

Neuromodulation: Present and Future

- **Nelson Svorkdal BSP, MD, FRCPC**
Anaesthesia and Interventional Pain Management,
Royal Jubilee Hospital, Victoria BC



Early Neuromodulation: Relevant to pain practice on the Coast : The “torpedoe fish”



NEUROMODULATION INDICATIONS

APPROVED

DBS / CORTICAL
Essential Tremor
Parkinson's • Dystonia

COCHLEAR
Profound Deafness

VNS
Epilepsy • Depression

PNS / PNIS
Chronic Pain

SCS
Chronic Pain

SPINAL
Chronic Pain
Malignant Pain • Spasticity

SNS
Incontinence

FUTURE

OTHER THERAPIES

Hypertension • Renal Failure
Diabetes II • CHF • Paralysis

FUTURE

DBS / CORTICAL
OCD • Depression • Tinnitus • Epilepsy
Stroke • TBI • Pain • Coma • Paralysis
Tourette's

BRAIN
Epilepsy • Parkinson's • Alzheimer's

ARTIFICIAL RETINA
Retinitis Pigmentosa

ONS
Headache

VNS
CHF • Obesity

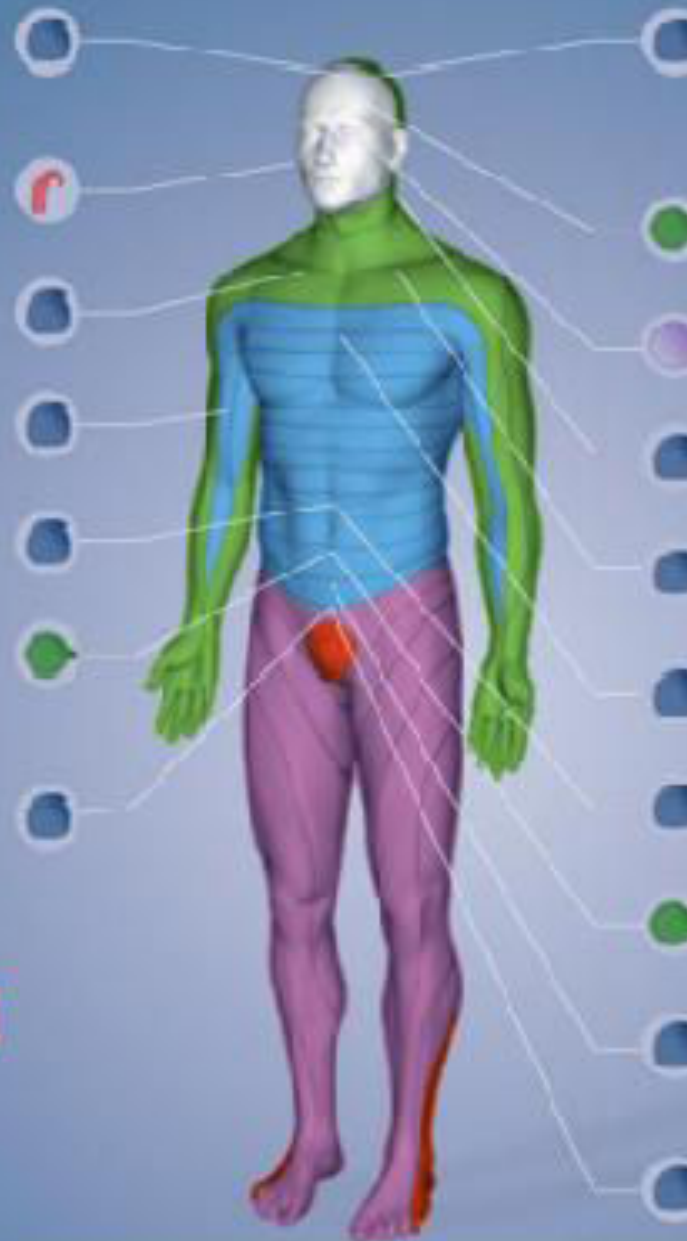
PULMONARY
Respiratory Support

SCS
Angina Pain • PVD Pain

SPINAL
ALS • Huntington's

GASTRIC
Obesity • Gastroparesis
Irritable Bowel Syndrome

SNS
Pelvic Pain • Sexual Dysfunction



Current Pain Indications

- **Therapeutic Adjunct** to behavioural modification, pharmacological therapy for;
 - Failed back surgery and failed neck surgery syndrome
 - CRPS
 - Ischemic disease –
 - Refractory angina / Peripheral vasocclusive disease
 - Pelvic Pain / Incontinence
 - Malignancy
 - Spasticity (spinal cord injury , spastic diplegia)



The British Pain Society's

Spinal cord stimulation
for the management of pain:
recommendations for best clinical practice

*A consensus document prepared on behalf of the British Pain Society in
consultation with the Society of British Neurological Surgeons*

April 2009

To be reviewed April 2012

Table 1 Indications for SCS (also see Appendix 2)

Good indications for SCS (likely to respond)	Neuropathic pain in leg or arm following lumbar or cervical spine surgery (FBSS/FNSS)
	Complex regional pain syndrome (CRPS)
	Neuropathic pain secondary to peripheral nerve damage
	Pain associated with peripheral vascular disease
	Refractory angina pectoris (RAP)
	Brachial plexopathy: traumatic (partial, not avulsion), post-irradiation
Intermediate indications for SCS (may respond)	Amputation pain (stump pain responds better than phantom pain)
	Axial pain following spinal surgery
	Intercostal neuralgia, such as post-thoracotomy or post-herpetic neuralgia
	Pain associated with spinal cord damage
	(other peripheral neuropathic pain syndromes, such as those following trauma may respond)
Poor indications for SCS (rarely respond)	Central pain of non-spinal cord origin
	Spinal cord injury with clinically complete loss of posterior column function
	Perineal or anorectal pain
Unresponsive to SCS	Complete spinal cord transection
	Non-ischaemic nociceptive pain
	Nerve root avulsion

- National Institute for Clinical Excellence (NICE) guidelines , 2008

Spinal cord stimulation: indications and outcomes

ANTHONY W. LEE, M.D.,¹ AND JULIE G. PILITSIS, M.D., PH.D.²

¹*Department of Neurosurgery, Wayne State University, Detroit, Michigan; and*

²*Department of Neurosurgery, Rush University Medical Center, Chicago, Illinois*

*Literature review of randomized controlled trials of SCS**

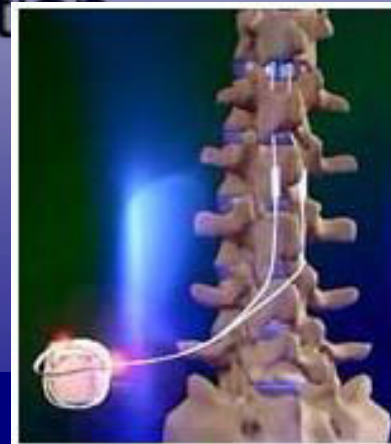
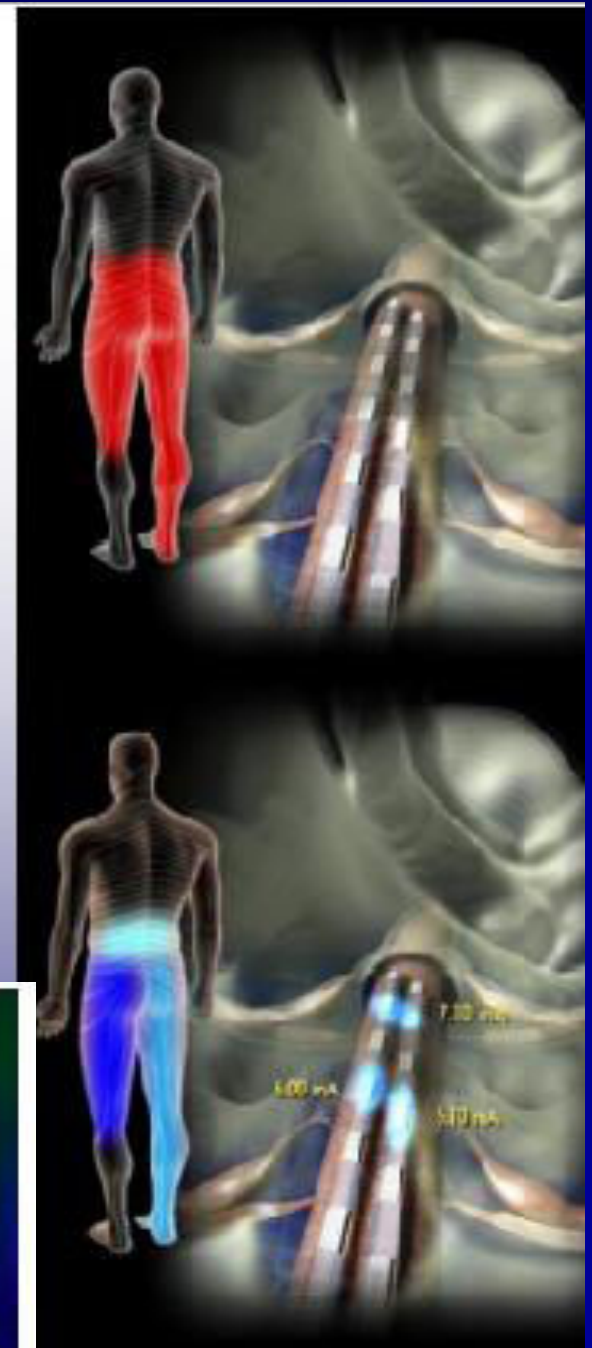
Authors & Year	Diagnosis	Cohort	Findings in SCS vs Control Group	Mean FU
North et al., 2005	FBSS	SCS vs back reop	less pain ($p < 0.01$), reduced opioid use ($p = 0.025$), less cross-over to alternative treatment ($p = 0.02$)	3 yrs
Kemler et al., 2000	CRPS I	SCS + PT vs PT alone	less pain ($p < 0.001$), improved QOL ($p = 0.02$)†	2 yrs
McNab et al., 2006	RAP	SCS vs myocardial laser revascularization	no difference in exercise capacity ($p = 0.989$), angina class ($p = 0.263$), or QOL	1 yr
de Jongste et al., 1994	RAP	SCS vs medical therapy	reduction in ischemia on ECG ($p < 0.05$), in pain relief ($p < 0.01$), & in nitrate use ($p < 0.01$); increase in exercise capacity ($p < 0.03$), QOL ($p < 0.005$)	1–2 mos
Hautvast et al., 1998				
Jessurun et al., 1999				
Suy et al., 1994	CLI	SCS vs medical therapy	improvement in clinical stage ($p < 0.05$)	1 yr
Jivegård et al., 1995	CLI	SCS vs medical therapy	reduced tissue loss ($p < 0.05$); no difference in limb survival	18 mos
Claeys & Horsch 1996	CLI	SCS + prostaglandins vs prostaglandins alone	significant improvement in clinical stage ($p = 0.0014$) & ulcer healing ($p < 0.0001$); no difference in limb survival	1 yr
Klomp et al., 1999	CLI	SCS vs medical therapy	improvement in clinical stage/mobility ($p = 0.0014$), less pain/opioid use ($p < 0.001$); no difference in limb survival ($p = 0.47$)	2 yrs
Spincemille et al., 2000				

* CLI = critical limb ischemia; ECG = electrocardiography; FU = follow up; NS = not significant; PT = physical therapy; RAP = refractory angina pectoris.

† The reduction in pain was no longer significant at the 5-year follow-up evaluation.

