P1. Variables Associated with Outcomes in Peripheral Nerve Repair

Beina Azadgoli, MS; Don Hoang, MD, MHS; Hyuma A Leland, MD; Nana-Yaw Bonsu, BS; Joseph Carey, MD
Keck School of Medicine, University of Southern California, Los Angeles, CA

Background: Data regarding outcomes after peripheral nerve injuries is limited, and the optimal management strategy for an acute injury is unclear. The aim of this study was to examine specific patient and surgical factors that impact motor and sensory outcomes after peripheral nerve injury.

Methods: This was a single center, retrospective study at a metropolitan level 1 trauma center. Patients with traumatic peripheral nerve injury from 01/2010 – 06/2015 were included. Patients who died, required amputation, suffered brachial plexus injury, or had missing motor-sensory exams were excluded. Motor and sensory exams were graded 0-5 by the Modified British Medical Research Council system. Operative repair of peripheral nerves was analyzed for patient characteristics, anatomic nerve injury, level of injury, associated injuries, days until repair, and repair method.

Results: 311 patients met inclusion criteria. 258 (83%) patients underwent operative management, and 53 (17%) underwent non-operative management. Those who required operative intervention had significantly more penetrating injuries 85.7% vs 64.2% ($p<0.001$), worse initial motor scores 1.19 vs 2.23 ($p=0.004$), and worse initial sensory exam scores 1.75 vs 2.28 ($p=0.029$). Predictors of improved operative motor outcomes on univariate analysis were Injury Severity Score (ISS) <15 ($p=0.013$), male sex ($p=0.006$), while upper arm level of injury was a predictor ($p=0.041$) of poor outcome. Nerve reconstruction type between primary, allograft, autograft, or nerve tube did not influence motor outcomes ($p=0.15$). Multivariate analysis did not confirm level of nerve injury to be predictive of outcome. Univariate analysis identified distal forearm level of injury ($p=0.026$) and autograft repair ($p=0.048$) as predictors of poor sensory outcome. These variables were not found to be significant on multivariate analysis. Days to nerve repair (² 24 hours versus >24 hours, $p=0.834$) did not influence motor-sensory outcome.

Conclusion: Outcomes were primarily influenced by patient characteristics, and injury level to a lesser degree, rather than operative repair characteristics.

	Level of Injury				
Outcome Level	Upper Arm n=21	Proximal FA n=11	Distal FA n=47	Palmar n=11	Digital n=78
Poor (0-1)	12 (57.1%)*	5 (45.5%)	14 (29.8%)	3 (27.3%)	22 (28.2%)
Fair (2-3)	2 (9.5%)	2 (18.2%)	6 (12.8%)	1 (9.1%)	10 (12.8%)
Good (4-5)	7 (33.3%)	4 (36.3%)	27 (57.4%)	7 (63.6%)	46 (60.0%)

*p-value=0.041

Table 1. Outcomes: Motor Recovery and Level Injury

Variables	Motor, n=170		Sensory n=220	
	p-value	OR (95% CI)	p-value	OR (95% CI)
Patient Characteristics				
ISS<15	**0.013**	10.14 (1.24-82.98)	0.519	1.86 (0.47-7.37)
Age<65	0.735	0.68 (0.18-2.63)	1.000	1.30 (0.30-5.59)
Sex, male	**0.006**	4.03 (1.39-11.67)	0.819	0.92 (0.44-1.93)
Mechanism, penetrating	0.308	0.62 (0.25-1.57)	0.196	1.67 (0.77-3.63)
Injured Peripheral Nerve				
Digital	**0.190**	1.50 (0.82-2.76)	0.209	1.41 (0.83-2.41)
Ulnar	0.849	0.92 (0.41-2.10)	0.793	0.91 (0.47-1.79)
Multiple Upper Extremity	**0.096**	1.86 (0.89-3.87)	0.830	0.93 (0.48-1.80)
Median	0.448	1.41 (0.71-2.08)	0.636	0.84 (0.40-1.75)
Radial	**0.089**	0.47 (0.19-1.14)	0.783	1.12 (0.49-2.55)
Level of Injury				
Upper Arm	**0.041**	0.38 (0.14-0.98)	0.430	1.46 (0.57-3.65)
Proximal Forearm	0.220	0.46 (0.13-1.63)	0.752	1.29 (0.36-4.58)
Distal Forearm	0.595	1.20 (0.61-2.37)	**0.026**	0.51 (0.28-0.93)
Palmar	0.514	1.52 (0.43-5.40)	0.595	1.30 (0.50-3.41)
Digital	0.244	1.44 (0.78-2.65)	0.251	1.37 (0.80-2.34)
Associated Injuries				
Tendon/Muscle	0.109	1.81 (0.87-3.76)	0.509	0.82 (0.45-1.50)
Vascular	0.818	0.93 (0.50-1.73)	0.590	0.86 (0.49-1.50)
Bone	0.484	0.78 (0.39-1.57)	0.981	0.99 (0.52-1.91)
Multiple Associated Injuries	0.364	1.33 (0.72-2.45)	0.841	1.06 (0.62-1.82)
Operative Characteristics				
Days from injury to repair ≤1	0.834	1.07 (0.56-2.06)	0.294	1.38 (0.76-2.50)
Short Tourniquet Time	0.660	1.19 (0.55-2.59)	0.100	0.56 (0.29-1.12)
Repair Method				
Primary Repair	0.467	1.29 (0.65-2.55)	0.091	1.76 (0.91-3.38)
Autograft	0.146	0.54 (0.24-1.25)	**0.048**	0.41 (0.17-1.01)
Allograft	0.452	2.24 (0.42-11.87)	1.000	1.30 (0.26-6.59)
Nerve Tube	0.944	1.05 (0.31-2.56)	0.672	0.81 (0.30-2.17)

Table 2. Predictors of Improved Motor-Sensory Outcomes: Univariate Analysis

Variables	Motor, n=170		Sensory, n=220	
	p-value	OR (95% CI)	p-value	OR (95% CI)
Patient Characteristics				
ISS<15	0.218	4.67 (0.403-54.07)	-	-
Sex, male	**0.017**	3.88 (1.28-11.80)	-	-
Mechanism, penetrating	-	-	0.061	3.13 (0.95-10.36)
Injured Peripheral Nerve				
Digital	0.946	1.03 (0.49-2.16)	-	-
Multiple Upper Extremity	0.116	2.00 (0.84-4.76)	-	-
Radial	0.274	0.57 (0.21-1.56)	-	-
Level of Injury				
Upper Arm	0.491	0.65 (0.19-2.21)	-	-
Distal Forearm	-	-	0.064	0.49 (0.23-1.04)
Associated Injuries				
Tendon/Muscle	0.847	1.09 (0.45-2.67)	-	-
Operative Characteristics				
Repair Method				
Primary Repair	-	-	0.973	1.02 (0.36-2.92)
Autograft	0.330	0.61 (0.22-1.66)	0.663	0.74 (0.19-2.91)

Table 3. Predictors of Improved Motor and Sensory Outcomes: Multivariate Analysis

P2. Focal Deficits In Myelination In Human Neuroma-in-Continuity

Fred De Winter, PhD[1]; Arie C Van Vliet, Msc[1]; Martijn R Tannemaat, PhD, MD[2]; Sjoerd G Van Duinen, PhD, MD[2]; Martijn J.A. Malessy, MD; PhD[2]; Joost Verhaagen, PhD[1]

[1]Netherlands Institute for Neuroscience, Amsterdam, Netherlands, [2]Leiden University Medical Center, Leiden, Netherlands

In 10% of the patients with neonatal brachial plexus palsy (NBPP) a neuroma-in-continuity (NIC) is formed that is thought to interfere with axonal outgrowth and prohibits functional recovery. However, the biological mechanisms underlying this problem are currently poorly understood. To increase our knowledge of NIC we initiated a characterization of NIC tissue resected during reconstructive surgery. In a microarray study we revealed that 722 genes are differentially regulated between the NIC and the proximal nerve. We observed that in the NIC, when compared to the proximal nerve stump, there is a decrease Schwann cell and myelin related gene expression in favor of more fibroblast and fibrosis related gene expression.

