studied the process of nerve regeneration, target reinnervation and functional recovery with chronic and acute recordings. In addition, we use retrograde tracing of neurons whose nerves have regenerated and *in situ* hybridization, RT-PCR, and immunohistochemical methods to document changes in gene expression. In rats, we either chronically axotomized lumbosacral motoneurons, chronically denervated Schwann cells, or chronically denervated target muscles to explore their role in time/distance in the success/failure of nerve regeneration. Also in rats, we examined the time course of femoral nerve regeneration and the effects of brief electrical stimulation, using retrograde tracing. We also explored the efficacy of exogenous neurotrophic factors and FK506 on nerve regeneration. We extended the study of brief low frequency electrical stimulation to explore its efficacy in promoting nerve regeneration after delayed nerve repair of hindlimb nerves, using a cross-suture approach. We extended this study to human subjects, using motor unit number estimation (MUNE) to document severe loss of motor units in chronic carpal tunnel syndrome prior to release surgery and monitoring of MUNE for a year following release surgery.

Results: We documented incomplete recovery of function after hindlimb nerve injuries, using chronic and acute recordings in cats. In rats, chronic axotomy of motor and sensory nerve reduced regenerative capacity with concomitant decline in expression of regeneration associated genes. Chronic Schwann cell denervation led to progressive atrophy and loss with progressive decline in regeneration through chronically denervated nerve stumps. Nonetheless, remaining Schwann cells retain capacity to support nerve growth. Chronic target denervation is *not* the limiting factor in poor recovery after chronic nerve injuries, remaining nerves making functional contacts with muscle and, in turn, resulting in muscle contraction. FK506 and exogenous neurotrophic factors, including low dose brain and glial derived neurotrophic factors, are effective in promoting nerve regeneration after chronic nerve injury as well as through acellular nerve allografts. However, upregulation of endogenous growth factors after brief electrical stimulation is effective in promoting axon outgrowth and accelerating target reinnervation in rats, both after immediate and delayed nerve repair. The same brief electrical stimulation regime is effective in promoting the reinnervation of the muscles of the median eminence by *all* the regenerating median nerves after carpal tunnel release surgery. In contrast, the reinnervation of the muscles a year after release surgery without the 1 hour 20 Hz stimulation at the time of surgery was insignificant.

Conclusions: A journey yielding promising outcomes of peripheral nerve surgery has been well worth taking with respect to both the outcomes and my personal enjoyment of an important area of research into the problems of peripheral nerve injuries.

Mouse Rapid-Stretch Nerve Injury Model: Severity Can Be Defined Biomechanically

Mark A Mahan, Wesley Warner, and Stewart Yeoh

Department of Neurosurgery, Clinical Neurosciences Center, University of Utah, Salt Lake City, Utah, USA; mark.mahan@hsc.utah.edu

Objective: 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. We sought to assess the regenerative capacity of nerves subjected to rapid-stretch injuries.

Methods: The sciatic nerves of 94 Thy-1-YFP transgenic mice were dissected and subjected to rapid-stretch injury methods. Rapid-stretch injury involved fixed direction strain produced via constrained weight drop applied to an intact nerve. Four injury severity levels were produced with rapid-stretch: sham, elastic (stretch with return to pre-existing length), plastic (persistent length change) and rupture. Animals underwent behavioral testing with Von Frey fibers, tapered-beam, paw-print analysis serially for 48 days and then were euthanized. Nerve histology, wet muscle weight, and muscle histology was performed.

Results: Decline in functional performance testing mirrored injury severity. In sciatic function index testing, sham animals demonstrated no change in performance; animals with an elastic-stretched nerve demonstrated modest functional deficits and returned to baseline by 15 days; animals with a plastic-stretched nerve demonstrated severe deficits and did not return to baseline at 48 days; animals with a ruptured nerve demonstrated the most severe functional deficits. All animals demonstrated deficits with tapered beam testing, but also improved performance over time. Wet muscle weight demonstrated profound decreases in both ipsilateral and contralateral triceps surae and tibialis anterior in both plastic and ruptured conditions. Nerve histology demonstrated infrequent neuroma-in-continuity in only plastic-stretched nerves; ruptured nerves all produced in-continuity stump neuromas – axons did not migrate across the injured zone. Elastic-stretched nerves demonstrated mild evidence of reorganization. Osmium staining demonstrated severe reduction in fiber counts that reflected nerve injury severity.

Conclusions: Rapid-stretch injuries to nerve in a rodent model appear to reproduce similar patterns of regeneration as human injuries, particularly similar to the pattern of recovery seen in birth brachial plexus palsy. Functional deficit severity and the likelihood for recovery was defined by the biomechanical strain applied during rapid-stretch. Neuroma-in-continuity could be clearly defined, but variably produced in a mouse model.

