Advances in Neurostimulation for Pain

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History of SCS

- 1965 – Melzak and Wall publish Gate Theory of Pain
- 1967 – Shealy 1st clinical use of SCS
- 1972 – First commercialized single electrode RF systems
- 1973 – Shealy stops using SCS after ~500 patients worldwide
- 1978 – New epidural electrode
- 1981 – First totally implantable stimulator
- 1981 – First 4 contact electrode
- 1984 –Itrel totally implantable stimulator
- 1986 – First 8 contact RF system
- 1987 – Holsheimer begins SCS modeling
- 1993 – Barolat et al. publish exhaustive map of SCS coverage pattern
- 1995 –Matrix: 8 contact 2 channel RF system
- 1999 –Renew 16 contact RF system
- 1999 –Synergy: 8 contact 2 channel totally implantable stimulator
- 2001 –Genesis 8 contact 2 channel totally implantable stimulator
- 2004 – First rechargeable IPG with 16 independent current sources
- 2009 – IPG with position-sensitive adjustments
- 2010 –5- column paddle electrode

Recent Developments

- 2013 MRI compatible IPG and percutaneous leads
- 2013 –32-contact/ current source IPG, 16-contact percutaneous electrodes
- 2014 –IPG with upgradeable firmware
- 2015 - HF10 therapy approval
- 2015 – Small RF SCS system approval
- 2015 –New SCS system approval
- 2015 DRG stimulation approval
- 2016 –Fully MRI compatible paddle system

Patient selection for Neurostimulation for Chronic Pain

- Most neuropathic pain syndromes
  - CRPS (RSD)
  - Painful neuropathies (Diabetic, small fiber, post-herpetic neuralgia)
  - Neuropathic facial pain/anesthesia dolorosa
  - Nerve injury pain
  - Failed back/neck surgery syndrome
  - Occipital neuralgia
  - Radicular 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

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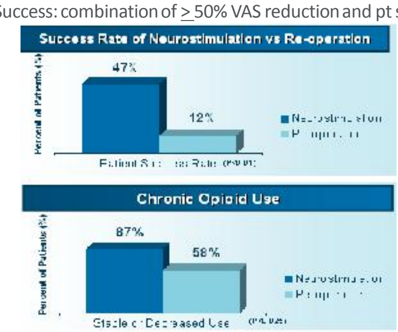
SCS vs. Reoperation

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



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North et al 2005

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

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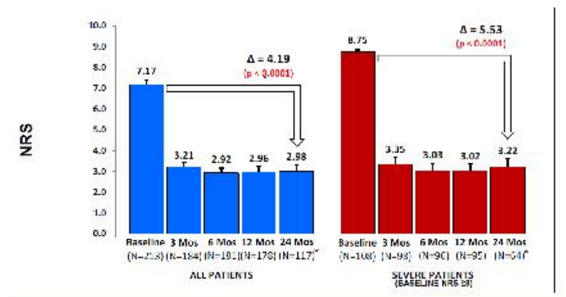
Real World SCS Outcomes



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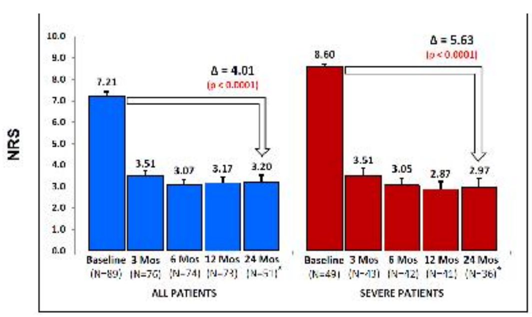
Real World SCS Outcomes – Back Pain Only



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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

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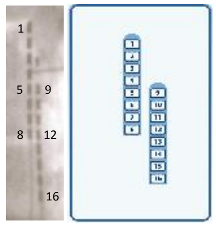
New SCS Programming

- 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



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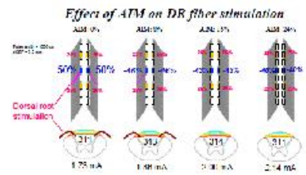
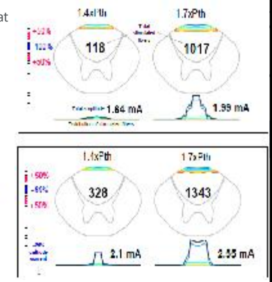
New SCS Programming