To examine the possible implication of a reduced Schwann cell/myelin profile we performed a systematic analysis of large series of NIC tissue (17 NBPP, 3 adult traumatic brachial plexus lesion) by immunohistochemistry. This revealed that in 74% of the patients, the NIC contains multiple focal myelin deficits (FMDs). These FMDs contain Schwann cells that enwrap axons but do not form myelin. Axons in the FMDs have disrupted nodes of Ranvier with decreased expression Caspr and Ankyrin, and reduced Na(v)1.6 channel clustering. Based on the number, shape and size of the FMDs we calculated that there is a ~95% change that an axon in a NIC will encounter 10 FMDs. Therefore FMDs may be a part of the pathobiologic basis for the absence of functional recovery in NBPP. These observations provide a basis for the development of novel strategies to promote functional recovery after neonatal plexus palsy by improving myelination in the NIC.

P3. Functional Motor Recovery Outcomes after Repair of Traumatic Nerve Injuries Using Processed Nerve Allograft

Jaimie T Shores, MD[1]; John V Ingari, MD[1]; Jozef Zoldos, MD[2]; Renata V. Weber, MD[3]; Mickey Cho, MD[4]; Wesley Thayer, MD, PhD[5]; Bauback Safa, MD[6]

[1]Johns Hopkins Medicine, Baltimore, MD; [2]Arizona Center for Hand Surgery, Phoenix, AZ, [3]Institute for Nerve, Hand, and Reconstructive Surgery, Rutherford, NJ, [4]Orthopedics, San Antonio Military Medical Center, San Antonio, TX, [5]Department of Plastic Surgery, Vanderbilt University, Nashville, TN, [6]The Buncke Clinic, San Francisco, CA

Introduction

While severe trauma to the upper extremities often results in the transection of major peripheral nerves, conducting controlled prospective clinical studies in this population remains a challenge. The RANGER® Registry is an ongoing observational study collecting data on the use and outcomes of processed nerve allograft (Avance® Nerve Graft, AxoGen, Inc.). The database includes a broad spectrum of nerve types, injury locations and mechanisms. In the current study, we reviewed the outcomes of using PNA to reconstruct mixed or motor nerve defect in the upper extremity, head and neck area. Meaningful recovery of motor function after these repairs is reported.

Methods

The RANGER database was queried for mixed or motor nerve injuries in the upper extremity, head and neck area that were repaired with PNA and reported sufficient follow-up assessments. Motor function assessments included range of motion and/or muscle strength tests. Reported quantitative outcome data were incorporated into the Medical Research Council Classification (MRCC) scale for motor function. Meaningful recovery was defined as ≥ M3 on the MRCC scale. Outcomes were compared to historical literature on nerve autograft and conduit.

Results

There were 31 nerve repairs in the cohort that reported sufficient outcome data for quantitative assessment of motor function after repair. The nerves repaired included: axillary, musculocutaneous, median, radial and ulnar nerve in the upper extremity, and spinal accessory, buccal, zygomatic, marginal mandibular nerve in the head/neck region. Mean age of the cohort was 40 ± 19(18 –77) years. Mean gap length was 28 ± 13(10–65) mm with a mean follow-up duration longer than a year (376 ±197 days). Meaningful recovery was observed in 81% of repairs. Analysis by mechanism of injury observed meaningful recovery in 88% of laceration and 73% of complex injuries. Demographics of these repairs are summarized in Table 1. No adverse events were reported.

Conclusion

Reconstruction of mixed and motor nerve defects using PNA resulted in good motor functional recovery in gaps between 10 and 65mm in length. Current data from the RANGER registry showed that 81% of these repairs achieved meaningful recovery of motor function after surgery. Outcomes compare favorably to historical controls from available literature for nerve autograft and exceed that of nerve conduit. The RANGER® registry is currently ongoing and future reports will provide additional clinical evidence on the expanding role of PNA in mixed and motor nerve repairs.

Table 1. Motor function recovery after PNA repair

Factor	Cumulative Cohort	Laceration	Complex Injury
Nerve Repairs, N	31	16	15
Age (years)	40 ± 19	44 ± 19	37 ± 17
Pre-operative Interval (days)	7 (0, 1067)	8 (0, 491)	6 (0, 1067)
Gap Length (mm)	28 ± 13	26 ± 11	32 ± 14
Follow-up (days)	376 ± 197	358 ± 199	386 ±195
Meaningful Recovery (MR), n	25	14	11
MR %	81%	88%	73%

- Age, gap length, follow-up duration are presented as Mean ± SD.
- Pre-operative interval is presented as Median (Min, Max).
- Complex injury included: gunshot/blast, amputation, crush/compression, tumor/neuroma excision and iatrogenic injuries.

P4. Sensory Outcomes Following Simultaneous Nerve Allograft and Mandibular Reconstruction for Benign Pathology

John randall Zuniga, DMD; MS, PhD[1]; John Peter Smith, MD[2]; Fayette Williams, DDS, MD[2]; Daniel Petrisor, DDS, MD[3]

[1]University of Texas, Dallas, TX, [2]Fort Worth, TX, [3]Oregon Health Sciences University, Portland, OR

Patients (age 5 -70) requiring resection of the unilateral or bilateral mandible for benign pathology which would include the continuity loss of the IAN were included. The length of the nerve allograft must be between 45 to 70 mm. Sensory nerve tests and three different surveys (Direct Path, Numerical rating scale, Word Choice) were collected before and at 3, 6 , and 12 months. Safety data were recorded.

Twenty-three patients were consented to this study. There were 2 patients with bilateral repairs and 3 patients who served as positive control since no nerve repair was performed. Three patients in the repair group and 1 patient in the positive control group were lost to follow up. Data over a 1 year time was collected on 17 patients. There were 7 males and 10 females, mean age were 26.4 years, range 10 to 64. The confirmed pathology of the mandible was ameloblastoma (n=11), central ossifying fibroma (n=4), myxoma (n=1), and sclerosing osteomyelitis (n=1). The mean length of the nerve defect was 59.75mm, range 45 to 70mm. The mean length of the nerve allograft was 62.7mm, range 45 to 70mm. The diameter was 2-3mm for each. Sixteen of 17 had S4 sensory scores preoperatively and the postoperative score was S4 at 3 months in 3, in 10 at 6 months, and in 12 patients at 12 months. The positive control patients reached S2 at 12 months. Numerical rating scales and word choices were not significantly different from presurgical scores at 6 and 12 months but remained significantly elevated in direct path scores (unusual feeling in face and left over food in cheek). There were no adverse events or recurrences of pathology at these postoperative times.