SCS--FBSS

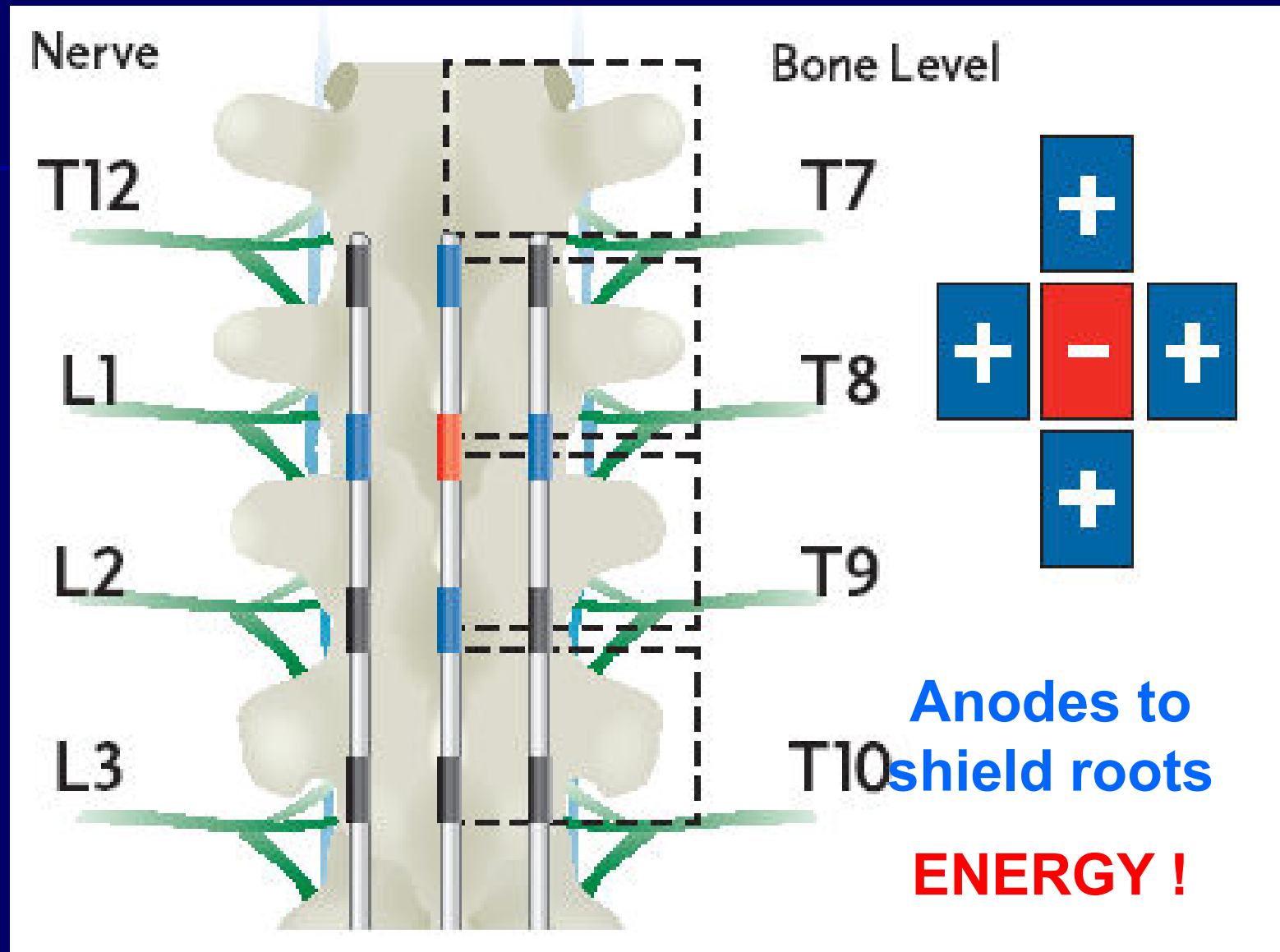
- SCS vs. Re-operation
- patients with persistent radicular pain
- primary outcome measure: frequency of cross-over
- At the 6-month crossover point: statistically significant ($p = 0.018$) advantage for spinal cord stimulation over re-operation



Spinal Stimulation Targets

Region	Position	Target
Cervical	C2 Lateral	Mandible, Neck
	C2-3	Shoulder
	C4-6	Arm
	C7	Anterior Shoulder, Chest
Thoracic	T1-3	Angina
	T4-6	Visceral Abdomen
	T7-9	Axial Back
	T10	Knee, Hip
	T11-12	Leg
Lumbar	L1	Foot
	L5-S1 Nerve Root	Foot
Sacral	S2-4	Pelvis, Rectum, Perineum

Three Leads / Columns for FBS



Prager JP & Chang JH, *INS meeting*, July 2000

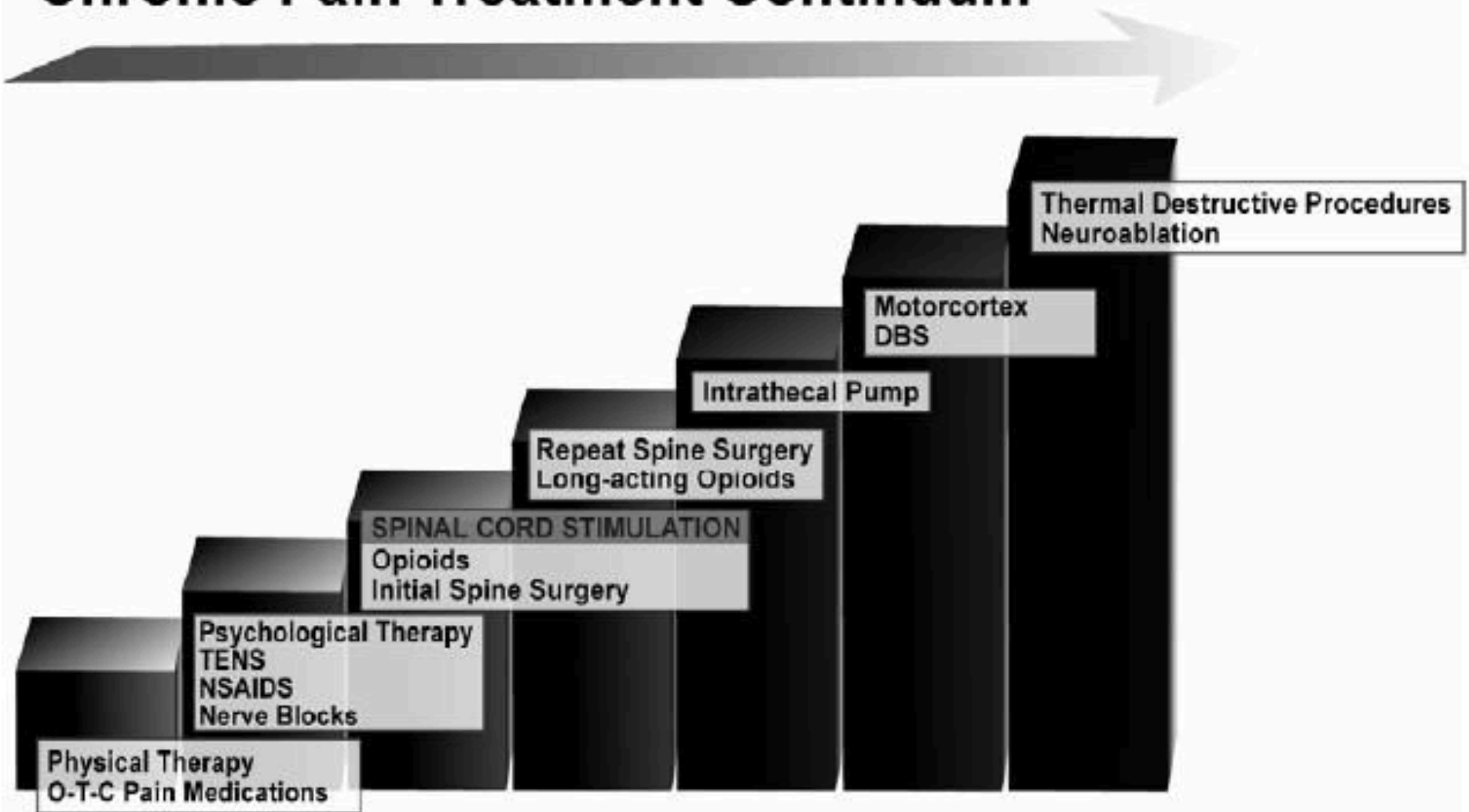
Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: randomized, controlled trial.

North RB et al.,*Neurosurgery* 56: 98-107, 2005.

<u>Outcome Measure</u>	<u>SCS</u>	<u>Repeat Back Surgery</u>	<u>p value =</u>
VAS ≤ 50%	47%	12%	<0.01
Decr Opiate	+	+/-	P=0.025
Treatment Crossover	21%	54%	P=0.02
<u>COST</u>	<u>\$ 31,530</u>	<u>\$ 38,160</u>	
(after cross-over)	<u>\$ 48, 357</u>	<u>\$105,928</u>	
	30-40%		