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





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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

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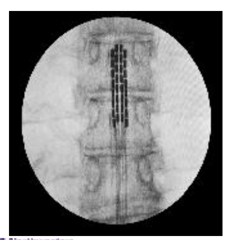
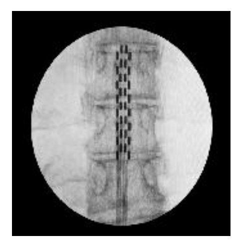
New SCS Electrodes

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





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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

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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

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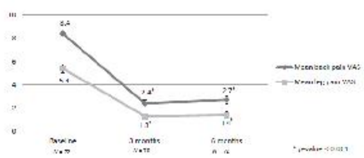
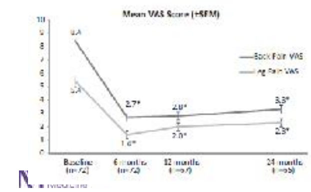
High Frequency SCS (10Khz)

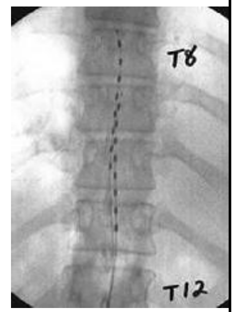
- van Buyten, *Neuromodulation* 2013
  - 83 trials, 72 successful, 6 month evaluation
  - 11/14 pts who failed prior SCS had successful trial
  - Back pain VAS – 8.4-2.7 – 78% improvement
  - Leg pain VAS 5.4-1.4 – 83% decrease
  - Daily charging needed



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

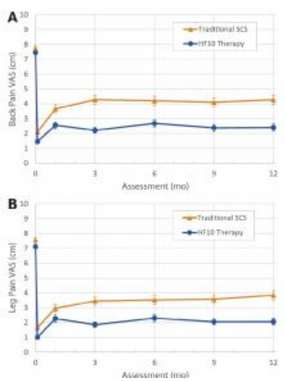




10KHz SCS RTC

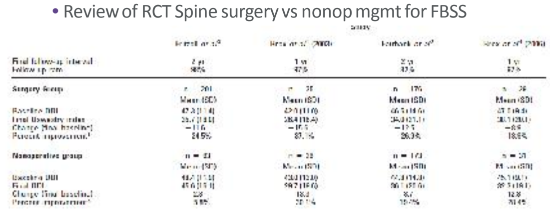
- 10KHz SCS vs traditional SCS
- 80% FBSS pts
- Pts randomized to treatment
- Not blinded, as HF SCS produces no detectable paresthesias
- Both treatments significantly reduced pain in a durable fashion, with HF SCS producing a larger VAS decrease in both back and leg pain

Kapural , Anesthesiology 2015



10KHz SCS vs Surgery for FBSS

- HF SCS RCT –
  - ODI improved average of 16.5 for HF SCS and 13.0 for traditional SCS
  - 65% of HF SCS and 31% 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
- Review of RCT Spine surgery vs nonop mgmt for FBSS



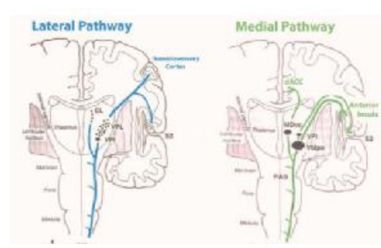
Mirza Spine 2007;32:816 – 823

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



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

	Placebo		Tonic		Burst		
	SD	%	SD	%	SD	%	P Value
Back pain	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

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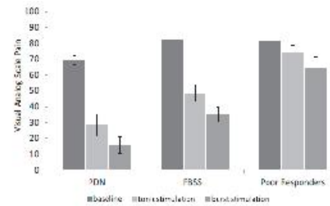
Burst SCS

- 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



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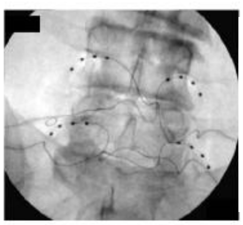
Dorsal Root Ganglion Stimulation

- 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 PLP, 14mo avg f/u, all with successful trials, prospective
  - 5/8 with pain relief ranging from 28-100%
- Liem, *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,
  - 25 successful trials, avg 27 wks 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%)

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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

