Krónikus fájdalom idegsebészeti kezelése

Balás István

PTE ÁOK Idegsebészeti Klinika

Krónikus fájdalom típusai

- Nociceptív
- Nem nociceptív

Nociceptív fájdalom

- Fájdalmas (nociceptiv) ingerrel kiváltott a perifériás **nociceptorok krónikus aktivációja**, vagy túlaktiválódása (pl. degeneratív, esetleg daganatos eredetű lágyrész, izületi, vagy csontfolyamatok).
- éles, markoló
- **csillapítható ópiátokkal**.
- **nincs idegrendszeri tünet** (érzészavar) a fájdalmas területen

Neuropathiás, neurogén fájdalom

- **Idegrendszeri sérülés** (érzőpálya) következménye
- **Idegrendszeri tünet**
- **Fájdalomvezető pályák** innervációjának elvesztése
- Égő, érzészavar
- **Nem reagál opiátokra**

Neuropathiás, neurogén fájdalom jellemzői

- Thermális (égő, hideg)
- exteroceptiv (elektromos, villámlásszerű, csípő, szúró)
- Proprioceptiv (szaggató, szorító, markoló)

dysaesthesia

állandó, időszakos, külső ingerekkel kiváltható (thermális, tactilis, proprioceptiv allodynia, hyperalgézia)

Idegsebészeti fájdalomcsillapítási lehetőségek neuropátiás fájdalomban

- **Ablatív**
- **Neuromoduláció**

Ablatív fájdalomcsillapító idegsebészeti beavatkozások

- fájdalomvezető pályákat átmetszése, roncsolása, destruktív, (rizotomia,DREZ,myelotomia,termocoaguláció)
- számos esetben hatástalan,
- hatás átmeneti,
- maradandó hiánytünet
- irreverzibilis, magasabb morbiditás
- ***deafferentációs fájdalmak kialakulása***.

Funkcionális idegsebészet

definíció

- **Kóros idegrendszeri működések (funkciók) műtéti úton történő befolyásolása (normalizálása).**

Funkcionális idegsebészet -alkalmazási területek

- **krónikus fájdalom**
- mozgászavarok
- spasticitás
- epilepszia
- psychochirurgia
- vegetatív zavarok

Neuromoduláció

- centrális-perifériás-autonom **idegrendszer működésének terápiás alterációja**
- implantált készülék
- elektromos, gyógyszeres
- non-destruktív
- reverzibilis
- betegséget nem gyógyít
- működést, életminőséget javít

Neuromoduláció típusai

- **Elektromos (neurostimuláció)**
- **Kémiai (gyógyszerpumpa)**

Neuropathic pain

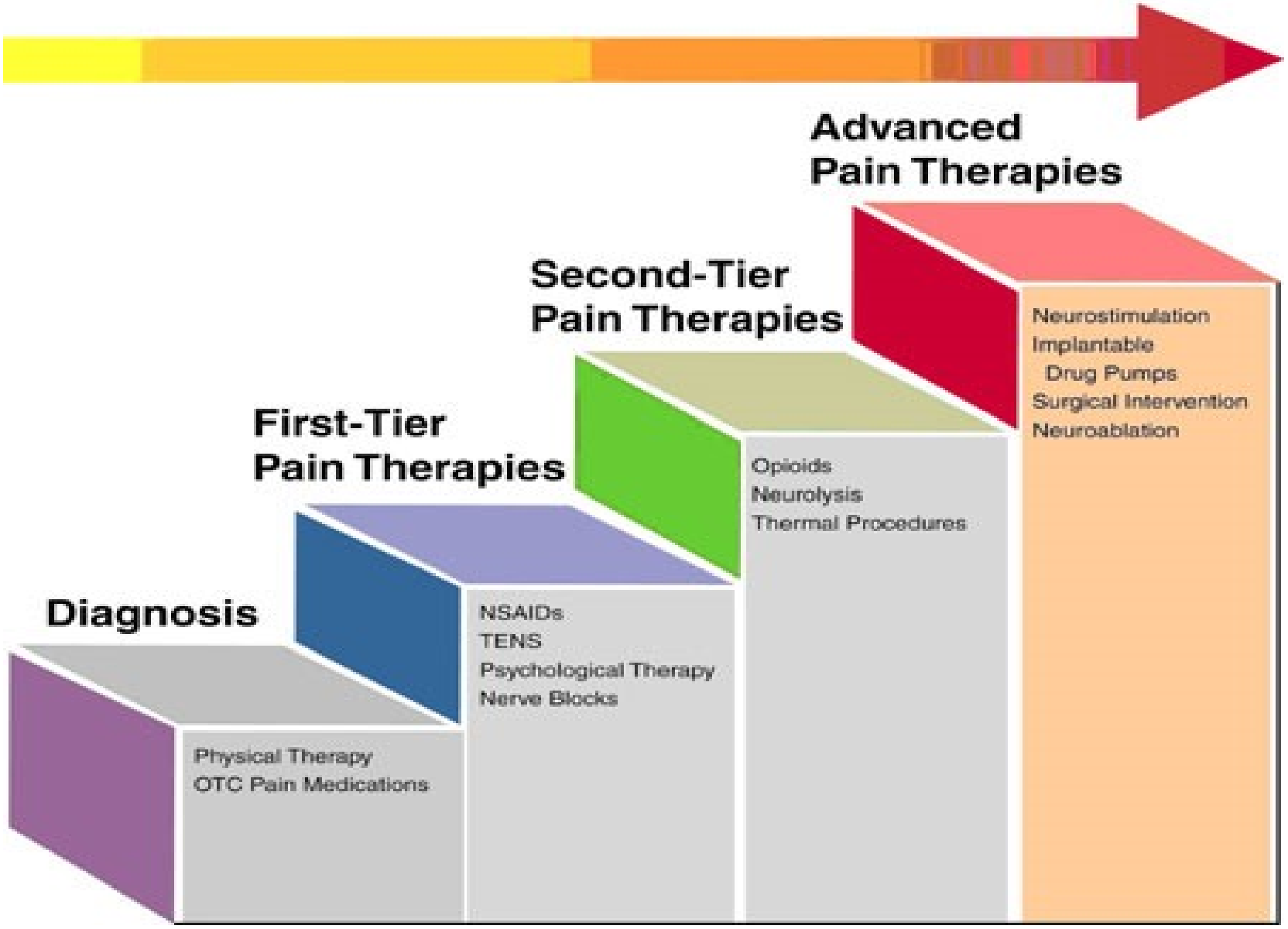
- International Association for the Study of Pain defines pain caused by **a lesion or disease** of the **somatosensory nervous system**.

- suffer more often from **insomnia, anxiety, and depression.**[1]

- analgetic **medication insufficient.**[2]

- SCS has undergone constant **technical advancement**

The Chronic Pain Treatment Continuum



Why Neuromodulation?

- Testable
- Completely reversible
- Non-destructive
- No limitation to future therapy

Neurostimuláció helye

- perifériás ideg — PNS, PNfS, DRGS
- gerincvelő — SCS
- mélyagyi — DBS
- motoros agykéreg — MCS

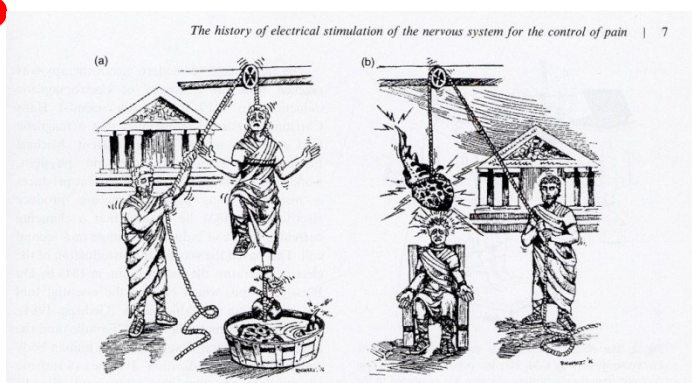


Fig. 1. Artist's impression of the treatment of gout (a) and headache (b) using torpedo fish. (Reproduced with permission: Perdikis, 1977.)

Neurostimulációs fájdalomcsillapító műtétek indikációjának felállítása

- fájdalom kezelésében járatos szakemberek **közös döntése**
- **centrumokban** (kivizsgálás, kezelés, szövődmények elhárítása)
- **multidisciplináris** (ideggyógyász, idegsebész, psychiáter, psychológus, anaesthesiológus, neuroradiológus, elektrofiziológus, mozgásterapeuta) munkacsoport

Neurostimuláció, általános kontraindikációk

(krónikus fájdalom)

- psychiátriai kórképek (aktív psychosis, súlyos depresszió, hipochondria, szomatizációs betegségek).
- nem együttműködő beteg
- alkoholizmus, kábítószer-élvezet
- súlyos kísérő betegség (coagulopathia, immundeficiencia)
- más implantált pacemaker (pl. szív) ?

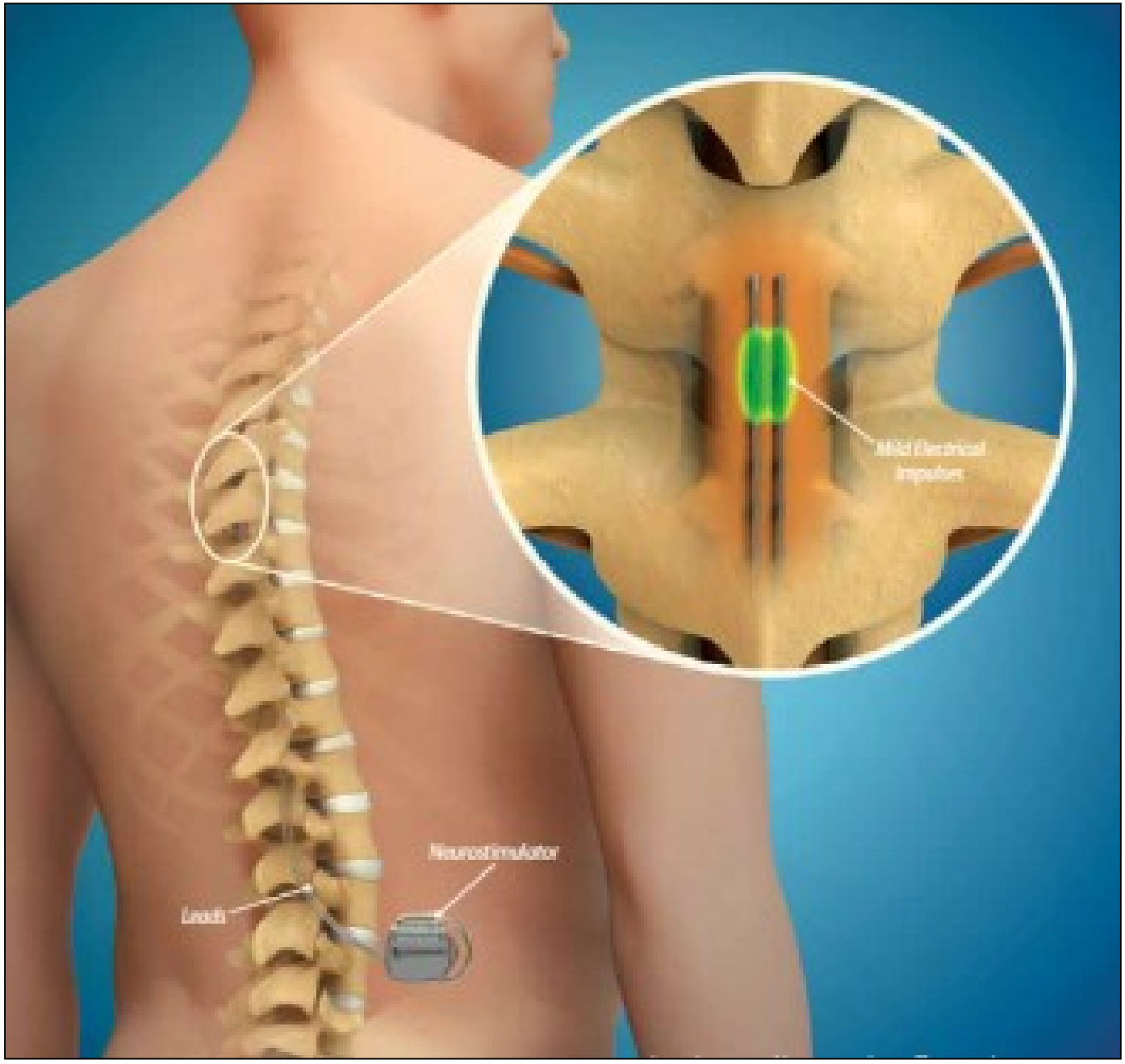
Neurostimuláció/ műtéti szövődmények

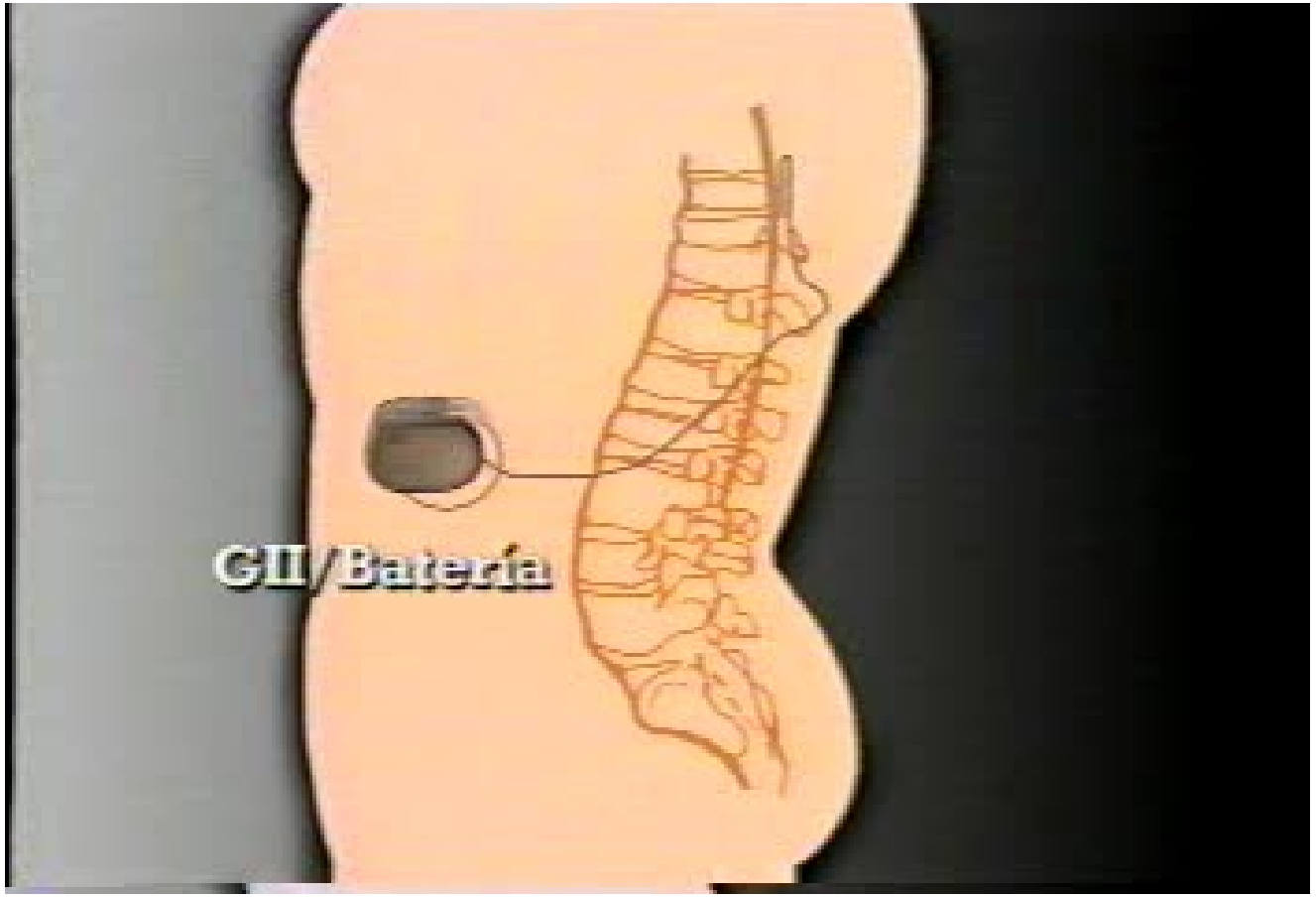
- korrigálhatók
- implantátummal (8-10%) kapcsolatos

  (elektróda elmozdulás, sérülés, elektromos működés zavar)
- vérzések (1-5%)
- gyulladások (5-7%).

Spinal cord stimuláció (SCS)

- Legnépszerűbb, leggyakrabban alkalmazott
- Első SCS daganatos fájdalom (Shealey 1967).