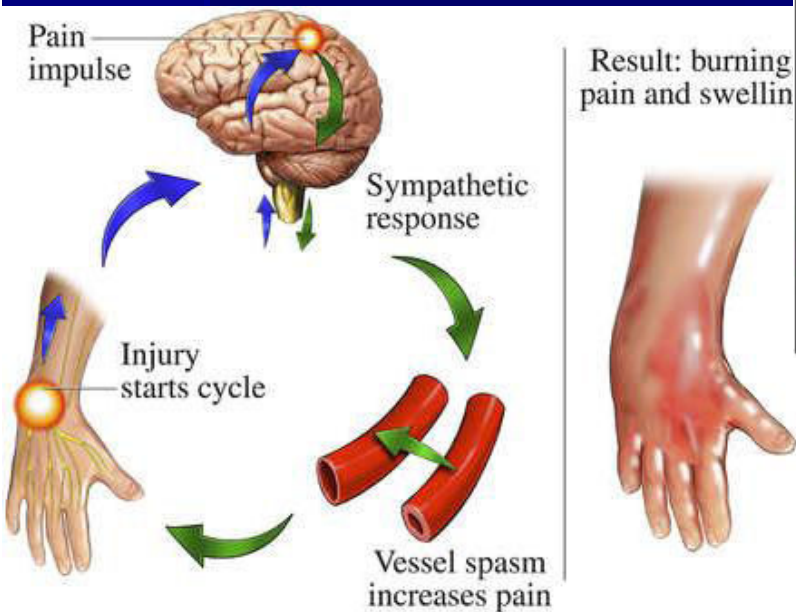
Updated Treatment Ladder

Chronic Pain Treatment Continuum

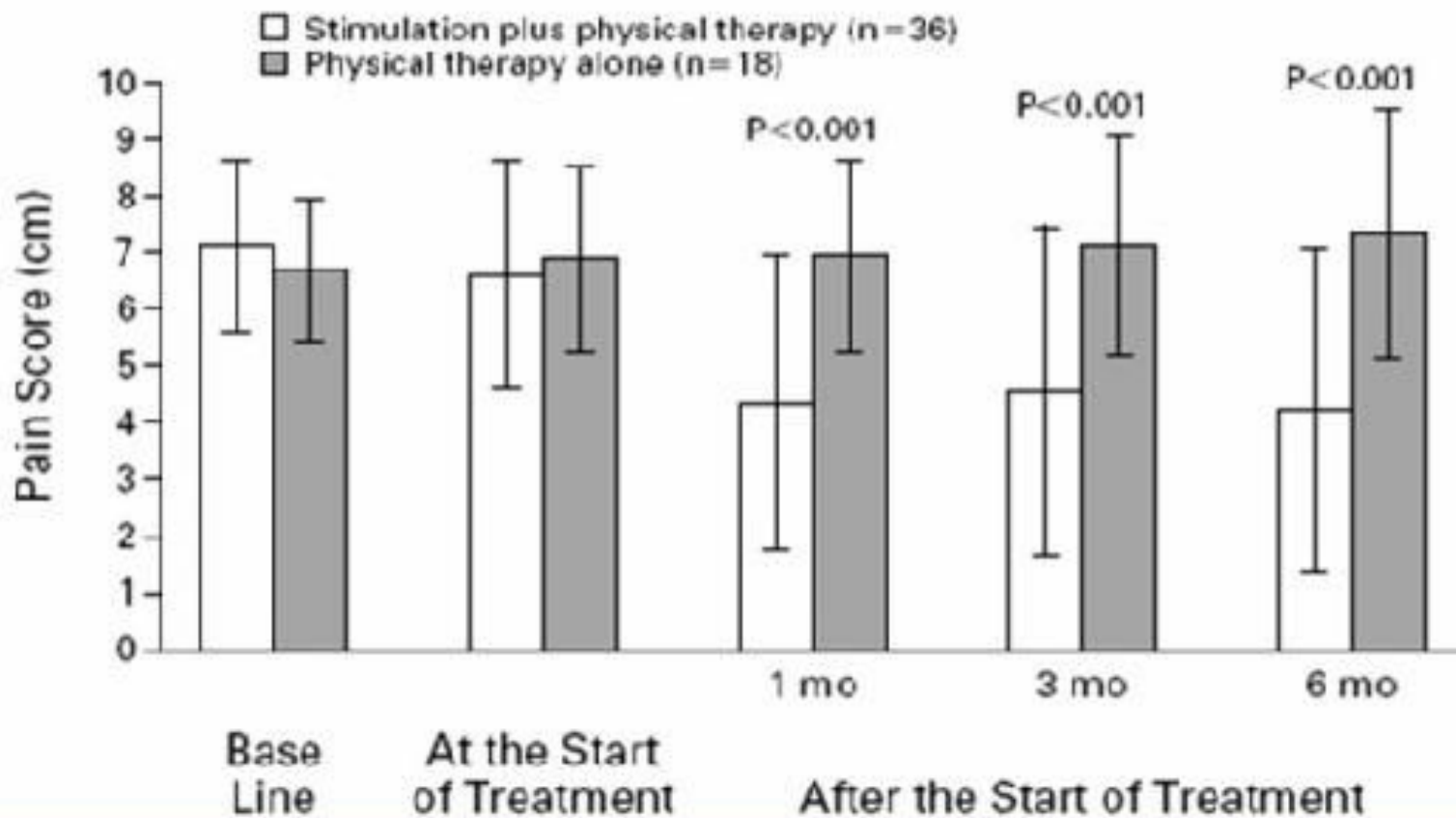


Neuromodulation in CRPS

- **SCS or Motor Cortex Stim**
- **RCT of SCS vs PT**
 - **VAS, QOL, cost**

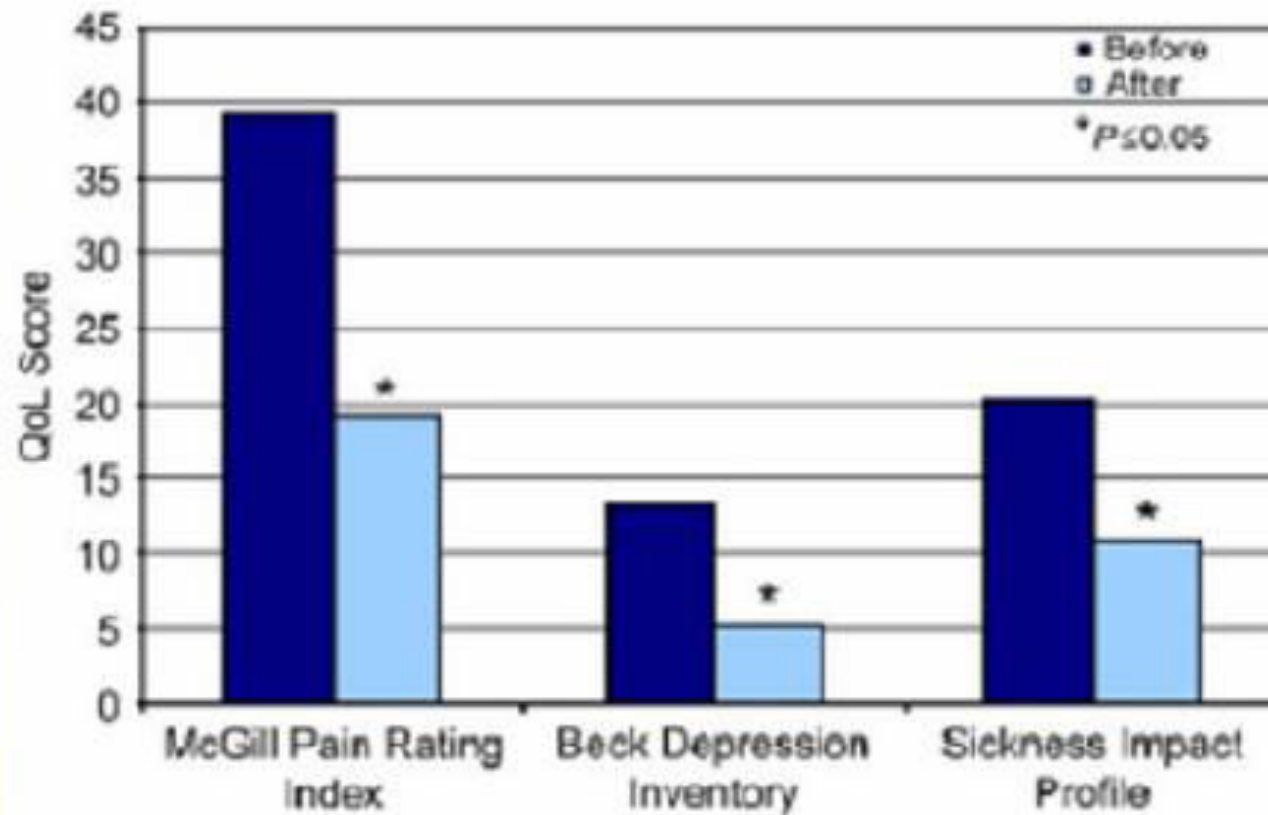


SCS--CRPS



Kemler MA et al., N Engl J Med.
2000 Aug 31;343(9):618-24

SCS in CRPS



Oakley JD & Weiner RL 1999,
Neuromodulation, 2:47-50

The Cost-Effectiveness of Spinal Cord Stimulation for Complex Regional Pain Syndrome

Marius A. Kemler Md, PhD¹, Jon H. Raphael MD², Anthony Bentley BSc(Hons)³, Rod S. Taylor PhD^{4,*}

Article first published online: 7 JUN 2010

DOI: 10.1111/j.1524-4733.2010.00744.x

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Issue



Value in Health

Volume 13, Issue 6, pages
735–742, September/October
2010

Table 2. Base-case incremental cost-effectiveness of SCS

	SCS	CMM	Difference
Total cost/patient	£86,770	£79,775	£6,994
QALYs/patient	4.84	2.88	1.96
Incremental cost per QALY	£3,562		

Note: Costs and QALYs discounted at 3.5% per annum, where £1.00 = US\$ 1.62.

CMM, conservative medical management; QALY, quality-adjusted life-year; SCS, spinal cord stimulation.

Economic evaluations of spinal cord stimulation for complex regional pain syndrome.

Kemler MA et al., *Neurology* 59: 1203-1209, 2002.

Taylor RS et al, *Eur J Pain* 10: 91-101, 2006.

<u>Outcome Measure</u>	<u>SCS + PT</u>	<u>PT alone</u>	<u>p value =</u>
VAS decr	3.6	Incr 0.2	<0.001
QOL improve	58%	6%	P=0.02
<u>COST</u>	<u>Year 1</u> <u>\$4000 ></u>		
--Lifetime--	<u>\$ 60,800 <</u>		
<u>QALY</u>	<u>\$8000</u>		

SCS in CRPS

J Neurosurg 2008; Feb 108(2);
292-8

*Alternative analyses at the 5-year follow-up**

Characteristic	Analysis w/ Original Group			Analysis w/ Patients in PT Group w/ Implant		
	SCS +PT	PT	p Value	SCS +PT	PT	p Value
no. of patients	36	18		31	17	
mean VAS score (cm)	-1.5 ± 2.3	-0.9 ± 2.8	0.22	-1.7 ± 2.3	-1.1 ± 2.8	0.25
no. of patients w/ ≥ much improved GPE (%)	8 (22)	2 (11)	0.14	7 (23)	2 (12)	0.17
health-related QOL measures (%)						
Nottingham Health Profile						
mobility	6 ± 17	7 ± 25	0.91	7 ± 15	8 ± 26	0.95
pain	-7 ± 26	-3 ± 24	0.55	-7 ± 27	-3 ± 24	0.57
sleep	-15 ± 31	-8 ± 30	0.47	-15 ± 30	-8 ± 31	0.41
energy	-1 ± 44	6 ± 47	0.66	5 ± 43	6 ± 49	0.91
social isolation	4 ± 17	1 ± 17	0.54	4 ± 18	0 ± 18	0.57
emotional reaction	-3 ± 25	1 ± 28	0.63	-2 ± 27	-3 ± 23	0.90
EQ-5D	14 ± 24	13 ± 40	0.90	16 ± 25	15 ± 41	0.94
Self-Rating Depression Scale	-1 ± 8	-2 ± 11	0.59	0 ± 9	-3 ± 10	0.40

* Values represent the means ± SDs

SPECIAL ARTICLE

Cost-Effectiveness of Implantable Cardioverter–Defibrillators

Gillian D. Sanders, Ph.D., Mark A. Hlatky, M.D., and Douglas K. Owens, M.D.

- N Engl J Med 2005; 353: 1471-80
- ICER of **\$34,000 - \$70,200 per QALY** in studies that demonstrate benefit when used as prophylaxis against sudden cardiac death.
- SCS – ICER of **\$33,930 - \$82,800**
 - Data collected Dec 2001- 2003

SCS for Refractory Angina

- **1982** – TENS for refractory angina , Mannheimer
 - European Heart Journal
- **1987** – Australia, First case report Murphy and Giles
- **1995** – European product compliance for refractory angina
- **1997** Health Protection Branch approves SCS for refractory angina in Canada
- **1998** ESBY Randomized trial
 - Mannheimer C, Eliasson T, Augustinsson L-E, et al. Electrical stimulation versus coronary artery bypass surgery for severe angina pectoris: the ESBY study. *Circulation* 1998;97:1157–1163.
- **2002** - Eur Heart J. 2002;23:355-370.
 - ESC Joint Study Group on the Treatment of Refractory Angina.
- **2003** – STARTSTIM study,

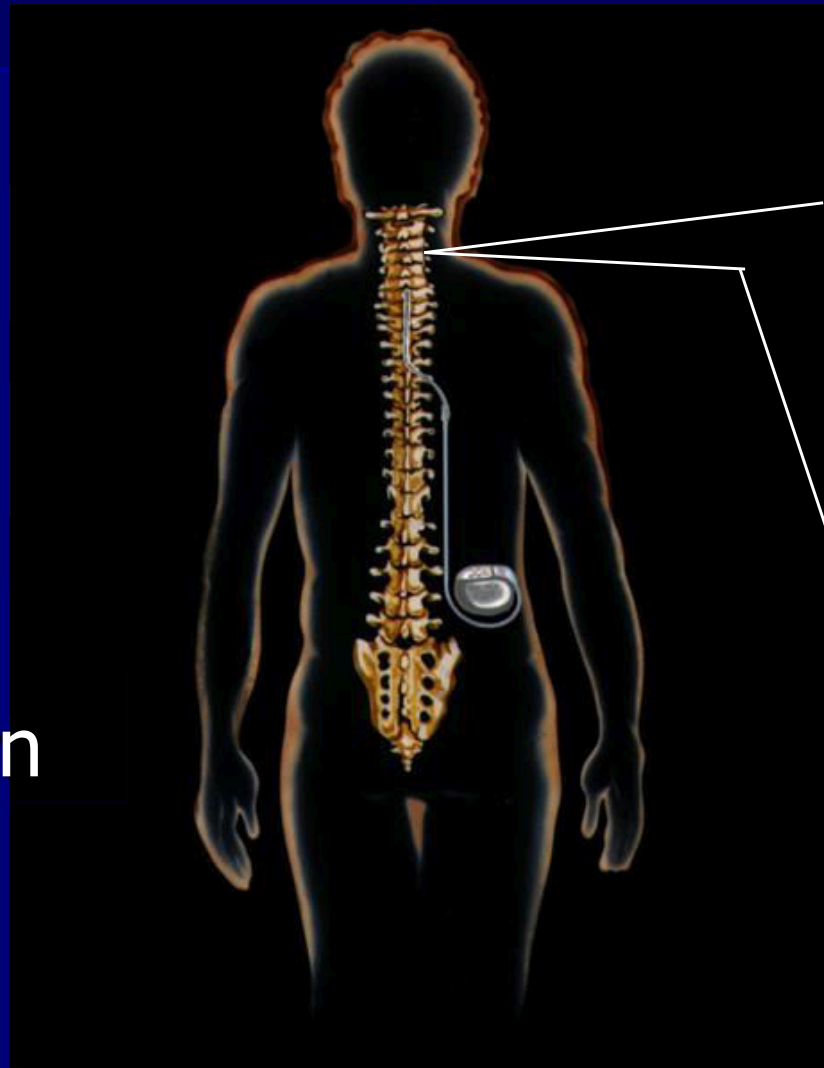
Case Reports & Clinical Practice



- 70 yo man, prev MI x 3,
- CABG 1980, redo 1994, EF 32%
- Pacemaker 2002
- 12 meds , NTG > 8/day
- SCS April 2004, St. Paul's Hospital, Vancouver
 - Pisces Quad Plus, Itrel 3
 - NTG 4 per month
 - CCS 4 to 1 in 6 months