Nerve allografts were found to be safe and effective in restoring both subjective and objective reports of sensation to the lip and chin in dramatic fashion with 94% reaching useful and functional sensory recovery and >80% reporting similar sensations to preoperative subjective values.

P5. Combining Nerve Autograft and Decellularized Allograft Cables with Epineurotomies Allows for Trans-Perineurial Schwann Cell Migration

Sami H. Tuffaha, MD; Joshua Budihardjo, BS; Amy Quan, MPH; Joseph Lopez, MD; Gerald Brandacher, MD; Jaimie T Shores, MD
Johns Hopkins University School of Medicine, Baltimore, MD

Background: When using a combination of autograft and decellularized allograft cables to reconstruct a large nerve defect, we hypothesize that epineurotomies in the grafts will allow side-to-side Schwann cell migration from the autograft cables to the decellularized allograft cables. We present a case series demonstrating outcomes using this technique and a rat study assessing whether epineurotomies allow for transperineurial migration of Schwann cells for autograft to decellularized allograft cables.

Methods: *Case series*: Motor and sensory outcomes data were collected retrospectively for seven patients who underwent reconstruction of large-caliber mixed motor nerves with a combination of autograft and decellularized allograft cable grafts. Longitudinal epineurotomies were made in the cable grafts before they were merged side-to-side with fibrin glue and sutured into the defects (Figures 1 and 2). *Animal study:* 4 cm sciatic nerve defects were created in Lewis rats and bridged with autograft + allograft with epineurotomies (group 1); autograft + allograft without epineurotomies (group 2); or allograft alone (group 3). (N=2 per group). At 2 weeks, mid-graft cross-sections were stained for S100 to assess for the presence of Schwann cells by immunofluorescence microscopy.

Results: *Case series*: Defects were reconstructed in ulnar (x2), median (x2), sciatic (x2) and posterior interosseus nerves. All defects were greater than 3cm in length. All patients with adequate follow up demonstrated favorable recovery of motor and sensory function. *Animal study*: In one of two animals in Group 1, S100-positive Schwann cells were found within allograft fascicles. (Figure 2) In the second animal of Group 1, Schwann cells were seen crossing the perineurium of the allograft, but none were found within the allograft fascicles. In Groups 2 and 3, there were no S100-positive cells observed within the allograft fascicles or crossing the perineurium in any animals.

Conclusions: Our case series demonstrates the feasibility of combining autograft and decellularized allograft cable grafts with epineurotomies to reconstruct large mixed-motor nerve defects with favorable outcomes. Epineurotomy allows for trans-perineurial side-to-side Scwhann cell migration from autograft to decellularized allograft cable grafts. Further studies are needed to delineate the degree and timing of Schwann cell migration, as well as the impact this has on axonal regeneration, muscle and sensory reinnervation and functional outcomes.

Figures 1 and 2. The senior author's (JS) technique illustrated and prior to implantation.

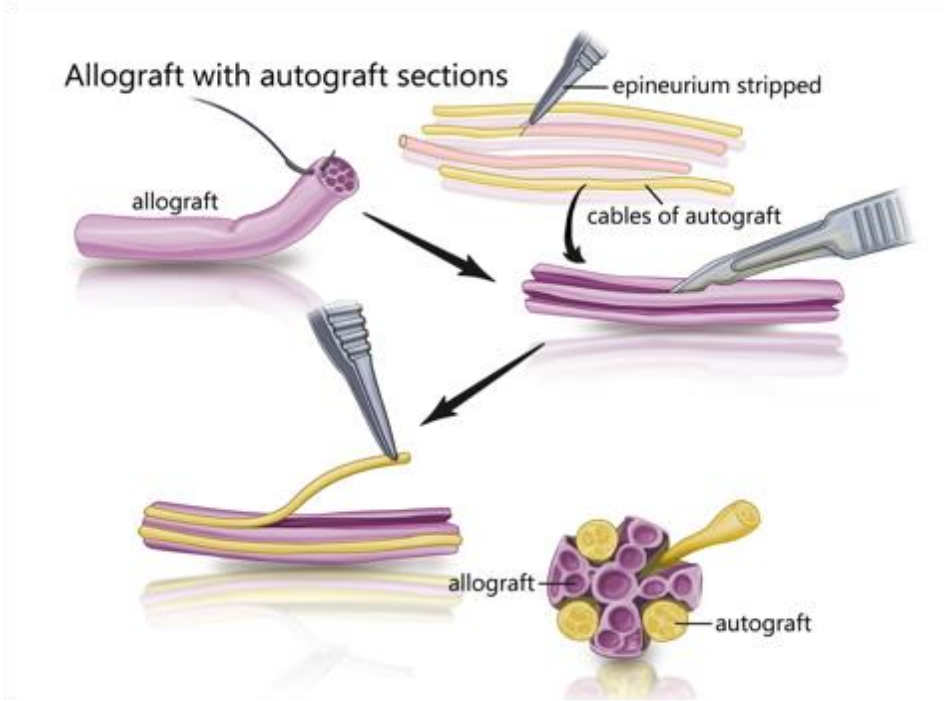
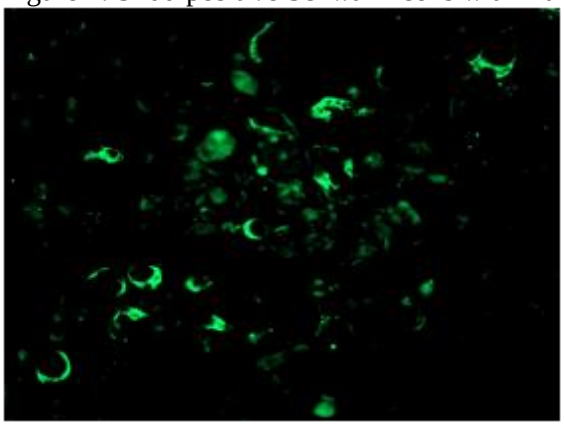


Figure 2: S100-positive Schwann cells within allograft fascicle (Group 1)



P6. Functional and Histological Evaluation of a Novel Branched Acellular Nerve Allograft and Processed Human Xenograft with and without FK506 in a Complex Branching Facial Nerve Defect: A Preliminary Study in Swine

Mario A. Aycart, MD; Muayyad Alhefzi, MD; Ericka M Bueno, PhD; Bohdan Pomahac, MD
Brigham and Women's Hospital, Boston, MA

Introduction: The gold standard for peripheral nerve gap repair remains the autologous nerve graft. However, "off-the-shelf" alternatives are appealing due to additional graft material, shorter operative times and avoidance of donor site morbidity. Such commercially available products may hold particular interest in large gap, complex branching nerve defects. This study aims to evaluate the functional and histological regeneration of a novel branched acellular nerve allograft (ANA) and processed human xenograft with and without oral FK506 in a 30mm complex branching facial nerve defect in a large animal model.

Methods: Yucatan miniature swine (n = 10) underwent transection of the inferior division of the facial nerve at a point 5mm proximal to the branching point of the marginal mandibular and cervical nerve branches and 25mm distal to the transection to create a 30mm nerve gap. The gap was addressed either by a species-specific ANA (n=4), a processed human xenograft with FK506 (n=4) or a processed human xenograft without FK506 (n=2). FK506 was given as a twice daily oral administration and continued for the entire duration of study. Goal whole blood trough levels were set to 4-8 ng/mL in order to evaluate the role of low-dose FK506 while minimizing the side effects of chronic FK506 and drug-related toxicity. Electrophysiologic assessments were performed at study end point (24 weeks) to assess functional recovery. Distal nerve stumps were harvested for immunohistochemical evaluation using neurofilament and S100 to observe the distribution and presence of Schwann cells in the respective nerve fibers.

