Peripheral Nerve Injury and Repair Options

Eric Hentzen, MD, PhD
Associate Professor, Orthopedic Surgery

University of California, San Diego
VA Medical Center, San Diego

May 20, 2017
Disclosures

• Synthes, Arthrex
Introduction

• Wide Spectrum of Disability

• Types of Injuries
  • Stretch/Traction
    • Most common
  • Crush
  • Laceration
  • Ischemic
  • Blast
  • Iatrogenic

• 75% Upper Extremity

• Prognosis
  • <50% regain useful function

• Tremendous amount of ongoing research…….
Anatomy – Cellular Level

• Axons
  – Transmit signals

• Schwann Cells
  – Supporting Cell of PNS
    • Produces Myelin
    • Secrete Neurotrophic Factors
  – Guides regrowth of axons
    • Cylindrical Orientation (Endoneurial Tubes)
    • Myelination of regenerating axons
Anatomy

- **3 Layers of a Nerve**
  - Epineurium
    - External Supportive Barrier
  - Perineurium
    - Surrounds individual fascicles
      - High Tensile Strength
  - Endoneurium
    - Loose Collagenous Matrix
    - Surrounds individual nerve fibers


Pathophysiology of Injury and Regeneration

- **Axon transected with traumatic degeneration in zone of injury**

- **Wallerian Degeneration** of distal nerve
  - Breakdown of neural and glial elements
  - Moderated by Schwann cells and macrophages
  - Only occurs with axon disruption
  - Starts 24-96 hours post injury
  - Completes by 6-8 weeks
Pathophysiology of Injury and Regeneration

- Growth cone regenerates
  - 1 mm/day, 1 inch/month
  - Basal lamina guides

- Schwann cells align to form Büngner bands

Injury Classification

- Seddon (1942)
- Sunderland (1951)

**Neurapraxia**: injury without physical disruption of axon or supporting structures *** No Wallerian Degeneration ***

**Axonotmesis**: disruption of axon but nerve in continuity (further subdivided by Sunderland based on structures disrupted)

**Neurotmesis**: complete transection of nerve
Prognosis

- Classification important for prognosis
- Neuropraxia - Full Recovery
- Neurotmesis - No Recovery
- Axonotmesis - Variable Recovery
Other Prognostic Factors

• **Age**
  – Younger do better
    • 3rd Decade

• **Level of the Lesion**
  – Distal better than proximal

• **Nature of the Nerve Injured**
  – Sensory recovers better than motor

• **Cause of the Injury**

• **Zone of Injury (soft tissue)**

• **Delay From Injury to Repair**
  – Surgeon has some control

Clinical Exam

• Careful documentation of neuro deficits
  – Define level and degree of injury
  – Baseline to compare for recovery

• Open injuries
  – Wound Evaluation
    • Clean/dirty
    • Zone of injury
  – Associated Injuries
    • Musculoskeletal
    • Vascular
Imaging

• Ultrasound
  – Reliable, cheap, available
  – Assess for continuity, neuroma, scar

• MRI
  – Nerves not accessible to ultrasound
  – Assess surrounding structures
    • Muscle atrophy, other soft tissues

Nerve Conduction Studies
Electromyography (NCS/EMG)

• Determine the site of injury
• Estimate severity of injury
• Follow and predict recovery

• NCS can localize the injury acutely

• EMG not useful acutely
  – becomes abnormal 3-6 wks after injury
  – acutely distinguish neuropraxia from axonotmesis/neurotmesis

• Indications
  – Closed Injuries/Fractures with Nerve Injury
    • e.g. Humeral Shaft Fractures, Knee Dislocations
  – Elective Procedures with Neuropraxia
    • e.g. Sciatic N after THA
Nerve Repair

• Indications
  – Open injuries
    • Neurotmesis (complete transection)
    • Acute repair
  – Closed injuries
    • Neuropraxia or Axonotmesis
    • Observe 3-6 wks
    • EMG
      – Baseline reinnervation, repeat in ~ 6wks
    • Imaging
      – Assess for continuity of nerve
      – US or MRI

• Delayed repair if discontinuous or no recovery in 3-6 months
Primary Repair

• **Best results: Immediate Primary Repair**

• Intraneural scarring with delay
• Earlier exploration provides easier diagnosis
  – Less scar tissue
  – Increased chance of matching fascicular arrangement

• **Prerequisites:**
  – Clean wound
  – Good vascular supply
  – No crush component
  – Adequate soft-tissue coverage
  – Skeletal stability
Primary Repair

• Goal = Tension-free repair
  – Tension causes
    • Gapping
    • Scar formation
    • Ischemia of nerve

• Mobilization of nerve
  – decrease tension
    • Transposition of Ulnar/Radial ➔ 3 cm
Primary Repair

• Technical Considerations
  – Neurolysis
    • Decrease tension
  – Resect to “healthy” nerve
    • Common cause of failure
  – Secondary Repair
    • Resect proximal neuroma and distal glioma
  – Gentle tissue handling
  – Microscope very helpful
Epineurial vs Fascicular Repair

• Equivalent results in most studies
• Exception is ulnar nerve near wrist
  – Motor fascicles definable
    • Ulnar side of nerve
• Epineurial Repair
  – 7-0, 8-0, 9-0 Nylon Suture
• Intra-fascicular Repair
  – 8-0, 9-0, 10-0
Nerve gap

• Precludes tension-free repair

• Occur with
  – Wide zone of injury
  – Delay in repair
    • Retraction
    • Scarring
  – Excision of neuroma or tumor
Nerve Gap Repair Options