SCS Implant Technique

- Tip to **T1** midline
- Single quadrapolar lead
- **Bilateral stimulation** (T2-T4)
- Continuous daytime stim and increase prn or pre-emptively

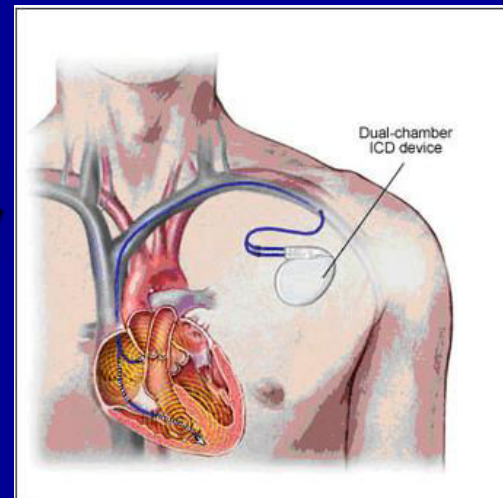


Case Reports & Clinical Practice



- Afib in 2006
 - CHF from NYHA I to III
- external cardioversion
 - Sinus rhythm
 - Power-off reset of IPG, no recoverable stim'n
 - CCS 3
- **Combined ICD and SCS battery Sep 2006**
 - Guidant Contak Renewal ICD
 - Synergy IPG
 - Intraoperative testing ICD x 6
 - Postoperative testing SCS with ICD on sense only
- Repeat cardioversions in 2007 and 2008
 - External and internal

Alive and Well!





■ CCS 0



...OUTCOMES....

The ESBY Study

(Electrical Stimulation versus Bypass Surgery in Severe Angina Pectoris)

European Heart Journal, 2002; 23: 1938-45

■ CABG Survival

- 6 months 46/51 (85%)
- 3 year 39/51 (76.5%)
- 5 years 35/51 (68.6%)

■ Quality of Life

Nottingham Health Profile
>30% improvement
Reduced pain and increased
physical capacity

■ SCS Survival

- 52/53 (98%) p<0.02
- 45/53 (84.9%) ns
- 40/53 (75.5%) ns

■ Quality of Life

- Nottingham Health Profile
- >30% improvement (ns)
- Reduced pain and increased
physical capacity

Systematic review and meta-analysis of controlled trials assessing spinal cord stimulation for inoperable critical leg ischaemia

D. T. Ubbink¹, H. Vermeulen¹, G. H. J. J. Spincemaille², P. A. Gersbach³, P. Berg⁴ and W. Amann⁵

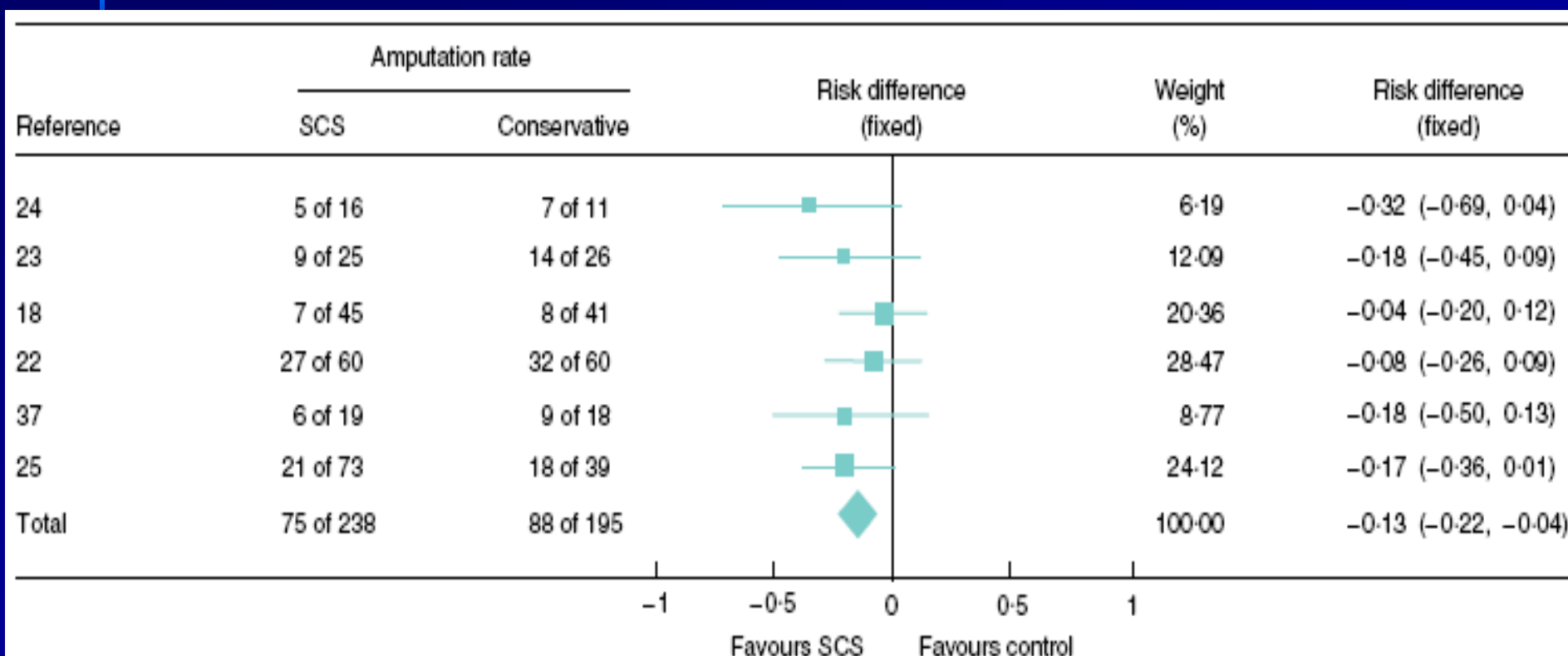


Fig. 1 Meta-analysis of 12-month amputation rates. Values in parentheses and whiskers represent 95 per cent confidence intervals. SCS, spinal cord stimulation. Test for heterogeneity: $\chi^2 = 3.03$, 5 d.f., $P = 0.70$, $I^2 = 0$ per cent. Test for overall effect: $Z = 2.88$, $P = 0.004$

CAUTION

**THIS SIGN HAS
SHARP EDGES**

DO NOT TOUCH THE EDGES OF THIS SIGN



ALSO, THE BRIDGE IS OUT AHEAD



Implementing the SAFE Principles for the Development of Pain Medicine Therapeutic Algorithms That Include Neuromodulation Techniques

Elliot Krames, MD* • Lawrence Poree, MD, PhD*,†,‡ • Timothy Deer, MD§,¶ • Robert Levy, MD**

NEUROMODULATION: TECHNOLOGY AT THE NEURAL INTERFACE

Volume 12 • Number 2 • 2009

- **Safety**
- **Appropriateness**
- **Fiscal Neutrality**
- **Efficacy**

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Neuromodulation Safety : 10 year example of SCS

Kumar et al: J Neurosurg 2006;5:191-203

■ Infection	4.4%
■ Seroma	3.1%
■ Neural injury	0%

“Appropriateness” of Neuromodulation

It is much more important to know what sort of patient has a disease than what sort of a disease a patient has. - Sir William Osler (1849-1910)

- **No surgical contraindication**
 - Infection, coagulopathy
 - Surgical inexperience
 - Emergency neurosurgery unavailable in case of complications
 - Frequent MRI (???)
- **No patient contraindications**
 - Uncommunicative
 - Noncompliance
 - Severe Psychiatric or psychological condition (catastrophizing)
- **Clinical response to reasonable trial**
 - Improvements in pain, objective measures of function
 - Multidisciplinary team
- **“Sniff test” – no secondary gain, spurious diagnoses**

Fiscal Aspects of Future Health Care

- Cost-utility will dictate spectrum of therapy
- Tech change > 60% of health cost increases
- Chronic disease 75% of health costs
- NIH statistic - \$100 billion on persistent pain
> cardiac, cancer and AIDS COMBINED !
- NSAIDs
 - 17% gastric ulcers
 - 100,000 hospitalizations
 - 16,500 deaths per year.

Current Trends in Neuromodulation

- Current Indications
- Current clinical environment
- SAFE principles
- Patients

Refractory Headaches

ORIGINAL

Peripheral Neurostimulation for the Treatment of Chronic, Disabling Transformed Migraine

Charles A. Popeney, DC; Kenneth M. Ald, MD

Background.—Up to 5% of the general population suffers from transformed migraine. This study analyzes clinical responses of transformed migraine to cervical peripheral nerve stimulation.

Methods.—Headache frequency, severity, and disability (Migraine Disability Assessment [MIDAS] scores) were independently measured in an uncontrolled consecutive case series of 25 patients with transformed migraine implanted with C1 through C3 peripheral nerve stimulation. All patients met International Headache Society (IHS) criteria for episodic migraine, as well as suggested criteria for transformed migraine, and had been refractory to conventional treatment for at least 6 months. Responses to C1 through C3 peripheral nerve stimulation were recorded.

Results.—Prior to stimulation, all patients experienced severe disability (grade IV on the MIDAS) with 75.56 headache days (average severity, 9.32; average MIDAS score, 121) over a 3-month period.

Following stimulation, 15 patients reported little or no disability (grade I), 1 reported mild disability (grade II), 4 reported moderate disability (grade III), and 5 continued with severe disability (grade IV), with 37.45 headache days (average severity, 5.72; average MIDAS score, 15). The average improvement in the MIDAS score was 88.7%, with all patients reporting their headaches well controlled after stimulation.

Conclusions.—These results raise the possibility that C1 through C3 peripheral nerve stimulation can help improve transformed migraine symptoms and disability. A controlled study is required to confirm these results.