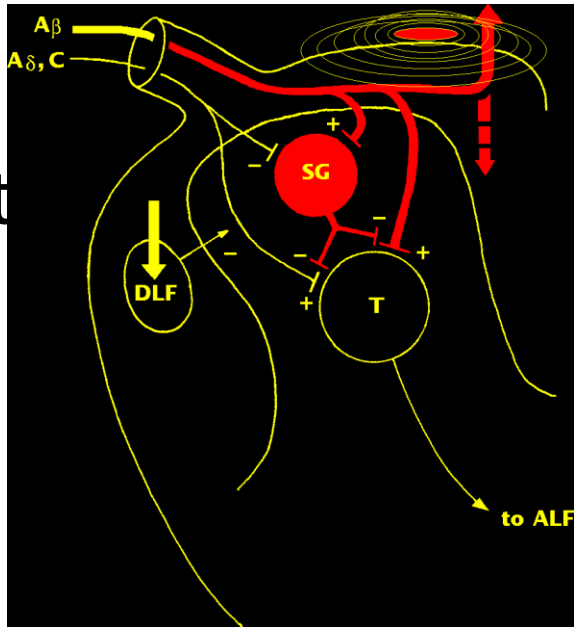

Mild Electrical Impulses
Neurostimulator
Leads


GII/Batería

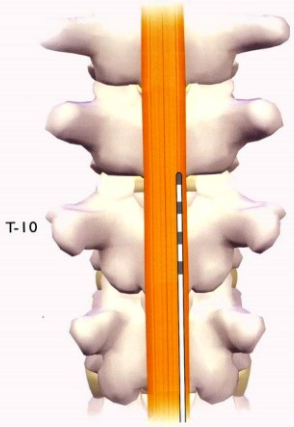
History of Spinal Cord Stimulation

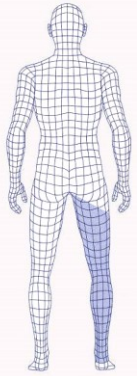
Shealy, 1969

- 1967 – Long and Wall, PNS
- 1969 – Shealy, SCS in humans
- 1975 – Dooley, perc. electrode
- Mid 1970s – self-powered battery
- 1980s - programmable quad elect
- 1980s -1990s – Primary cell IPG
- 2004 – Rechargeable IPG



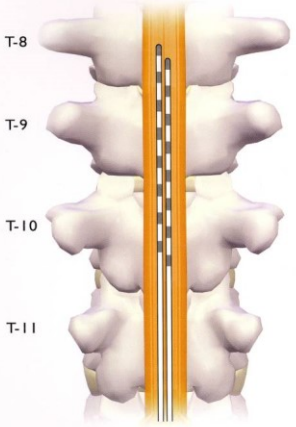
Quattrode® Lead





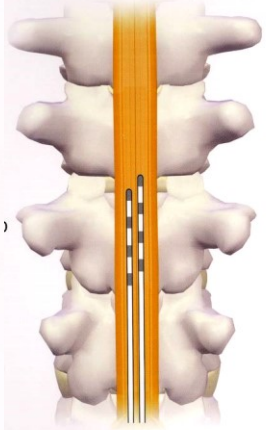
Unilateral Leg

Dual Octrode® Leads

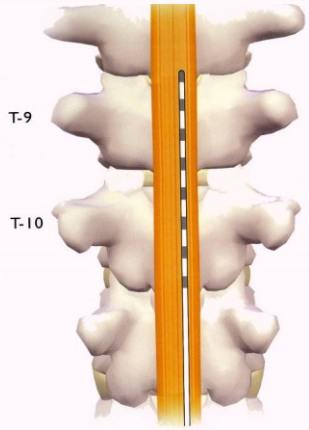


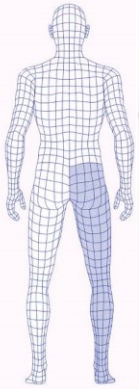
Bilateral Leg and Back

Dual Quattrode® Leads

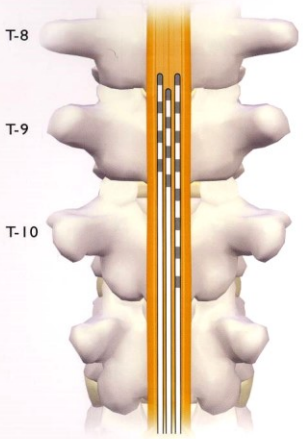


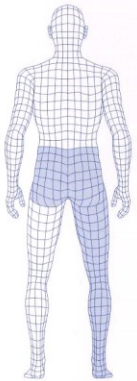
Bilateral Leg



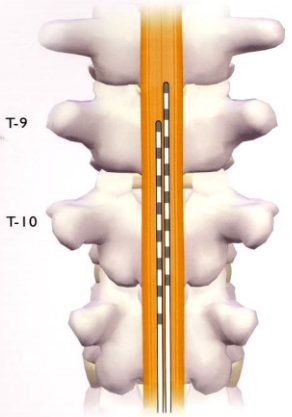


Unilateral Leg and Unilateral Low B

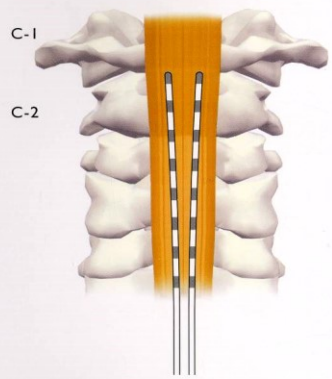


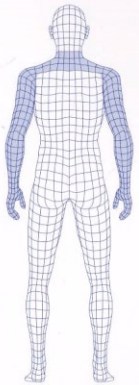


Unilateral Leg and Back

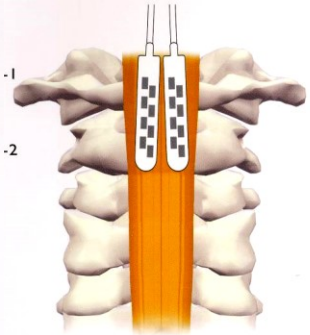


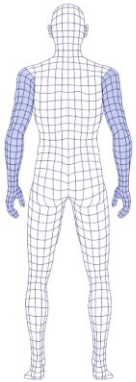
Bilateral Leg and Low Back



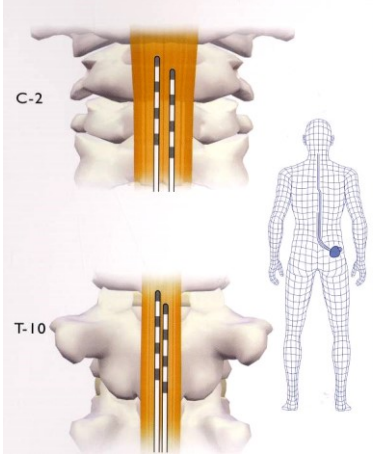


Bilateral Arm and Shoulders



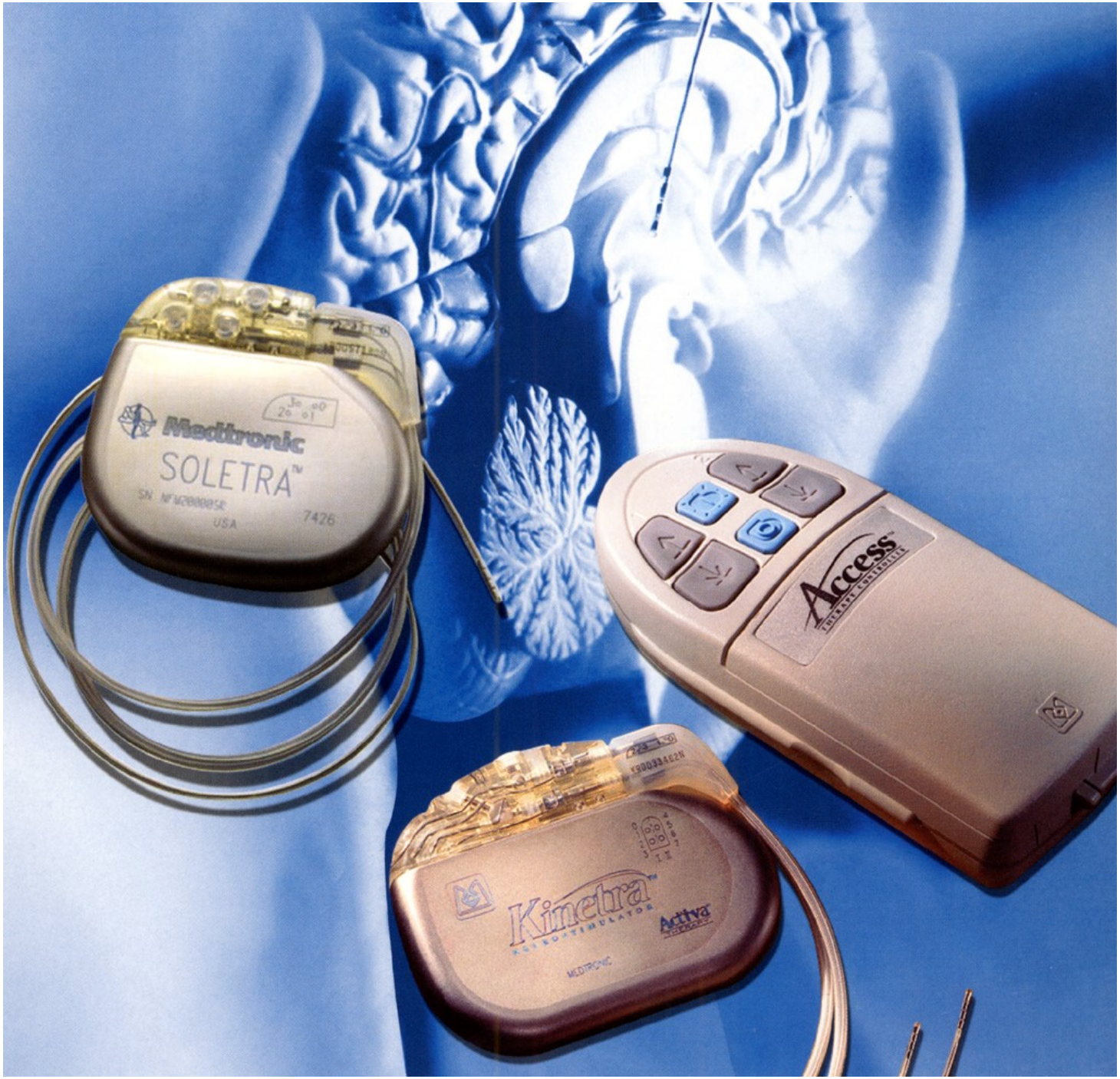


Bilateral Arm



Complex Multi-Extremity

Pain location	Tip of the electrode
Foot	T12 – L1
Leg and ankle	T11 – T12
Thigh and knee	T9 – T10
Axial low back and inferior limb	T7 – T12
Low back	T8 – T10
Precordial (for refractory angina)	C6 – T1 (at the left of the midline)
Upper limb	C5 – T1
Neck and arm	C1 – C2 (it may be placed via a retrograde C0 – C1 insertion)
Head and face	C1 (cervicomedullary junction)
Chronic visceral abdominal pain	T5 – T6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Reduction of Pain

Clinical studies on SCS continue to support the effectiveness of this therapy. The following charts summarize studies of SCS and its effects on the quality of life of patients.

Reference	Number of Patients	Follow Up	Results
Kumar[17]	410	8 years	74% had ≥50% relief
North[14]	19	3 years	47% had ≥50% relief
Barolat[9]	41	1 year	50%-65% had good to excellent relief
Van Buyten[18]	123	3 years	68% had good to excellent relief
Cameron[19]	747	Up to 59 months (4.9 years)	62% had ≥50% relief or significantly reduced pain scores

SCS indikációk I.

Neuropáthiás (neurogén) fájdalom

- **Perifériás idegek *sérülése***: gyökök, plexusok (idegrendszeri hiánytünet).
  sérülés okai: baleseti, műtét pl lumbális discectomia (gyök), nőgyógyászati (inguinalis ideg), térdműtétek (infrapatelláris ideg), mastectomia (costo-brachiális ideg).
- végtag-amputáció ***csonkfájdalom*** jobban, mint a ***fantom*** *fájdalom*.
- *post-**herpeses neuralgia***, amennyiben a bőrérzés részlegesen megtartott
- *post-**irradiációs*** **plexopátia**
- ***polyneuropátiák*** (diabeteses, alkoholos), post-kemoterápiás (amennyiben a vastag rostok működése részlegesen megtartott)
- ***gerincvelő incomplett sérülése*** -amennyiben a vastag érzőrostok működése megtartott és a segmentális fájdalom a sérülés magasságában lép fel
- cervicális és lumbosacralis ***radiculopátiák*** (compresszió, ischaemia, sebészi, baleset, arachnoiditis.
- ***CRPS II.*** (causalga)
- **DE !!!**
- plexus avulsió, syringomyelia fájdalom nem csillapíthatók !!!.
- nincs egyetértés a CRPS I (reflex sympaticus dystrophia).

SCS indikációk II.

- ***Kevert fájdalom szindrómák***

  Falied back surgery syndroma = FBSS korábbi gerincsebészeti beavatkozás (postoperatív fibrosis, arachnoiditis)

Posztlaminektomiás szindróma

angolszász: failed back surgery szindrómának **(FBSS)**

- **fájdalom lokalizáció:** alsó ágyéki gerinc, far, alsó végtagok
- **etiológia**: arachnoiditis, epidurális heg, radiculitis, mikro-instabilitás, rec. porckorongsérv, gyulladás
- **tapasztalatok:** alsó végtagba terjedő fájdalomra SCS hatékony
- axiális fájdalmakra nem bizonyított.

Incidencia FBSS

- ranges 5 - 50%
- postdiscectomy 10-40%

Etiologia FBSS

- Scar tissue that forms around the surgery site, interrupting normal neurological functioning.
- technicalities of the operation are not successful, the performing surgeon had poor technique, and/or there is iatrogenic injury present.
- surgery is not performed at the site that causes the pain.
- surgery performed is not actually necessary.
- patient is a poor fit for a successful surgery.
- diagnosis was incorrect.
- Complications of surgery arise.

FBSS okai és tünetei

- **FBSS cause:**[1-7]
  - **irreversible nerve injury**
  - **surgical complications**
  - **psychosocial problems**
  - **inappropriate selection of patients for surgery**
  - **recurrent herniation**
  - **wrong level of operation**

- **FBSS symptoms:**[3,4,8]
  - **lumbosacral postoperative fibrosis and/or arachnoiditis**
  - **root lesion**
  - **dorsal compartment syndrome**
  - **lateral spinal stenosis**

1. Anderson VC et al. *Current review of pain* 2000;**4**:105-11
2. Leveque JC et al. *Neuromodulation* 2001;**4**:1-9
3. Dario A et al. *Neuromodulation* 2001;**4**:105-110
4. Ohnmeiss DD et al. *The Spine Journal* 2001:358-363
5. Vaccaro AR et al. *Spine* 2001;**26** (24): S111-8
6. Spengler DM et al. *Spine* 1980;**5**:356-60
7. Fager CA, Freidberg SR. *Spine* 1980;**5**:87-94
8. Long DM. *Surgical management of pain* 2002: 354-64

SCS indikációk III.
Angina pectoris

- New York Heart Association III.-IV. csoport (szignifikáns coronária stenosis egy, vagy több szűkület >70 %),
- **myocardiális ischaemia reverzibilis, angina gyógyszeres, revascularizációs beavatkozásokkal nem enyhíthető**.
- életminőség↑, nitro-glicerin felhasználás↓, anginás rohamok száma↓, járástávolság↑ .
- SCS anti-ischaemiás hatás
- nincs bizonyíték SCS hatékonyságra instabil angina, acut myocardiális infarctus, vazospasticus angia, más szívbetegség okozta anginás fájdalmak csillapítására

Anginás fájdalom
SCS tanulmányok, hatékonyság I.

- **Nienke** [45] PT, 1 év követés, **életminőség, szociális, mentális, fizikális teljesítmény szignifikánsan javul**
- **Hautvast** [46] stabil angina pectorisban, RT, 6 hét követés. Randomizálás: a. stimulátor OFF, b. csoport 3x1 óra/nap ON vagy hirtelen anginában:

  anginás rohamszám csökken

  fizikai teljesítőképesség javul

  sublinguális nitrát felhasználás csökken

  EKG-n az ischaemiás epizódusok csökkennek

  ST depresszió enyhül, életminőség javul,

  anginás fájdalom csökken

SCS indikációk III.

Angina pectoris

- tanulmányok eredményei kedvezőek [39-43].
- terápiás hatás hosszú távú
- nitrát bevitel csökkenthető
- fájdalomcsillapító hatású
- szívizom vérkeringés javul
- PET tanulmány:
  ischaemiás szívizomban keringésében
  redistribucio alakul ki nyugalomban,
  és gyógyszer indukált stresszben[44].

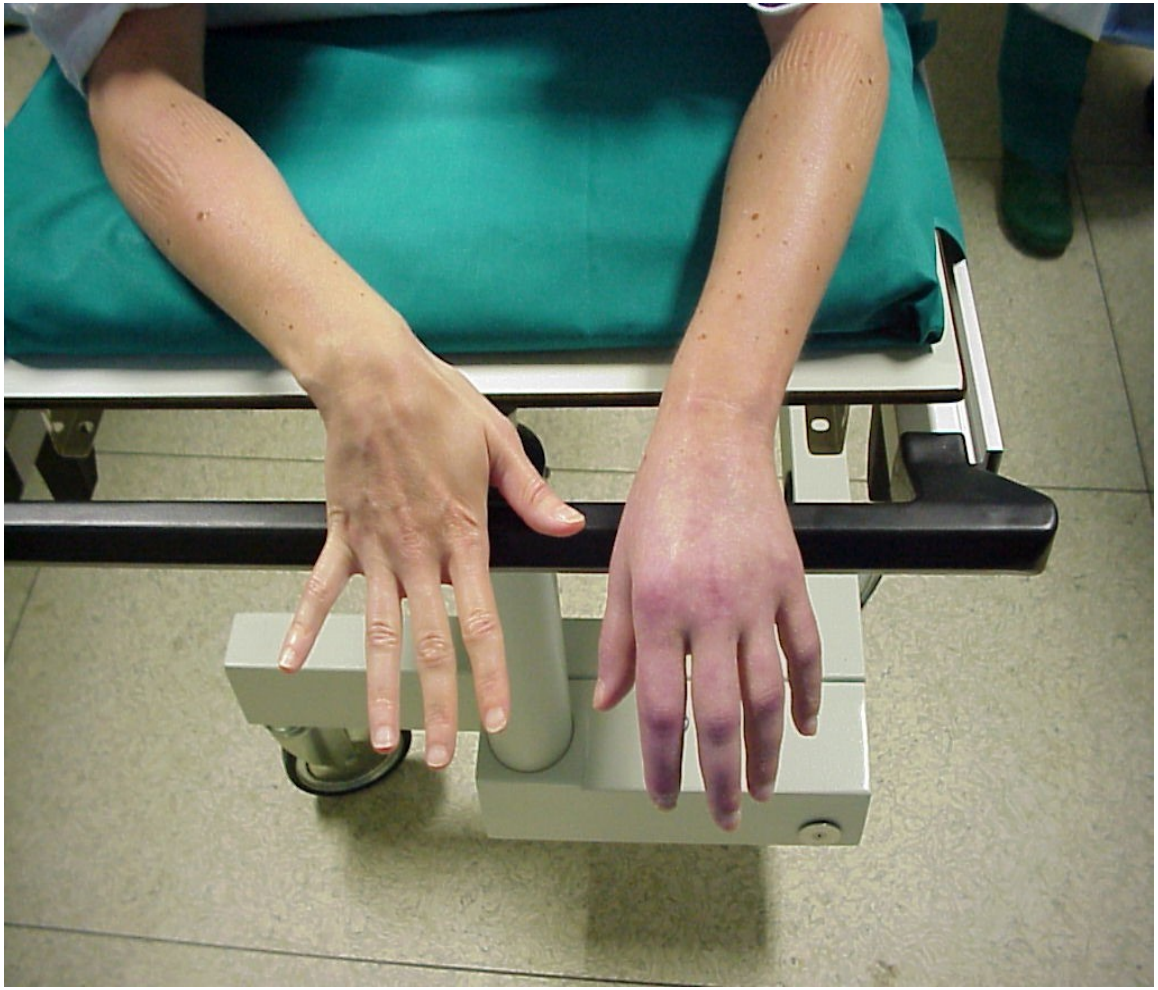
SCS indikációk IV.

Perifériás vasculáris betegségek

- lassan progrediáló perifériás vasculáris ischaemia -atherosclerosis (Fontaine 3., 4. stádium)
- vazospasticus betegség (pl. Raynaud, frostbite) **gyógyszeresen, érsebészeti műtéttel nem uralható végtagfájdalom**.
- Buerger-kór
- kontraindikált !!!.: lábszárfekély> 3 cm, gangréna

SCS indikációk V.

