Challenges and Opportunities in Restoring Function after Paralysis

IEEE Life Sciences Grand Challenges

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I am a stock holder in NDI Medical and member of the SAB. I will mention one of their products.

I have no other conflicts.
Number of People Living with Paralysis in US*

N = 5,596,000

- Spinal Cord Injury: 1,275,000 (23%)
- Multiple Sclerosis: 939,000 (17%)
- Stroke: 1,608,000 (29%)
- Unspecified Birth Defect: 110,000 (2%)
- Neurofibromatosis: 212,000 (4%)
- Traumatic Brain Injury: 242,000 (4%)
- Cerebral Palsy: 412,000 (7%)
- Post-Polio Syndrome: 272,000 (5%)
- Other: 526,000 (9%)

*Paralysis = CNS disorder resulting in difficulty or inability to move upper or lower extremities
Body Systems Affected by Paralysis

• Virtually all body systems can be affected
• Paralysis often affects multiple body systems in a single person
• Significant impact on independence and quality of life
Manifestation of Paralysis:

- Loss of voluntary movement
- Undesired involuntary movement (spasticity and spasms)
- Loss of sensation (skin breakdown and perception)
- Pain
Desired Functional Recovery Identified by People with SCI

(K. Anderson, 2004)
Treatment Options

• Therapy and Medical Management
• Assistive Technology – individually augmentative
  Orthoses (braces), Mobility aids (Wheelchairs, Braces,
  Crutches, Cushions, Urinary collection devices,
  Robotics…
• Restorative therapies (Robotics, e.g. BWST,…)
• Surgical Interventions
  Few are available (tendon transfers, full muscle transfers,
  tenomoties, neurotomies, …)
• Electrical Stimulation
  – Therapeutic intervention (restorative)
  – Neuroprosthetic intervention
• Neural Regeneration (biological)
• Combinational Interventions
Opportunities

• Recovery of Voluntary Function
• Restoration of Function – substitution via neuroprosthetics
• Linkages between Recovery and Restoration
Challenges

• Clinical
  – In some disorders, such as Spinal Cord Injury, relatively small numbers of patients (who will be effected for decades of their lives = enormous societal costs)
  – Heterogeneous injuries – one solution does not apply to all
  – Early intervention

• Technical and Scientific
  – Often expensive technology – Class III
  – Insufficient designs
  – Inaccessible for trials
The CRM market registered double digit growth rates in early 90s but, the market is not likely to return to these high double digit growth rates… analysts are hopeful of the market maintaining a mid-single digit growth rate in the coming years.

Source: Global Cardiac Rhythm Management (CRM) Market Report: 2009 Edition (Koncept Analytics)

1 Cardiac: Pacemakers, Implantable Cardioverter Defibrillator (ICDs), and Cardiac Resynchronization Therapy Device (CRTs)
2 Non-Cardiac: All non-cardiac implantable pulse generators
Where does Electrical Stimulation Fit?

**Delivery of Electrical Stimulation**

**Surface Stimulation**
- Biofeedback
- FES Bikes
  - * Electrodes placed onto the skin to cause a temporary contraction of the muscle

**Percutaneous Stimulation**
- Temporary use or demonstration phase
- * Needle electrodes through the skin connected to an external stimulator

**Neuro-Prosthesis**
- Fully implanted, long-term use to restore a function lost
  - * Surgically implanted device connected to an array of electrodes with custom programming ability
1. Electrodes
   – Surface – thousands in use
   – Percutaneous – in pivotal clinical trials (NDI Medical)
   – Implanted – used with IPG
     • Intramuscular and Epimysial electrodes – thousands in human subjects – excellent performance
     • Nerve – several designs – many in clinical use commercially; evolving designs with multiple contacts
     • Spinal Cord epineural electrodes – thousands in clinical use (particularly for SCS)
     • Intraspinal Microstimulation (ISMS) – evolving from pre-clinical use
Electrodes Developed by CWRU/Cleveland FES Center
1970s - present

- Spiral Nerve Cuff
- Epimysial Myoelectric Recording Electrode
- Intramuscular Stimulating Electrode
- Epimysial Stimulating Electrode
- In-line Connectors

Electrodes Developed by CWRU/Cleveland FES Center
1970s - present
2. Stimulators

- Surface – many; most open loop
- Percutaneous – low profile design in pivotal trial
- Implanted – many designs
  - RF powered and battery powered (primary and secondary cells)
  - Most have only a single or few channels
  - Programmable – to some extent
  - Most operate open loop
  - Advanced designs – emerging to clinic now
    - BIONS
    - Networked Neuroprosthesis
Networked Neuroprosthesis

- Applicable to multi-system dysfunction
- Fully implantable
- No external components during functional use
- Modular
- Scalable
- Upgradeable components
- Externally programmable
Networked Neuroprosthesis Components

- Power Module
- Network Cable And Connector
- Remote Modules
- 4 Channel Stimulator
- 2 Channel Myoelectric Signal
- Stimulating And Recording Electrodes
Summary of Tools

