Advances in Neurostimulation for Pain
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Disclosures
Corporate Ownership, Equity, Stocks, Bonds
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Corporate Fiduciary or Board Positions
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Patents
None

1965 – Melzak and Wall publish Gate Theory of Pain
1967 – Shealy 1st clinical use of SCS
1972 – Shealy stops using SCS after ~500 patients worldwide
1973 – Shealy 1st commercially available RF systems
1981 – First totally implantable stimulator
1982 – First 4-contact electrode RF systems
1984 – First totally implantable stimulator
1987 – Shealy begins SCS modeling
1988 – First 8-contact electrode RF system
1993 – Barolat et al. publish exhaustive map of SCS coverage pattern
1995 – Matrix: 8-contact 2-channel RF system
1999 – Synergy: 8-contact 2-channel totally implantable stimulator
2000 – Genesis II: 2-contact 3-channel totally implantable stimulator
2001 – Synergy II: 6-column paddle electrode
2004 – First rechargeable IPG with 16 independent current sources
2009 – IPG with position-sensitive adjustments
2010 – 5-column paddle electrode
2013 MRI compatible IPG and percutaneous leads
2015 MRI compatible IPG with upgradeable firmware
2015 – HF10 therapy approval
2015 – Small RF SCS system approval
2016 – Fully MRI compatible paddle system
2016–2013 – Small RF SCS system approval
2015 – Genesis II: 2-channel totally implantable stimulator
2014 – IPG with upgradeable firmware
2013 – Small RF SCS system approval
2013 – MRI compatible IPG and percutaneous leads

History of SCS

Recent Developments

Patient selection for Neurostimulation for Chronic Pain

• Most neuropathic pain syndromes
  – CRPS
  – Painful neuropathies (Diabetic, small fiber, post herpetic neuralgia)
  – Neuropathic facial pain/anesthesia dolorosa
  – Nerve injury pain
  – Failed back/neck surgery syndrome
  – Radical pain with the absence of surgical lesions and possible presence of arachnoiditis, fibrosis
• Patients with surgical pathology but predominant neuropathic or burning pain secondary to prolonged nerve compression or injury
• Poor response to conservative treatment
• Remedial surgery inadvisable
• No major psychiatric disorder, including somatization complaints
• Willingness to stop inappropriate drug use before implantation
• Minimized secondary gain
• Patient preference over repeat surgery

SCS Advances

• SCS Evidence
• Stimulation programming
• Stimulation leads
• Stimulation methods
• Stimulation indications
RCT of SCS vs. Reoperation

• North et al 2005, Neurosurgery
• Fifty patients
  – Equipoise between SCS and repeat surgery
  – Allowed to cross over to other therapy at 6 months
  – Followed for a mean of 3 years.
• Crossover rates significantly different
  – 17% of SCS patients opted for repeated operation
  – 67% of reoperation patients opted for crossover to SCS (p = 0.02).
• Success after crossover –
  – 0% (0/4) SCS patients
  – 43% (6/14) repeat surgery patients

SCS vs. Reoperation

Success: combination of ≥ 50% VAS reduction and pt satisfaction

Crossover Rates

SCS Cost effectiveness

• Data from first 42 patients of RCT by North et al. (Neurosurgery 2007)
  – Mean 3.1 year follow up
  – The cost per patient who achieved long-term success with SCS alone was $48,357.
  – The cost per patient who achieved long-term success with reoperation alone was $105,928.
  – Crossovers to SCS achieved success (5/13) at mean cost of $117,901
  – Crossovers to repeat surgery achieved no success despite mean cost of $260,584

Real World SCS Outcomes

Real World SCS Outcomes – Back Pain Only

New SCS Programming

• I am not an electrical engineer
• The number of possible anode/cathode combinations with a 16- or 32-contact SCS system is tremendous
• Improved software automates programming
New SCS Programming

- Even small lead migration causes loss of pain relief
- The stimulation system can now detect changes in the relative position of contacts
- In the future the stimulator will automatically compensate for this and change contact combinations to maintain a similar charge field