CRPS



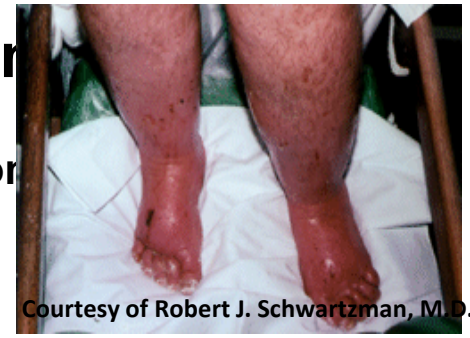
CRPS tünetei

Sensory

Intense pain[1,2]
Allodynia[1,3]
Hyperesthesia[1,3]
Hyperalgesia[1,3]
Sensory deficits[4]

Motor dysfunction

Weakness
Decreased range of motion
Tremor[1,6]
Dystonia[7]
Myoclonus[7]
Decreased muscular strength[8]


Courtesy of Robert J. Schwartzman, M.D.

Autonomic

Swelling[1]
Colour/temperature changes[6]
Sweating abnormalities[6]

Dystrophic

Increased/decreased nail/hair growth
Skin changes (e.g. palor, plantar fibrosis, hyperkeratosis and thin glossy skin[9])

1. Harden RN et al. *Pain* 1999;**83**:211-219
2. Galer BS et al. *J Pain Symptom Manage* 2000;**20**:286-92 *Neurosurgery* 1990;**40**:57-61
3. Birklein F, Handwerker HO. *Pain* 2001; **94**:1-6
4. Rommel O et al *Pain* 1999;**80**:95-101 1998;**16**:851-68

5. Thimineur M et al. *Clin J Pain* 1998;**14**:256-67

6.Birklein F et al. *Pain* 1997;**69**:49-54
7. Schwartzman RJ, Kerrigan *J. Neurosurgery* 1990;**40**:57-61

8. Zyluk A. *J Hand Surg* 2001;**26**:151-154
9. Wasner G et al. *Neuro Clin* 1998;**16**:851-68

SCS indikációk VI.
Abdominális és viscerális fájdalom szindrómák

- Fájdalom etiológiája változatos.
- Ok: gastrointestinális, gastro-urinális, musculosceletális, idegrendszeri
- Megfigyelés: Th. X myelotomia daganatos pelvicus fájdalmat csillapít.

Mechanisms of SCS

- Gate control theory
- Direct inhibition of spinothalamic neurons
- Descending modulatory effects
- Alteration of sympathetic activity
- Neurochemical modulation

GATE CONTROL THEORY

Ron Melzack & Patrick Wall, 1967

SCS mechanisms of action

Wolter T et. al November 2014 Volume 2014:7 Pages 651—663
http://dx.doi.org/10.2147/JPR.S37589

- **gate control theory**: nociceptive signal in the dorsal horn would be inhibited by antidromic activation of collateral fibers of the dorsal columns. This explanation only **partially true**. (only a **little knowledge about supraspinal control of pain transmission**, and **SCS was thought to act at the segmental level**.[15])
- wide dynamic range (**WDR**) **neurons** in the **dorsal horn** (convergent, multireceptive)

SCS mechanisms of action

- **Overexcitability of WDR neurons in the dorsal horn can be overcome by SCS.**[16]
- related to an **increased basal release of glutamate and to a dysfunction of (GABA) system.** in animals
- SCS **decreased extracellular glutamate concentration in the dorsal horn**.[18]
- **activation of the $GABA_B$ receptor** play a crucial role.[18–20]
- **Release of acetylcholine** under SCS
- **activation of the M4 muscarine receptor.**[21] **muscarine receptor agonists led to amplification of the SCS effects in rats,**[22]
- **serotonergic pain-modulating descending pathways** were involved in this effect.[23]
- **SCS inhibited wind-up in the WDR neurons, whereas stimulation of the spinal ganglia did not.** Guan et al[27].

CSC hatásmechanizmus
Neuropathiás fájdalom I.

- **Melzak és Wall 1965** „kaputeória”

  vastag myelinizált „A” rostok ingerlése gátolja a transmissiót a vékony , myelin nélküli „C” primer afferens rostokban. Epidurális elektróda stimulálja a hátsó köteget, ami gátolja vagy modulálja a bejövő nociceptív inputot a vékony rostokban.

- **Ruhston 2002** SCS a hátsószarvi neuronokat, radiculusokat és hátsó kötelet is aktiválja.

  Tractus spinothalamicus transmissio gátlása:

  centrális gátlómechanizmusok aktiválása révén sympaticus efferens neuronok közvetítésével

  gátló neurotransmitterek révén

CSC hatásmechanizmus
Neuropathiás fájdalom

- **Stojanovic 2001**, hátsó szarvi neuronok aktivitását gátolja
- **Cui 1997,** fokozza a *GABA* hátsó szarvra kifejtett gátló hatását
- **Meyerson 1997,** intrathecalis *GABA agonista* (baclofen) fokozza az SCS hatását.

  adenozin: fájdalomcsillapító pályák disinhibiciója a periaqueductalis szürkeállományban.
- **Linderot 1992, Meyerson 2000, fokozza a** *serotonin* és *substance P* felszabadulást.

Pain. 1996 Aug;66(2-3):287-95

Effects of spinal cord stimulation on touch-evoked allodynia involve GABAergic mechanisms. An experimental study in the mononeuropathic rat.

Cui JG, Linderoth B, Meyerson BA.

- in **mononeuropathic animals** with definite signs of tactile allodynia, **which did not respond to SCS, GABA-A and the GABAB-agonist baclofen were administered intrathecally**
- SCS may operate by upgrading the spinal GABAergic
- **effects of SCS are more linked to GABAB-than to GABAA-receptor system**

Eur J Pain. 2008 Jan;12(1):132-6. Epub 2007 May 1.

Baclofen-enhanced spinal cord stimulation and intrathecal baclofen alone for neuropathic pain: Long-term outcome of a pilot study.

Lind G, Schechtmann G, Winter J, Meyerson BA, Linderoth B.

intrathecal baclofen (GABA-B receptor agonist) delivery **together with SCS**

deficient SCS effect in neuropathic pain considerably **improved by intrathecal baclofen administration** enhanced effect **persists for a long-time**.

Spine. 2008 Feb 15;33(4):E90-3

Neurophysiological evidence of antidromic activation of large myelinated fibres in lower limbs during spinal cord stimulation.

Buonocore M, Bonezzi C, Barolat G.

- **Perifériás idegek antidrómos aktivációja.**

CSC hatásmechanizmus PVD-ben

- **Linderot 1999, Kemler 2000,** oxigén ellátás reballanszírozásával megelőzi az ischaemiát.

Test stimulation

- **full paresthesia coverage** of the painful area.
- **test phase**, 6–12 days.
- decision whether or not to implant an IPG
- more than **50% pain reduction**
- **quality of life** and moods are improved,
- analgetic **medication** can be reduced,
- **patient wants** the implant.

Patient selection/screening, including psychological

- **some patients do not profit from SCS** (17%–20%) negative trial result[28])
- SCS **effects diminish** over time : electrode problems (dislocation, breakage) psychological factors.
- **negative correlation** between the level of **depression** and SCS efficacy,[31,32]
- **Demand for technological developments**

Stimulation Modes

Conventional stimulation

SCS using **biphasic**, (40-100 Hz) **below 300 Hz**, previously considered to be the highest physiological response rate of neural tissue (22).

Current technological development

Burst stimulation

- **“bursts”** of 5 impulses of 1 ms duration followed by a 1 ms interval, applied at a frequency of 500 Hz.
- **pain was strongly relieved compared with conventional** stimulation.
- **no stimulation-induced paresthesia** necessary to obtain a pain-relieving effect.
- **leg pain** also **back pain was relieved.**[34,35]

Current technological development

High-frequency (kilohertz) stimulation

- **continuous** stimulation with 10 kHz
- prospective multicenter study, favorable results.[36]
- radicular **leg pain also back pain**
- results **stable** after 24 months.[37]
- **no paresthesia is perceived** (desensitization of hyperactive WDR neurons and control of wind-up phenomenon of WDR neurons.
- no experimental evidence provided.[36]

Current technological development/ **paresthesia**

- Although **paresthesias are assumed essential for pain relief when using conventional SCS** (32,33),
- **paresthesia can be uncomfortable** (34).
- **Pain relief without paresthesia would expand the role of SCS**.
- **Burst and kilohertz-frequency stimulation are potential solutions to the paresthesia problem.**
- **Currently,** multicenter randomized **studies are under way in the USA**.

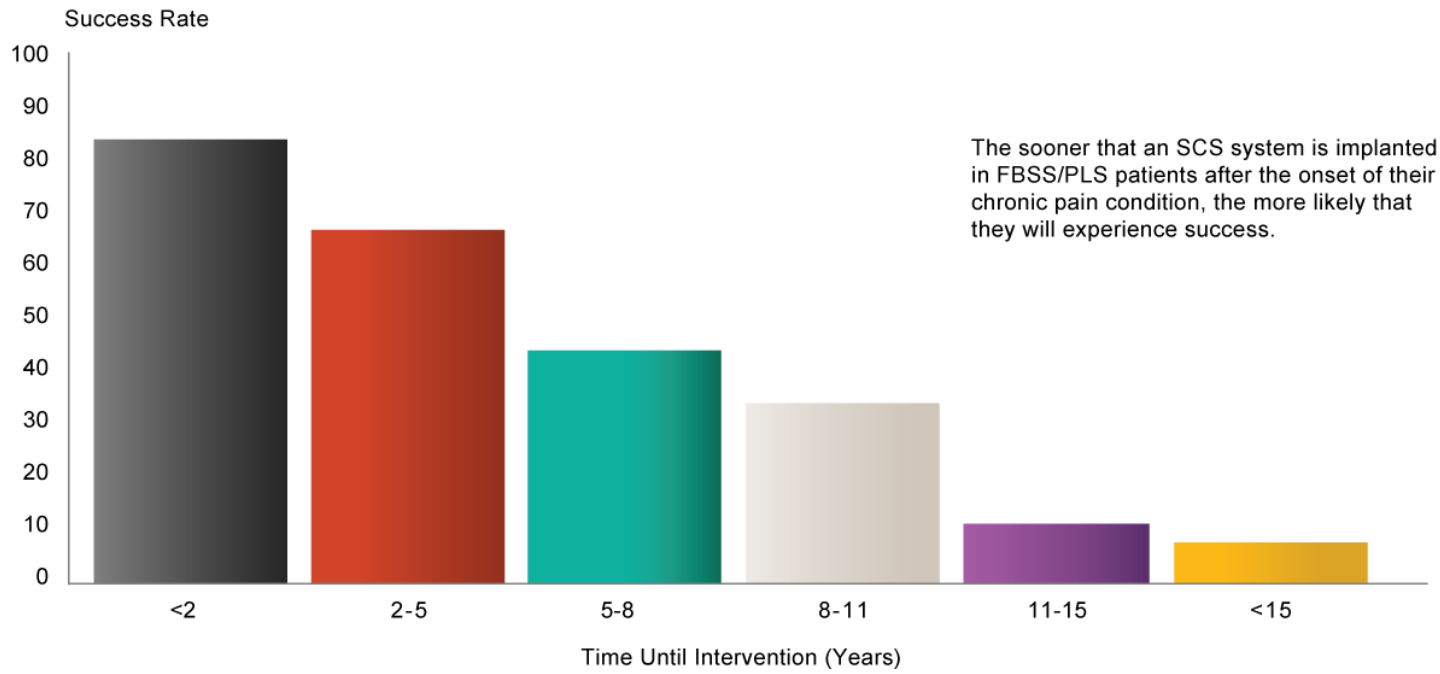
Current technological development

Position-adaptive SCS

- SCS-induced **paresthesia is dependent on body position.**[39–41]
- more intensely in the **supine position than in an upright position**.
- **variable thickness of the cerebrospinal fluid layer around the spinal cord**.
- position of the spinal cord within the spinal canal exhibited considerable **interindividual differences**. Holsheimer et al[42]
- computer model, they calculated the expected thresholds
- **devices are able to detect whether the patient is lying down or standing**
- **automatic sensor-driven stimulation** pt. significantly more satisfied than with manually stimulation.[45]


Medtronic
Upright
Prone
Supine
Amplitude
AdaptiveStim™ exclusively available with RestoreSensor™

Importance of Timing With SCS in the Treatment of FBSS



- SCS for patients with FBSS is more effective the sooner an SCS system is implanted from the date of the previous failed surgery.[17]

Reduction in Medication

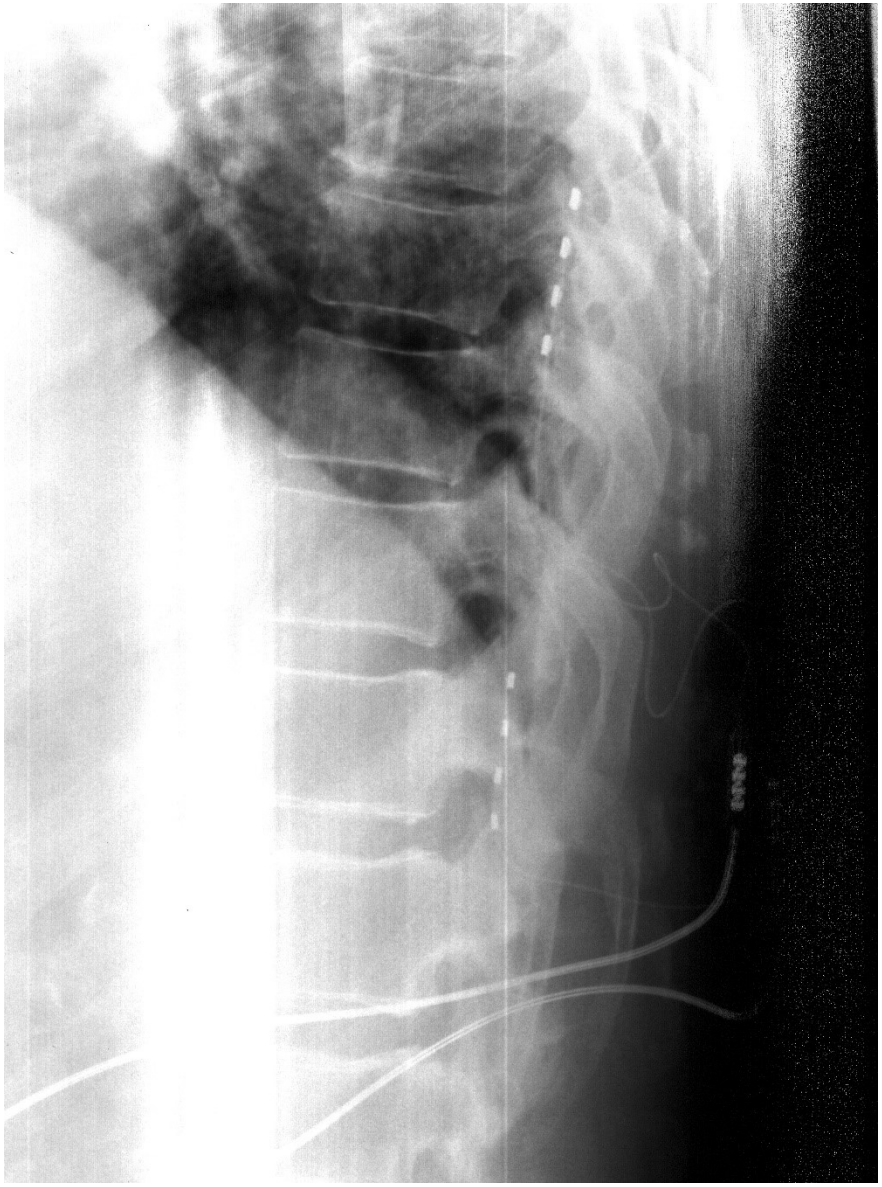
Reference	Number of Patients	Follow Up	Results
North[14]	19	3 years	~50% reduced their medications
Van Buyten[18]	123	3 years	As a group, reduced medication use by >50%
Cameron[19]	766	Up to 84 months	45% reduced their medications
Taylor[20]	681	n/a	68% no longer needed analgesics