• Operative Treatment
  – Grafting
  • Autograft
    – Cable
    – Trunk
  • Allograft
    – Transplantation
    – Decellularized
  • Conduits
    – Biologic
    – Synthetic
Nerve Autografts

- Gold Standard
  - Nerve architecture
  - Growth factors
  - Nonimmunogenic

- Drawbacks
  - Donor site morbidity
    - Scar
    - Sensory deficit
    - Potential neuroma
  - Limited availability
Donor Autografts

- Requisites:
  - Tolerable donor site morbidity
  - Sufficient length
  - Appropriate caliber
  - Ease of harvest

- Cutaneous Sensory nerves

- Sural Nerve most common donor
  - 40 cm length

- Multiple Other Donors
  - Upper Extremity
    - MABC, LABC, SRN, PIN, AIN
  - Lower-Extremity
    - SPN, LFCN, Saphenous
Autograft

- Technical Considerations
  - Same principles as primary repair but 2 repair sites
  - Tension-free repair
    - Graft 10-20% longer than defect
- Cabled Grafts
  - Injured nerve often larger than donor nerve
  - Multiple lengths of donor placed in parallel
  - Match diameter of severed nerve
  - Fascicular repair
4 cm Gap w/ Sural Nerve Cabled Autograft

Prox Ulnar Nerve

Distal Ulnar Nerve

Cabled Sural Nerve
Nerve Allograft

• Advantages
  – No donor site morbidity
  – Unlimited Supply
  – Potential recovery near autograft

• Two Options
  – Tissue allograft
  – Decellularized allograft
Tissue Allograft Nerve

- **Allotransplantation**
  - Alberts 1885 -> 1st allograft transplant
  - Primary drawback – immunogenicity

- Graft processing can decrease MHC II
  - Chemical treatment
  - Cold Preservation
  - Irradiation
  - Repetitive Freeze-Thaw
  - Lyophilization
  - University of Wisconsin Storage Solution
    - Pen G + Dexamethasone + Insulin + 5 Celsius x 7 days

- Patients still require 24 months of immunosuppression
- Has place for patients with very large nerve deficits to crucial nerves
Decellularized Allografts

- Acellular - Non-immunogenic
- Highly processed
  - Detergent, Gamma Irradiation
  - Enzymatic Degradation
    - Modulate surface molecules that regulate axon ingrowth
- Structural architecture maintained
  - Microtubules, laminins
  - Support nerve regrowth

- Results equivalent to autograft for sensory nerve gaps up to 3 cm

- Larger gaps or Motor or Mixed nerve
  - Less data, more mixed results in humans
  - Poorer results in animals
Conduits

• Simple tubes to direct nerve regeneration
  – Direct axon regrowth
  – Provide barrier to fibrosis
  – Concentration of growth factors in gap
  – Lack Schwann cells, neurotrophic factors and architecture

• Biologic
  – Vein/Artery

• Synthetic
  – Collagen (NeuraGen, Integra)
  – Polyglycolic Acid (NeuroTube)
  – Caprolactone (Neurolac)
Conduits

• Uses
  – Small sensory nerves
  – Short gaps < 3 cm
    • Inferior for larger gaps and also head to head compared to allografts and autografts in animal studies
  – Augmentation of primary repair or grafting

• Advantages
  – Directs nerve regrowth
  – Prevents fibrosis
  – Ease of use
  – Structural support for repair

• Disadvantages
  – Cost
  – No Schwann cells or nerve architecture
  – Only for small gaps in sensory nerves
# Summary

<table>
<thead>
<tr>
<th></th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Repair</td>
<td>• <strong>Best Outcomes</strong></td>
<td>• Must be tension free</td>
</tr>
<tr>
<td>Autograft</td>
<td>• <strong>“Gold-Standard” for Gaps</strong></td>
<td>• Donor Site Morbidity</td>
</tr>
<tr>
<td></td>
<td>• Non-Immunogenic</td>
<td>• Scarring</td>
</tr>
<tr>
<td></td>
<td>• Bridges Long Gaps</td>
<td>• Neuroma Formation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Limited Supply</td>
</tr>
<tr>
<td>Allograft</td>
<td>• Abundant Supply</td>
<td>• Expensive $$$$ (Decellularized)</td>
</tr>
<tr>
<td></td>
<td>• No Donor Site Morbidity</td>
<td>• Immunosuppression (Allo)</td>
</tr>
<tr>
<td></td>
<td>• Non-Immunogenic</td>
<td>• Less experience</td>
</tr>
<tr>
<td></td>
<td>(Decellularized)</td>
<td></td>
</tr>
<tr>
<td>Conduits</td>
<td>• Abundant Supply</td>
<td>• Expensive $$$</td>
</tr>
<tr>
<td></td>
<td>• No Donor Site Morbidity</td>
<td>• No Architecture for Regrowth</td>
</tr>
<tr>
<td></td>
<td>• Less Scarring</td>
<td>• Only short gap, sensory</td>
</tr>
<tr>
<td></td>
<td>• Accumulate NGF’s</td>
<td></td>
</tr>
</tbody>
</table>
Summary

- Primary repair without tension always preferred

For Gaps
- Autograft → GOLD STANDARD
  - Nothing shown better than autograft in any clinical situation
- "Classic" Allograft with immunosuppression
  - Very large defects when autograft not available
- Decellularized Allograft
  - Gaps from 1 – 5 cm
    - Preference for sensory and < 3 cm
- Conduits
  - Sensory Nerves with gap < 1.5 cm
  - Adjunct to Direct Repair
Summary

Length of nerve gap (cm)

- Autograft
  - Decellularized Allograft
- Conduit
- Primary Repair
Thanks!