Anode intensity Management transfers some of the cathodal current to a distant location (like the IPG) at subthreshold levels

The theoretical result is increased dorsal column stimulation with reduced dorsal root stimulation

New SCS IPG

- More power sources in the IPG power more contacts
  - 32-contact paddle leads
  - Multiple 4-8- or 16-contact leads
  - Allows for addition of more leads in future if pain location changes

New SCS Electrodes

- More power sources in the IPG power more contacts
  - 32-contact paddle leads
  - Multiple 4-8- or 16-contact leads

New Stimulation Paradigms

- Current practice –
  - 40-80 Hz
  - Paresthesia mapping
  - Patient cooperation
  - Back pain relief problematic
- High frequency SCS
  - 10,000 Hz
  - No paresthesia mapping
  - No patient cooperation
  - Improved back pain relief

High Frequency SCS

- Schecter, et al. Anesthesiology 2013
  - Rat sensory nerve ligation model of neuropathic pain
  - SCS at 50Hz, 1kHz, 10kHz
  - kHz SCS reduced hypersensitivity better than 50Hz
  - However, 50Hz stimulation better reduced windup in dorsal horn cells
High Frequency SCS (10Khz)

- van Buyten, Neuromodulation 2013
  - 83 trials, 72 successful, 6 month evaluation
  - 11/14 pts who failed prior SCS had successful trial
  - Back pain VAS − 8.4 ± 2.7 – 78% improvement
  - Leg pain VAS 5.4 ± 1.4 – 83% decrease
  - Daily charging needed

10KHz SCS RTC

- 10KHz SCS vs traditional SCS
- 80% FBSS pts
- Pts randomized to treatment
- Not blinded, as HF SCS produces no detectable paresthesias
- Both treatments significantly reduced pain in a durable fashion, with HF SCS producing a larger VAS decrease in both back and leg pain
Kapural, Anesthesiology 2015

HF SCS 24 month f/u

- Al-Kaisy, pain med 2014
  - 24-month prospective f/u
  - 2 explants due to poor pain relief
  - Mean ODI decrease of 15 points (55-40)
  - Significant decrease in opioid use
  - 6% infection rate, 4.8% lead migration

10KHz SCS vs Surgery for FBSS

- HF SCS RCT
  - ODI improved average of 16.5 for HF SCS and 13.0 for traditional SCS
  - 69% of HF SCS and 51% of traditional SCS pts had LBP VAS <2.5
  - 76% of HF SCS and 38% of traditional SCS pts had leg pain VAS <2.5

Burst SCS

- The thalamus communicates in burst patterns
- Delivers "packets" that have more charge per second than tonic stimulation
- Requires less temporal integration than tonic stimulation
- Often does not produce paresthesias

Burst SCS

- Thought to involve the “medial pathway” of pain signaling
- Controls affective components of pain

Review of RCT Spine surgery vs nonop mgmt for FBSS

**Burst SCS**

- De Ridder, World Neurosurgery 2013
- 15 patients
- Each randomly received 1 week burst, tonic and placebo
- Burst and tonic better than placebo
- Burst better than tonic for back and general
- No difference between burst and tonic for leg pain

<table>
<thead>
<tr>
<th>Feature</th>
<th>Tonic</th>
<th>Burst</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>Test 1</td>
<td>6.4%</td>
<td>8.1%</td>
<td>5.2%</td>
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<tr>
<td>Test 2</td>
<td>7.3%</td>
<td>7.5%</td>
<td>6.8%</td>
</tr>
<tr>
<td>Test 3</td>
<td>6.3%</td>
<td>7.1%</td>
<td>5.8%</td>
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<tr>
<td>Mean</td>
<td>6.9%</td>
<td>7.6%</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

**Burst SCS**

- De Vos, Neuromodulation 2014
- 48 patients with FBSS and PDN, some who became refractory to tonic SCS
- 2 weeks burst stimulation
- Pain—additional 44% improvement in PDN and 28% in FBSS