Visualization of Human Posterior Interosseous Nerves In Healthy Subjects And In Patients With Type 1 and 2 Diabetes By X-ray Phase Contrast Zoom Tomography

Lars B Dahlin, K R Rix, V A Dahl, A B Dahl, J Nørtoft Jensen, P Cloetens, A Pacureanu, S Mosheni S, N Thomsen, and M Bech

Department of Translational Medicine – Hand Surgery, Lund University, Sweden. Department of Hand Surgery, Skåne University Hospital, Malmö, Sweden; lars.dahlin@med.lu.se

Introduction: Light and electron microscopy allow two-dimensional visualization of peripheral nerves. We hypothesized that synchrotron imaging techniques obtain better morphological information and provides detailed three-dimensional (3D) images of peripheral nerves in healthy subjects and in subjects with type 1 and 2 diabetes.

Methods: Biopsies of the posterior interosseous nerve at wrist level, taken from patients with carpal tunnel syndrome in conjunction with carpal tunnel release from otherwise healthy subjects and from subjects with type 1 and 2 diabetes, were prepared for morphological analyses. One biopsy from each patient category (i.e. healthy subject, subject with type 1 or type 2 diabetes) was investigated with x-ray phase contrast zoom tomography at the European Synchrotron Research Facility (ESRF, Grenoble, France) at the ID16-NI beamline. Each sample was scanned at four different sample to detector distances, using the so-called zoom tomography imaging mode, allowing us to obtain soft tissue contrast with an isotropic voxel size of 130 nm.

Results: Subcomponents of the nerve (e.g. myelinated nerve fibers, myelin sheaths, axons, nodes of Ranvier, Schmidt-Lanterman incisures and blood vessels) as well as fewer myelinated nerve fibers in type 1 diabetes, could be visualized, simultaneously in transverse and longitudinal sections, from tomograms of the biopsies. Segmentation of data revealed the 3D structure of healthy myelinated nerve fibers with 3D visualization of the nodes of Ranvier. Furthermore, subcomponents, as regenerative clusters of regenerated nerve fibers as well as altered blood vessels, could be shown with this technique in type 1 diabetes.

Conclusions: Using synchrotron technique with x-ray phase contrast zoom tomography, detailed 3D structure of peripheral nerves can be visualized in human posterior interosseous nerve biopsies from healthy and diabetic subjects. This technique provides novel insights into diabetic neuropathy; a relevant factor for determining outcome of surgery in diabetics with carpal tunnel syndrome.

A Clinical Retrograde Study of the Effectiveness and Safety Of Thread Carpal Tunnel Release (TCTR)

Danzhu Guo, Danqing Guo, Rachel Lytie, and Steven Schmidt

Baycare Clinic, Green Bay, WI, USA; danzhuguo@gmail.com

Introduction: Thread Carpal Tunnel Release (TCTR) has been studied previously with cadavers and in the clinic at a small scale. The aim of this study is to evaluate the safety and efficacy of this technique for longer term and at a larger scale.

Methods: TCTR was performed on 532 hands since June 23, 2015. The diagnosis of CTS was based on clinical symptoms and findings supported by EMG/NCS testing, sonographic study of cross sectional area, and diagnostic carpal tunnel steroid injections. All patients either failed conservative management or requested a surgical release. All patients that had a steroid injection during the procedure were excluded from this study. The Boston Carpal Tunnel Syndrome Questionnaire was used to assess the outcomes, with patients following up at 1 week, 2 weeks, 1 month, 3 months, 1 year and 2 years. 190 patients have been followed for more than 1 year and 54 patients have now been followed for more than 2 years. Statistical analysis was used to compare the outcomes with available data from open and endoscopic techniques.

Results: One patient, with a history of a work-related injury and s/p C5-6 and C6-7 spinal fusion and posterior decompression, had no significant relief after TCTR with 6 month follow up. One patient had returning numbness and tingling affecting the surgical arm and hand two years after TCTR. She was diagnosed with C4-5 HNP and underwent surgery. One patient had TCTR done outside our facility with increased symptoms. This patient had an incomplete release and underwent a redo TCTR by us with significant symptom relief. Five patients developed wrist pain at the palm area 4-6 weeks post TCTR due to overuse of the hand; however, symptoms were relieved after conservative management. All other patients had significant relief of symptoms 3-5 hours post procedure. Outcomes were better at short-term and long-term time points when compared with open and endoscopic releases. Patients reported sleep quality was improved on the day of surgery. Most patients with office jobs could return to work on post-operative day one. Patients with repetitive jobs returned to work in about 1-2 weeks. There were no neurovascular complications in any case. There have been no recurrent cases.

Conclusions: Our results suggest that TCTR is a reliable alternative treatment for carpal tunnel syndrome with a high success rate. The TCTR procedure has been shown to be a safe and effective technique for carpal tunnel release if performed by surgeons who are familiar with ultrasonic hand anatomy and anatomic relationships within the carpal tunnel combined with experience in manipulating a needle under ultrasound guidance.

A Cadaveric Study of Thread Cubital Tunnel Release

Danqing Guo, Danzhu Guo, Logan McCool, Alex Senk, Brionn Tonkin, and Michel Kliot

Pain & Rehab Medicine, BayCare Clinic, Green Bay, WI, USA; danqingg@gmail.com

Introduction: The ultrasminimally invasive ultrasound guided thread cutting technique has been successfully applied for thread carpal tunnel release and thread trigger finger release. This cadaveric study was designed to test othe surgical feasibility of performing a cubital tunnel release of the ulnar nerve across the elbow using the same ultraminimally invasive technique. In addition, we wanted to verify adequate decompression of the ulnar nerve could be performed percutaneous complete with minimal or no collateral damage to important adjacent structures such as the sensory branch of the medial antebrachial cutaneous nerve.