Results: After 24 weeks, processed human xenografts treated with FK506 demonstrated a non-statistically significant (p=0.16) improvement across functional parameters, as measured by electrophysiologic studies (mean marginal mandibular nerve amplitude 3.82 ±0.69 mV) against species-specific ANA (mean marginal mandibular nerve amplitude 2.96 ±0.32 mV) and processed human xenografts without FK506 (mean marginal mandibular nerve amplitude 2.94 ±0.95 mV). Mean FK506 trough levels were 5.76 ± 4.9 ng/mL with no mortalities. Nerves repaired with a xenograft and FK506 had greater appreciable costaining of neurofilament and S100 distal to the repair site compared to other groups.

Conclusion: In this study, we demonstrate the use of a novel branched ANA and processed human xenograft with and without oral FK506 in a complex branching facial nerve defect in a large animal model. Low-dose FK506 appears to enhance and support a processed human xenograft across a large gap, branched nerve defect. Ongoing efforts are being directed towards isograft and histomorphometric outcomes.

P7. Return of Motor Function After Segmental Nerve Defect In A Rat Model: Comparison Between Two Collagen Nerve Conduits And Nerve Autograft

Eliana Saltzman, BA; Jordan Carolina Villa, M[D]; Joseph H Feinberg, MD; Steve K Lee, MD; Scott W Wolfe, MD
Hospital for Special Surgery, New York, NY

Introduction: Current synthetic conduits fail to provide equivalent motor recovery compared to autologous nerve repairs of peripheral nerve injuries. Autograft repairs are additionally associated with donor site morbidity and are limited by tissue availability. A synthetic conduit that enables equivalent motor recovery would thus provide an ideal graft alternative. A novel polyglycolic acid conduit (Nerbridge, Toyobo Co., Ltd., Osaka, Japan), uniquely contains collagen fibers within the tube to provide support and guidance for regenerating peripheral nerves through the transected site. We hypothesized that this collagen-filled conduit would generate motor recovery equivalent to that of autograft, and superior to a hollow collagen conduit (NeuraGen *nerve guide,* Integra, Plainsboro, NJ) as a result of its internal scaffold.

Methods: 72 Lewis rats were randomized into 3 experimental groups, in which a unilateral 10-mm sciatic defect was repaired using nerve autograft, collagen-filled conduit, or hollow collagen conduit. Outcomes were measured at twelve and sixteen weeks postoperatively, and included bilateral tibialis anterior muscle weight, voltage and force maximal contractility, assessment of ankle contracture, and nerve histology. Results were expressed as a percentage of recovery from the contralateral side. Kruskal-Wallis analysis was utilized with an alpha level of $p < 0.05$ to determine significance, and post-hoc Bonferroni-correction was used for multiple comparisons.

Results: At twelve weeks, mean muscle force compared to that of the contralateral control side was 50% ±21 for autograft, 9% ±6 for the collagen filled conduit, and 32% ±21 for the hollow collagen conduit. After sixteen weeks, the mean muscle force was 72.4% ±22.5 for autograft, 58.0% ±19.3 for collagen-filled conduit, and 61.1% ±24.8 for collagen hollow conduit. Autograft was statistically superior to both conduits for all outcomes except histology (Fig 1). The conduits demonstrated equivalence to each other across outcomes. Although all three groups experienced improved outcomes from twelve to sixteen weeks, the collagen filled conduit demonstrated the greatest rate of recovery in axonal density over this period.

Conclusion: Autograft repair provided superior motor recovery than the use of two distinct collagen conduits for a 10-mm nerve gap in a rat model. Nevertheless, the collagen filled conduit demonstrated encouraging improvement in muscle force and axon density between 3 and 4 months postoperatively, highlighting its utility in spanning nerve gaps, particularly when autograft is unavailable.

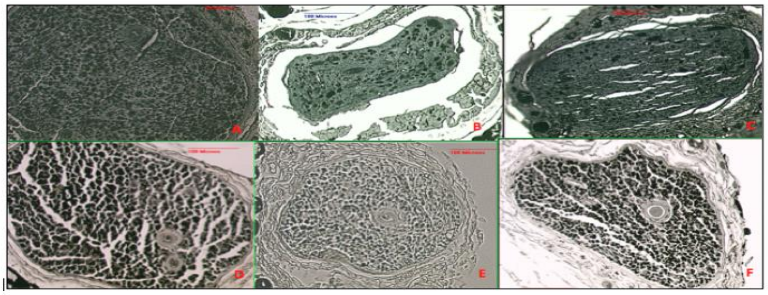


Fig 1. Transverse sections of rat tibial nerve (100 microns): autograft group (A), collagen-filled conduit group (B), and hollow collagen conduit group (C) at 12 weeks. Autograft group (D), collagen-filled conduit group (E), and hollow collagen conduit group (F) at 16 weeks.

P8. Chitosan Tubes for Peripheral Nerve Regeneration

Giulia Ronchi, PhD[1]; Stefania Raimondo, PhD[1]; Giovanna Gambarotta, PhD[1]; Benedetta Elena Fornasari, BSC[1]; Alessandro Crosio, MD[2]; Pierluigi Tos, MD; PhD[3]; Bruno Battiston, MD[2]; Thomas Freier, PhD[4]; Kirsten Haastert-Talini, PhD[5]; Claudia Grothe, PhD[5]; Stefano Geuna, MD[1]

[1]University of Turin, Orbassano, Torino, Italy, [2]Microsurgery Unit, CTO Hospital, Torino, Italy, [3]UO di microchirurgia ricostruttiva, Ospedale Gaetano Pini, Milano, Italy, [4]Medovent GmbH, Mainz, Germany, [5]Hannover Medical School, Hannover, Germany

Introduction: Recent studies demonstrated that the chitosan guides used for peripheral nerve repair showed results similar to those obtained using autologous nerve grafts after immediate repair of rat sciatic nerve gaps. These promising pre-clinical results led to approval of the chitosan tubes for clinical use in 2014 as Reaxon® Nerve Guide. In this study we show a strategy to further improve the performance of the chitosan tube by the introduction of longitudinal skeletal muscle fibers. As previously demonstrated, muscle fibers used to fill a vein ("muscle-in-vein" conduit) improve peripheral nerve regeneration when used to bridge a nerve defect up to 2cm.

Materials & Methods: The rat median nerve was repaired by means two different conduits: (i) 10 mm hollow chitosan tube; (ii) 10 mm chitosan tube enhanced by the introduction of skeletal muscle fibers (a longitudinal piece of the pectoralis major muscle was introduced inside the tube, muscle-in-tube). 10 mm autologous nerve graft was used as a positive control. Samples were harvested at both early (7, 14, 28 days after nerve repair) and late time points (3 months), and functional, morphological, stereological and biomolecular analysis were carried out.

Results: The biomolecular analysis carried out on early time points shows that the muscle inside the tube produces and releases neuregulin1, a key factor for the survival and activity of Schwann cells usually released following nerve injury. Indeed, neuregulin1 is also expressed in the autologous nerve graft, but is not detectable in the hollow chitosan tube, suggesting that the presence of the muscle compensates this lack. Moreover, the morphological analysis shows that few fibers are already present after 14 days from nerve repair only in the muscle-in-tube conduit.