**Dorsal Root Ganglion Stimulation**

- Located in neural foramen
- Contains A-beta, C fibers and A-delta fibers
- Physiologic changes in these neurons in chronic pain states
- Stimulation here may exert different effects than DCS
- Stimulation produces very selective distribution of paresthesias
  - Can selectively target foot, groin, etc without overflow

**Dorsal Root Ganglion Stimulation**

- Eldabe, Neuromodulation, 2015
  - 8 pts with PLC, 14mos avg f/u, all with successful trials, prospective
  - 5/8 with pain relief ranging from 26-100%

- Lim, Neuromodulation, 2015
  - 51 trials, 32 implants, variety of pain etiologies, 1 year prospective f/u
  - Overall pain VAS improvement from 77.6 to 33.6 at 1 year (similar for back and leg pain)
  - Motor stimulation in 14%, infection 8.5%, CSF leak 8.5%

- Schu, Pain Practice 2015
  - 29 patients, total 49 leads, avg 27 week f/u, retrospective
  - Etiologies—herniorrhaphy (13), vascular access (2), other surgery (7) and others
  - VAS improved from mean 74.5 to 20.7 (71.4%)  

**Craniofacial Pain**

- Occipital nerve stimulation
  - Greater occipital nerve
  - Lesser occipital nerve
  - Third occipital nerve
- Supraorbital nerve stimulation
- Infraorbital nerve stimulation
- Auriculotemporal nerve stimulation
- Sphenopalatine ganglion stimulation

**Trigeminal Branch**

- Supraorbital or infraorbital
- Mandibular stim usually avoided due to lead mobility
- Target – 1cm above supraorbital rim or below infraorbital notch
- Percutaneous trial
- Craniofacial Pain
  - Papers mostly case series
    - Retrospective, small, VAS-based
    - Many corporate funded trials not published
  - Hardware not designed for this indication
  - Complication rate high
    - Migration as high as 40%
    - Tip erosion

- Craniofacial Pain
  - Bilateral occipital neuralgia with tinel's signs, allodynia and good transient response to ONB

- Craniofacial Pain
  - Chronic bifrontal migraine headache

- Craniofacial Pain
  - Chronic holocranial pain following meningitis

- ONSTIM Trial
  - Corporate-funded trial of ONS for migraine
    - US, Canada and UK centers
    - Old hardware – Pisces quads and Synergy/Versitrel
  - Randomized 2:1:1 between adjustable stim:preset stim:medical
    - Preset stim – 1 min per day only, no titration
    - Positive temporary response to ONS
    - No trial – full implant if coverage achieved in OR
  - 110 subjects enrolled, 75 randomized, 67 completed 3 month f/u

- ONSTIM Trial
  - VAS change
    - AS – 1.5 ± 1.6
    - PS – 0.5 ± 1.3
    - MM – 0.6 ± 1.0
  - SF-36 and other functional measures not significantly improved
ONS RCT for Migraine

- Corporate-funded trial of ONS for migraine
- Only trial successes (>50% pain reduction) randomized
- Randomized 2:1 between active and sham stim
- 12 week phase
- 268 subjects trialed over 5 years
- 157 implanted and randomized
- 105 active, 52 control
- “Responder” – reduction of pain of >50% with no increase in avg headache duration

ONS RCT for Migraine

- ITT analysis
- 18 responders in active group (17.1%)
- 7 responders in control group (13.5%)
- P=0.55
- Significantly more pts in active group achieved 10%, 20%, and 30% improvement
- MIDAS significantly improved in active group c/w control group (p=0.001)
- Active group – 27.2% reduction in headache days
- Control group – 14.9% reduction in headache days

ONS RCT for Migraine

- Lead migration – 16.6%
- Infection – 6.4%
- IPG site pain/discomfort – 17.8%
- 51 pts (32%) required 93 additional surgical procedures
- IPGs in the abdomen and buttocks were associated with a significantly higher percentage of AEs
- AEs decreased with increasing implanter experience