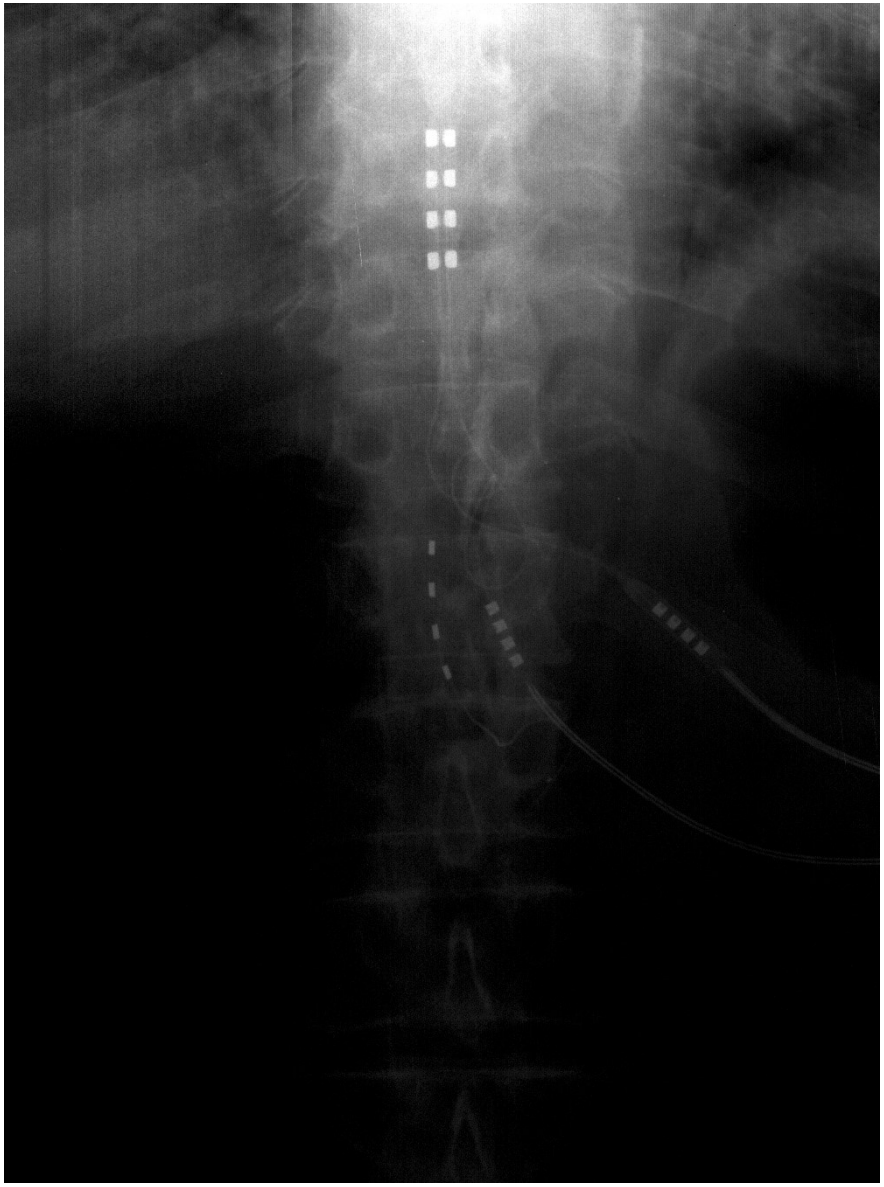
Improvements in Daily Activities

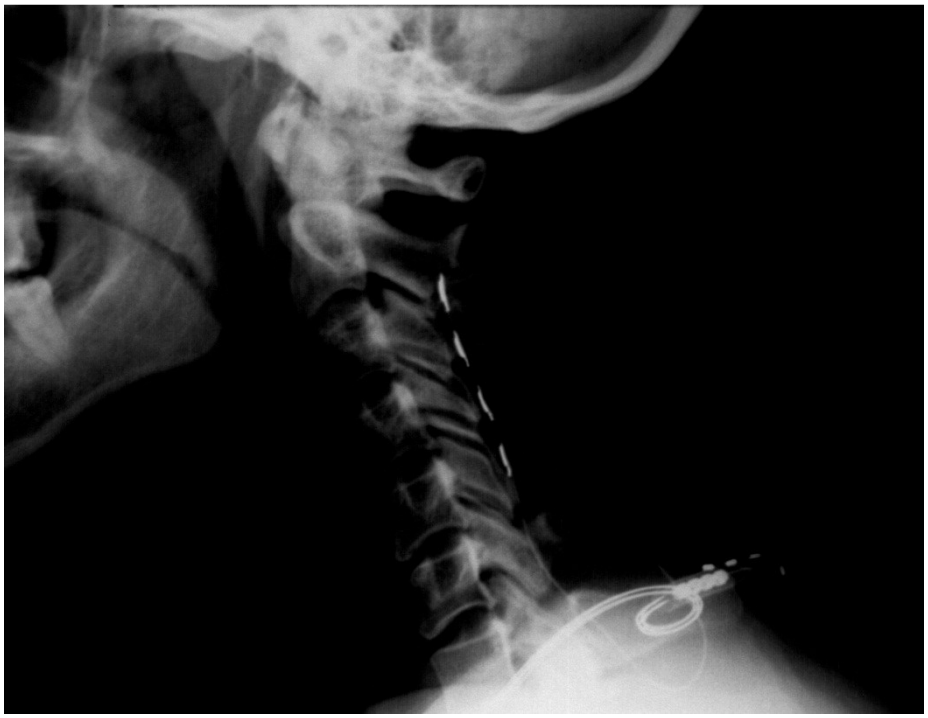
Reference	Number of Patients	Follow Up	Results
Barolat[9]	41	1 year	As a group, significantly improved function and mobility
North[14]	19	3 years	As a group, improved in a range of activities

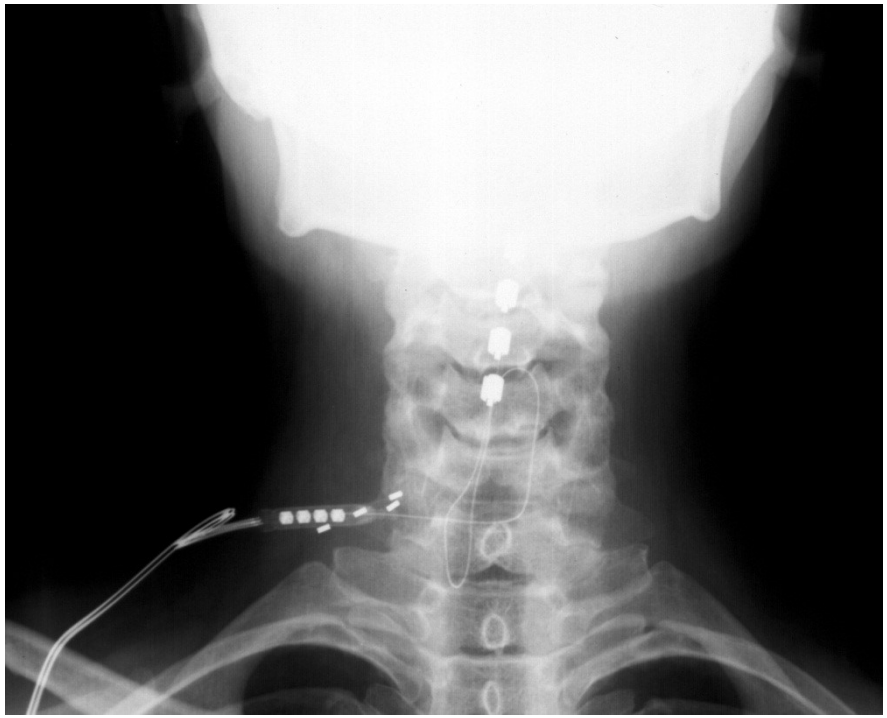
Return to Work

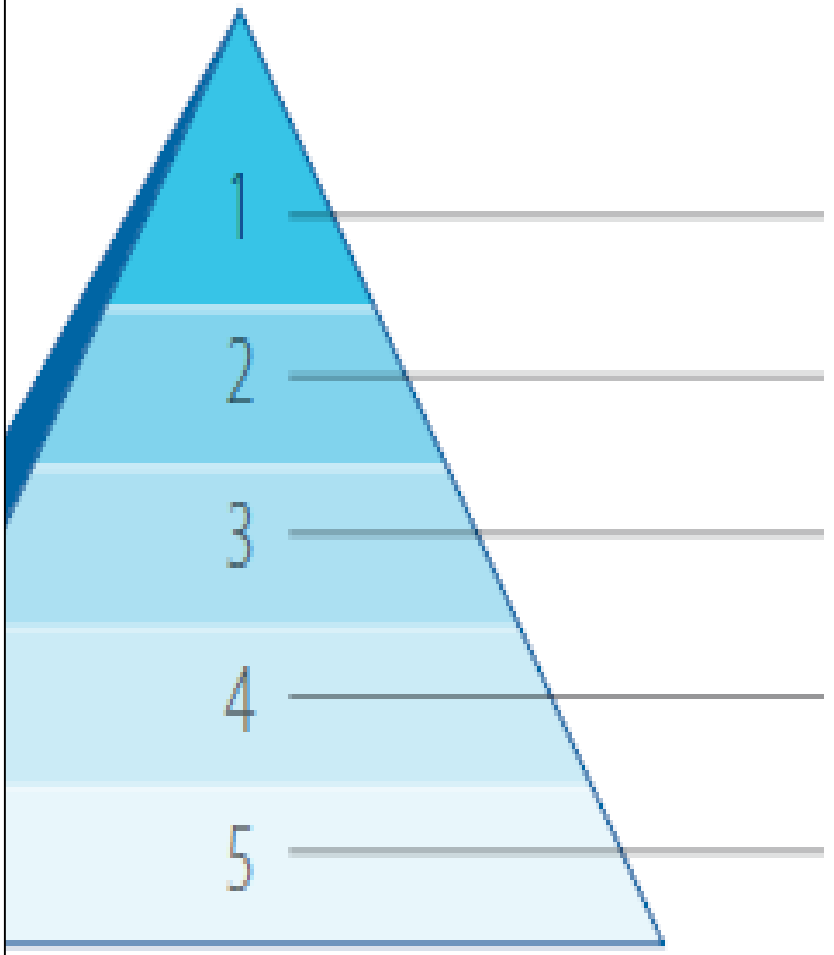
Reference	Number of Patients	Follow Up	Results
Van Buyten[18]	123	3 years	31% returned to work
Taylor[20]	1,133	n/a	40% returned to work
Dario[21]	23	3 years	35% returned to work











*Levels of Evidence**

1. Properly-designed, Randomized Controlled Trials (RCTs)
2. Controlled trials without randomization
3. Cohort- or case-controlled studies from more than one center or research group
4. Multiple-time series with or without the intervention, uncontrolled trials or case reports
5. Opinions of respected authorities based on clinical experience

*Based on the Oxford Centre for Evidence-Based Medicine

Neuromodulation. 2014 Aug;17(6):515-50;. Deer TR[1]

The appropriate use of neurostimulation of the spinal cord and peripheral nervous system for the treatment of chronic pain and ischemic diseases: the Neuromodulation Appropriateness Consensus Committee.

- **International Neuromodulation Society (INS) evaluated evidence regarding the safety and efficacy of neurostimulation** to treat chronic pain, chronic critical limb ischemia, and refractory angina and recommended appropriate clinical applications.
- **literature reviews, expert opinion, clinical experience, and individual research. systematic reviews** (1984 to 2013), and **prospective and randomized controlled trials** (2005 to 2013)
- **RCS support the efficacy of SCS in FBSS, and CRPS**
- International **guidelines recommend spinal cord stimulation to treat refractory angina**
- **studies of neurostimulation are needed** for peripheral neuropathic pain, postamputation pain, postherpetic neuralgia, and other causes of nerve injury

Mélyagyi stimuláció (DBS)

Activa™ Tremor Control Therapy can treat bilateral tremor with two implanted systems.

Első DBS a fájdalom kezelésében

- **VPL** (Mazars 1960)
- **Capsula interna hátsó szár** (Adams 1974)
- **PAG** (Reynolds 1969)
- **CM-PF** (Thoden 1979, Boivie-Meyerson 1982)

Acta Neurochir Suppl. 2007;97(Pt 2):111-6.
Deep brain stimulation for neuropathic pain.
Owen SL, Green AL, Nandi DD, Bittar RG, Wang S, Aziz TZ

- **PVG/PAG complex**
- **PVG-thalamus gyüttes stimulázója eredményezi a legnagyobb fájdalomcsillapodást**
- **Kimenetel az etiológiától függ**
- **Legjobb hatás: fantom fájdalom, arc-fej területi fájdalom, és anaesthesia dolorosa.**
- **post-stroke fájdalomra nem hatásos**

Neurosurg Focus. 2006 Dec 15;21(6):E8
Deep brain stimulation for the treatment of various chronic pain syndromes.

Rasche D, Rinaldi PC, Young RF, Tronnier VM.

- **56 pts** with different forms of neuropathic and mixed nociceptive/neuropathic pain syndromes
- follow-up 1 to 8 years, mean 3.5 years.
- Electrodes somatosensory **thalamus and the periventricular gray region**.
- The **best long-term results: chronic low-back and leg pain, (FBSS), neuropathic pain of peripheral origin (CRPS Type II).**
- **Disappointing results: central pain syndromes, (spinal cord injury and poststroke pain).**

Neurol Sci. 2008 May;29 Suppl 1:S65-8
Neuromodulation in treatment of refractory headaches.

Franzini A, Leone M, Messina G, Cordella R, Marras C, Bussone G, Broggi G

- **cluster fejfájás, trigeminus neuralgia**
- Deep Brain Stimulation (DBS)
- **Target: Posterior Hypothalamus**

Mélyagyi stimuláció

krónikus fájdalom

- **neospinothalamicus pályák**, vagy átkapcsoló állomásai VPL, IC, PVG, PAG, VM, PF, septalis magok, hypothalamus, tegmentum
- **több központ együttes ingerlése** (csak thalamus 58%, PVG/PAV és thalamus/capsula interna együtt 87%)
- **nociceptív fájdalom eredmények jobbak**, mint deafferentációs típusnál (63% vs 47%).
- **leghatékonyabb FBSS (>80%).**
- **phantom fájdalom,**
- **anaesthesia dolorosa.**
- **cluster fejfájás, arcfájdalom**

- **Hatástalan: central fájdalom (gerincvelő sérülés, poststroke fájdalom).**

Neuromodulation. 2014 Aug;17(6):551-70; discussion 570. doi: 10.1111/ner.12213.

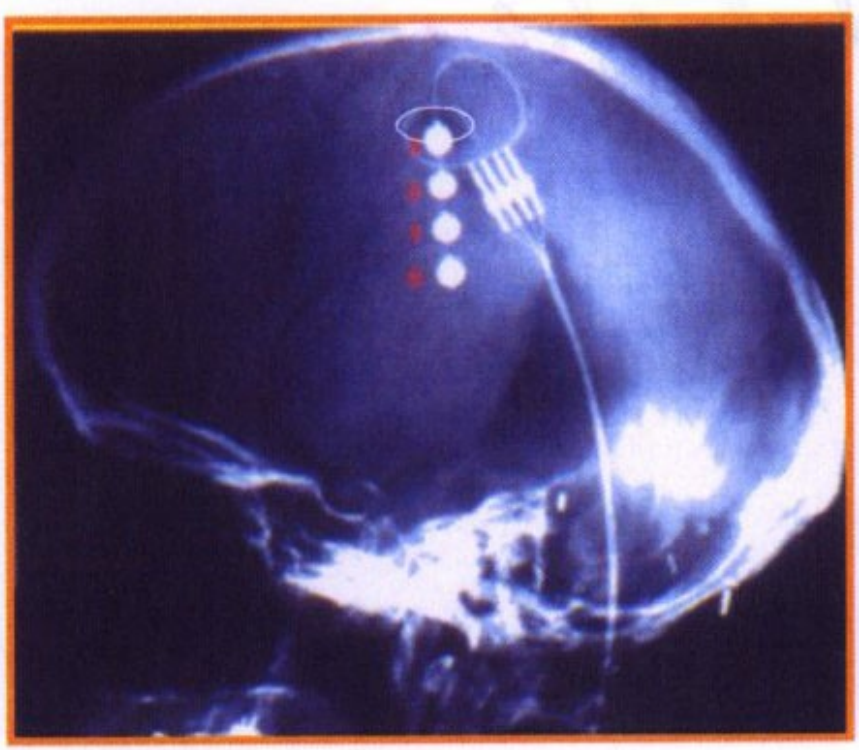
The appropriate use of neurostimulation: stimulation of the intracranial and extracranial space and head for chronic pain. Neuromodulation Appropriateness Consensus Committee.

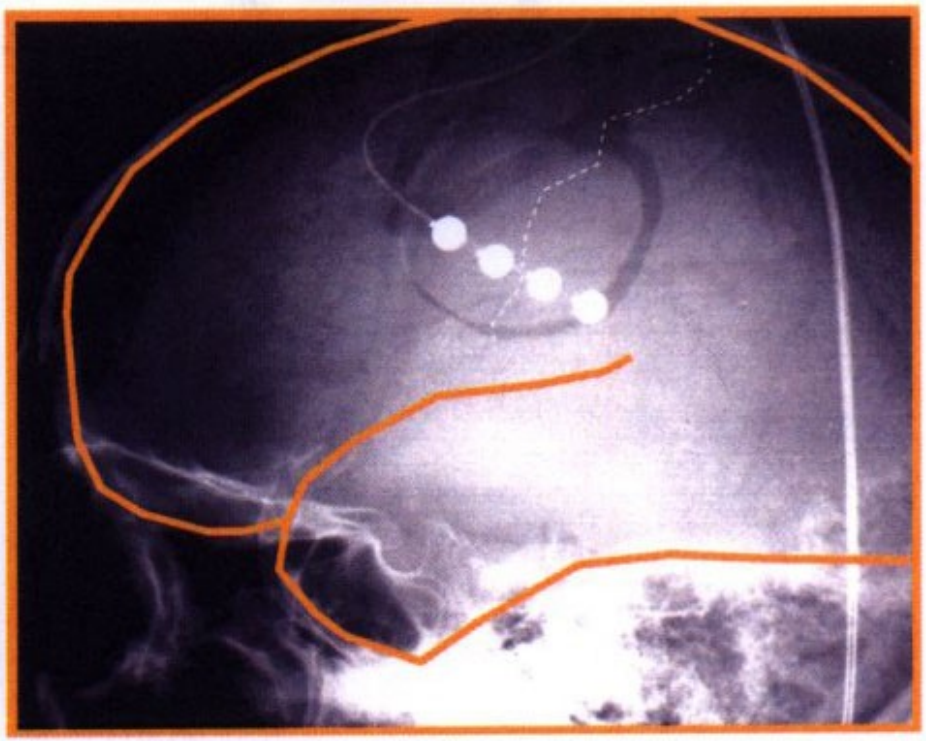
Deer TR[1], Mekhail N, Petersen E, Krames E, Staats P, Pope J, Saweris Y, Lad SP, Diwan S, Falowski S, Feler C, Slavin K, Narouze S, Merabet L, Buvanendran A, Fregni F, Wellington J, Levy RM; Neuromodulation Appropriateness Consensus Committee.