Methods: 19 unembalmed fresh frozen and then thawed cadaveric upper extremities including shoulders were used to perform thread cubital tunnel release (TCuTR) across the elbow. The procedure involved two separate steps. First, the portion of the nerve just proximal to the medial epincondyle and extending at least 8 cm distally within the flexor-pronator muscle mass was decompressed using an 18 gauge 6 inch long Thuy needle which then served as a conduit for passing the thin metal cutting wire with care taken to preserve the sensory nerve by creating a plane between the nerve and underlying muscle fascia. Second, the ulnar nerve at least 8 cm proximal to the medial epicondyle was decompressed. Hydrodissection was performed as necessary to separate adhesions between the ulnar nerve and surrounding soft tissues. The whole process was performed under real-time ultrasound guidance. All elbows were then immediately dissected so as to carefully free the skin away from the underlying tissues permitting us to directly visually inspect and evaluate the extent of ulnar nerve decompression as well as any damage to surrounding tissues.

Results: The cubital tunnel and deep fasciae 8 cm proximal and distal to the medial epicondyle were completely cut in all cases. The ulnar nerve appeared to be completely and adequately decompressed in all cases as well. There was no obvious collateral damage to important structures such as the ulnar nerve and distal medial forearm branch of the medial antebrachial cutaneous nerve.

Conclusions: This cadaveric study demonstrated the feasibility of employing the ultraminimally invasive ultrasound guided thread cutting technique, successfully employed to decompress the median nerve in the Carpal Tunnel, to decompress the ulnar across the elbow adequately and with minimal collateral damage to the ulnar nerve an surrounding tissues. Additional preclinical and clinical studies are necessary to demonstrate the clinical feasibility, applicability, and effectiveness of this new procedure in patients with ulnar nerve entrapment across the elbow.

Transposition of the Lateral Femoral Cutaneous Nerve

Amgad S Hanna

University of Wisconsin, Madison, WI, USA; hanna@neurosurgery.wisc.edu

Introduction: Meralgia paresthetica causes pain, in the anterolateral thigh, associated with dysesthesia and decreased sensation in the lateral femoral cutaneous nerve (LFCN) territory. Surgery is offered when conservative measures fail. Simple decompression is associated with a high failure rate. Neurectomy leaves the patient with an area of loss of sensation in the thigh. A new technique of LFCN transposition is described. Anatomical feasibility and early case
series are presented.

Methods: Three embalmed cadavers had the LFCN dissected in the upper thigh and retroperitoneum. The LFCN canal was opened and the nerve mobilized medially. Nineteen cases of meralgia paresthetica were surgically treated between 2011 and 2016. We had 3 groups: simple decompression, deep decompression, and transposition.

Results: In all cadavers, it was possible to mobilize the LFCN medially for about 2 cm. Four patients underwent simple decompression, 5 deep decompression, and 10 transposition. The average preoperative Numerical Rating System (NRS: 0 no pain and 10 most severe pain) for superficial decompression was 7; 3.2 at 3 months postoperatively, and 1 at 1 year ($p = 0.0867$). The average preoperative NRS for deep decompression was 6.4; 1.6 at 3 months postoperatively, and 2.2 at 1 year ($p = 0.0148$). The average preoperative NRS for transposition was 6.5, 3 months postoperatively 1.5, and 1 year 1 ($p < 0.0001$). When comparing the reduction in NRS between the three groups, the results were not statistically significant. In the superficial decompression group, 2 patients underwent reoperation for nerve transection. In the deep decompression group, one patient was reoperated for an infected hematoma. In the transposition group, no patient underwent reoperation ($p = 0.0454$).

Conclusions: In most cases of meralgia paresthetica, the LFCN is too close to the ASIS which probably accounts for most recurrences. The nerve needs to be mobilized medially. Transection should not be the primary treatment, but saved for recurrences.

Changes In Electromyographic Patterns And Global Masticatory Force After Masseter Nerve Transfer In Patients With Unilateral Facial Paralysis

Alexander Cardenas-Mejia, Alejandro Orihuela-Rodriguez, Adriana de Lourdes Rivera-Priego, Fernando Angeles-Medina, Julio Morales-Gonzalez, Jose E Telich-Tarriba, Ignacio Mora-Magaña

Division of Plastic and Reconstructive Surgery, Hospital General "Dr. Manuel Gea Gonzalez", Mexico city, Mexico; alexcardenas@hotmail.com

Introduction: The masseter nerve has become a standard source of innervation in patients with facial paralysis due to its limited donor site morbidity, ease of identification and proximity to the facial nerve. However, despite its widespread use, few studies have described the functional impact this nerve transfer might have on masticatory function. The objective of this work is to evaluate the changes masseter nerve transfer has on electromyographic activity of the masseter muscle and on masticatory force.