Cluster Headache and Sphenopalatine Ganglion

- Cluster headache involves autonomic responses of the trigeminal system
- SPG innervated by parasympathetics from nervus intermedius via the greater petrosal n.
- SPG projects to lacrimal glands, nasal mucosa
- Postganglionic parasympathetics also travel with trigeminal n
- Postganglionic fibers sympathetic from superior cervical ganglion also pass through
- Innervates eye, nose, soft palate, pharynx
- Via the trigeminal system SPG has connections to dura

SPGS Implant

- Schoenen, Cephalgia 2013
- 28 patients
- Corporate-funded trial
- 4wk baseline, 6 wks titration, 3-8 wks randomized, open label out to 1 yr
- Randomized period – shortest period needed to treat 30 attacks
- Full stim vs sub perception stim vs sham (remote randomized stims)
- Paresthesias felt in the nose
- Stim used on demand
- Avg 20 attacks treated per patient
**SPGS Trial**

- Pain judged on 0-4 scale
- Pain relief (0-1) achieved in 15 mins in 67% of full stim treated attacks vs 7.4% sham stim attacks
- Pain freedom (0) achieved in 15 mins in 34% of full stim treated attacks vs 1.5% sham stim attacks

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<thead>
<tr>
<th>Full stimulation</th>
<th>Submaximal stimulation</th>
<th>Sham stimulation</th>
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<tbody>
<tr>
<td>Hb%</td>
<td>Hb%</td>
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<tr>
<td>median</td>
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<tr>
<td>0.74%</td>
<td>0.74%</td>
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<td>0.72-1.00%</td>
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<tr>
<td>Global comparison</td>
<td>p &lt; 0.001</td>
<td>= 0.001</td>
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**Motor Cortex Stimulation**

- Tsubokawa – 1991
  Deafferentation pain best treated with stimulation above level of deafferentation
  Where to stimulate for thalamic pain?

- Post-central cortical stimulation failed
- PRE-central cortical stimulation succeeded!

**MCX Stim: Technique**

- Must understand homunculus organization
- Target craniotomy and electrode localization

**MCX Stim: Electrodes**

**MCX Stimulation Problems**

- No uniformity in results reporting
- Optimal stimulation parameters?
- Optimal hardware?
- Seizures
- Tachyphylaxis

**MCX Stimulation Tachyphylaxis**

- Affects almost all patients
- Reprogramming time-intensive
- Higher risk of seizure
- Rarely permanent
- ?Cortical plasticity
DBS for Pain

- Vc Sensory Thalamus (VPM / VPL)
- Paresthesia producing
- PVG
- Endorphin release
- Pain pathway modulation

DBS for Pain

- Levy 1987
  - 141 patients average F-U 80 mo.
  - 84 with deafferentation pain and 57 with nociceptive pain
  - Deafferentation pain treated predominantly with VPM/VPL stimulation and nociceptive pain with PVG stimulation
  - 83 (59%) implants following the trial
  - At 80 mo, 31% maintained significant pain relief

DBS for Pain

- Coffey 2001
  - Multi-center trial of DBS with 2 phases, the second using the modern 3387 DBS electrode
  - 15 diagnosis: Thalamic (11) accident (6) and post laminectomy (8)
  - 50 implants / 37 internalizations
  - 22% of internalized with >50% at 3 mo and 14% at 24 mo
  - No correlation between efficacy and electrode location
  - Sponsor did not pursue DBS FDA labeling for chronic pain

DBS for Pain

Owen and Aziz 2006:

- 15 patients with post-stroke pain
- 24 mo FU
- A implanted initially with PVG and Vc for trial
- 12 implanted following trial (7 PVG/4 PVG/Vc/ 1 Vc)
- 2 patients with >50% relief
- 7 with >40% relief
- Cortical strokes with better outcomes than subcortical

Thank you for coming!

E-mail: jrosenow@nm.org
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Come to Chicago in 2016!

April 30, 2016

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