- evidence supports **extracranial stimulation for facial pain, migraine, and scalp pain**
- **evidence is limited for intracranial neuromodulation.**
- **High cervical spinal cord stimulation is an evolving** option for facial pain.
- **Intracranial neurostimulation for pain should be seen as investigational.**
- **extracranial nerve stimulation should be considered in the algorithmic treatment of migraine and other disorders of the head.**

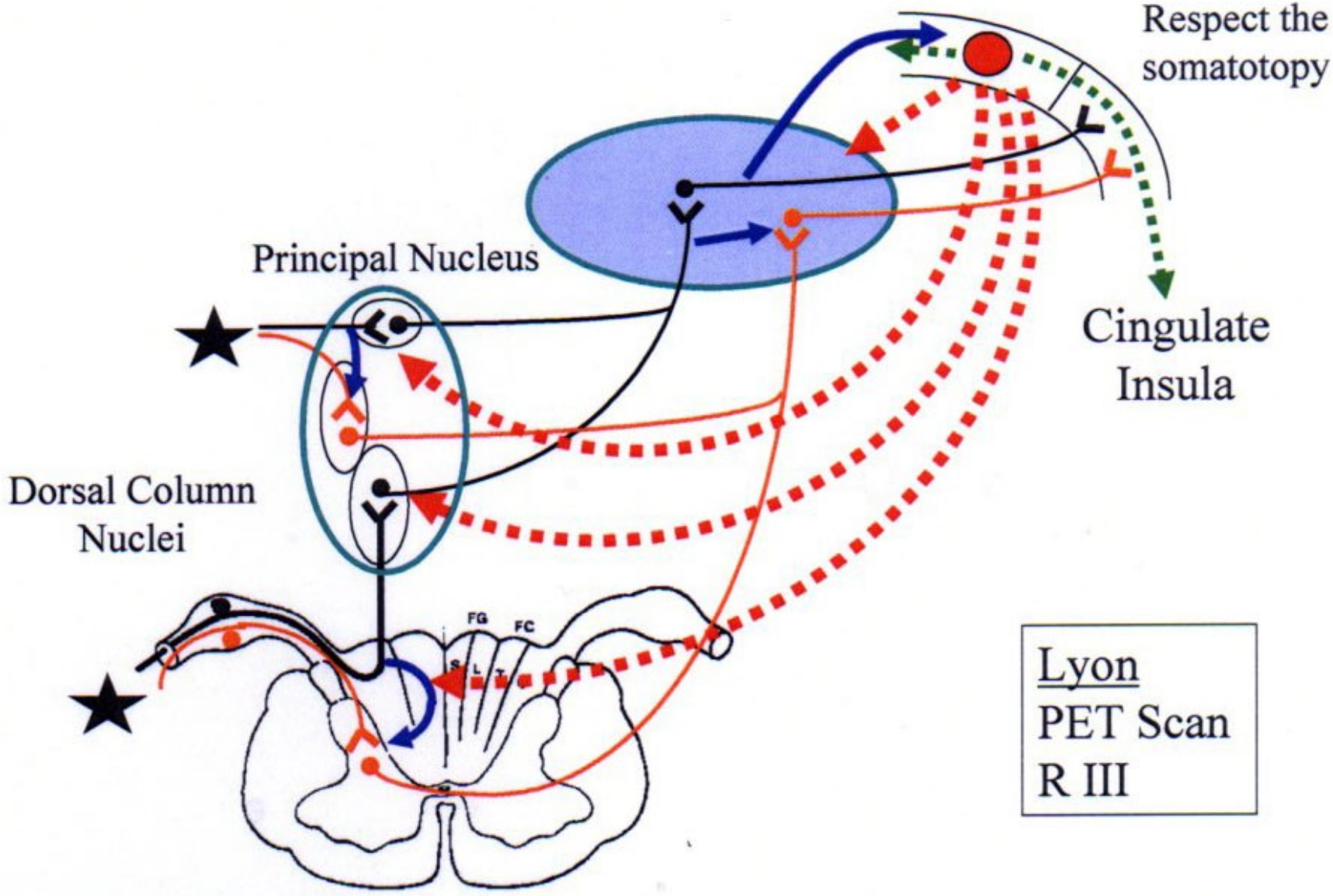
Motor cortex stimuláció

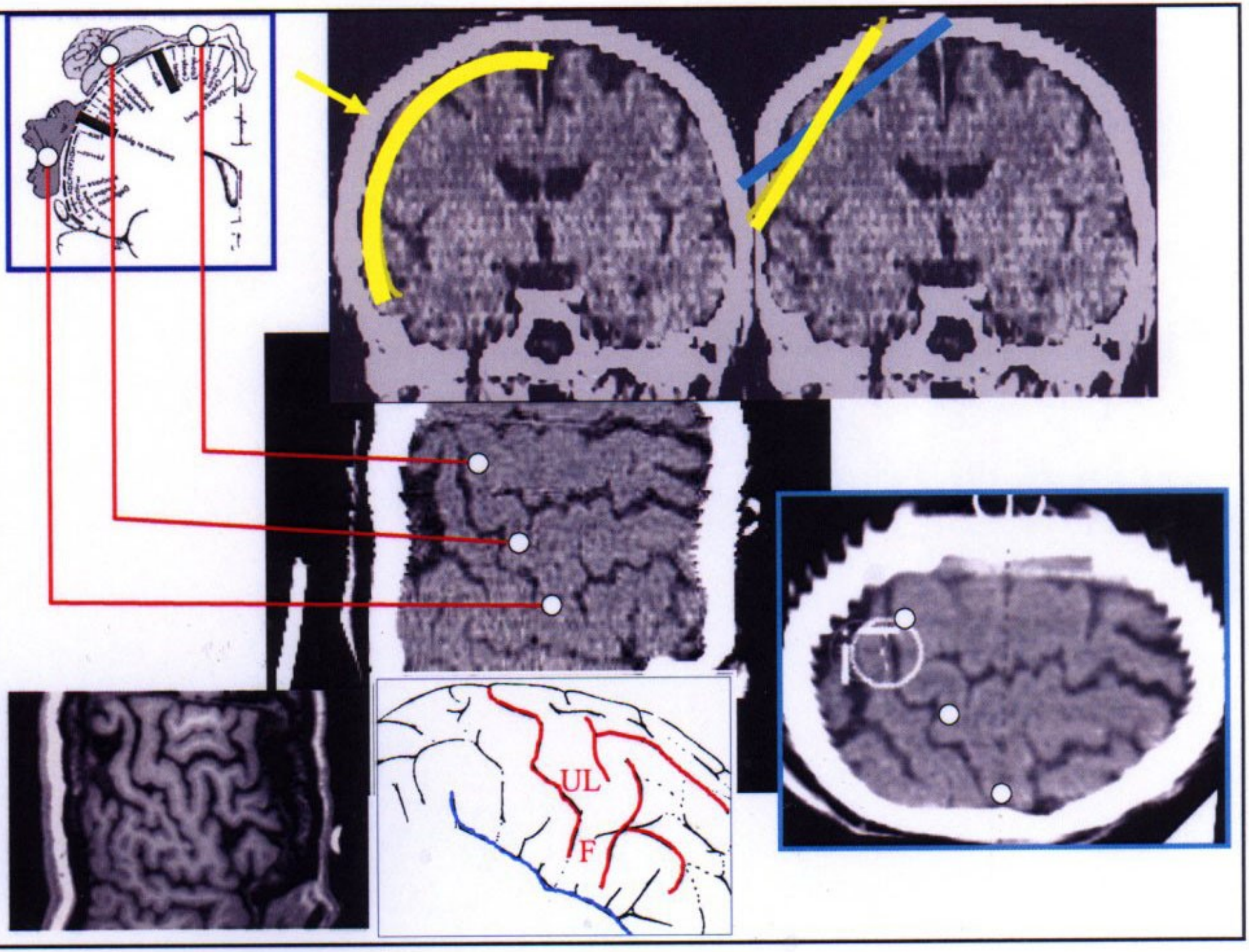
Motor cortex stimulation





« The most important, widespread source of top-down pain modulation arises from the cortex »

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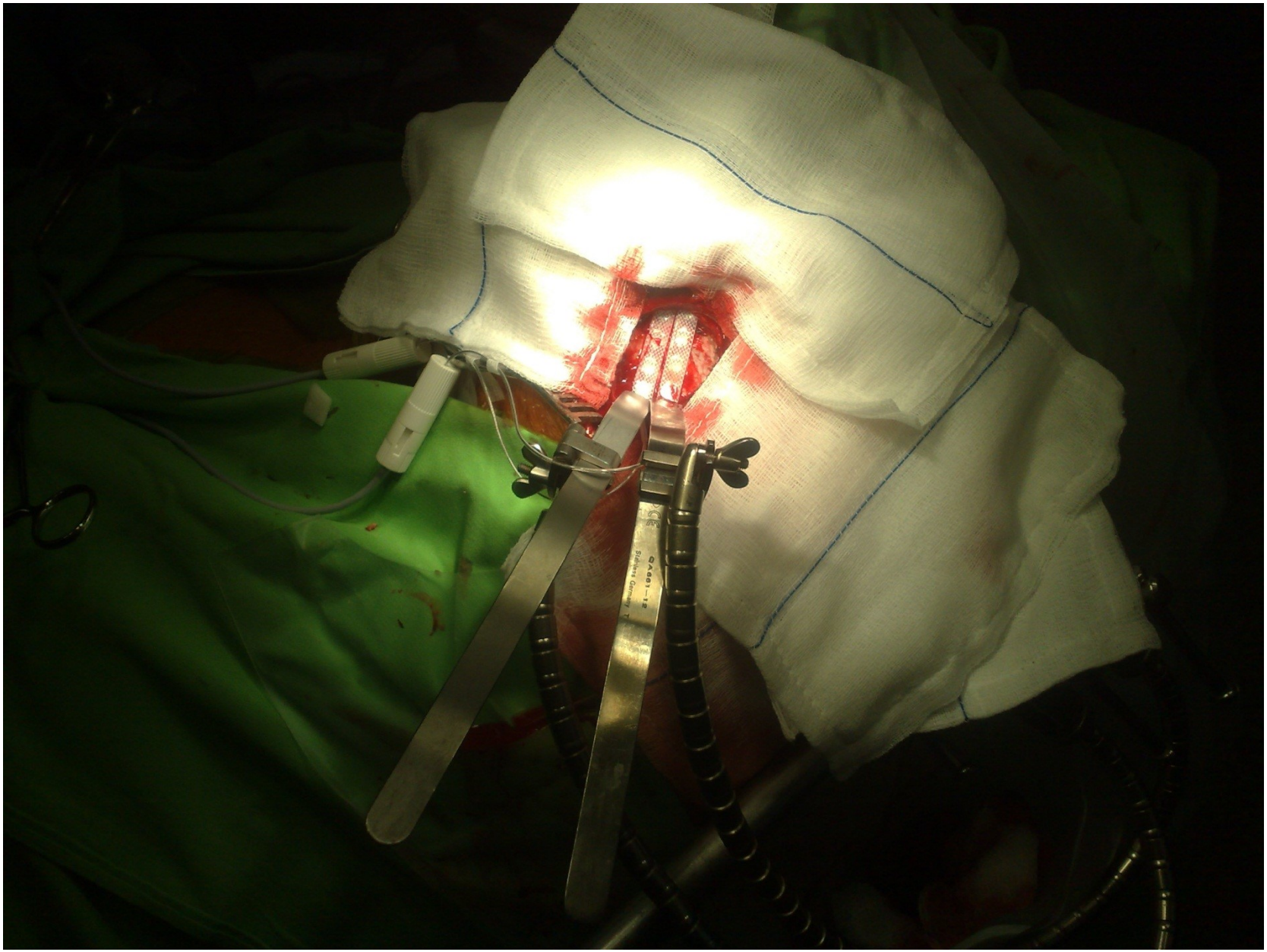


Motoros cortex stimuláció (MCS)

- Centrális, deafferentációs fájdalom, neuropathiás arcfájdalom nem reagált a klasszikus stimulációs technikákra a thalamusban
- Tsubokawa 1991 centrális laesio (thalamus fájdalom) abnormális neuronális aktivitás a thalamusban, ami a MCS-val csillapodik.

MCS indikációk

- **deafferentációs arcfájdalom**
- **centrális fájdalom**

DE !!!

- **teljes deafferentációs** arcfájdalom, teljes bénulással, **súlyos motoros deficittel** járó fájdalom **rossz prognosztikai faktor !!!.**

Hatásmechanizmus (MCS)

- **rCBF változás**: Középvonali **thalamus magok, anterior gyrus cinguli, agytörzs felső része (Garcia-Larrea 1999)**
- A pyramis pálya direkt hatást gyakorol a **g.velő hátsó szarvra (Coulter 1974)**
- Ingerlés a **somatotopiának megfelelő** területen hatékony **(Nguyen 1999)**

MCS feltételezhető hatásmechanizmusai

- A nem nociteptív **szenzoros inputok** nociteptív rendszer fölötti megerősítése révén fejti ki hatását a **thalamus szintjén.**

- Csökkenti a fájdalom **emocionális komponenseit** az **anterior cinguláris cortex és az anterior inzula** aktiválása révén.

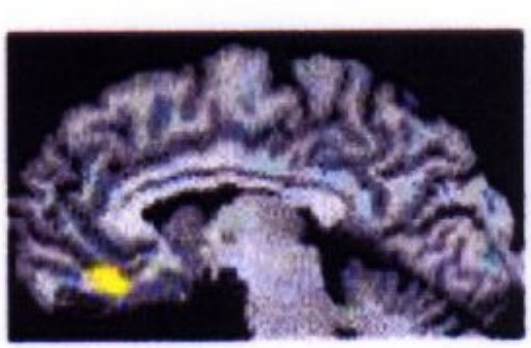
J Neurosurg. 2015 Aug 14:1-11. [Epub ahead of print]

Motor cortex stimulation and neuropathic pain: how does motor cortex stimulation affect pain-signaling pathways?

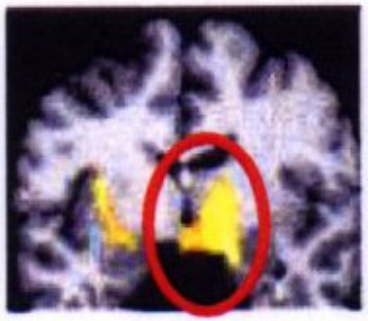
Kim J[1,2,3], Ryu SB[4], Lee SE[5,6], Shin J[1,2], Jung HH[2], Kim SJ[5,6,7], Kim KH[4], Chang JW[1,2].

- MCS **modulated ascending and descending pain pathways**.
- It regulated neuropathic pain by affecting the **striatum, periaqueductal gray, cerebellum, and thalamic area,** which are thought to regulate the descending pathway.
- MCS also **suppress activation of the VPL**, which is part of the ascending pathway.

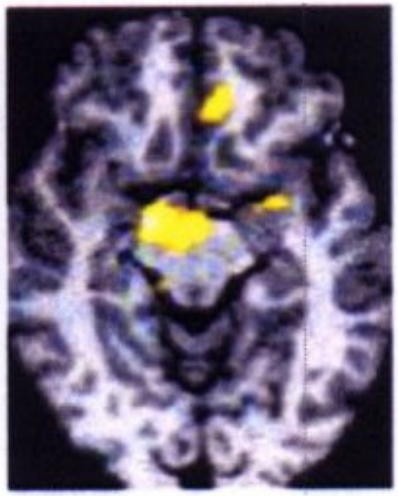
Main brain regions activated by precentral cortex stimulation



Anterior Cingulum



Thalamus



Mesencephale

Peyron et al., Pain 1995, 62: 275-86
Garcia-Larrea et al., Pain 1999, 83: 259-73
Arch Med Res 2000, 31: 248-57

J Neurol Surg A Cent Eur Neurosurg. 2015 Sep 9. [Epub ahead of print]

Treatment of Central Deafferentation and Trigeminal Neuropathic Pain by Motor Cortex Stimulation: Report of a Series of 20 Patients.

Kolodziej MA[1], Hellwig D[2], Nimsky C[3], Benes L[3].

- **Conclusions** **MCS is an effective treatment** modality for central neuropathic pain and trigeminal pain with low morbidity and mortality.
- **Future studies are necessary** to evaluate and optimize this treatment option in more detail.

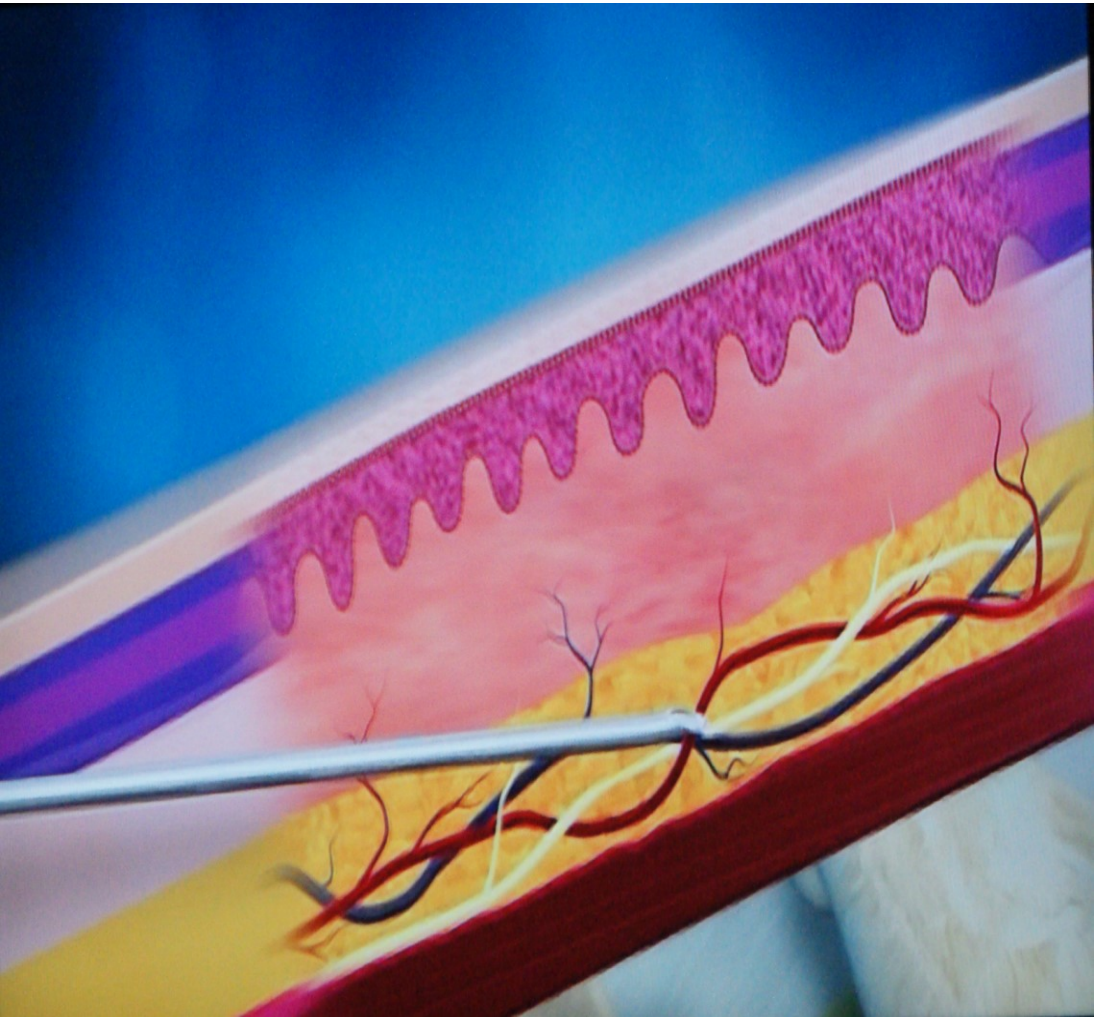
Can J Neurol Sci. 2013 Sep 1:1-9. [Epub ahead of print]

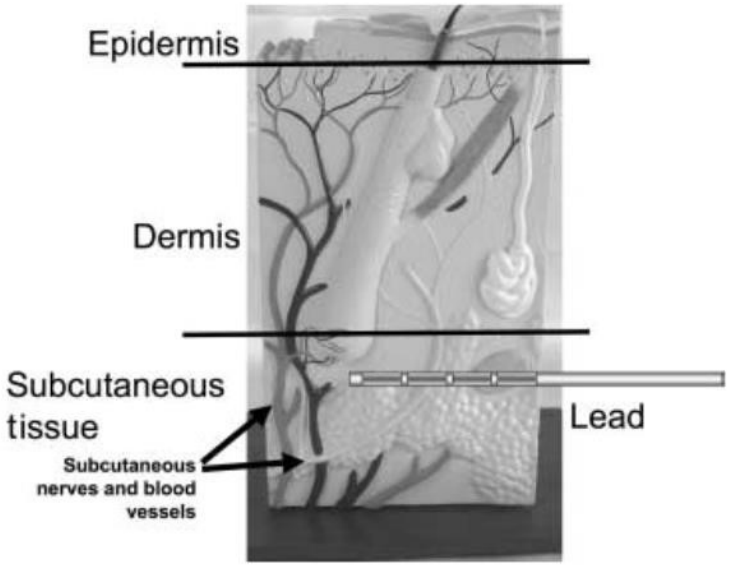
Motor Cortex Stimulation for Neuropathic Pain: A Randomized Cross-over Trial.