Conclusions: These preliminary results are very promising, because they combine the simplicity and rapidity of the use of the chitosan tube, with the effectiveness of the muscle fibers to promote axon regeneration. From the clinical point of view, this conduit might be used instead of the autologous nerve graft which, although still considered the "gold standard" technique, has some well known disadvantages.

P9. Retropharyngeal Contralateral C7 Nerve Transfer to the Lower Trunk for Brachial Plexus Birth Palsy: Technique and Results

Anthony Thanh Vu, MD
Cincinnati Children's Medical Center, Cincinnati, OH

Introduction: Brachial plexus birth palsies can lead to significant long-term morbidity, even when surgical treatment is attempted. Multiple nerve root avulsions present a particularly difficult problem for reconstruction due to the limited amount of donor nerves. The contralateral cross-C7 (CC7) nerve has been described for use as a donor nerve but mostly in adolescents and adults. More recently, the CC7 transfer via the retropharyngeal route has been described in attempt to improve outcomes owing to shorter nerve grafts. We present our technique and early results for the retropharyngeal CC7 nerve transfer to the lower trunk.

Methods: A retrospective review over the past 4 years was performed. We included any child less than 2 years of age who received a CC7 nerve transfer via the retropharyngeal route to the lower trunk for brachial plexus birth palsy. Charts were analyzed for patient demographic data, operative variables, postoperative motor and sensory recovery, length of hospital stay, and length of follow up. Complications related to the retropharyngeal dissection and the donor limb were also recorded.

Results: We had a total of five patients. Average age at the time of surgery was 157 days. Average operative time was 5.7 hours. Average hospital stay was 2 days. Average nerve graft length was 3cm. Variable degrees of hand sensation were present in all patients by 9 months. All patients had unprompted use of the recipient limb, independent of the donor limb. All patients had at least an AMS of 2/7 for finger and thumb flexion; one patient had an AMS of 7/7 for finger and thumb flexion. Only one patient has had return of intrinsic hand function with an AMS of 3/7. Regarding donor site complications, two patients had temporary triceps weakness and one patient had clinically insignificant temporary phrenic nerve paresis. There were no complications related to the retropharyngeal nerve dissection in any patient. Average length of follow up was 3.3 years.
A retrospective review of nine patients who also underwent the CC7 nerve transfer for other reasons did not demonstrate any permanent complications related to the donor limb or retropharyngeal dissection.

Conclusion: The retropharyngeal CC7 nerve transfer is a safe way of supplying extra axons to the severely injured arm in birth-related brachial plexus injuries without any permanent donor limb deficits. Early functional recovery in our patients with regard to hand function and sensation is promising.

P10. Validation of Anatomy and Motor Functional Outcome in a C7 to Biceps Rabbit Model of Brachial Plexus Injury

Kathleen Kollitz, MD; Guilherme Giusti, MD; Patricia F. Friedrich, BA; Allen T. Bishop, MD; Alexander Y. Shin, MD
Mayo Clinic, Rochester, MN

Introduction: Proximal brachial plexus injuries pose a reconstructive challenge to surgeons. While the rabbit has been used to model brachial plexus injury previously, reports conflict in anatomic detail and do not validate a nerve-muscle pair to measure motor function recovery after injury. The purpose of the current study is to 1) describe the innervation pattern of the rabbit biceps and 2) validate a technique for measurement of isometric tetanic force in the rabbit biceps muscle in order to establish an animal model of brachial plexus injury.

Methods: Part 1: Anatomy. Eight rabbits underwent electrophysiologic investigation. A bipolar nerve stimulator was used to systematically stimulate the roots, trunks and divisions and nerve branches of the rabbit brachial plexus and compound muscle action potential (CMAP) was used to record muscle response to stimulation.
Part 2: Motor Recovery Validation. Eighteen rabbits were anesthetized. The trunk formed by C6, C7 was clamped in a bipolar electrode. Compound muscle action potential (CMAP) was obtained. The proximal tendinous portion of the biceps was clamped in a force transducer. Muscle preload and electrical stimulation variables were optimized to obtain the highest tetanic muscle contraction. Wet muscle weight and nerve histomorphometry were also analyzed.

Results: Part 1: The C7, C8, and TI nerves form the middle and lower portions of the brachial plexus to terminate in the axillary, radial, median, and ulnar nerves. The musculocutaneous nerve innervates the biceps and branches from the median nerve. The biceps was innervated primarily by C7.
Part 2: The rabbit biceps muscle force demonstrated side-to-side equivalence. The maximum force for the right side averaged 2247.71g ± 378.20g (95%CI 2038.27-2457.15g) and for the left side was 2302.16g ±401.29g (95%CI 2079.94-2524.39g). The right side expressed as a percentage of the left averaged 99.7% (95%CI 88.9-110.5%). The wet muscle weight of the right expressed as a percentage of the left was 98.9% (95%CI 95.8-101.9%).

Discussion: The trunk formed by C6, C7 and the biceps muscle are an ideal model for studying reconstruction techniques after brachial plexus injury. Isometric tetanic force is equivalent from side-to-side in the rabbit as demonstrated by the high degree of overlap in the 95% confidence intervals for each side. The width of the 95% confidence interval demonstrates that there is more variability in the rabbit upper extremity than there is for the lower extremity or for the rat, and researchers should take this into account when performing power analyses in pre-experimental planning.

P11. Elbow Flexion Contractures in Obstetrical Brachial Plexus Palsy: Factors Associated with Decision to Pursue Treatment

Emily S. Ho, BSc OT Reg (Ont), Med[1]; Raheel Sheikh, BSc[2]; Howard M. Clarke, MD, PhD; FRCS(C) [1]
[1]University of Western Ontario, London, ON, Canada, [2]Hospital for Sick Children, Toronto, ON, Canada

Introduction: The prevalence of elbow flexion contractures reported in children with Obstetrical Brachial Plexus Palsy (OBPP) ranges from 48 to 85%. Children with OBPP and their families can opt to pursue a surgical or non-surgical treatment to improve the range of motion of the elbow and the cosmetic appearance of the limb. The decision to pursue treatment appears largely dependent on functional concerns and personal factors such as aesthetics and developmental age. The objective of this study was twofold: 1) Determine the clinical factors that predict whether a child with OBPP will pursue treatment for an elbow contracture and, 2) Explore the experience of young adults who had serial casting and splinting to elucidate factors associated with decisions to pursue treatment Materials and

Methods: A retrospective study of youth between 7 to 18 years who attended the authors? brachial plexus clinic in a 7-year period. The degree of contracture and functional outcome measured by the Brachial Plexus Outcome Measure (BPOM) Activity and Self-evaluation Scales were extracted from the clinic?s database. In-depth interviews were conducted with a purposeful sample of 6 young adults from this sample that had non-surgical treatment as a child.

Results: 287 children were identified, 87 excluded due to missing documentation. Average age was 11.1 + 3.1 years, females (58%) and upper plexus (77%) injuries. 25% (n=50) made the decision to pursue treatment for an elbow contracture (1 surgical release, 49 serial casting/splinting). 8 declined treatment. Average degree of contracture was 23.5 + 17.5 (Range: 20-90) degrees. 13% did not have a contracture. Stepwise logistical regression model indicated that greater severity in elbow contracture, higher BPOM Activity sum score and lower BPOM Appearance Scale scores were predictive of whether a child will pursue treatment for an elbow contracture. Five main themes emerged from the interviews: 1. Functional and aesthetic reasons to pursue and continue treatment were intertwined, 2. Youths? perspective of function and appearance changed over time, 3. Splinting and casting treatment had challenges, 4. Intrinsic versus extrinsic motivation was associated with success and adherence of treatment, and 5. Early knowledge and trial of treatment were important to the youth.