Methods: This is a prospective study including 15 patients with unilateral facial paralysis (mean age 24.06 years). Maximum masticatory force (MMF) was evaluated with a computerized occlusal analyzer; electrical activity of the masseter muscle was evaluated with surface electromyography during Maximum Intercuspation (MIC) and No Denture Contact (NDC). All patients were evaluated prior to the surgical procedure and three months after the nerve transfer was performed. Clinical characteristics are presented as means or percentages; comparisons between means were made using the T-test.

Results: Mean basal MMF in kgF on the paralysed side was 22.67 (SD 16.69) and decreased to 15.56 (SD 7.91) after nerve transfer; these results did not show statistical significance. Electromyographic activity (expressed as root mean square, RMS) during MIC was 140.86 (SD 65.94) preoperatively and decreased to 109.68 (SD 68.04) after the nerve transfer ($p = 0.017$; during NDC basal value was 123.68 (SD 75.64), and was reduced to 82.64 (SD 66.56) after the procedure ($p = 0.02$).

Conclusions: The masseter muscle has decreased electrical activity after a masseter nerve transfer is performed, however global masticatory function remains unaltered. The masseter nerve remains an effective donor nerve in patients with facial paralysis, with minimal donor-site functional impact.

Facial Reanimation In The 7th and 8th Decades Of Life

Alexander Cardenas-Mejia, Bridget Harrison, Daniel Labbe, Chalil Chamseddin, Austin Hemd, and Shai Rozen

Plastic and Reconstructive Surgery Division, Hospital General "Dr. Manuel Gea González" and Postgraduate Division of the Medical School, Universidad Nacional Autonoma de Mexico, Mexico City, Mexico; alexcardenas@hotmail.com

Introduction: Dynamic reanimation is the optimal goal in patients with facial palsy. Achieving symmetry, synchronicity, and spontaneity is the ideal, but not always consistently obtainable in every patient or population. Select populations are often excluded from the option of dynamic reanimation. One such group is older patients usually in their 7th and 8th decade of life. Since facial reanimation is often not offered to the older population, and detailed literature is scarce in this age group, we present the combined experience from three facial palsy centers

Methods: Between the years, 1997 to 2015 a total of 30 patients over the age of 60 y/o from 3 centers were included in the study. Twelve patients were treated with LTM, fourteen patients were treated with a FFMT innervated by the masseter nerve, and four patients by direct nerve transfer. All patients were evaluated for demographics, etiology, time-interval from palsy to surgery, pre-operative grading, time interval to achieve motion, previous surgeries, and complications. Pre-and post- operative measurements were performed with the MEEI-FACE gram system in both repose and animation.

Results: This series includes 30 patients over the age of sixty y/o, consisting of 10 males and 21 females with an average age of 64.7 years (Range 53-86) for the entire group consisting of 64 years in the LTM group, 64 years in the FFMT group, and 65 years in the nerve transfer group. The LTM group included 12 patients, the FFMT group included 14, and the NT group consisted of 5 patients. Average follow up was 48 months in the regional muscle transfer group, 34 months in the FMT group, and 30 months in the nerve transfer group. The average pre-op HB score was 5.6 in the LTM group, 4.9 in the FMT group, and 5 in the NT group. The mean duration of paralysis prior to reanimation was 181 months in the LTM group, 74 months in the FFMT group, and 7.5 months in the NT group. The average time from surgery until observed motion (either in clinic or by patient report) was 10.6 days in the regional muscle transfer group, 4.5 months in the FFMT group (12 of 14) since one patient died and 1 never developed motion and declined a second surgery), and 5.8 months in the nerve transfer group.

Conclusions: Facial reanimation in the older adult has been relegated to static procedures or conservative care for fear of poor outcomes or complications. This study refutes this pervasive viewpoint and demonstrates evidence of success for one-stage dynamic reanimation including muscle advancements, free functional muscle transfers, or nerve transfers. For the appropriate patient, age alone should not eliminate surgical options for dynamic facial reanimation, and striving for near normalization of appearance and function should always be the goal.

Targeted Cutaneous Nerve Biopsy

Tomas Marek, B Matthew Howe, Kimberly K Amrami, and **Robert J Spinner**

Department of Neurologic Surgery, Mayo Clinic, Rochester, MN, USA; spinner.robert@mayo.edu

Introduction: Nerve biopsy is an important part of a diagnostic algorithm in some patients who have persistent or progressive neuropathy, often despite empiric therapeutic trials. Non-targeted distal cutaneous nerve biopsy (e.g., sural nerve) is most frequently performed; it is an easy procedure, usually well tolerated, but is of relatively low yield. Targeted fascicular biopsy of proximal major nerves was introduced 15 years ago in a subgroup of these patients in whom high resolution MR imaging revealed abnormalities; the diagnostic yield has improved significantly and the morbidity of the procedure has been acceptably low. Is there an opportunity and is this the time to consider targeted cutaneous nerve biopsy?