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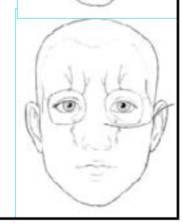
Trigeminal Branch

- Supraorbital or infraorbital
- Mandibular stim usually avoided due to lead mobility
- Target – 1cm above supraorbial rim or below infraorbital notch
- Percutaneous trial



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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

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Craniofacial Pain

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

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Craniofacial Pain

- Chronic bifrontal migraine headache

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Craniofacial Pain

- Chronic holocranial pain following meningitis

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ONSTIM Trial

Saper, *Cephalgia* 2011

- 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 ONB
  - No trial – full implant if coverage achieved in OR
- 110 subjects enrolled, 75 randomized, 67 completed 3 month f/u

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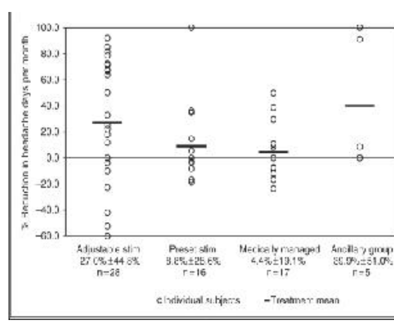
ONSTIM Trial

- 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



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ONS RCT for Migraine

Silberstein, *Cephalgia* 2012

- 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

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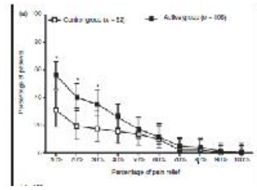
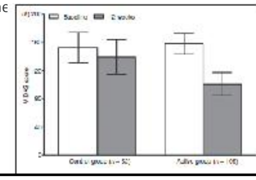
ONS RCT for Migraine

- 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





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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 significa higher percentage of AEs
- AEs decreased with increasing implanter experience

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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 sympathetics from superior cervical ganglion also pass through
- Innervates eye, nose, soft palate, pharynx
- Via the trigeminal system SPG has connections to dura

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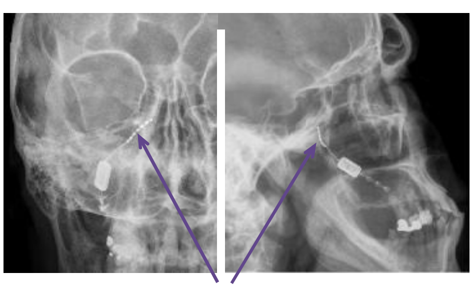
SPGS Implant



Microstimulator lead within the pterygopalatine fossa
Stimulator fixed to maxilla with lead extending into pterygopalatine fossa

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SPGS Trial

- Schoenen, *Cephalgia* 2013
- 28 patients
- Corporate –funded trial
- 4wk baseline, 6 wks stim 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

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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

	Full stimulation		Sub-perception stimulation		Sham stimulation	
	Relief	Freedom	Relief	Freedom	Relief	Freedom
Probability of pain Relief/freedom (GEE LSM)	67.1%	34.1%	7.3%	1.6%	7.4%	1.5%
95% CI (GEE LSM)	50.2–80.5%	18.5–54.1%	4.0–13.2%	0.5–5.1%	3.5–13.7%	0.5–4.9%
p value compared to sham (GEE LSM)	<0.0001	<0.0001	0.96	0.97	—	—

GEE generalized estimating equation; CI: confidence interval.

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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!

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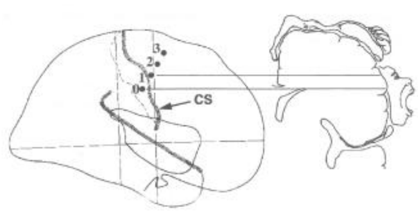
MCX Stim: Technique

- Must understand homunculus organization
- Target craniotomy and electrode localization



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MCX Stim: Electrodes

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MCX Stimulation Problems

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

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MCX Stimulation Tachyphylaxis

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


Clinical Paper

Recovery of Pain Control by Intensive Reprogramming after Loss of Benefit from Motor Cortex Stimulation for Neuropathic Pain

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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 (9) 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 f/u
- 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!

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Come to Chicago in 2016!

April 30, 2016 — American Association of Neurological Surgeons

June 2016 — ASSFN American Society for Stereotactic and Functional Neurosurgery

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