Conclusions: The degree of elbow contracture, perceived satisfaction with the appearance of the limb and objective upper extremity function were predictors of whether a child will pursue treatment for an elbow contracture. Elucidating the functional and aesthetic concerns that motivate the youth to pursue treatment is important.

P12. Severe Recurrent Cubital Tunnel Syndrome Treated With Revision Neurolysis And Amniotic Membrane Nerve Wrapping

Michael P. Gaspar, MD[1]; Patrick M. Kane, MD[1]; Michael M. Vosbikian, MD[2]; Hesham Abdelfattah, MD[1]; Mark S. Rekant, MD[1]

[1]Philadelphia Hand Center of Thomas Jefferson University, Philadelphia, PA, [2]Beth Israel Deaconess Medical Center of Harvard University, Boston, MA

Introduction: Perineural scarring of the ulnar nerve is a predominant cause of symptom recurrence following surgical treatment for primary cubital tunnel syndrome (CuTS). We report our preliminary experience with revision ulnar nerve decompression and nerve wrapping using an amniotic membrane allograft adhesion barrier.

Methods: We performed a retrospective review with prospective follow-up of patients with recurrent CuTS who were treated with revision neurolysis with amniotic membrane nerve wrapping. Preoperative grip strength, Visual Analog Scale (VAS) rated pain level, and Quick Disabilities of the Arm, Shoulder and Hand (QuickDASH) functional outcome score were compared to postoperative values using paired t-testing. Changes in symptom characteristics and physical exam findings over the course of treatment, incidence of complications, and level of satisfaction, were also obtained.

Results: Eight patients (mean age, 47.5 years) satisfied study inclusion. All 8 patients had undergone at least two prior ulnar nerve surgeries before revision neurolysis with amnion placement. At a mean follow-up interval of 30 months after surgery, significant improvements were noted in VAS pain levels (-3.5 vs. preoperatively; $P < 0.0001$), QuickDASH scores (-30 vs. preoperatively; $P < 0.0001$), and grip strength (+25 pounds vs. preoperatively; $P < 0.0001$) All patients expressed some degree of subjective satisfaction with their results. Importantly, no adverse reactions or complications occurred in any patients.

Conclusions: Ulnar nerve wrapping with an amniotic membrane adhesion barrier in conjunction with revision neurolysis, is a safe and effective treatment option for patients with severe and debilitating recurrent cubital tunnel syndrome.

P13. Weakness At Presentation Does Not Affect Outcome In Motor Nerve Malignant Peripheral Nerve Sheath Tumors

Ross Puffer, MD; Robert J. Spinner, MD
Mayo Clinic, Rochester, MN

Introduction: Malignant peripheral nerve sheath tumors of major motor nerves often present with pain and/or weakness. It is not known whether weakness as a presenting symptom confers any change in outcome compared to patients without weakness at presentation

Methods: A retrospective search involving MPNST cases at our institution since 1994 was performed. Cases not involving a major motor nerve were excluded. Outcomes and other factors were compared between patients presenting with documented weakness and those that did not

Results: A total of 181 cases of MPNST were reviewed. Of these, 65 involved a major motor nerve. Thirty-six patients (55%), presented with weakness, while 45% had only pain, sensory abnormality or no symptoms at all. MPNST location included 25 (38%) in the upper extremity, and 41 (62%) in the lower extremity. Complete excision (negative histologic margins) was performed in 51 (78%) patients. Adjuvant chemotherapy/radiation was performed in 52 (80%) patients. At the time of this abstract, 23 (35%) patients had died, and the mean time to death or last follow-up for the entire cohort was 35.9 +/- 4.9 weeks. There was no statistically significant difference between age, histologic grade, presence of metastases at presentation, ability to perform complete excision or outcome between patients presenting with weakness and those that did not.

Conclusion: In cases of MPNST involving a major motor nerve of the upper or lower extremity, weakness at presentation may not affect long term outcome.

P14. Brain Metastasis from Malignant Peripheral Nerve Sheath Tumors

Ross Puffer, MD; Christopher Graffeo, MD; Grant Mallory, MD; Mark E. Jentoft, MD; Robert J. Spinner, MD
Mayo Clinic, Rochester, MN

Introduction

Metastatic disease is a well-known sequela of malignant peripheral nerve sheath tumors (MPNSTs). Metastatic spread to the brain is unusual.

Case Report

A 56-year-old man was found to have a high grade MPNST of the sciatic nerve. Despite en-bloc excision of the sciatic nerve and local radiation post-operatively, he developed pathologically confirmed systemic metastases: 25 months after the diagnosis he was found to have lung nodules and received chemotherapy; and thirty-two months after initial diagnosis, he presented with left leg weakness and sensory changes and was found to have a lesion of the frontal lobe, received palliative radiation following which he developed systemic metastases and died 35 months after initial presentation.

Review of a clinical cohort

We retrospectively reviewed the charts of 179 patients treated at our institution with MPNSTs since 1994. This was the only case of a pathology proven brain metastasis, resulting in an incidence of 0.5%.

Discussion

Literature review revealed 22 total cases. The mean age was found to be 37.5 years, and mean survival after development of a brain metastasis was 9.9 months.

Conclusion

Brain metastases from MPNSTs are very rare and represent a poor prognosis, with survival after brain metastasis reported to be approximately 10 months. Early and effective initial diagnosis and treatment of MPNSTs likely represent the best opportunity for increased overall survival.

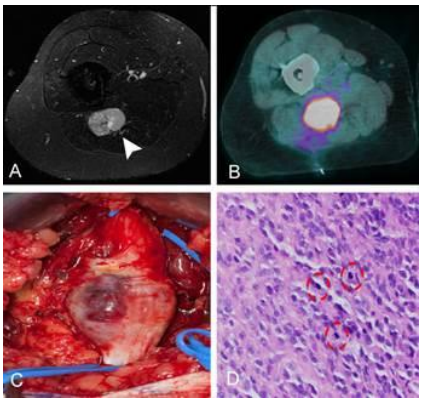


Figure 1. (A) T1-weighted, fat-saturation MRI scan with gadolinium demonstrating a heterogeneous mass arising from the sciatic nerve (arrowhead). (B) Avid FDG-PET uptake. (C) Intraoperative photograph demonstrating uniform enlargement of the sciatic nerve. (D) Pathologic specimen demonstrating a highly cellular tumor with multiple mitotic figures (circles).

Figure 2. En-bloc resection.

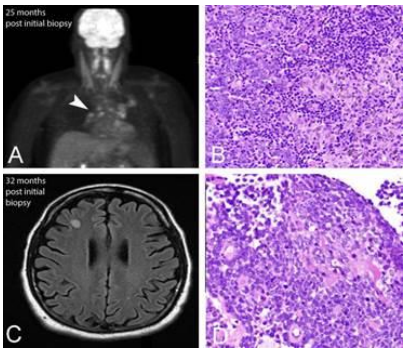


Figure 3. (A) Follow-up PET scan demonstrated evidence of FDG uptake within the peri-hilar lymph nodes. (B) Peri-hilar lymph node biopsy demonstrating evidence of metastatic MPNST. (C) An MRI was performed for new onset left sided symptoms demonstrating a non-enhancing mass in the right frontal lobe on T2-weighted FLAIR sequence. (D) Subsequent brain biopsy pathologic specimen again demonstrates metastatic MPNST.