Materials and Methods: Four patients are illustrated with "idiopathic" brachial plexopathy to demonstrate the utility of this technique. All cases had MRI abnormalities were detected in the brachial plexus in 4 cases, and on closer review, in the contiguous cutaneous nerves in 3 cases. Instead of targeting the pathology in the brachial plexus, the great auricular or supraclavicular nerve was biopsied.

Results: One case confirmed an inflammatory condition (CIDP n = 1) and three, perineural spread of a previously treated skin cancer (melanoma n = 2, squamous cell CA n = 1). The procedures were done safely through limited small incisions in 3 cases and in 1 case, percutaneous fine needle aspiration was performed. All patients then received specific treatment for their condition.

Conclusions: Improved imaging resolution (technology) and appreciation of the 3-dimensional anatomy on imaging allows radiologists to help surgeons diagnose and deliver targeted treatment for patients and understand disease pathophysiology more fully. There is no need to do a more invasive procedure (i.e. targeted fascicular nerve biopsy) if we can do a less invasive one (i.e. targeted cutaneous nerve biopsy) instead.

Distal Peroneal Nerve Decompression After Sciatic Nerve Injury Secondary To Total Hip Arthroplasty

Thomas J Wilson, Grant M Kleiber, Ryan M Nunley, Susan E Mackinnon, and Robert J Spinner

Department of Neurosurgery, Stanford University School of Medicine, Stanford, CA, USA; wilsontj@stanford.edu

Introduction: Particularly when a posterior approach is utilized during total hip arthroplasty (THA), the sciatic nerve, especially its peroneal division, is at risk of injury. With injury to the peroneal division of the sciatic nerve during THA, only 1 in 3 patients spontaneously recover. Typical points of entrapment may then secondarily become sites of conduction block or impediments to axonal regeneration due to nerve swelling, constriction of the tunnel, or both. For the peroneal nerve, the typical site of entrapment is the fibular tunnel. Thus, conceptually, distal decompression of the peroneal nerve at the fibular tunnel may improve the degree of recovery.

Methods: Retrospective study was performed of all patients who underwent peroneal decompression for the indication of sciatic nerve injury following THA. The primary outcome was dorsiflexion strength at latest follow-up. Multiple variables were assessed for their ability to predict a good surgical outcome.

Results: The total included cohort consisted of 37 patients. Dorsiflexion improved from a median preoperative grade of MRC 0 to ≥ 3 for 24 (65%) patients and to ≥ 4- for 15 (41%) patients. Logistic regression analysis identified motor unit potentials in the tibialis anterior and in the peroneus longus on preoperative electromyography as significant predictors of a good surgical outcome.

Conclusions: Performing peroneal nerve decompression at the fibular tunnel following sciatic nerve injury related to THA may significantly improve maximal recovery.

The Natural History Of Schwannomas

Alireza Mansouri and **Allan Belzberg**

Department of Neurosurgery, The Johns Hopkins Hospital, Baltimore, MD, USA; belzberg@jhu.edu

Introduction*:* Though benign, extra-cranial nerve sheath tumors (ENSTs) can become symptomatic through growth and mass effect on adjacent structures. While the mainstay of management for symptomatic tumors is microsurgical resection, some can be observed long-term. Currently there is a lack of clinical evidence guiding the decision-making for patients with ENSTs. Our objective was to identify predictors of successful long-term observation of ENSTs.

Methods: A retrospective review of the JHU radiology database was conducted. Patients were categorized into "long-term observation", "upfront surgery", and "delayed surgery". The proportion and rate of tumor growth in the observation cohort was calculated. Multivariate logistic regression was used to identify predictors of successful long-term observation.

Results: 265 patients were identified: 124 (47%) long-term observation, 24 (9%) delayed surgery, and 117 (44%) upfront surgery. In the long-term observation cohort, incidental presentation was most common (85, 68%), only 41(33%) demonstrated growth (mean follow-up 32 months), among which the annual growth rate was 2.2mm/year. A location outside the spinal canal ($p<0.01$) and symptomatic presentation ($p<0.01$) were independent predictors of upfront surgical intervention. Among spinal tumors, cord compression and size >25mm were predictors of failed observation. Perioperative and neurological complication rates among delayed and upfront surgical cohorts were similar.

Conclusions: Many ENSTs do not grow. Among those that grow, the annual growth rate is low. The outcomes of upfront and early surgical intervention are similar. Asymptomatic spinal tumors may be most amenable to long-term observation. A preliminary pathway for management of patients with sporadic ENSTs is proposed, which can guide clinical decision-making.

Whole Exome Sequencing Of Growing And Non-Growing Cutaneous Neurofibromas From A Single Patient With Neurofibromatosis Type 1

Daniel L. Faden, Saurabh Asthana, Tarik Tihan, Joseph DeRisi, and **Michel Kliot**

Department of Neurosurgery, Stanford University Medical Center, Stanford, CA, USA; michelkliot@gmail.com

Introduction: The growth behaviors of cutaneous neurofibromas in patients with Neurofibromatosis Type I (NF1) are highly variable. The role of the germline NF1 mutation, somatic NF1 mutation, and mutations at modifying loci, are poorly understood. We performed whole exome sequencing of three growing and three non-growing cutaneous neurofibromas from a single individual with NF1. Cells from the blood were also analyzed.