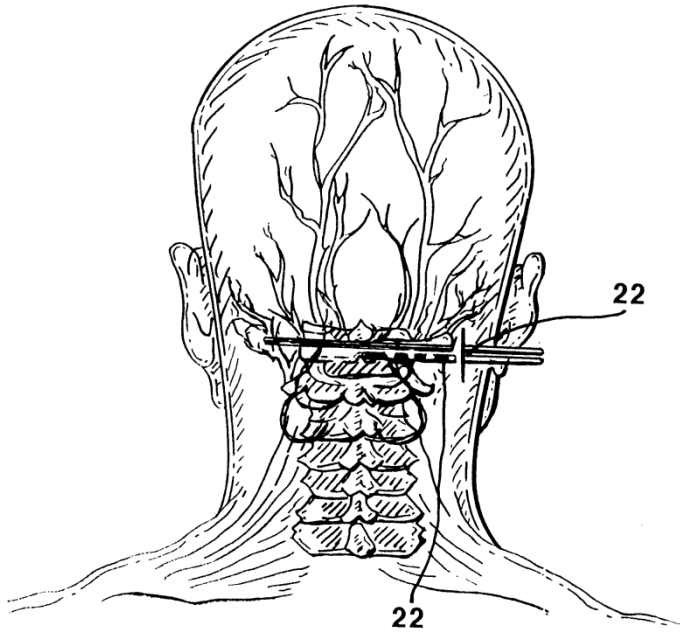
Radic JA[1], Beauprie I[2], Chiasson P[1], Kiss ZH[3], Brownstone RM[1].

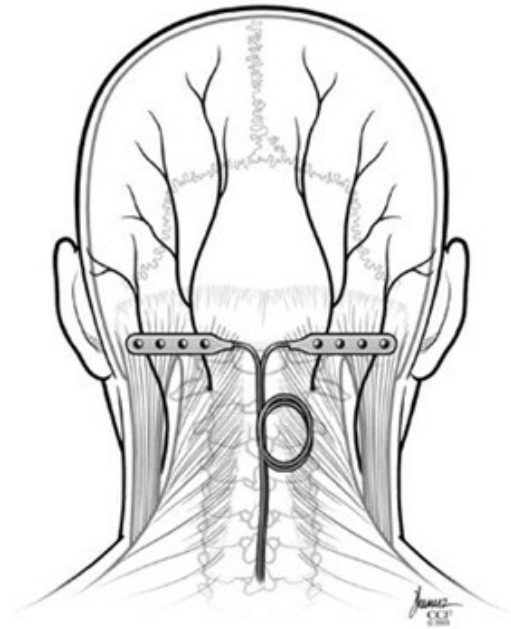
- **CONCLUSIONS:**
- **We failed to show that MCS is an effective** treatment for refractory upper extremity neuropathic pain
- We suggest that a **healthy degree of skepticism is warranted when considering** this invasive therapy for upper extremity pain syndromes.

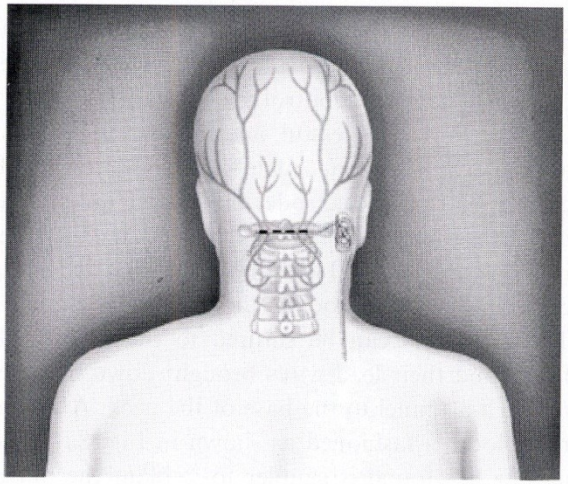
Peripheral Nerve Field Stimulation











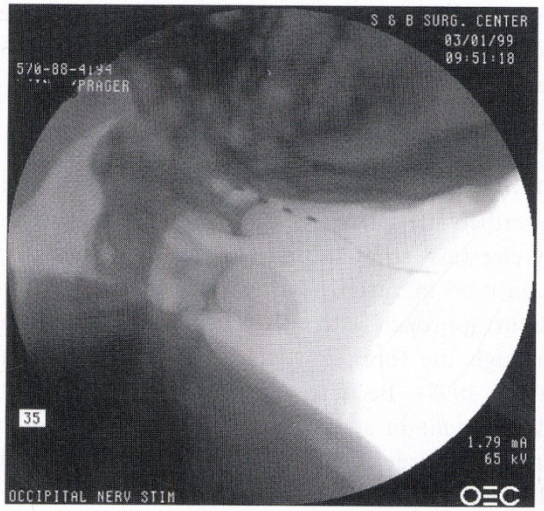
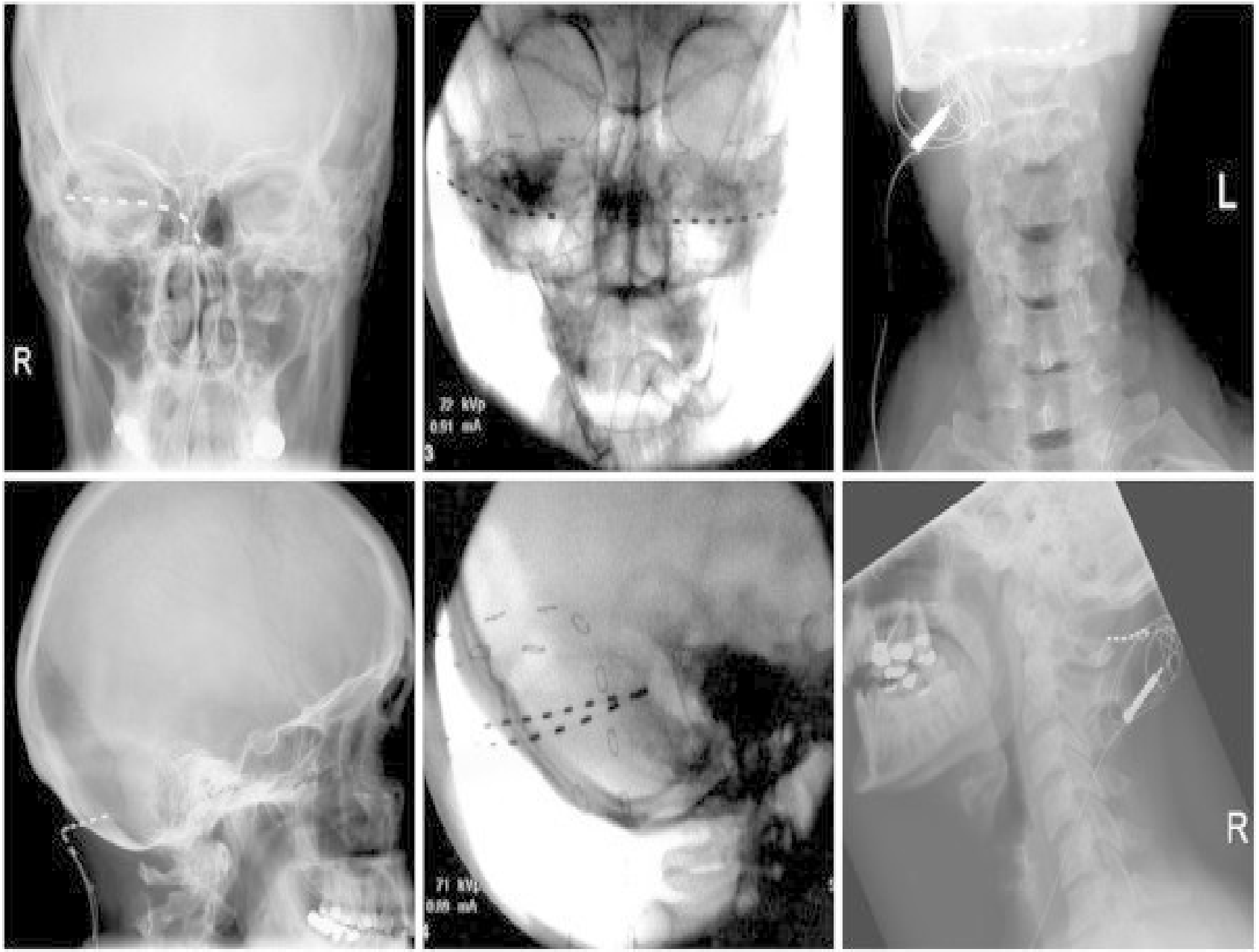


Fig. 8. (a) A sketch showing position of a percutaneous quadrapolar electrode for treatment of occipital neuralgia. (Courtesy of Richard L. Weiner, M.D., Dallas Neurological Associates, 8230 Walnut Hill Lane, Suite 220, Dallas, TX 75231, USA). (b) Radiograph showing an occipital nerve electrode from an oblique projection. (Courtesy of Joshua Prager, M.D., 100 UCLA Medical Plaza, Suite I 760 SP, Los Angeles CA 90095, USA).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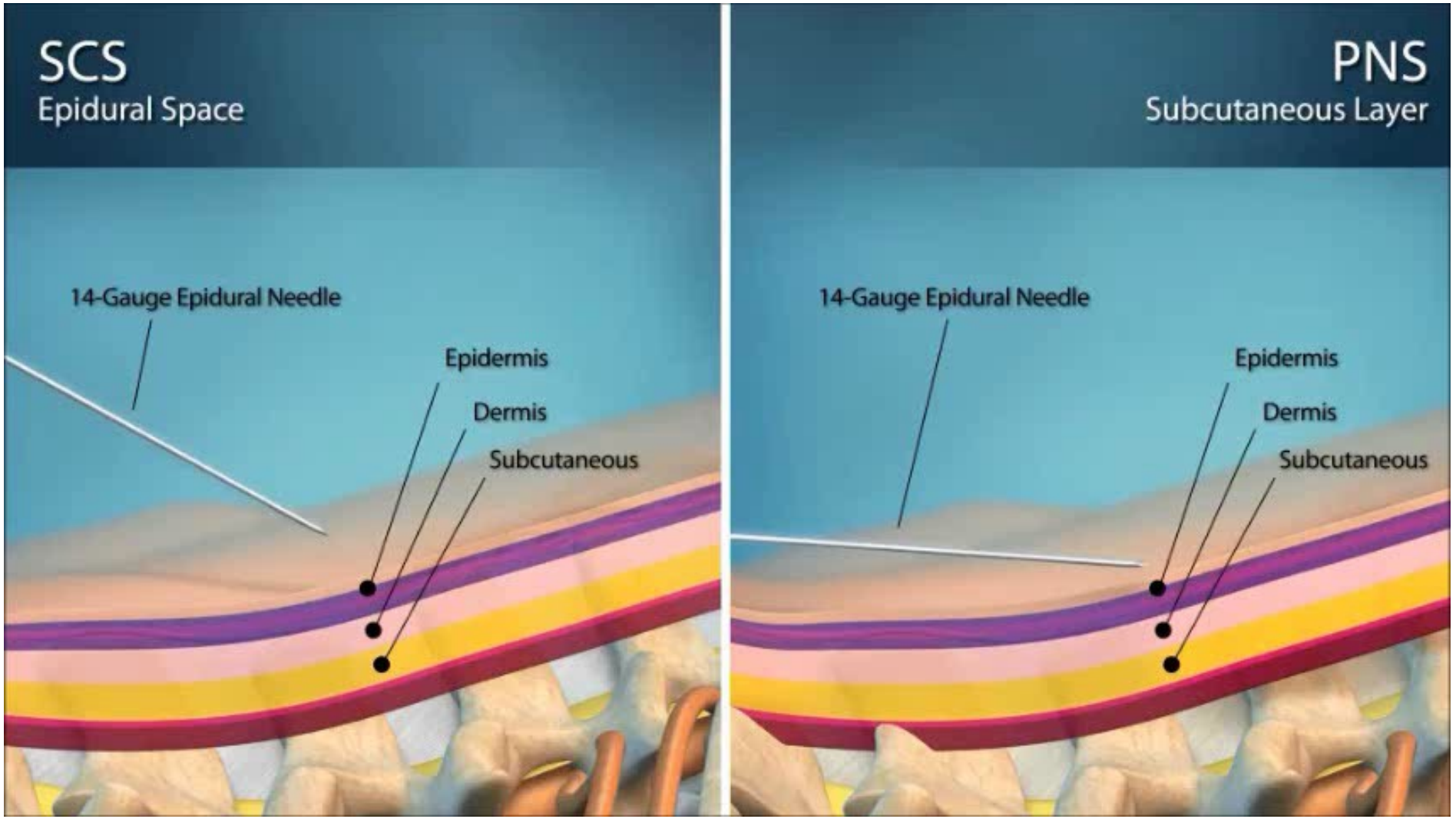
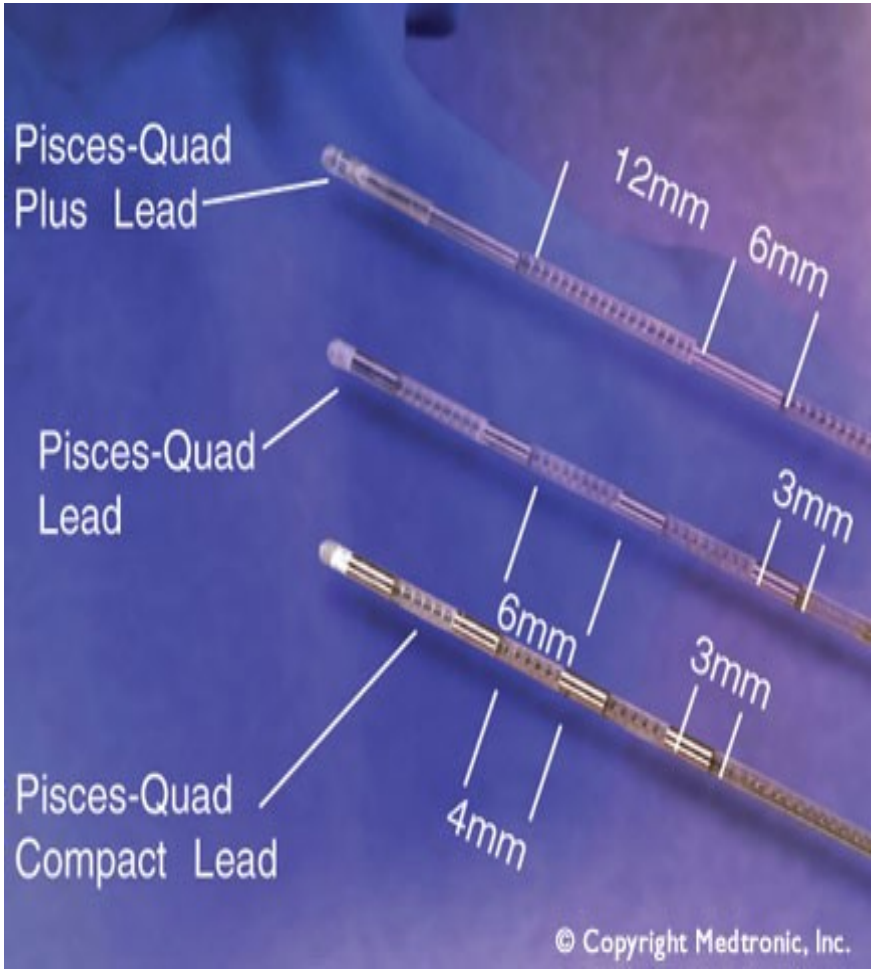

SCS
Epidural Space
14-Gauge Epidural Needle
Epidermis
Dermis
Subcutaneous
PNS
Subcutaneous Layer
14-Gauge Epidural Needle
Epidermis
Dermis
Subcutaneous


Pisces-Quad
Plus Lead
12mm
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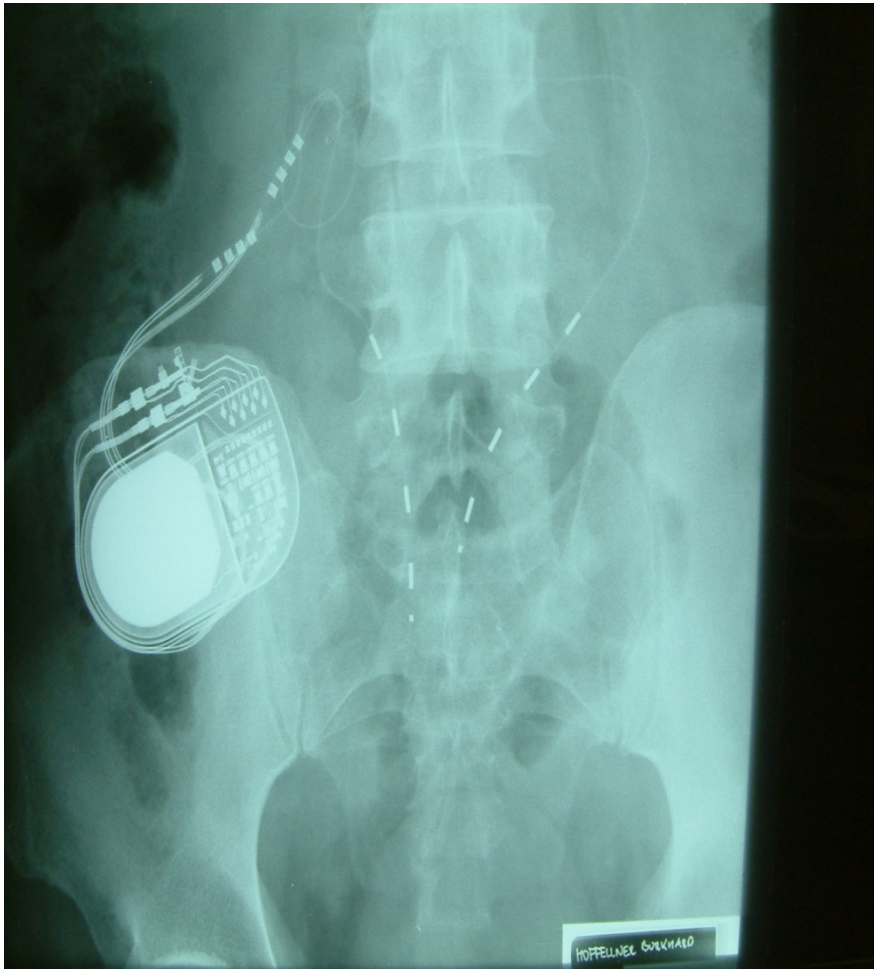