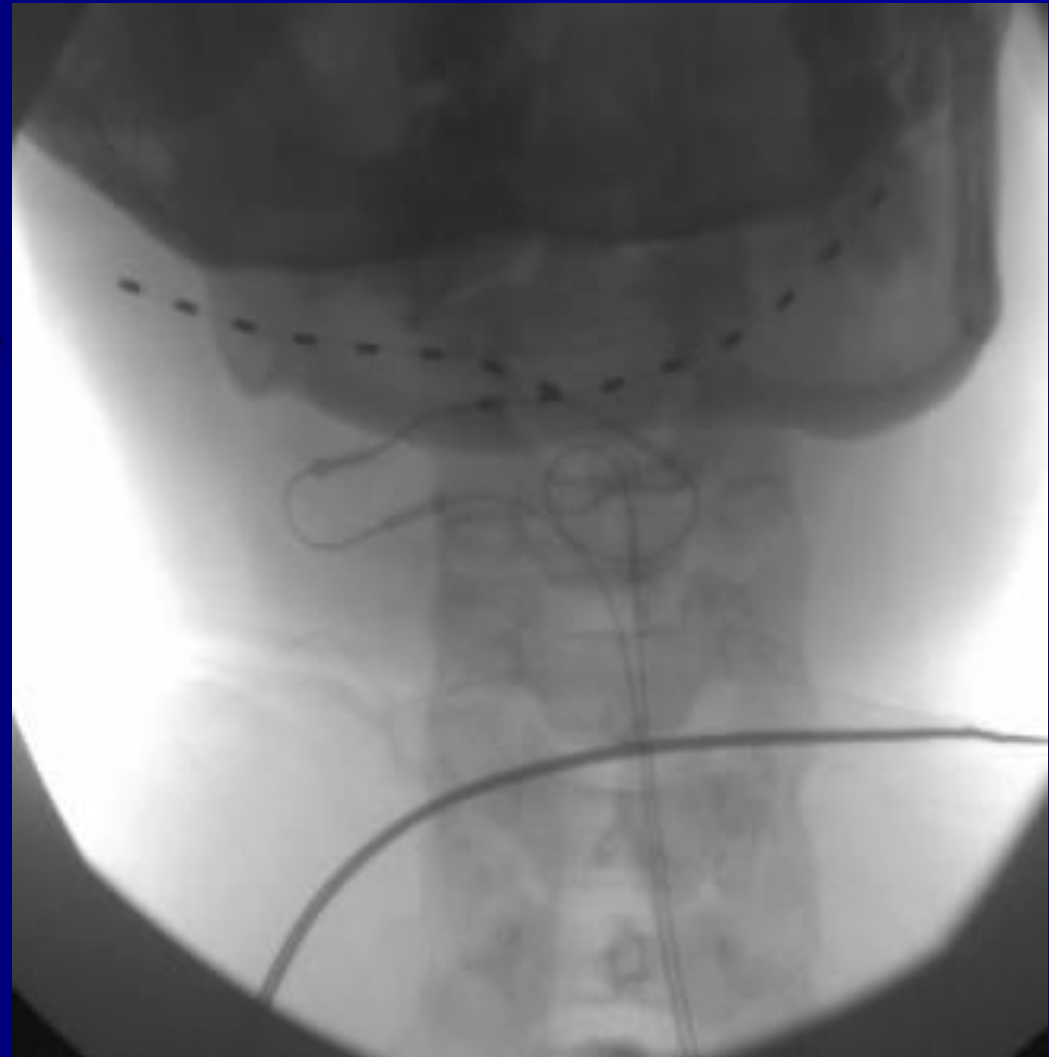
Key words: headache, migraine, transformed migraine, peripheral nerve stimulation, MIDAS score, neurostimulation

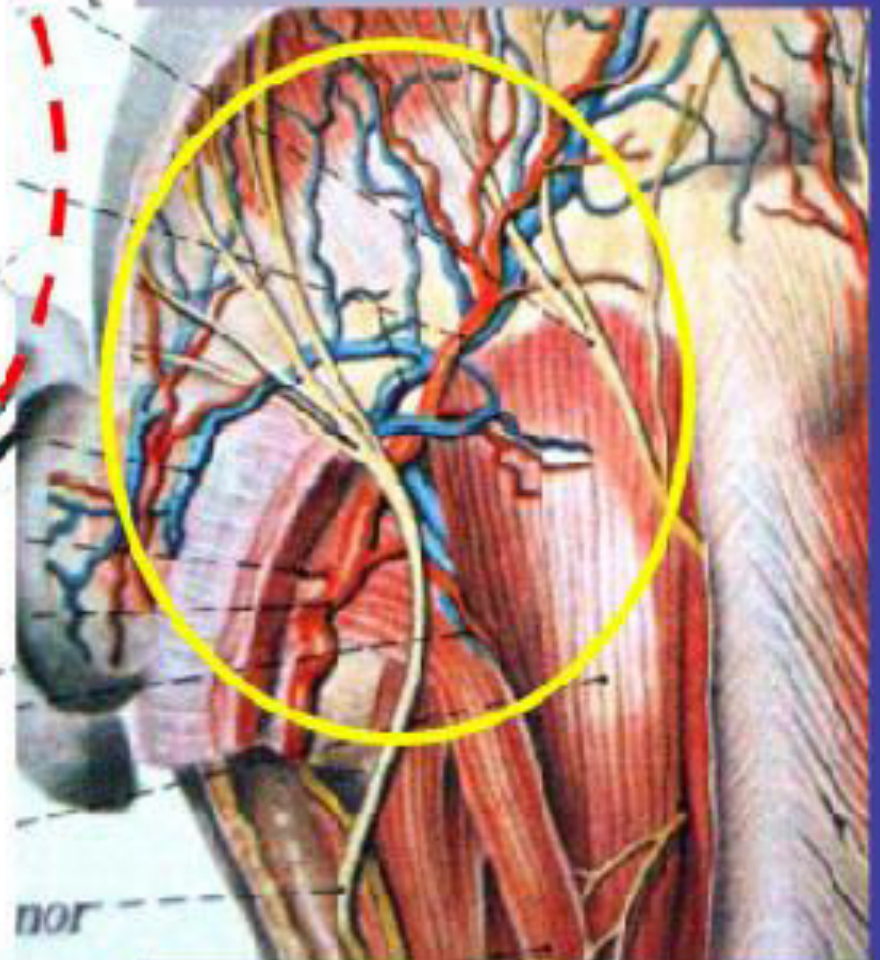
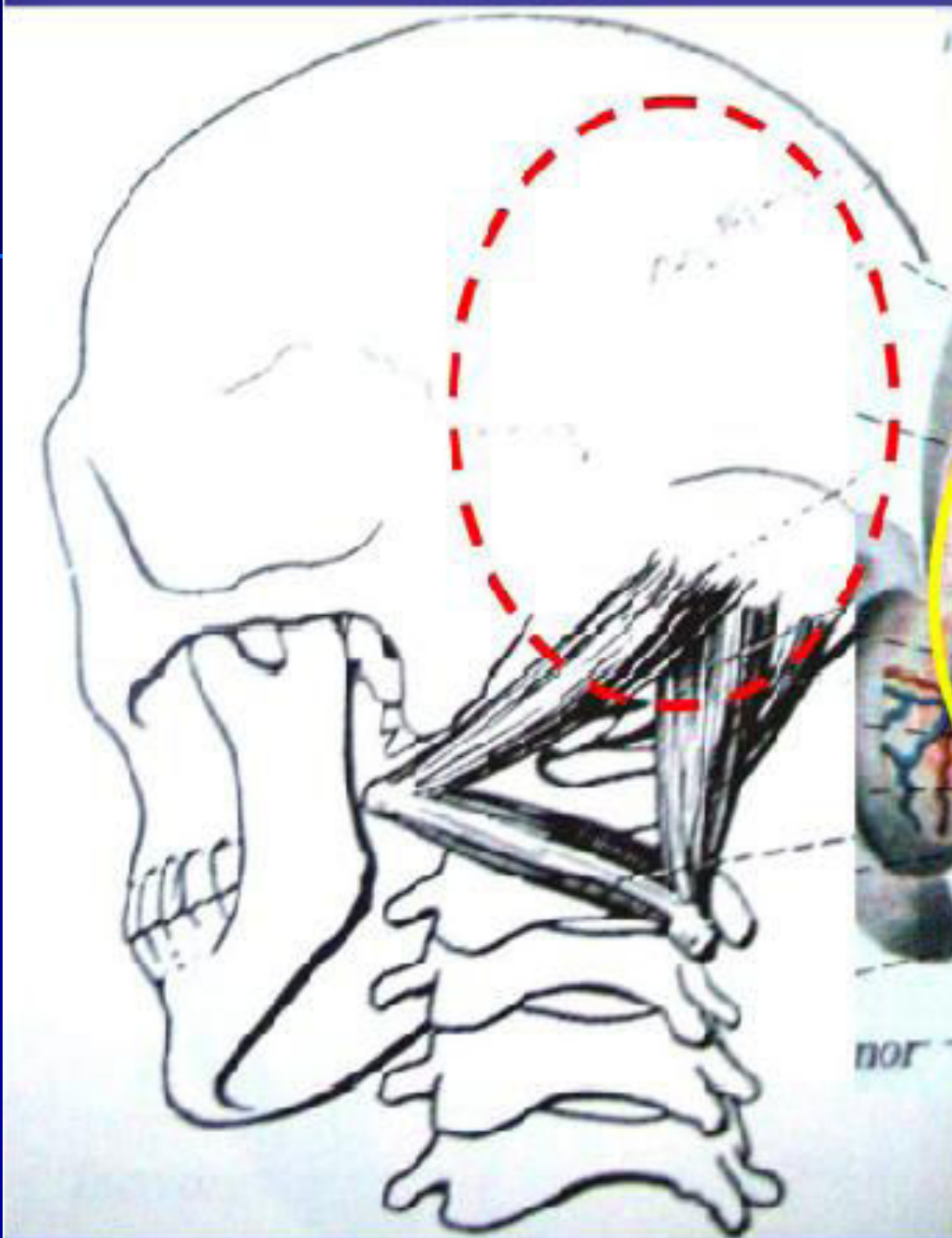
Abbreviations: PNS peripheral nerve stimulation, MIDAS Migraine Disability Assessment

(*Headache* 2001;41:369-375)

Mrs. NR

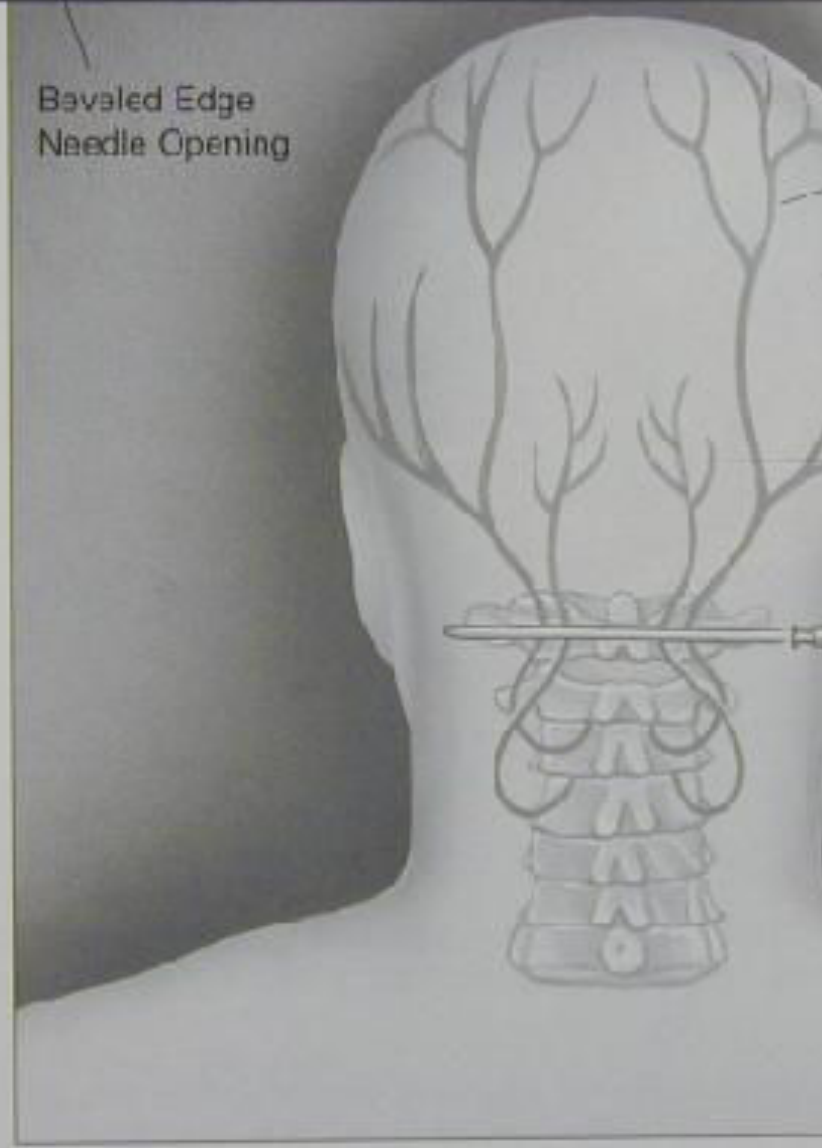
- 38 yo woman
- MVA while pregnant with triplets
- Occipital neuralgia
- C1-2 arthropathy (bone scan positive)
- Multiple injections, RF in USA, prolotherapy
- Morphine, NSAID, TCA,
 - gabapentin
- Trial of PNS