- Many implanted designs, but often not accessible
- Most IPG’s are for specific specialized indications
- Most FDA approved IPG devices are not available for off label clinical use
- Good “stable” of subcontract manufacturers exists
- FDA familiar with the overall field
- Evolving tools provide platform technology for new clinical discovery and application
- Need to design the entire system – not just the individual components
Major Unsolved Clinical Problems

- Restoring movement
- Providing command control inputs
- Restoring sensation
- Suppressing spasticity
- Controlling pain

- Examples of Approaches Follow -
Recovery: Relearning in the Nervous System in Chronic Stroke Survivors

Contralaterally Controlled FES Therapy Lab Sessions

Work of Knutson & Chae - CWRU
Cervical intraspinal stimulation to promote recovery after Spinal Cord Injury

Recovery after injury?
- Rats trained at forelimb reaching task (FRT)
- C4-C5 unilateral contusion injury
- Implanted with intra-spinal stimulating electrodes below injury
- Paired based on deficit in FRT & cylinder exploration
- Randomly assigned to:
  - Stimulated group (N = 11)
  - Unstimulated group (N = 11)
- Stimulated 7hp, 5dpw, 12 wk

Modified from Mushahwar et al., *J Neural Eng* (2007)

Kasten & Moritz (IFESS 2012)
Intra-spinal stimulation (7 hrs/day) improves forelimb reaching

Kasten & Moritz (IFESS 2012)
Sagittal Shifting

L TA

R TA

L MG

R MG

0.4 mV

3 sec

Lateral Shifting

0.4 mV

3 sec

Harkema, Edgerton et al
Standing with Implanted Neuroprosthesis
2nd Generation Hand Neuroprosthesis
Bilateral Implanted EMG Control

Annette
C6 Tetraplegia
NP user for 22 mo.
Service dog trainer

Research studies of Keith, Kilgore, Peckham
Tyler Lab Peripheral Nerve Stimulation for Sensory Restoration

Stable response since implant on 5/24/12

Electrodes under socket

19 Stimulation Channels →
19 Unique Locations / Sensations
PA: 0.6 – 0.9 mA; PW: 80 – 250 usec

Funding:
VA Merit Review
TATRC

Acknowledgements:
Daniel Tan; Michael Keith, MD; Robert Anderson, MD; Joyce Tyler, OTR/L, CHT; Melissa Schmitt, RN; Matthew Schiefer, PhD; Christiane Mhanna; Jennifer Wall

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High Frequency Alternating Current Nerve Block

Rat Sciatic

Test Stimulus On 0.5 Hz, Supramaximal Twitch

Block On 10kHz, 4Vpp, Sinusoid

Tendon Tension

Time (seconds)

Proximal P.S.  Block  D.S.  Distal

Work of Kilgore & Bhadra, CWRU
Potential Applications for HFAC Block

• Motor Block
  – Spasticity control in Stroke, Multiple Sclerosis, Cerebral Palsy, Head Injury
  – Bladder/bowel sphincter relaxation
  – Block of movement in movement disorders such as Dystonia, Torticollis, Tourette Syndrome
  – Spasm block post-operatively
  – FES-related spillover block

• Sensory Block
  – Neuroma pain
  – Chronic peripheral nerve pain
  – Cancer pain block
  – Post-operative pain block
  – Spasticity control through sensory block, including continence control

• Autonomic Block
  – Sympathetic block for hyperhidrosis
  – Celiac plexus block for pancreatic cancer
Multi-Function System

Hand/Reach
8-12 Muscles
2-4 Myoelectric
Control Channels

Cough
2-3 Spinal Cord
Stimulation Channels
1 External Switch

Bladder/Bowel
3 Spinal Root
Stimulation Channels
2 Nerve Block
Channels
1 External Switch

Trunk Support
4-6 Muscles
Per Side
1-2 Myoelectric
Control Channels
1 External Switch

Multi-Function System
Techniques to Interface with Nervous System

- **Electrical** - most advanced and proven
  - Mostly for stimulation
    - Safe
    - Reversible
    - Precise – but not at cellular level
  - Techniques for inhibition being tested in humans
- **Drugs**
  - Systemic delivery (intrathecal)
  - Need precise delivery
- **Magnetic**
- **Optical**
  - Discovery phase
Longer Term Challenges

• New cellular level neural interfaces at peripheral nerve and spinal cord levels
• Advanced neuroprosthetic systems employing closed loop control
• Cortical interfaces that provide “natural – thought generated” control (Dr. Gao)
• Tissue engineered scaffolds that enhance neural regeneration (& guiding axonal growth)
• Combinatorial strategies
Summary

- Manifestations of paralysis are enormous personally and to society
- Heterogeneity of injuries between paralyzed people presents challenges in deployment
- Tools are emerging – safety is proven for many; must design for entire system
- Opportunities in both recovery and restoration of function
- Several examples of deployment into clinic – clinicians and patients desire and will accept these solutions
- Need to train workforce (students) for translational future to see results brought to clinic
- Innovative translational approaches will be necessary to realize the clinical benefits