P15. Surgical Treatment of Refractory Migraine Headaches: Preoperative Utility Assessment and Post-Operative Symptomatic Evaluation

Radbeh Torabi, MD[1]; Jacob P Veith, BS1[1]; Lynn A Bourn, BS[1]; Ahmed Ibrahim, MD, PhD[1]; Matthew J Bartow, MD[1]; William G Austen Jr., MD[2]; Tessler Oren, MD[1]

[1]Louisiana State University Health Sciences Center, New Orleans, LA, [2]Massachusetts General Hospital, Boston, MA

Background: Surgical treatment for migraine headaches, refractory to medical treatment, has recently produced promising results for patients with limited options. Utility scores are standardized tools offering validated means of measuring the health state preference of a health condition or disease state. The aim of this study was to prospectively determine the impact of the health state burden, prior to surgical treatment, to characterize the quality of life for this patient population and the symptomatic outcome post-operatively.

Methods: 28 consecutive patients [2 male (7.1%), 26 females (92.9%)], age of 48.1 years (SD=14.7) undergoing surgery for migraines were prospectively assessed to establish utility scores [visual analogue scale (VAS), time-trade off (TTO), and standard gamble (SG)] and Migraine-Specific Symptoms and Disability (MSSD) prior to surgical treatment. 15 patients reached 3 months follow up and completed MSSD.

Results: Despite medical treatment, MSSD demonstrated mean 17.3 headaches per month (SD=9.7), lasting 9.5 hours (SD=9.4) per episode, with a mean pain score of 7.6 (SD=1.6) for patients prior to surgical treatment. Utility scores (VAS, TTO, SG) for migraine headaches were 0.54 (SD=0.25), 0.57 (SD=0.25), and 0.62 (SD=0.27) respectively; similar to those for monocular blindness (0.49, 0.64, 0.61) but higher than binocular blindness (0.26, 0.32, 0.27), pre operatively. MSSD completed at 3 months demonstrated an overall improvement with mean 5.9 headaches per month (SD=6.2), lasting 5.3 hours (SD=7.9) with a mean pain score of 5.6 (SD=3.6). Of the 15 patients evaluated at 3 months, 9 patients demonstrated a symptomatic improvement >75% when multiplying number of headaches per month, length of headaches and pain score, including 5 patients with complete resolution of symptoms. Evaluation of the number of trigger points of the 6 patients that did not respond, demonstrated a mean of 3.6 trigger points pre-operatively (SD=1.1) and 2.6 trigger points post-operatively (SD=1.1).

Conclusion: Migraine headaches refractory to medical treatment can be objectively assessed using utility scores. Utility scores for migraine headaches were comparable to previously published data for unilateral facial paralysis and lower extremity lymphedema, and worse in comparison to common cosmetic deformities such as breast ptosis and an aging neck. Symptomatic evaluation at 3 months post-operatively showed the majority of the patients (n=9) undergoing surgery improved, while the non-responders (n=6) had a decreased number of trigger points. We have described the health state burden, in a prospective manner, in order to expand the benefits of surgical treatment of refractory migraine headaches.

P16. Supraorbital Rim Syndrome (SORS): Definition, Surgical Treatment, and Outcomes for Frontal Headache

Robert R Hagan, MD[1]; Jeffrey Janis, MD[2]; Michael A Fallucco, MD[3]
[1]Neuropax Clinic, St. Louis, MO, [2]Ohio State University, Columbus, OH [3]Florida Plastic Surgery Group, Jacksonville, FL

Background: Supraorbital Rim Syndrome (SORS) is a novel term attributed to a composite of anatomically defined peripheral nerve entrapment sites of the supraorbital rim region. The SORS term establishes a more consistent nomenclature to describe the constellation of frontal peripheral nerve entrapment sites causing frontal headache pain. In this article, we describe the anatomical features of SORS as well as evidence to support its successful treatment using the trans-palpebral approach that allows direct vision of these sites and the intraconal space.

Methods: A retrospective review of 276 patients who underwent nerve decompression or neurectomy procedures for frontal or occipital headache was performed. Of these, 96 patientsÕ treatment involved frontal surgery, and 45 of these patients were pure SORS patients that underwent this specific frontal trigger site deactivation surgery only. All procedures involved direct surgical approach through the upper eyelid to address the nerves of the supraorbital rim at both the bony rim and myofascial unit sites.

Results: Pre- and post-operative data from the migraine disability assessment questionnaire (MIDAS) was analyzed with paired t-test. Following surgical intervention, MIDAS scores decreased significantly at 12 months post-operatively ($p<.0001$).

Conclusions: SORS describes the totality of compression sites both at the bony orbital rim as well as the corrugator myofascial unit for the supraorbital rim nerves. Proper diagnosis, full anatomical site knowledge and complete decompression allows for consistent treatment. Further, the direct, transpalpebral surgical approach provides significant benefit to allow complete decompression.

P17. Inter-Rater Reliability of the SMILE System in Children with Möbius Syndrome

Tommy Nai-Jen Chang, MD[1,2]; Emily S. Ho, MD[2]; Alexandra Weinberg, MD[2]; Ronald M. Zuker, MD[2]; Gregory H. Borschel, MD[2]

[1]Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan, [2]The Hospital for Sick Children, Toronto, ON, Canada

Introduction: The SMILE system is a reliable grading system of facial reanimation that measures critical landmarks on pre-operative and post-operative 2D photographs in Adobe Photoshop®. The inter-rater reliability of the SMILE system has been established in adults, but not yet in a pediatric population.

Materials and Methods: A total of 107 patients with Möbius syndrome from a single cohort at The Hospital for Sick Children underwent facial reanimation surgery with free segmental gracilis muscle transplantation between 1985 to 2014. A retrospective analysis of 2D photographs was used to evaluate the inter-rater reliability of the SMILE system. Two independent raters evaluated the pre- and post-operative pictures of patients with Mobius syndrome. Inter-rater reliability of the excursion angles on both right and left sides were analyzed between the two raters.

Results: Sixty-two children had pre- and post-operative photos available for analysis. Nine cases were excluded because of poor photo quality and/or missing data. Of the 53 patients analyzed, 41 underwent motor nerve to masseter transfers and 12 had cross face nerve grafts to reinnervate the gracilis muscle flap for facial reanimation. The mean age was 9.2 ± 4.0 years old at the time of surgery. Intraclass Correlation Coefficient ($ICC_{(2,1)}$) of left /right angle measurements between the two raters were 0.957/0.904 pre-operatively and 0.974/0.951 post-operatively.

Conclusion: The SMILE system demonstrated excellent inter-rater reliability to evaluate preoperative and postoperative outcomes of facial reanimation in a pediatric population.

P18. Sensory Nerve Ending Structures After 5 Weeks of Vibration Exposure

Chaowen Wu, MD-PhD[1], Jordan Zimmerman, BS[2], James Bain, MS[2]; Danny Riley, PhD[12]
[1]Plastic Surgery, Medical College of Wisconsin, Milwaukee, WI, [2]Marquette University, Milwaukee, WI

Hand arm vibration syndrome (HAVS) is an occupational disease that causes debilitating numbness and vasospasm of the fingers. The mode of injury remains poorly understood which also inhibits preventative measures. Previous work has shown that one bout of 12 min vibration with a riveting hammer causes decreased sensation in the rat tail. However the effects on mechanosensory receptors of the skin have not been characterized. We aimed to study the effects of vibration on rat tail sensory nerve endings on the skin by examining changes after 5 weeks of vibration exposure.