Beveled Edge
Needle Opening



Greater
Occipital Nerve

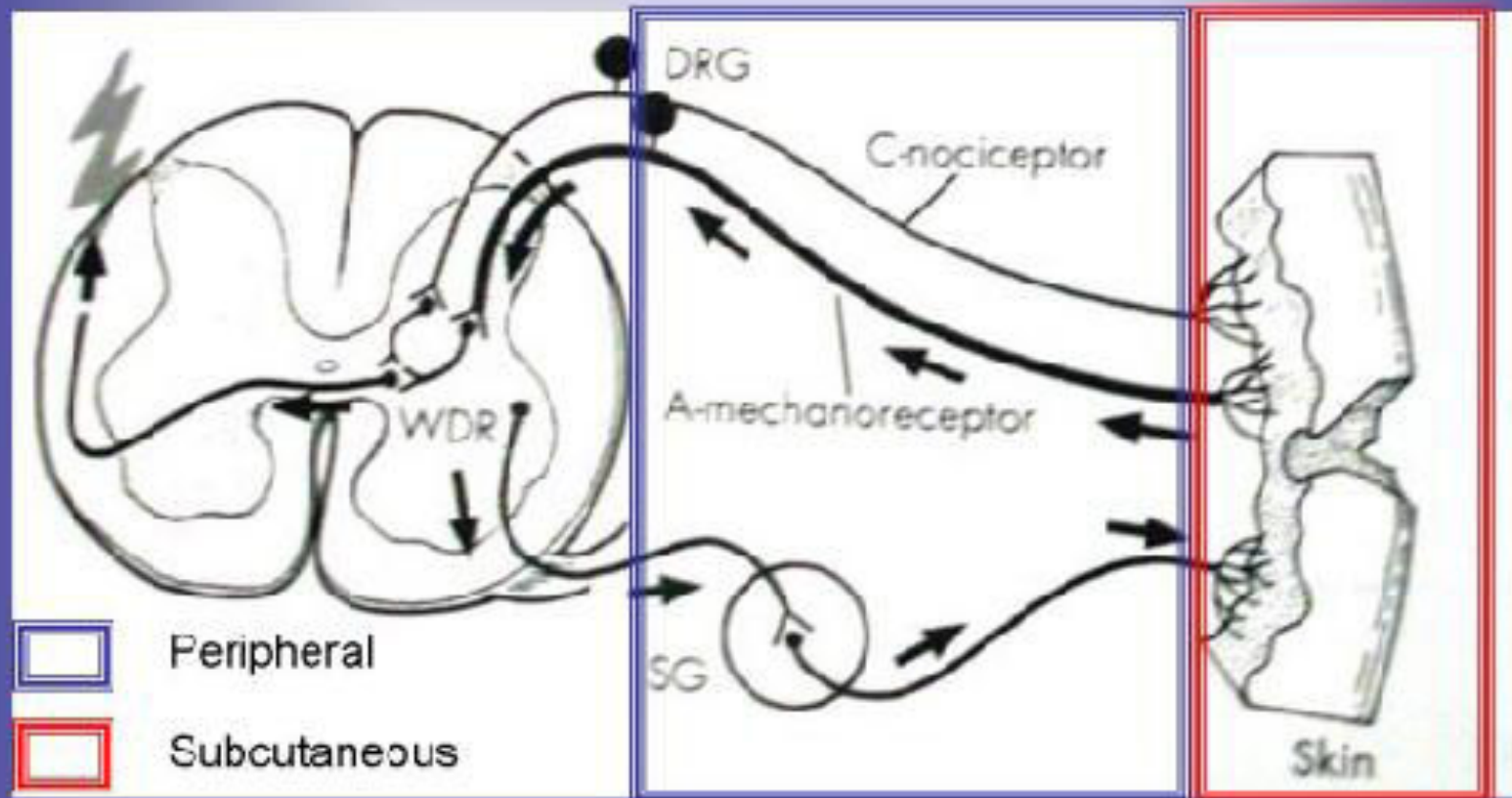
Lesser
Occipital Nerve

Third
Occipital Nerve

Introducer
Needle



Extraspinal stimulation

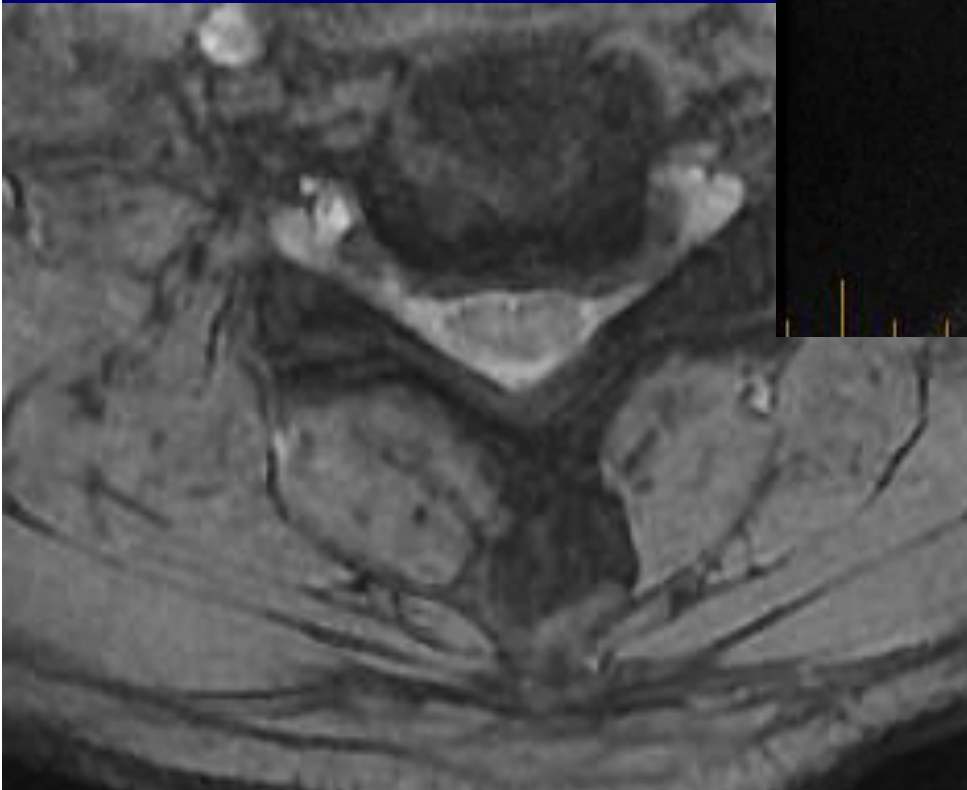


Mr. E. C.

- 72 yo man
- Prev MI X 3, plasty x 2, Stent x 2
- EF 32%, CCS III,
- extol < 1 block
- Metoprolol, amlodipine, NTPatch, ASA, Plavix, atorvastatin, NT spray 6/day
- TENS trial then SCS 2007
 - Quad Plus and Itrel 3
 - CCS I – No NTG for 1 year