Methods: The growth and non-growth of the six cutaneous neurofibromas from a single patient with NF1 was based on serial clinical observations at 3-6 month intervals over a one year period. At surgery all tumor samples were collected and snap frozen and stored at -80 degrees Centigrade until processed. These samples were analyzed by frozen section to assess neoplastic cellularity. DNA was extracted followed by library preparation and whole exome sequencing performed at Centrillion Technologies (Palo alto, CA) using Agilent Sure Select Human All Exon v5 (Santa Clara, CA) on an Illumina HiSeq 2000 (San Diego, CA). 100bp paired-end reads were aligned against NCB1 build 37 of the human genome with BWA-MEM. Duplicate reads were marked-, local index realignment performed, and base-quality scores recalibrated with the Picard Suite and Genome Analysis Toolkit. Novel point mutations were identified and copy number segmentation performed. Visual inspection of mapped reads within the entire NF1 gene and identified mutations as well as pathway and network analysis were performed.

Results: We identified 1-11 mutations per samples with deleterious NF1 mutations in two samples. While provocative mutations were identified in each of the samples at potential modifying loci, no trends were present between the types of somatic mutations identified and growth behavior of the cutaneous neurofibromas. Mutations in the HIPPO signaling pathway, which is thought to play a role in tumor initiation and progression, appeared to be overrepresented.

Conclusions: Additional studies of the exome and transcriptome, as well as of epigenetic modifications, in larger cohorts of NF1 patients with image documented evidence of both growing and non-growing cutaneous neurofibromas are needed.

Brachial Plexus Tumors – A Personal Series

Eric L Zager, Jared M Pisapia, Giscard Adelcat, Sanford Roberts, Li Yun, Zarina S Ali, and Gregory George Heuer

Department of Neurosurgery, The Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; eric.zager@uphs.upenn.edu

Introduction: To review a personal series of operative cases of tumors involving the brachial plexus in adults.

Methods: A retrospective chart review of a consecutive series of surgical cases by a single neurosurgeon at an academic center from 2001-16. The patients' demographics, clinical and radiographic presentations, tumor locations, surgical approaches, pathological diagnoses and postoperative neurological function were collected and analyzed.

Results: 103 operated brachial plexus region tumors in 98 patients were identified. The mean age was 47, the mean follow-up time was 10 months and the genders were equally represented. 90% of patients presented with a palpable mass, and sensory deficit or paresthesia was the presenting symptom in 40%. The supraclavicular region was the most common tumor location (56%). The anterior supraclavicular (48%) and infraclavicular (34%) approaches were the dominant surgical approaches, with transaxillary (9%), combined anterior approach (5%), posterior cervical (3%) and thoracotomy (1%) being used less frequently. The benign nerve sheath tumors (schwannoma 45% and neurofibroma 23%) were the most common pathological diagnoses, while a variety of unusual histologies comprised the other third of lesions. Nearly 15% of lesions were malignant. At follow up, pain responded very well to surgical intervention, with 85% reporting stable or improved pain, and neurological function was unchanged or improved in 75%. In 51 patients with no preoperative motor weakness, strength was worse in 18 (35%) but recovered to at least 4/5 in half of these patients.

Conclusions: This represents a relatively large series of tumors involving the brachial plexus in adults, operated on at an academic institution over a 15 year interval. The tumor presentations, pathologies and surgical indications were quite typical for this location, and the surgical approaches were dictated by the tumor location and size. The outcomes in terms of pain relief were quite gratifying, but motor function suffered in the early postoperative period in a third of patients. Fortunately, motor function recovered to serviceable levels with time and physiotherapy in the majority of patients. In summary, brachial plexus region tumors in adults can be managed surgically with good outcomes with careful attention to proper surgical indications, and operative approaches and techniques for tumor resection.

Tailored Approach To Retroperitoneal Lumbosacral Plexus And Nerve Associated Tumors

Thomas Kretschmer, Thomas Schmidt, and Christian Heinen

Department of Neurosurgery, Klinikum Klagenfurt, Klagenfurt, Austria; kretschmerthomas@mac.com

Introduction: Nerve or nerve associated tumors of the retroperitoneal space are rare. They are frequently situated within or close to the lumbosacral plexus. Diagnosis and grade are unclear prior to surgery. If tumors extend into neighbouring anatomical regions, and are of considerable length, approach related morbidity and risk increase. There is considerable variety of approaches and techniques available. Choice of approach decisively influences surgical risk and outcome.

Methods: We reviewed our patients with retroperitoneal tumors for outcome and surgical strategy to scrutinize and possibly support our localization and extent related approach system.