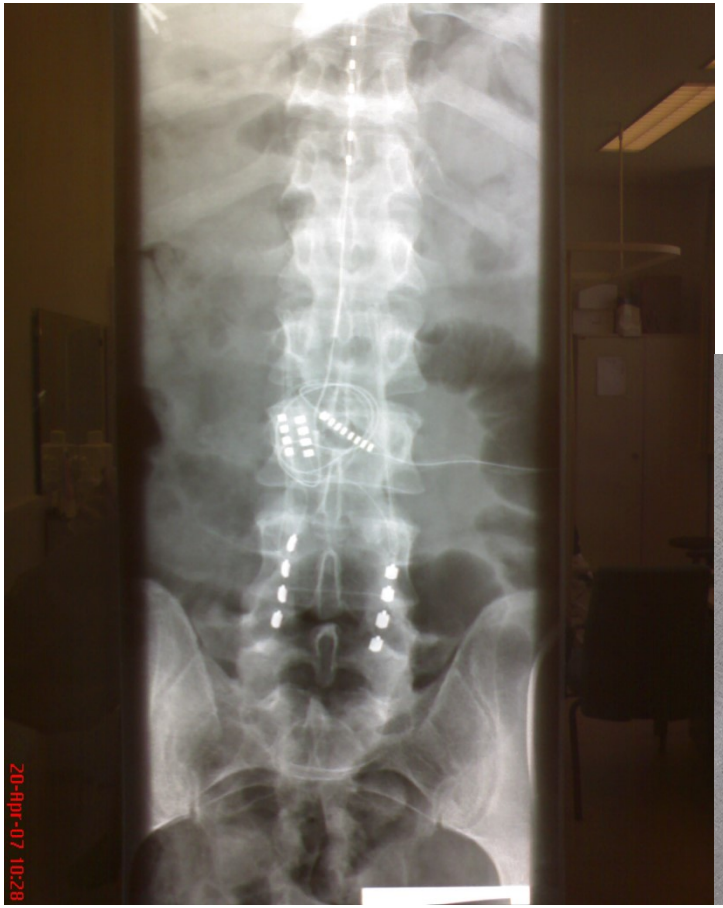
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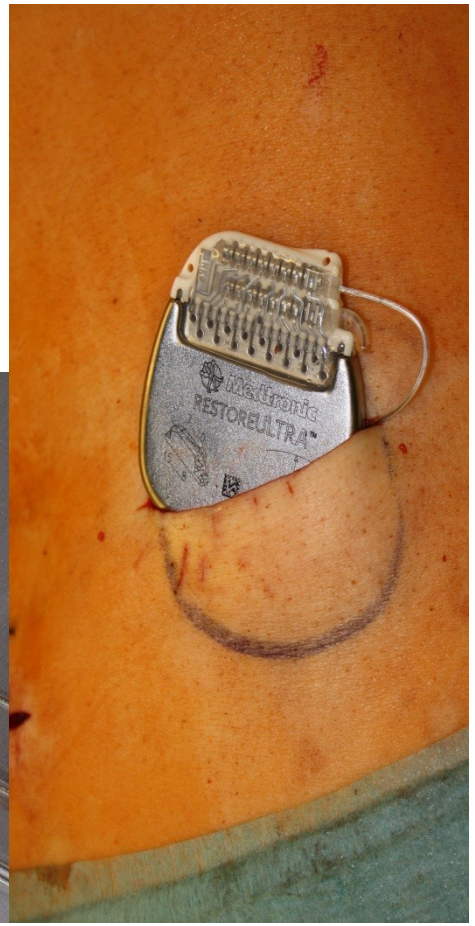
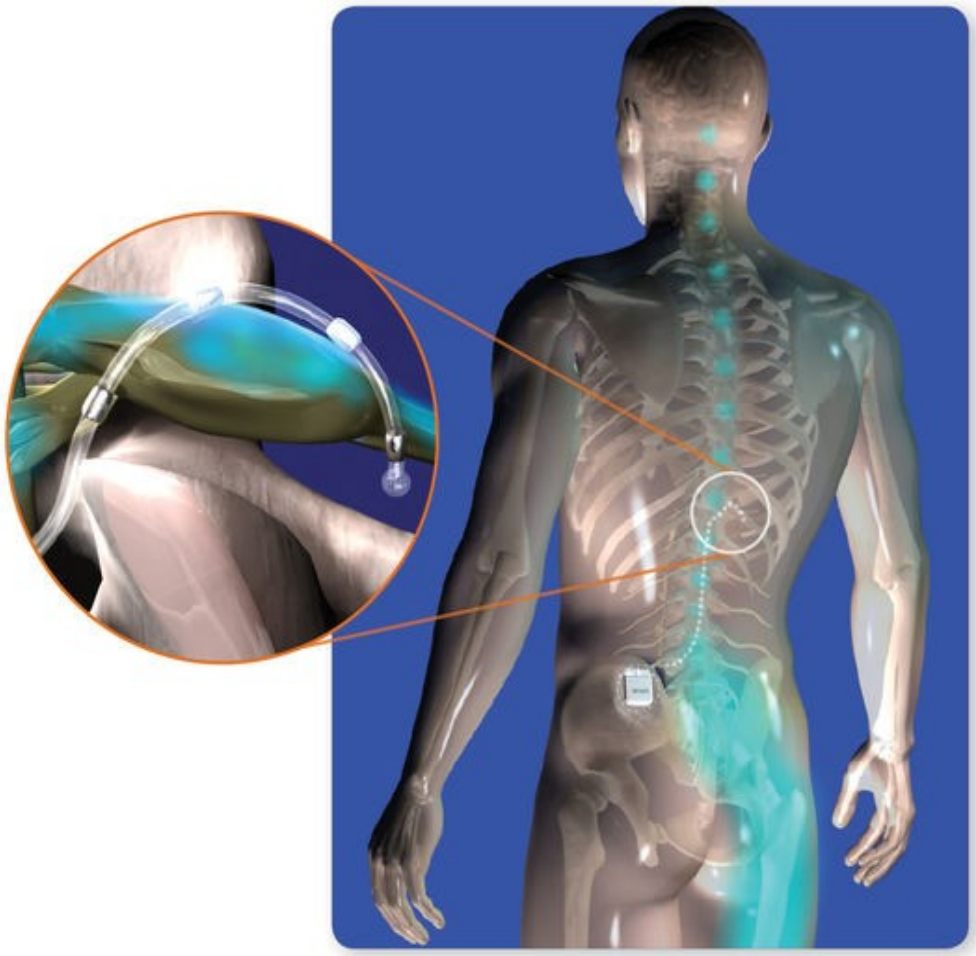

Medtronic
RESTORE ULTRA™

Dorsal Root Ganglion Electrical Stimulation



The DRG lead lies directly adjacent to the spinal cord

Dorsal Root Ganglion Electrical Stimulation

- **DRG** integral to the **development of both nociceptive and neuropathic pai**n (53)
- The **development of neuropathic pain** is **complex and involves different cell types** that include **DRG cell bodies, satellite glial cells** that wrap and surround the pseudo-unipolar DRG somata, glial cells, **astrocytes and Schwann cells, the immune system, and neuronal pathways** (55).
- A **massive spontaneous discharge within** large axotomized **A-neurons within the DRG occurs after cutting spinal nerves distal to the DRG** (56). Sukhotinsky et al. (56) support the **hypothesis** that **"ectopic firing in DRG A-neurons induces central sensitization" (57) and clinical allodynia**.

Current technological development

Dorsal root ganglion stimulation

- electrode is placed **adjacent to the spinal ganglion**
- **paresthesia within a single dermatome**
- **energy consumption significantly less.**[76]
- **pain relief strongest in the feet and weakest in the low back.**[77]
- **in monoradicular pain**
- **limited number of dermatomes**.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The Appropriate Use of Neurostimulation of the Spinal Cord and Peripheral Nervous System for the Treatment of Chronic Pain and Ischemic Diseases: The Neuromodulation Appropriateness Consensus Committee

Timothy R. Deer, MD[1]; Nagy Mekhail, MD, PhD[2]; David Provenzano, MD[3]; Jason Pope, MD[1]; Elliot Krames, MD[4]; Michael Leong, MD[5]; Robert M. Levy, MD, PhD[6]; David Abejon, MD[7]; Eric Buchser, MD[8,9]; Allen Burton, MD[10]; Asokumar Buvanendran, MD[11]; Kenneth Candido, MD[12]; David Caraway, MD, PhD[13]; Michael Cousins, MD[14]; Michael DeJongste, MD[15]; Sudhir Diwan, MD[16]; Sam Eldabe, MD[17]; Kliment Gatzinsky, MD, PhD[18]; Robert D. Foreman, PhD[19]; Salim Hayek, MD, PhD[20,21]; Philip Kim, MD[22,23]; Thomas Kinfe, MD[24]; David Kloth, MD[25]; Krishna Kumar, MD[26]; Syed Rizvi, MD[26]; Shivanand P. Lad, MD, PhD[27]; Liong Liem, MD[28]; Bengt Linderoth, MD, PhD[29]; Sean Mackey, MD, PhD[30]; Gladstone McDowell, MD[31]; Porter McRoberts, MD[32]; Lawrence Poree, MD, PhD[33]; Joshua Prager, MD, MS[34]; Lou Raso, MD[35]; Richard Rauck, MD[36]; Marc Russo, MD[37]; Brian Simpson, MD[38]; Konstantin Slavin, MD[39]; Peter Staats, MD[40,41]; Michael Stanton-Hicks, MD[42]; Paul Verrills, MD[43]; Joshua Wellington, MD, MS[44]; Kayode Williams, MD, MBA[41]; Richard North, MD[41,45]*

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International Neuromodulation Society Critical Assessment: Guideline Review of Implantable Neurostimulation Devices

Timothy R. Deer, MD*; Simon Thomson, MBBS†; Jason E. Pope, MD*; Marc Russo, MD§; Francis Luscombe, MD¶; Robert Levy, MD‡

Introduction: Spinal cord stimulation (SCS) is well accepted for the treatment of chronic pain since its beginning in 1967. As its use continues to enter into the chronic pain treatment algorithm earlier, conscience patient selection and durability of the therapy are clearly clinically relevant. To improve treatment efficacy, consensus statements and guidelines were developed.

Objective: The purpose of this work is to review the relevant guideline statements for implantable neurostimulation therapies to treat chronic pain and to identify guideline gaps and future directions for recommendation platforms.

Materials and Methods: A systematic literature search through EMBASE, Medline, Cochrane data base, as well as peer-reviewed, nonindexed journals and materials presented at national and international meetings was performed to chronologically identify consensus statements or guideline statements for use of neurostimulation therapies to treat chronic neuropathic pain limited to the English language.

Results: From 1998 to 2013, 22 guideline statements were identified. Thirteen of the 22 guidelines were society-sponsored guideline statements from ten societies. Two guideline statements were from research foundations, two were government supported, and one statement was published as a position statement.

Conclusions: The current available guideline statements have clear deficiencies in either scope of coverage, evidence synthesis, or lack of transparency of funding. Improved evidence and best practice/guideline assessment may improve patient outcomes and accessibility to these important modalities. Further prospective comparator randomized data are required to not only provide data of clinical and cost-effectiveness in other indications but also to better describe the position of neurostimulation application within the disease management pathway. Therein cases where there appears to be sufficient evidence and consensus, every effort should be made to secure access to these effective therapies. Importantly, each guideline only has a useful clinical half-life, if not updated. This should be acknowledged by both clinicians and third-party payers. Based on these deficiencies, the International Neuromodulation Society recommended the creation of a consensus conference to examine the appropriate use of neurostimulation for pain and ischemic disease.

Keywords: Chronic pain, implant, neuropathic pain, neurostimulation, review article

Conflict of Interest: The authors reported no conflict of interest.

Neuromodulation. 2014 Oct;17(7):678-85; discussion 685. doi: 10.1111/ner.12186. Epub 2014 May 6.

International neuromodulation society critical assessment: guideline review of implantable neurostimulation devices.

Deer TR[1], Thomson S, Pope JE, Russo M, Luscombe F, Levy R.

- to **review the relevant guideline statements for implantable neurostimulation therapies to treat chronic pain** and to identify guideline gaps and future directions for recommendation platforms.
- A systematic **literature search through EMBASE, Medline, Cochrane data base**
- Based on these deficiencies, the International **Neuromodulation Society recommended the creation of a consensus conference to examine the appropriate use of neurostimulation for pain and ischemic disease.**

SAFETY OF NEUROSTIMULATION Compared With High-Dose Opioids

- **high-dose, long-term opioid side effects hormonal and immune system dysfunction, depression, weight gain, tolerance, opioid-induced hyperalgesia (OIH), and the potential for dependence, abuse, and addiction** (141– 145).
- **overdose deaths** (146,147), with opioid **74%** (14,800 of 20,044) in 2008
- oral opioids **long-term** (more than six months) **efficacy are lacking** (148,149).
- **opioid therapy questionable in neuropathic pain** (150,151).

Compared with Conservative Medical Management

- PROCESS study (161) comparing SCS withCMM in a randomized and controlled manner, **SCS is superior to CMM**.
- Literature reviews in 2011 and 2013 of the safety, appropriateness, fiscal neutrality, and effectiveness (SAFE) of **SCS** suggest that it be **considered before submitting patients to long-term opioid therapy** for chronic pain from FBSS and CRPS (163,164).

Compared With Spine Surgery

- North (127) randomized 60 **FBSS** patients to either SCS or repeated lumbosacral spine surgery with an average follow-up of three years
- **SCS is more effective than reoperation** for radicular pain after lumbosacral spine surgery.

Failure of Conservative Medical Management

Neuromodulation. 2014 Aug;17(6):515-50;. Deer TR[1]

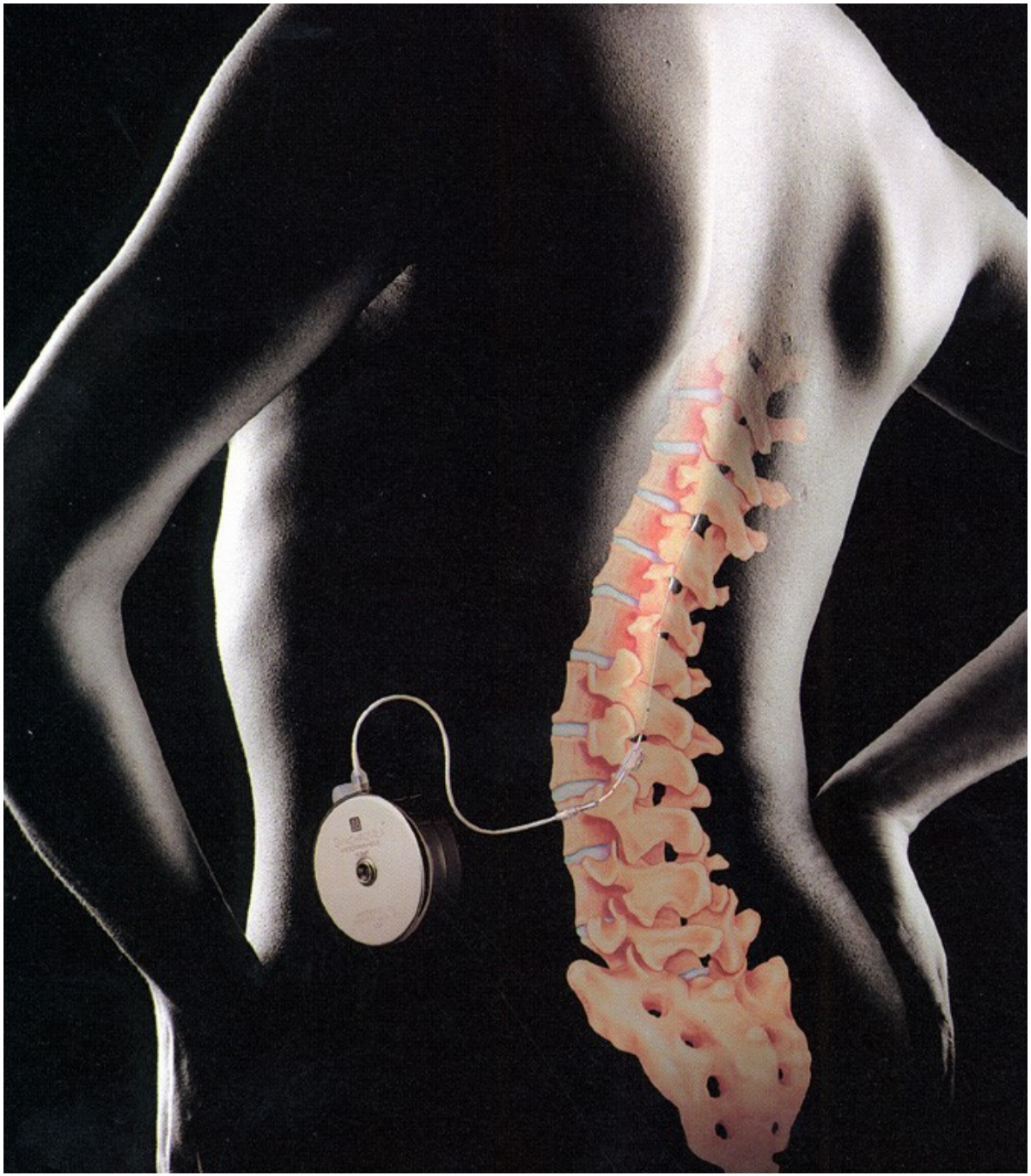
- **NACC recommends**
- **neuromodulation** should be used in patients **who fail to have acceptable relief** /or have **unmanageable side effects with conservative treatment**.
- evidence that **SCS should be used before another back surgery for FBSS (127) and**
- **before starting** systemic **long-acting opioids** (163).

Contraindications

- **active, uncontrolled psychiatric disorder**
- **infection, immunosuppression, and anticoagulant or antiplatelet therapy** that cannot be suspended (191).
- **Previously failed trial, but** kilohertz-frequency SCS, burst SCS, DRG stimulation suggests that there is **not necessarily a correlation between a failed trial with conventional SCS** and **future success** (20–22,27,192).
- **NACC recommends: consider using new technologies who have failed trials of conventional SCS.**

Kémiai neuromoduláció - gyógyszeradagolás helye

- intraspinális (IS)
- intracerebroventricularis (ICVDDS)



IDA DDS indikációk

- diffúz daganatos fájdalom
- somaticus viscerális fájdalom (daganat, chr. pancretitis)
- osteoporosis
- nociceptív fájdalom
- multiplex fájdalom (trunkális/axiális)

Pain Physician. 2011 May-Jun;14(3):219-48.

Intrathecal therapy for cancer and non-cancer pain.

Hayek SM[1], Deer TR, Pope JE, Panchal SJ, Patel VB.