Mr. RK
FNSS

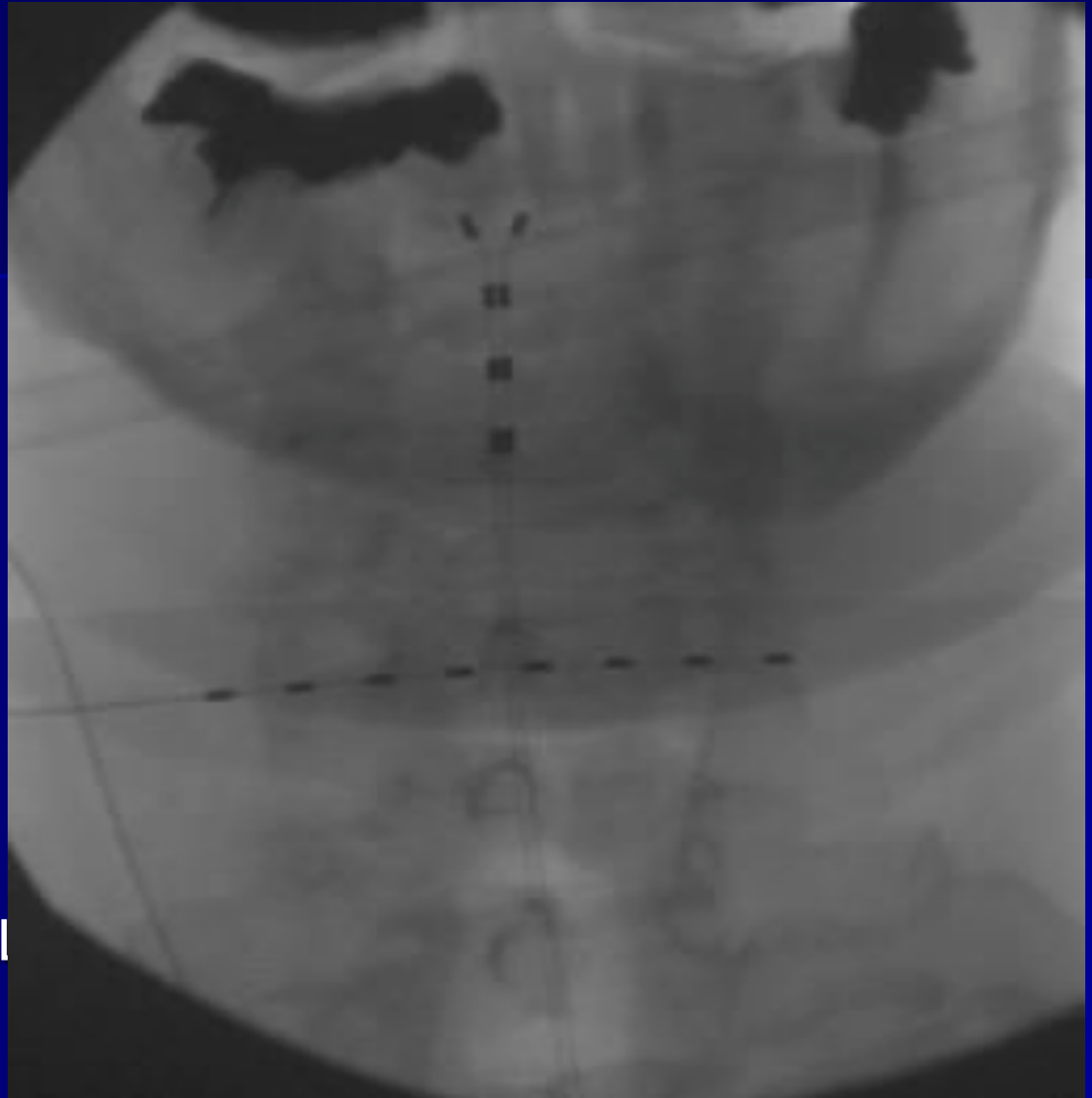


Mr. RK

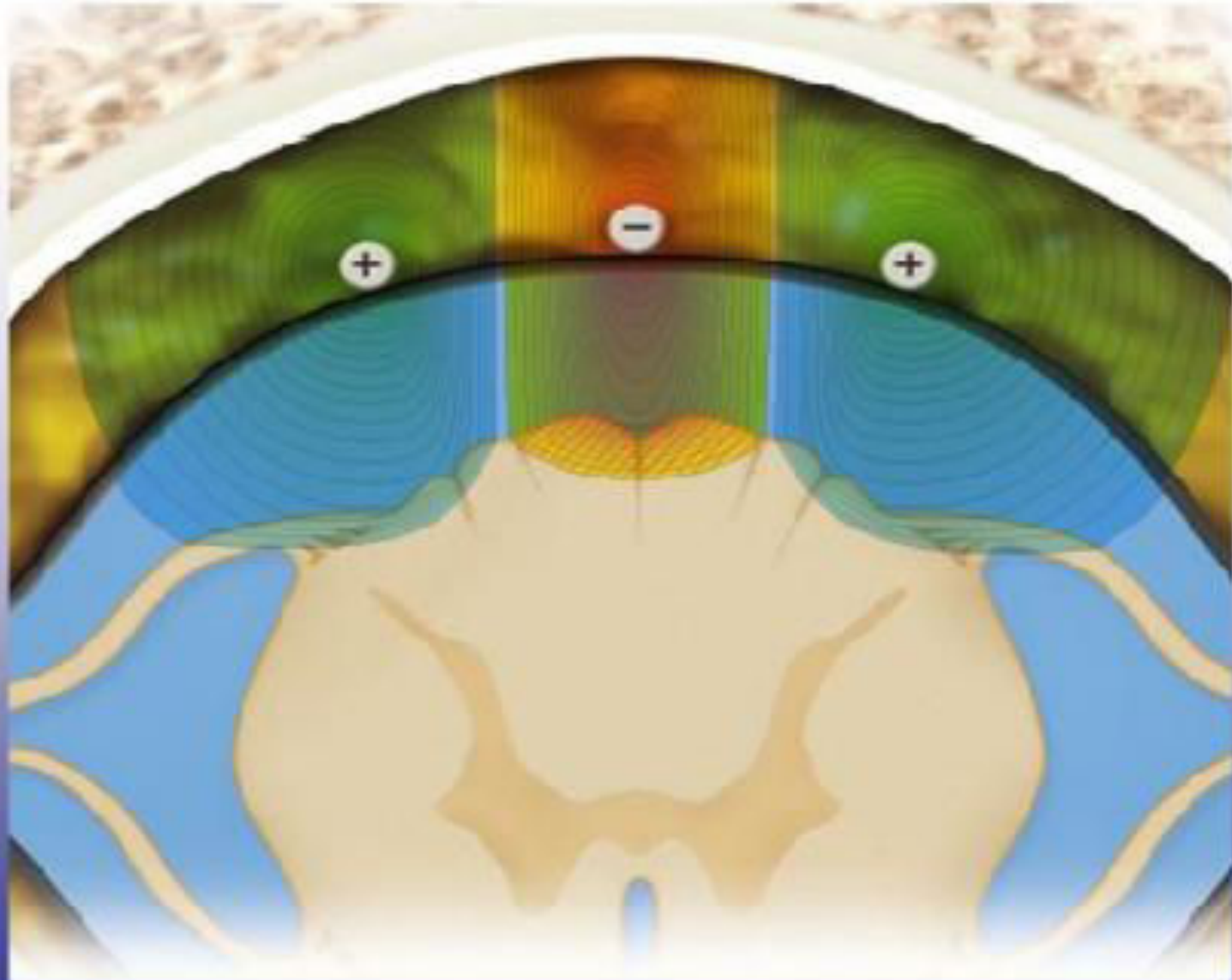
- Hydromorph Contin, pregabalin, duloxetine, lidocaine infusions, Cervical epidural, prolotherapy,
- \$\$
- Walk therapy, pain education series
- Psychological screen,
- Trial of spinal cord stimulation : great for radiculopathy...not neck pain...
- **CHANGE STRATEGY**

Mr. RK

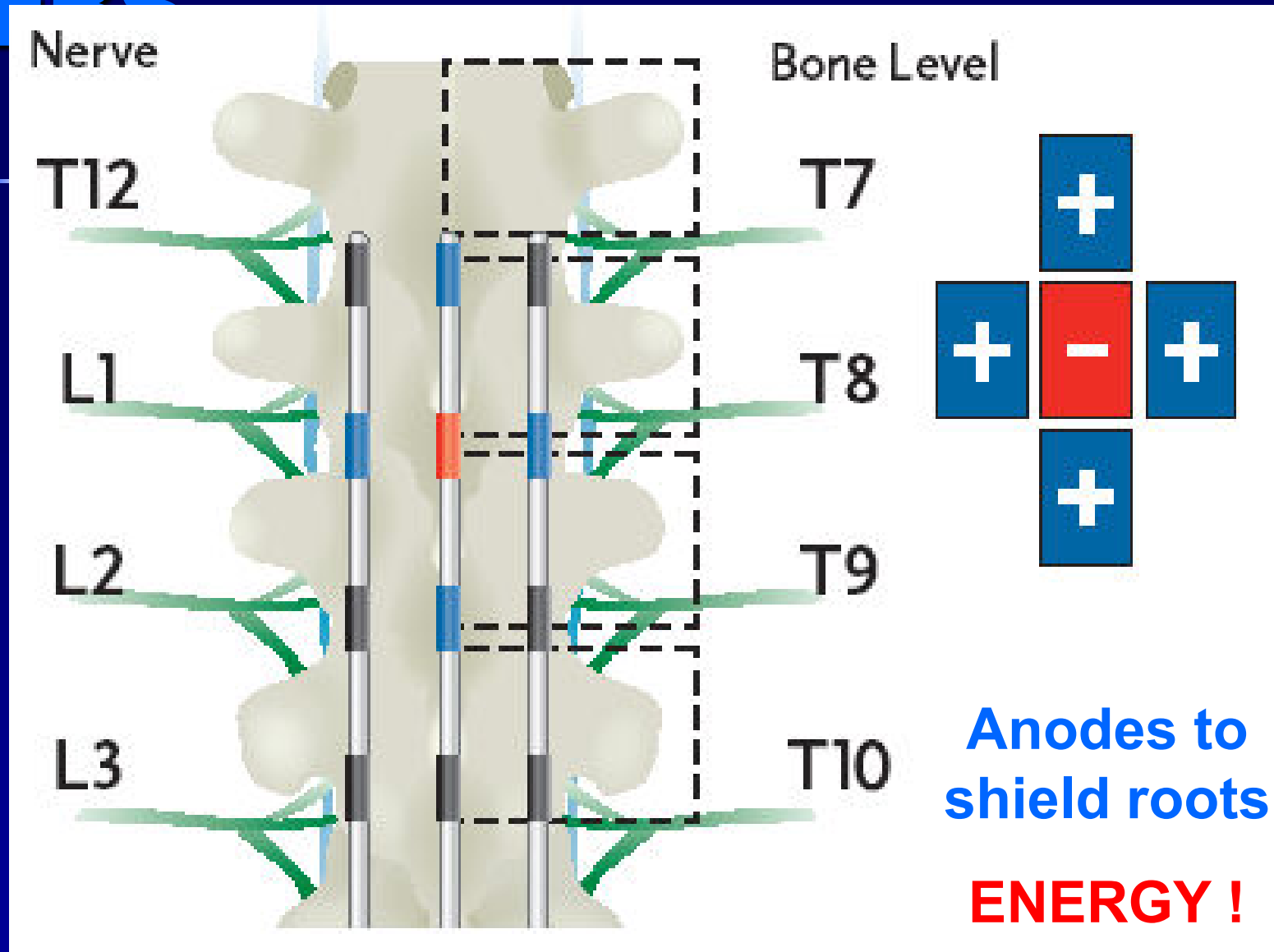
- GAME CHANGER ...
- “TRIANGULATION” OF ELECTRICAL FIELD –
 - Spinal cord stim with guarded cathode PLUS
 - PNS using subcutaneous anode
 - VERY LARGE ELECTRICAL FIELD
 - Almost off meds ; very active - elated



Transverse Tripolar Array



Three Leads / Columns for FPC

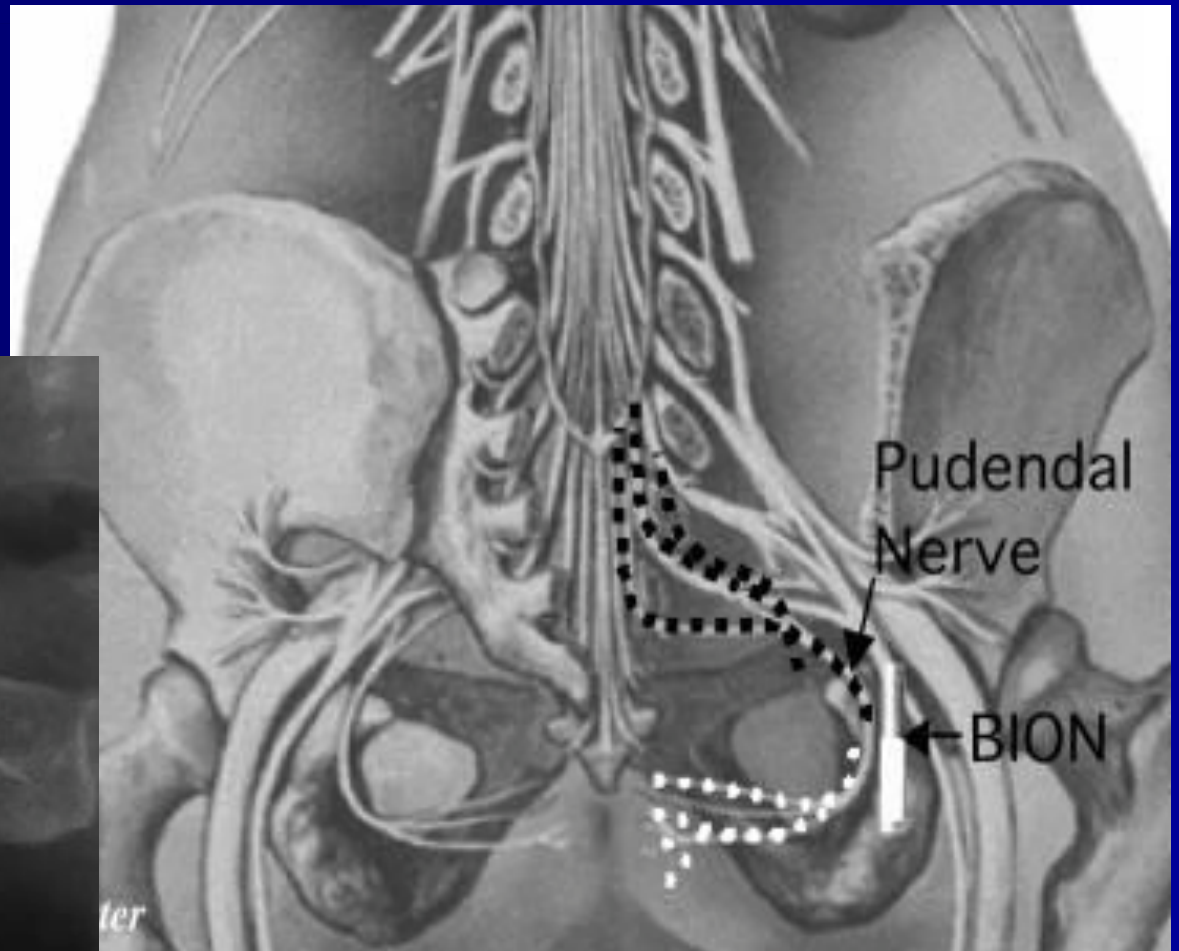


Prager JP & Chang JH, *INS meeting*, July 2000

Future Trends

- Blended therapy
 - “Multimodal” synergy – meds / devices
 - Electrical field changes – PNS and MCS or SCS
- Patient Selection
 - Genetic screening
 - Psychological / collaborative
- Regulatory and Economic
 - “Pay for Performance”
- Mechanism and adjunct
- Study design
 - More science less “magic”
- Imaging compatibility
- Reduce
- Neuroprosthetics
 - Closed loop systems
- Device – Nerve Interface