Results: From 2012 to 2016 n=12 patients were operated, n=9 female, n=3 male. Histological findings included n=5 schwannomas, n=2 malignant peripheral nerve sheath tumors (MPNST), n=1 sarcoma of unknown origin (GOS), n=1 perineurioma, n=1 intraneural ganglion cyst, n=1 lymphoma, and n=1 paraganglioma. Approaches used were monoportal retroperitoneal (n=3), combined retroperitoneal to inguinal (n=2), monoportal transabdominal (n=3), combined transabdominal to dorso-sacral (n=2), and dorsal (n=2). One patient required two-staged surgery (GOS). Techniques applied ranged from open biopsy in n=2 (perineurioma/paraganglioma), to tumor enucleation in n=5 (schwannoma), to subtotal function sparing resection in n=3 (MPNST/sarcoma/lymphoma), complete resection of MPNST in n=1, to removal of residual schwannoma with graft reconstruction, and n=1 intraneural fenestration and decompression (ganglion cyst). Four patients required further radio-oncological treatment, one patient developed a new motor deficit.
Based on imaging data we could plan different approach ports to maximize dissection freedom, and reduce morbidity. An approach scheme based on anatomical regions involved, length of lesion, and extent of dissection anticipated is suggested.

Conclusions: Retroperitoneal nerve or nerve associated tumors encompass a large variety of entities. Due to extent of individual tumors patients benefit from use of individually tailored approaches based on imaging data. Frequently different approach ports can be combined in a single session to ease surgery and improve outcome.

Persistent Sciatic Pain Following Back Surgery

Israel P Chambi and Lawrence Miller

Brachial Plexus and Peripheral Nerve Institute, Santa Ana, CA, USA; drisraelchambi@yahoo.com

Introduction: Surgery following a symptomatic lumbar disc herniation or instability at the L4-5, L5-S1 has been associated with favorable results. However in patients that present with a history of a fall and continued complains of persistent sciatic pain in the face of a normal post-operative MRI, CT scan, or x-rays of the lumbar spine are a unique group of individuals. These patients with persistent sciatic pain following back surgery have been analyzed.

Methods: This is a prospective clinical study including 15 patients that developed a back and leg pain as a result of a fall and sustaining trauma to lumbar and gluteal areas. These patients were referred from various pain management clinics both in Los Angeles and Orange Counties in the state of California. Six patients underwent a microdiscemetomy at the L5-S1 level. Three patients underwent a microdiscectomy at the L4-5 level and six patients underwent lumbar fusion for instability. There were an additional four patients at the L5-S1 Level and two patients at the L4-5 level. In the microdiscemtomy cases, patients experienced a temporally relief, lasting form 3-6 months, and in the lumbar fusion cases. There were temporal improvements for a period of 2 - 4 months. The Lumbar fusion cases demonstrated axial pain improvement but continued to complain of severe sciatic pain, in spite of physical therapy, medications, acupuncture, epidural injections, spinal cord stimulation and/or sacro-iliac fusion. These patients underwent an ultrasound imaging study of the gluteal area, demonstrating fibrosis of the piriformis muscle causing distortion and compression of the sciatic nerve and an ultrasound guided diagnostic injection in the piriformis muscle provided an excellent but a temporary relief of the sciatic pain. The EMG demonstrated an absent H-reflex and on clinical examination, there was a positive Tinel's sign, in the gluteal area there was noted in the distribution of the sciatic nerve a weakness and sensory loss of the sciatic nerve. The piriformis stress test was positive in all fifteen patients.

Results: Fifteen patients underwent surgical decompression of the piriformis muscle and underlying sciatic nerve. In every patient, there was fibrosis of the piriformis muscle causing compression of the sciatic nerve. A favorable result was seen in 13 patients. In 2 patients, the patients continued to complain of mild sciatic pain that had been relieved with anti-inflammatory medications.

Conclusions: Patients that present with a history of a fall with a background history of lumbar surgeries may sustain a double crush syndrome affecting the lumbar spine and the gluteal area leading to an injury to the lumbar disc and a trauma to the piriformis muscle. This can result in fibrosis and compression of the sciatic nerve due to scarring of the piriformis muscle.

To Use Or Not To Use Viable C5-C6 Stumps In Brachial Plexus Traction Injuries?

Lukas Rasulić

School of Medicine University of Belgrade, Belgrade, Serbia; lukas.rasulic@gmail.com

Introduction: Brachial plexus injuries, especially traction injuries, are still a challenging issue due to difficulties in differentiating between supra- and infra- ganglionic lesions, lots of different strategies for its reconstruction, and uncertain recovery regardless of which treatment modality is used. The pooled international data strongly favors targeted nerve transfers over nerve grafting because when nerve grafting is used, the percentages of successful regeneration are diminished by factors such as a longer path which regenerating nerve fibers have to pass and an additional suture line. On the other hand, there are authors who favor exploration of the whole brachial plexus and nerve grafting as the treatment modality of choice due to avoidance of possible additional neurological deficit by donor nerve harvesting and the possibility of reserving nerve transfers for second stage procedures in case of failure. Clearly, it is very important to select the appropriate treatment modality, because the right choice could lead to optimal functional recovery.

Material and Methods: The goal of this study was to evaluate outcomes of priority functions in 36 patients with upper or complete brachial plexus palsy in whom we performed solely nerve grafting from viable proximal nerve stumps to targeted nerves over a period of fifteen years (January 1999 to December 2013). All the patients whom we prospectively analyzed in this study had preserved function of the trapezius muscle, levator scapula muscle, rhomboid muscle and serratus anterior muscle, registered action potentials in paraspinal muscles during EMNG testing, and showed no signs of pseudomeningoceles at levels C4-C5 and C5-C6 on MR scans and CT myelograms. The decisive inclusion criteria was the intraoperative registration of motor action potentials during transcranial electric stimulation. Patients were followed-up for at least two years.