- Literature search through EMBASE, Medline, Cochrane databases, and systematic reviews as well as peer-reviewed non-indexed journals from 1980 to December 2010.
- **CONCLUSION:**
- evidence for **cancer-related pain is moderate**
- evidence **limited to moderate** from non-randomized studies **for non-cancer related pain.**

Examples of Chronic Pain Treated with SCS and TDD

Condition	Spinal Cord Stimulation	Targeted Drug Delivery	
		Morphine	Ziconotide
Failed Back Syndrome	✓	✓	✓
Spinal Stenosis		✓	
Radicular Pain Syndrome	✓	✓	
Complex Regional Pain Syndrome	✓	✓	✓
Cancer Pain		✓	✓
Compression Fractures from Osteoporosis		✓	

Medtronic Spinal Cord Stimulation Indication Statement (US), A03526001, 2004.
For a more comprehensive list, and a list of references, see professional.medtronic.com/pain-indications.

Konklúzió

PNS (PNfS) for pain

Neuromodulation. 2014 Aug;17(6):515-50;. Deer TR[1]

- For **head and neck, the committee said that when possible, extracranial stimulation should be "an earlier option** in the treatment algorithm.„

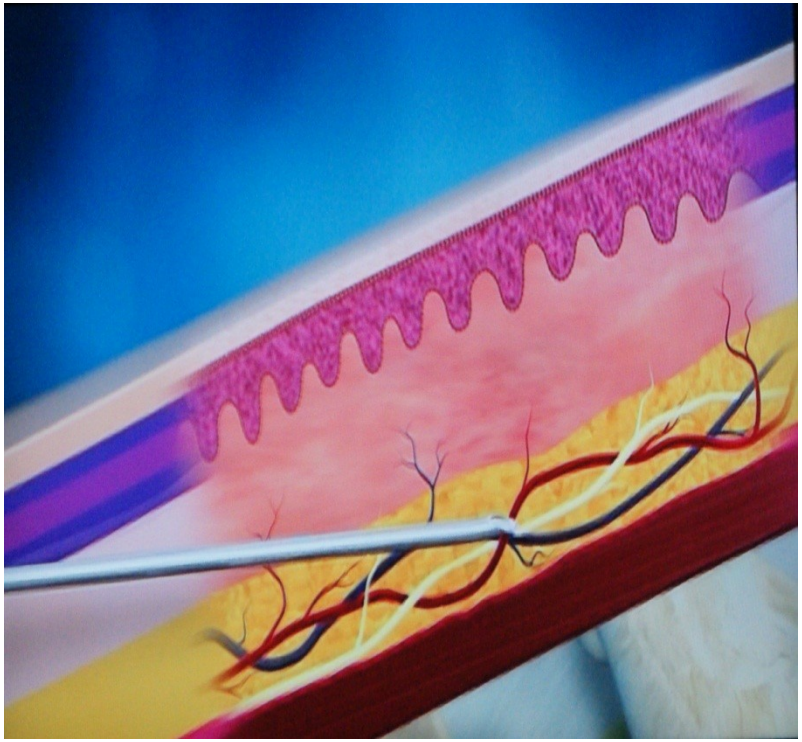
- **CE mark** approved in Europe

-occipital neuralgia

-chronic migraine

- Medtronic **CE Mark**

-Chronic Back Pain



SCS for pain

Neuromodulation. 2014 Aug;17(6):515-50;. Deer TR[1]

- **approved by the FDA for**

-failed back surgery syndrome,

-complex regional pain syndrome,

-radiculopathy, (traumatic neuropathies, diabetic neuropathy, postherpetic neuralgia).

- **In Europe CE mark for**

-refractory angina pectoris

-peripheral limb ischemia

DBS for pain

Neuromodulation. 2014 Aug;17(6):515-50;. Deer

- DBS is **limited** by its inherent **invasiveness and risks.**
- for certain painful conditions, including **facial pain due to damaged trigeminal nerves**,
- **may not be the best treatment for pain**
- **has not been tested for this in randomized clinical trials,**

MCS for pain Surg Neurol Int. 2012; 3(Suppl 4): S290–S311.

- **facial chronic neuropathic pain**
- **safe and efficacious** when previous managements have failed;
- most successful for:
- **trigeminal neuropathic/deafferentation pain**
- **central poststroke pain**,
- however, there is **still lack of strong evidence** (larger randomized controlled multicentre studies)

Neuromoduláció
neuropátiás fájdalom konklúziók

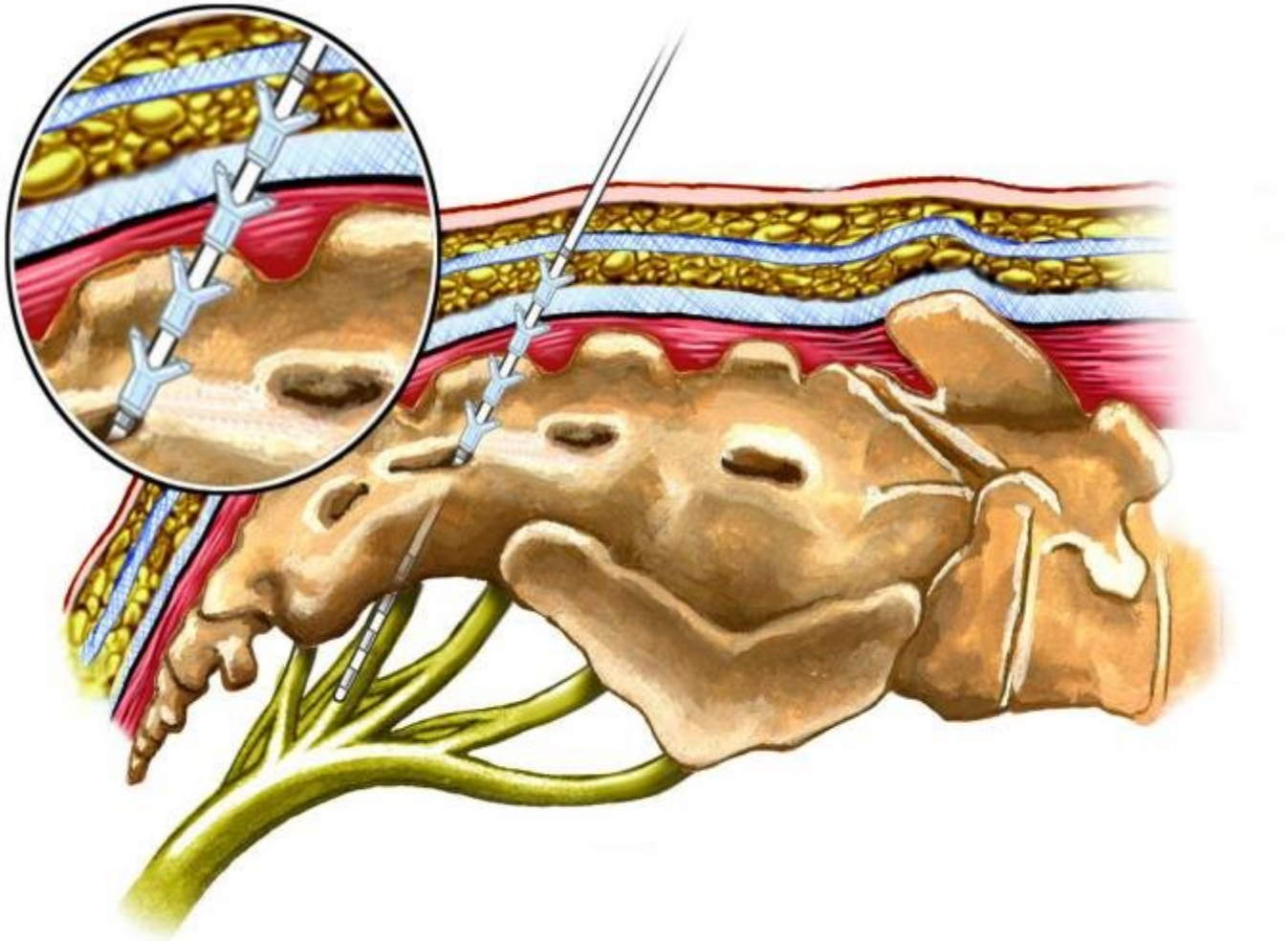
- **SCS:** „on- label” **FBSS, CRPS** (level B), **angina, PVD**
- **PNS:** „on- label”
  - **migrén, occipitális neuralgia, (fej-nyak fájdalom)**
  - **LBP (derékfájdalom)**
- **IDA:** „on -label” **diffúz, multiplex fájdalmak főleg daganatos**

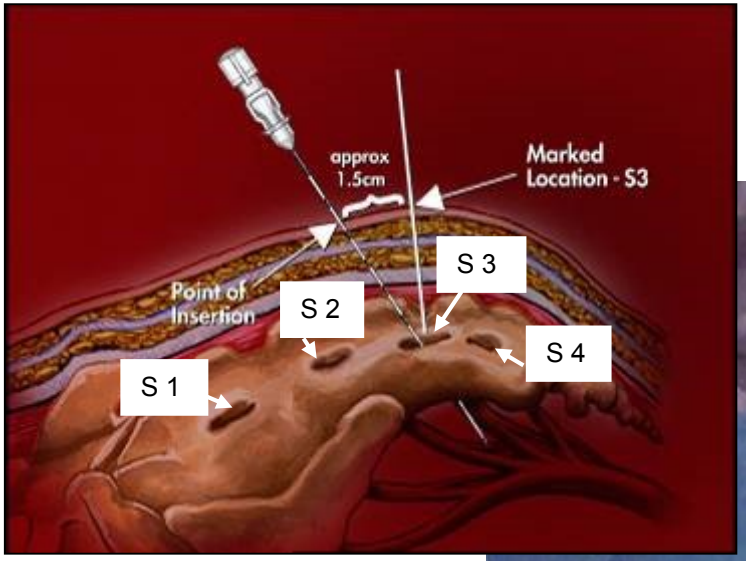
- **DBS:** „off label” **arc-fej fájdalom, cluster.**
- **MCS:** „off label” **centrális post-stroke és deafferentációs arcfájdalom** (level C).

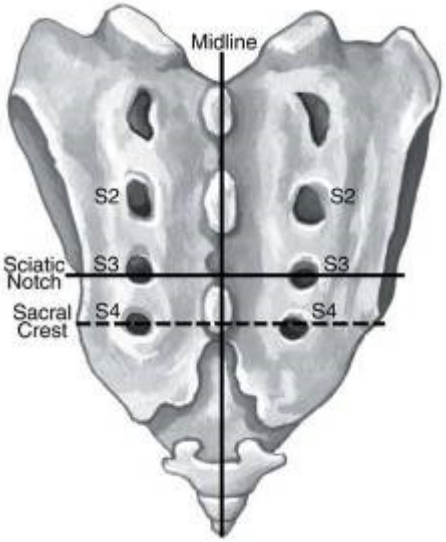
SCS indikációk VI.
Sacralis ideg stimláció (SNS)

- Alo 1999, Chancellor Chartier-Kastler 2000, Windaele 2000.

Tined Leads Models
Anchoring with Tines




approx
1.5cm
Marked
Location - S3
Point of
Insertion
S 1
S 2
S 3
S 4


Midline
S2
S2
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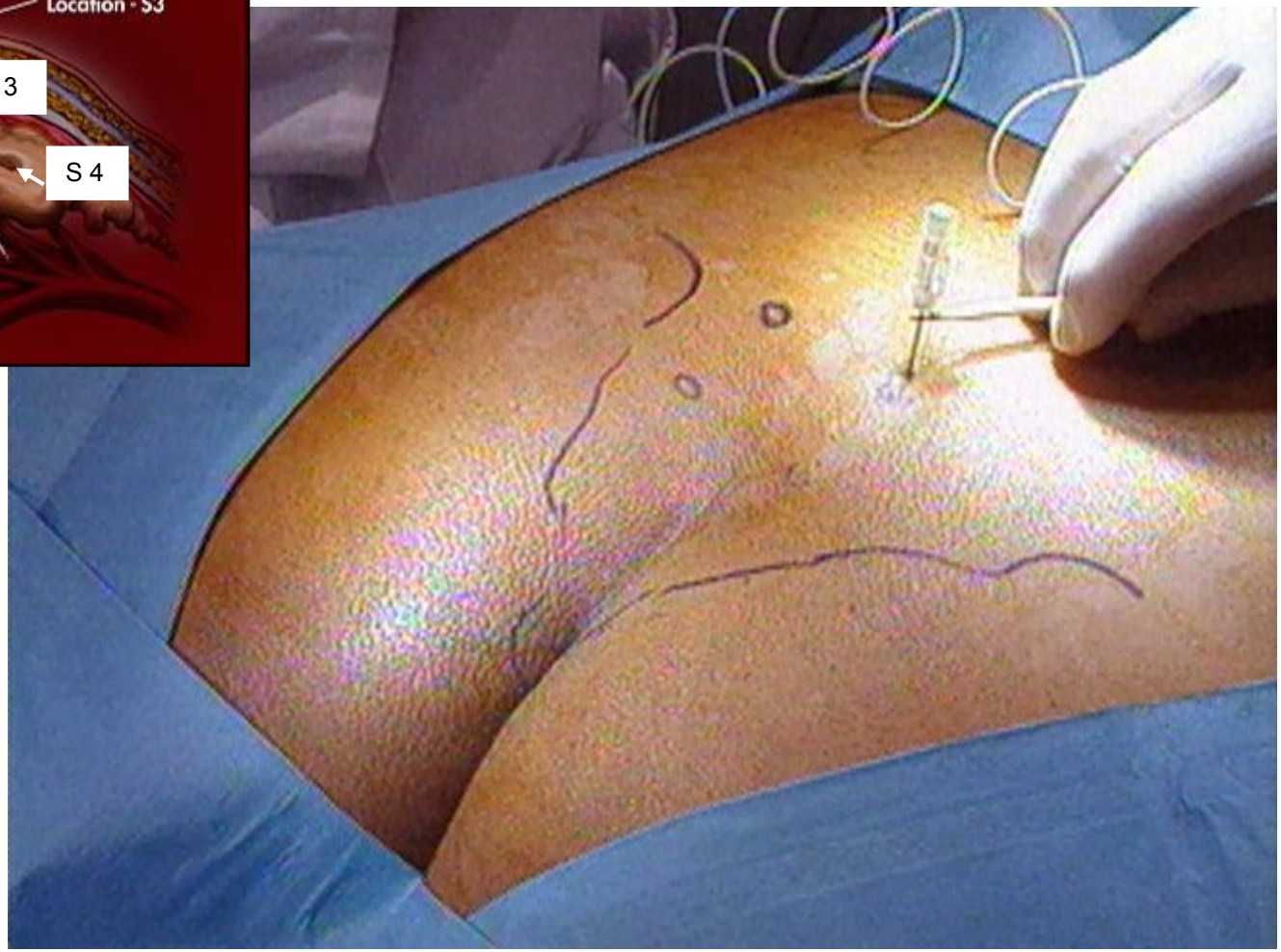
Notch
S3
S3
Sacral
Crest
S4
S4



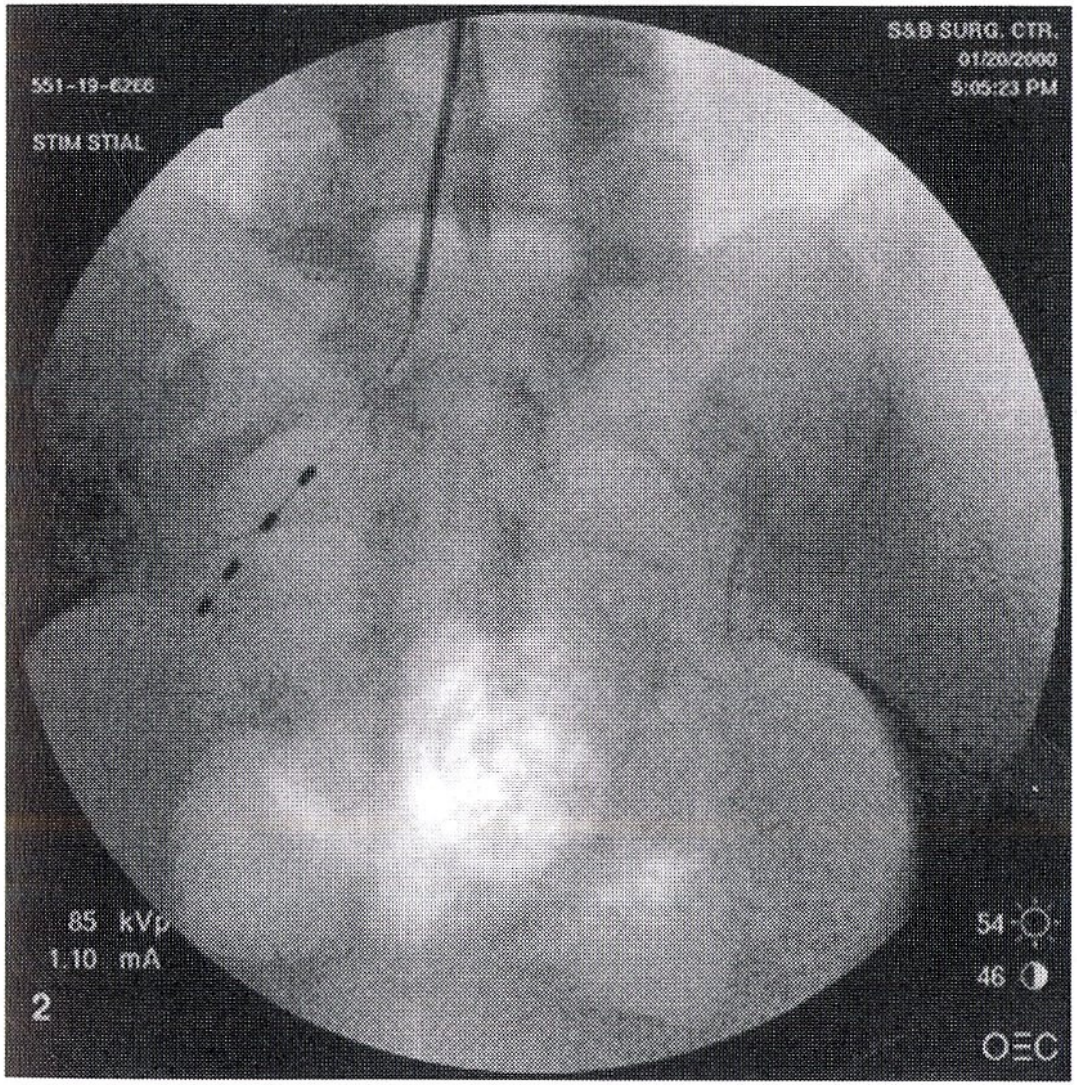


Fig. 10. Radiograph showing retrograde placement of electrodes on the S3 and S4 roots for the management of pelvic pain.

Sacralis ideg stimláció (SNS) indikációk

- **Urologiai betegségek** (sürgősségi-incontinencia,OAB, retenció).
- **Székletszabályozási** zavarok
- **Perineális, genitális, rectális, pelvis fájdalom (pl.** interstitial cystitis) csak ha sphincter zavarral kombinálódik !!!!


Köszönöm a figyelmet !