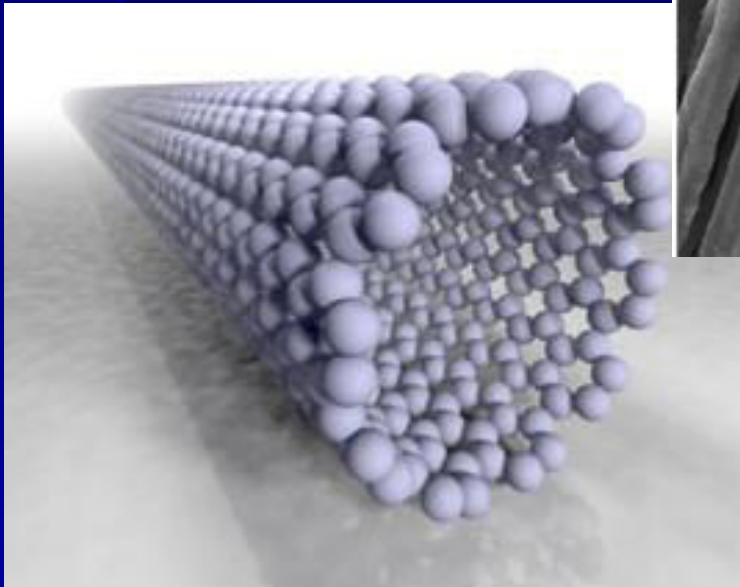
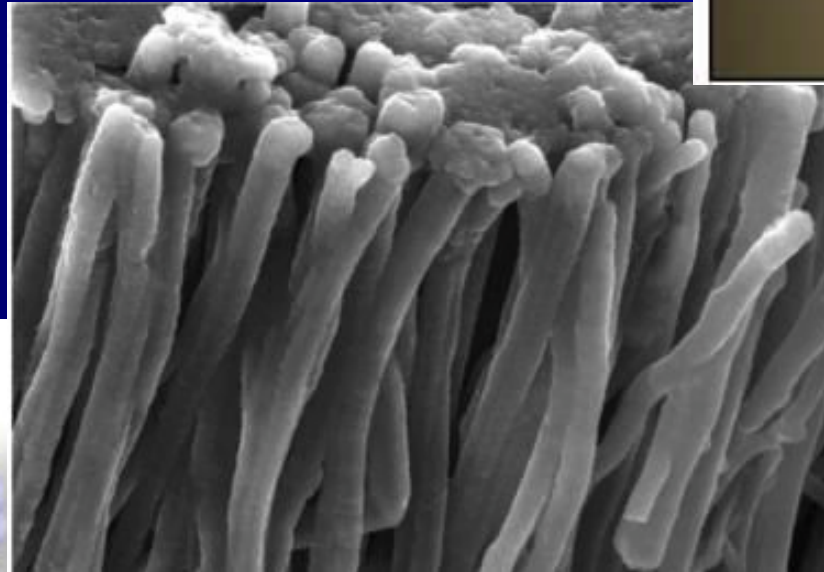
Miniaturization for Peripheral Nerve stimulation : BION for Pudendal nerve in pelvic pain



Future: Compatibility with imaging and new materials

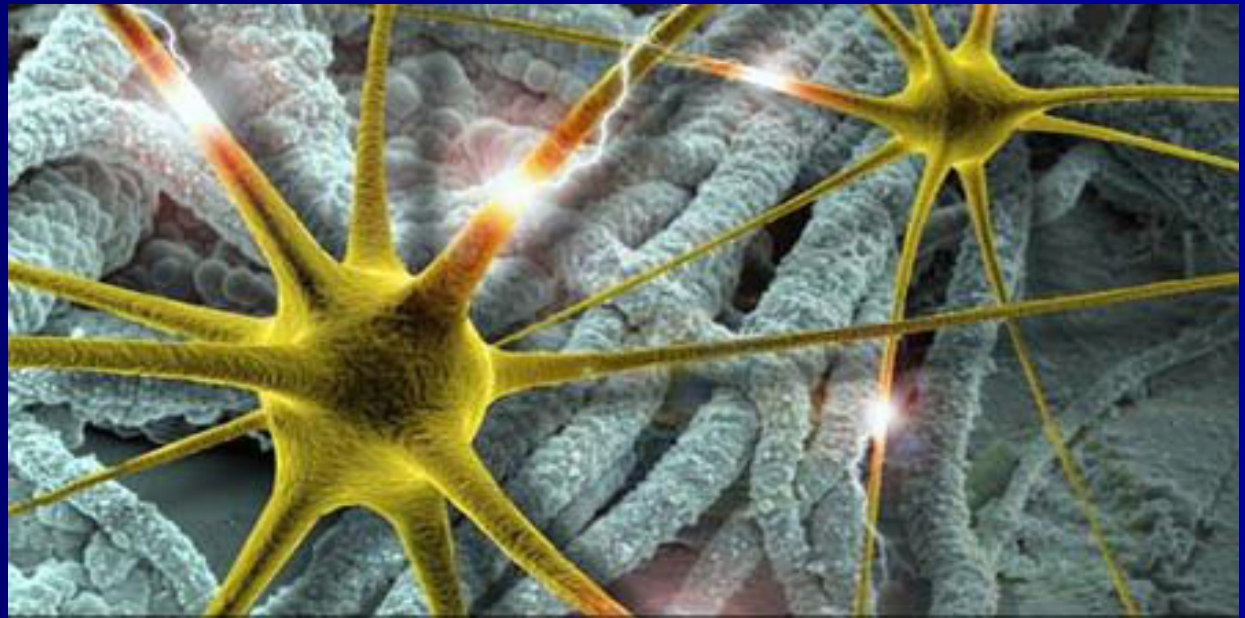


Carbon Nanotubes biomaterial of future



Future Neuroprosthetics; – Device Neuro Interface nanotubes of carbon polymer

- biocompatible**
- electronic and ionic conductivity**
- effective neural interface to function
as biosensor or as a drug delivery
system**

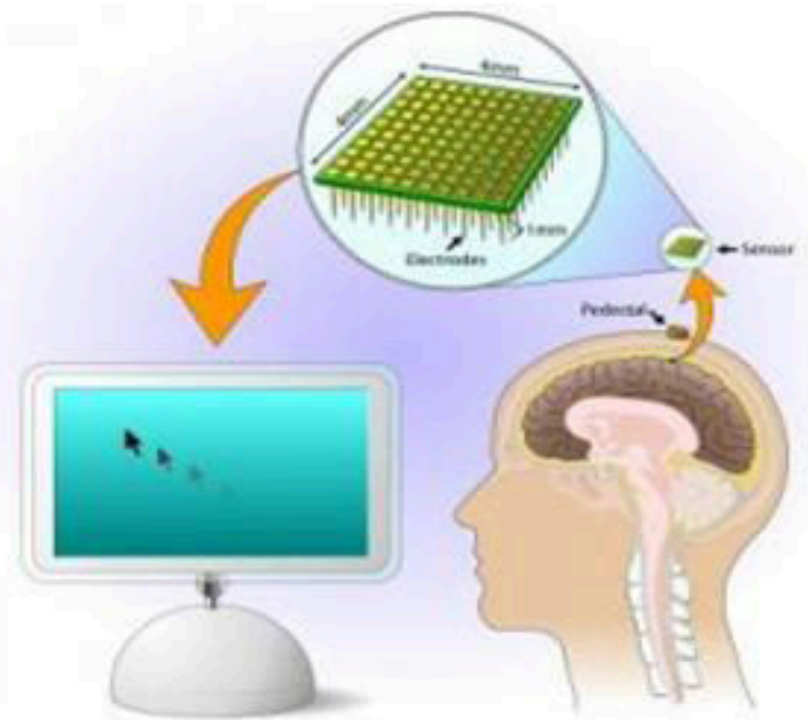


Neuroprosthetics

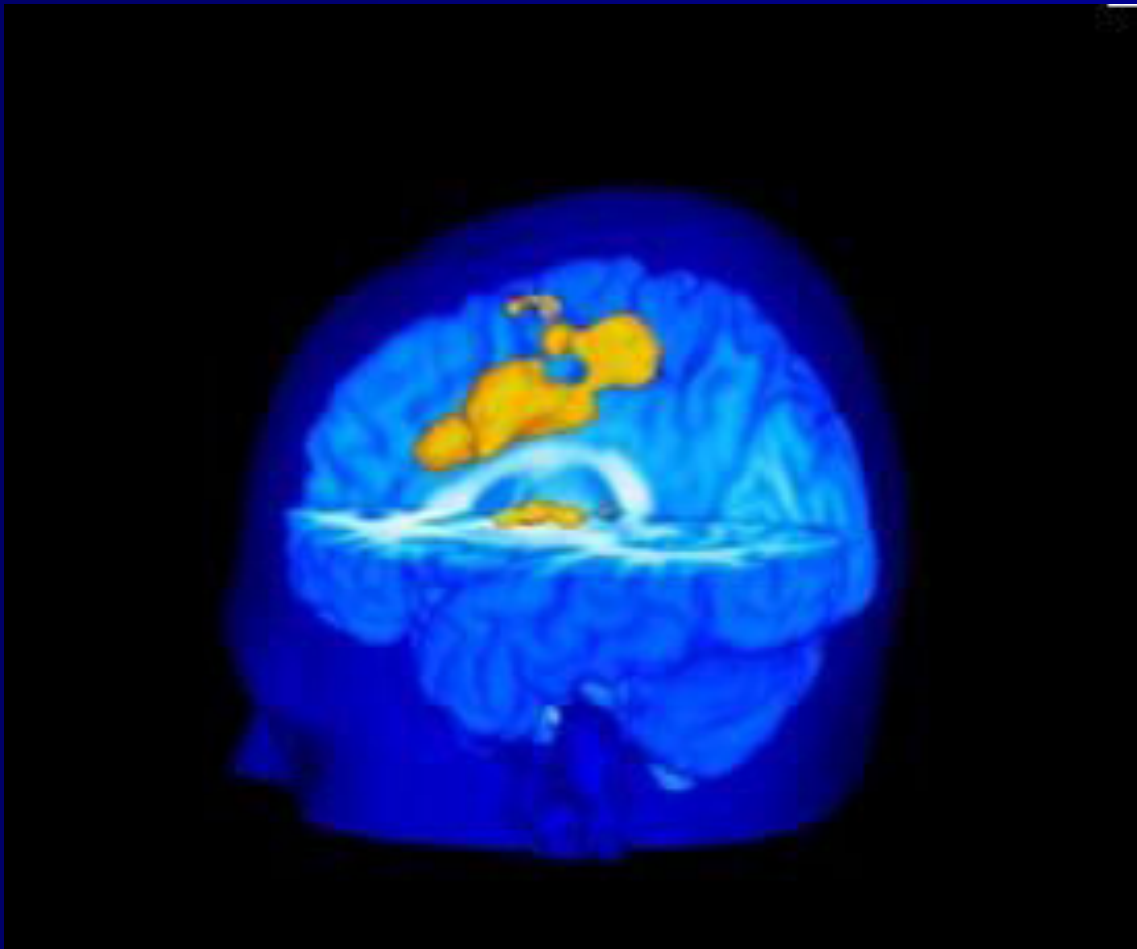
- overt action that the BCI accomplishes



- Robotic arm
- Driving a wheelchair
- Physiological processes (limbs, bowel, bladder)



Neuro-Device interface:
Location, location, location...
is there the potential for “Closed-Loop systems”
in Pain management similar to..



Evolution of Deep Brain Stimulation: Human Electrometer and Smart Devices Supporting the Next Generation of Therapy

Kendall H. Lee, MD, PhD* • Charles D. Blaha, PhD† • Paul A. Garriss, PhD† •

NEXT GENERATION DEEP BRAIN STIMULATORS 99