Results: The mean age of patients was 21 years (16-31 y/o range) and the most common etiology was vehicular accident. Commonly associated injuries were rib fractures, fractures of the long bones, and brain contusion. 22 of 36 patients underwent emergency surgery for associated injuries. The average interval between the injury and nerve grafting surgery was 4 months (3-7 month range). 24 patients manifested with complete brachial plexus palsy, and 12 patients manifested upper brachial plexus palsy. *See Figure 2 on page 52.*

Conclusions: One of the main goals of preoperative and intraoperative diagnostic procedures in traction brachial plexus injuries is the differentiation of preganglionic injuries, postganglionic injuries, or a combination of both. Namely, functioning ventral roots can be used as the proximal stumps for nerve grafting. There is not a single diagnostic procedure with a sensitivity of 100%. Therefore, use of a combination of diagnostic procedures in the preoperative evaluation is mandatory.

Usage of longer nerve grafts that connect viable proximal stumps of spinal nerves (usually C5 and sometimes C6) with targeted nerves allows avoidance of misdirection and wasting of regenerating axons and directs them to the targeted muscles. Exploration of the whole brachial plexus enables us to discover potential double lesions of the nerves so we could by-pass them.

Satisfactory functional results could be achieved by grafting of C5 to the musculocutaneous and the axillary nerves and by grafting of the dorsal scapular nerve to the branch of the radial nerve to the long head of the triceps muscle in the majority of such cases. This is our treatment of choice in cases of the early reconstruction of the total brachial plexus palsies in young patients with a viable proximal stump of C5.

Figures

Figure 1

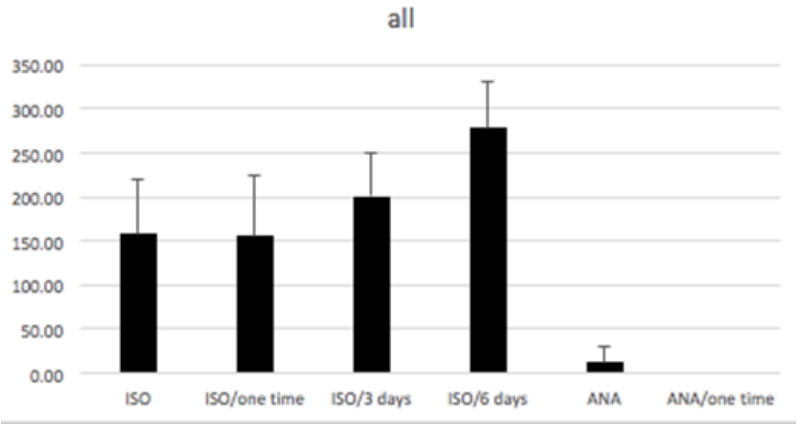


Figure 2

Donor nerve	Recipient nerve	Number of patients	Functional satisfactory recovery
C5	Musculocutaneous nerve	36	72,2% elbow flexion: M3 in 4 patients, M4 in 20 patients M5 in 2 patients
C5	Axillary nerve	36	61,1% shoulder abduction: M3 in 5 patients M4 in 17 patients ---------- 33,3% external rotation: M3 in 8 patients M4 in 4 patients
C6	Radial nerve	10	50% elbow extension: M3 in 3 patients M4 in 2 patients
C6	Medial pectoral nerve	10	50% shoulder adduction: M3 in 2 patients M4 in 3 patients
Dorsal scapular nerve	Branch of the radial nerve to long head of the triceps muscle	14	71,4% in elbow extension: M3 in 9 patients M4 in 1 patient

Prior Meetings

Year	Site	President
1980	Glen Cove, NY	Morton Spinner
1981	New Orleans, LA	David Kline
1983	Santa Fe, NM	George Omer, Jr
1984	Baltimore, MD	Shaw Wilgis
1986	Vienna, Austria	Hanno Millesi
1988	Durham, NC	Leonard Goldner
1990	Louisville, KY	Joseph Kutz
1992	Malmo, Sweden	Goran Lundborg
1993	Seattle, WA	Edward Almquist
1995	Zurich, Switzerland	Victor Meyer
1997	Vail, CO	Michael Jabaley
1999	London, England	James Urbaniak
2001	San Diego, CA	Richard Braun
2002	Baltimore, MD	Thomas Brushart
2004	Toronto, Canada	Rajiv Midha
2007	Manchester, England	DA (Gus) McGrouther
2008	Rochester, MN	Robert Spinner
2009	Shanghai, China	Long-en Chen
2011	New York, NY	David Chiu
2013	Leiden, Holland	Martijn Malessy
2015	Ann Arbor, MI	John McGillicuddy & Lynda Yang
2016	Frankfurt, Germany	Kartik Krishnan & Thomas Kretschmer
2018	Stanford, CA	Michel Kliot

SUNDERLAND SOCIETY