8-wk-old Sprague-Dawley rats were divided into a tail-vibration group (n=8) and a sham-vibrated control group (n=8). The vibration group received 12 min of riveting hammer vibration exposure per day, 5 days per week for a total of 5 weeks. The Control group received the same treatment in terms of restraint and noise exposure, however they were not subjected to tail vibrations. When treatments were completed, the rats were euthanized and perfusion fixed with buffered formaldehyde. Mid-tail segments were removed, decalcified and frozen for cryostat sections. Lanceolate mechanosensory nerve endings surrounding hairs in the skin were immunostained by PGP9.5 and examined by fluorescence microscopy.
Interestingly, results showed that lanceolate nerve ending complexes appeared largely unchanged in number and organization between the vibrated and control non-vibrated groups. These findings may suggest that altered sensory perception is not a result of damage to sensory nerve endings at the skin level, but rather it may be secondary to changes in signal transduction in the peripheral or central nervous system. Alternatively, since PGP9.5 also stains Schwann cells, the observed complexes may represent preserved Schwann cell processes with or without intact nerve endings. Future experiments will be conducted to differentiate between Schwann cell processes and nerve endings of the lanceolate complex. This will determine whether vibration causes injury at the cutaneous mechanoreceptor level which may help in targeting preventative or treatment therapies for HAVS.

P19. Motor Unit Muscle Fiber Clumping in Large but not Small Reinnervated Muscles as an Indicator of Reduced Innervation after Peripheral Nerve Injuries and the Return of Fiber Type Compartmentalization

Tessa Gordon, PhD; DSc; Joanne Totosy de Zepetnek, PhD
University of Alberta, Edmonton, AB, Canada

Introduction: Motor unit (MU) muscle fibers innervated by one motoneuron, and muscle fiber types are normally distributed in a mosaic pattern in muscle cross-sections. A muscle nerve normally branches to supply muscle fibers in separate muscle compartments with slow and fast nerve fibers innervating deep and superficial compartments, respectively. We showed that this distribution is restored after reinnervation of large hindlimb muscles with MU and fiber type clumping apparent only when the nerve supply was reduced. Here we asked whether 1) MU muscle fiber and muscle fiber types 'clump' (defined as a significant increase in numbers of the fibers that are adjacent to one another) in a smaller reinnervated rat tibialis anterior (TA) muscle, and 2) regenerating slow and fast nerves reinnervate their original muscle compartments as they do in larger muscles.

Materials and Methods: TA muscle and MU contractile forces were recorded in normal muscles and in reinnervated muscles, 4-6 months after common peroneal nerve transection and surgical repair with random alignment of the nerve stumps. Glycogen-depletion for visualization and enumeration of MU muscle fibers was accomplished by exhaustive electrical stimulation of the nerve supply. Muscle fiber types identified with histochemical staining, were counted.

Results: First, the MU muscle fibers occupied defined territories in serial muscle cross-sections. The territories were significantly smaller in reinnervated TA muscles despite all motoneurons regenerating their nerves and reinnervating the muscles. The reinnervated MU muscle fibers and fiber types were clumped within 1 to 3 groups with significantly more MU muscle fibers lying adjacent to one another in parallel with a corresponding increase in muscle fiber type adjacencies. Second, reinnervated slow muscle fibers were localized to the deep muscle compartment as they are normally despite the failure of regenerating nerve fibers to reinnervate their former muscle fibers. Numbers of reinnervated slow muscle fibers were significantly increased and a significant proportion were located abnormally in the superficial compartment.

Conclusions: We conclude that 1) reinnervated rat MU muscle fibers clump within smaller muscle territory areas and 2) most but not all reinnervated slow muscle fibers locate normally to the deep muscle compartment. The significance of the findings is that fiber type clumping in small muscles that have relatively few MU muscle fibers in small territories, is *not* a reliable indicator of the extent of nerve regeneration whereas, in large muscles, 'clumping' may serve to indicate reduced numbers of intact MUs after complete or partial nerve injuries.

P20. Novel Rat Forelimb Model Optimizes Measurement of Functional Recovery after Chronic Denervation of Peripheral Nerves

Amy Quan, MPH, Joseph Lopez, MD MBA, Joshua Budihardjo, BS, Sara Mermulla, MBBS, Tariq Jawadi, BS1; Howard D Wang, MD; Ahmet Hoke, MD PhD; Sami Tuffaha, MD; WP Andrew Lee, MD; Gerald Brandacher, MD

Johns Hopkins University School of Medicine, Baltimore, MD

Introduction: Chronic denervation of upper and lower extremity motor nerves causes significant damage to peripheral nerves: Schwann cells undergo apoptosis, axonal basal laminae deteriorate, and target muscles atrophy. Thus, chronic denervation of peripheral nerves results in decreased nerve regeneration potential and negatively impacts clinical outcomes after extremity nerve trauma. Although the cellular and molecular effects of chronic denervation on peripheral nerve regeneration are well understood, previous studies have failed to correlate these results to behavioral functional results. To address this problem, we have developed a novel murine, upper extremity nerve injury model that optimizes measurement of functional recovery after chronic denervation injury.

Methods: We developed a forelimb chronic denervation model in which the median nerve was transected at the mid-humerus level and left in discontinuity for 0, 8 or 12 weeks. After the period of chronic denervation was complete, the distal median nerve stump was co-apted to the proximal end of a freshly axotomized ulnar nerve. Group 1 rats underwent 8 weeks of chronic denervation (n= 8); Group 2 rats underwent 12 weeks of chronic denervation (n=8); Group 3 rats (positive control) underwent immediate neurorrhaphy of the ulnar and median nerves (n = 8); and Group 4 rats (naïve control) did not undergo any surgical procedure (n = 8). Functional recovery was tested weekly by measuring grip strength using a force transducer, scoring the injured forelimb during feeding, and recording compound muscle action potentials (CMAPs) in the abductor pollicis brevis muscle of the injured limb. Animals were sacrificed at 14 weeks after ulnar-median neurorrhaphy for assessment of axonal regeneration and degree of muscle atrophy.

Results: Fourteen weeks after ulnar-median neurorrhaphy, Group 3 rats demonstrated significant functional recovery, as compared with Group 1. Group 3 rats demonstrated greater grip strength than Group 1 (2.2 ± 0.3 Newtons vs. 1.0 ± 0.1 Newtons, $P=0.001$), improved feeding (score of 7.3 ± 0.05 vs. 6.0 ± 0.04, $P<0.0001$), and greater CMAPs (1.7 ± 0.07 millivolts vs. 0.5 ± 0.04 millivolts, $P=0.0001$). Furthermore, forelimb flexor muscle weights were significantly different between Group 3 and 1 (0.82 grams vs. 0.53 grams; $P<0.00001$). Results for Group 2 and 4 animals are pending.

Conclusions: This novel forelimb chronic denervation model provides the first translatable animal model to assess functional recovery after peripheral nerve chronic denervation injury. This model provides a reliable model to assess future therapeutics aimed at augmenting extremity function following chronic denervation injury of peripheral nerves.