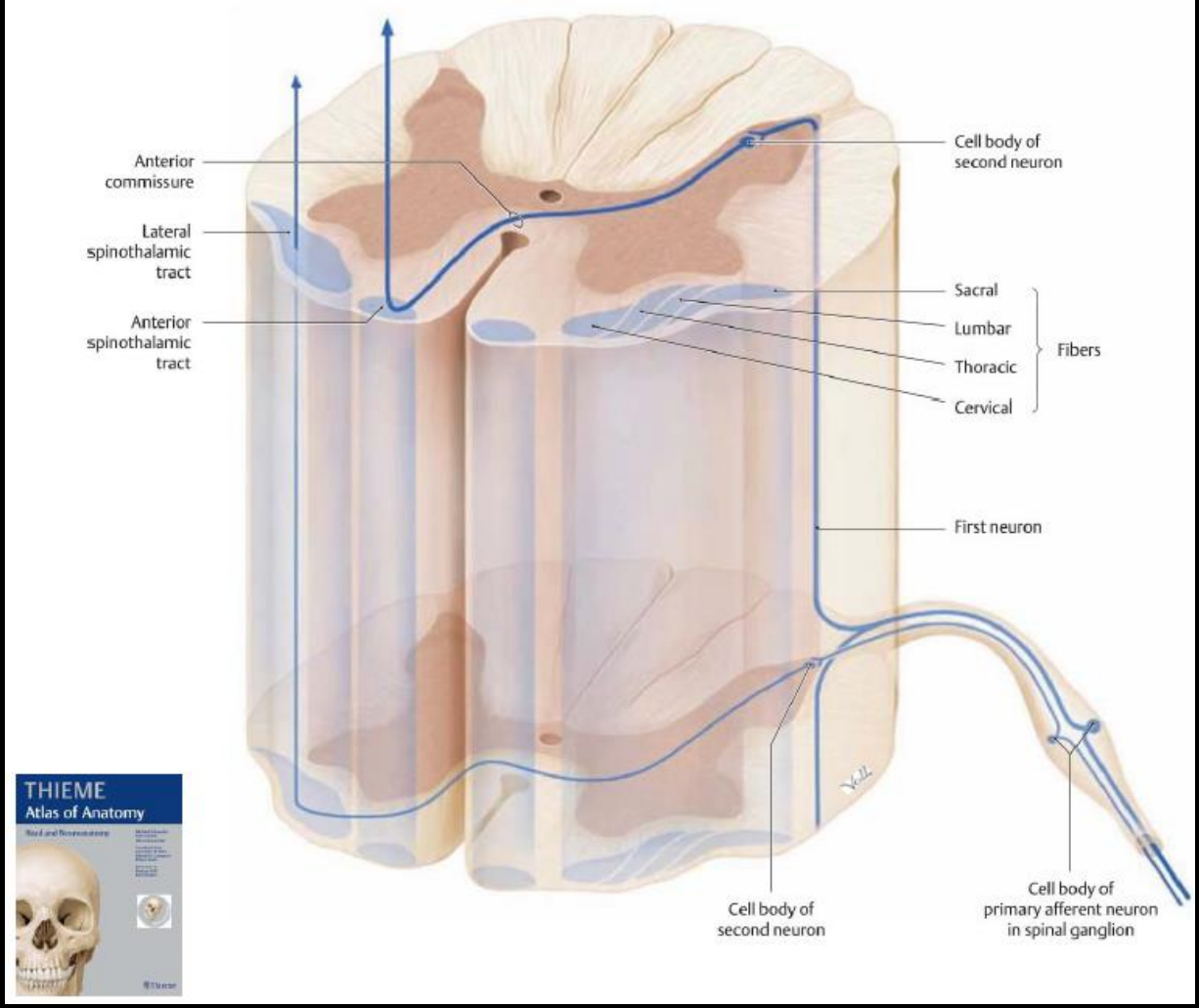
Traitement de la douleur en neurochirurgie

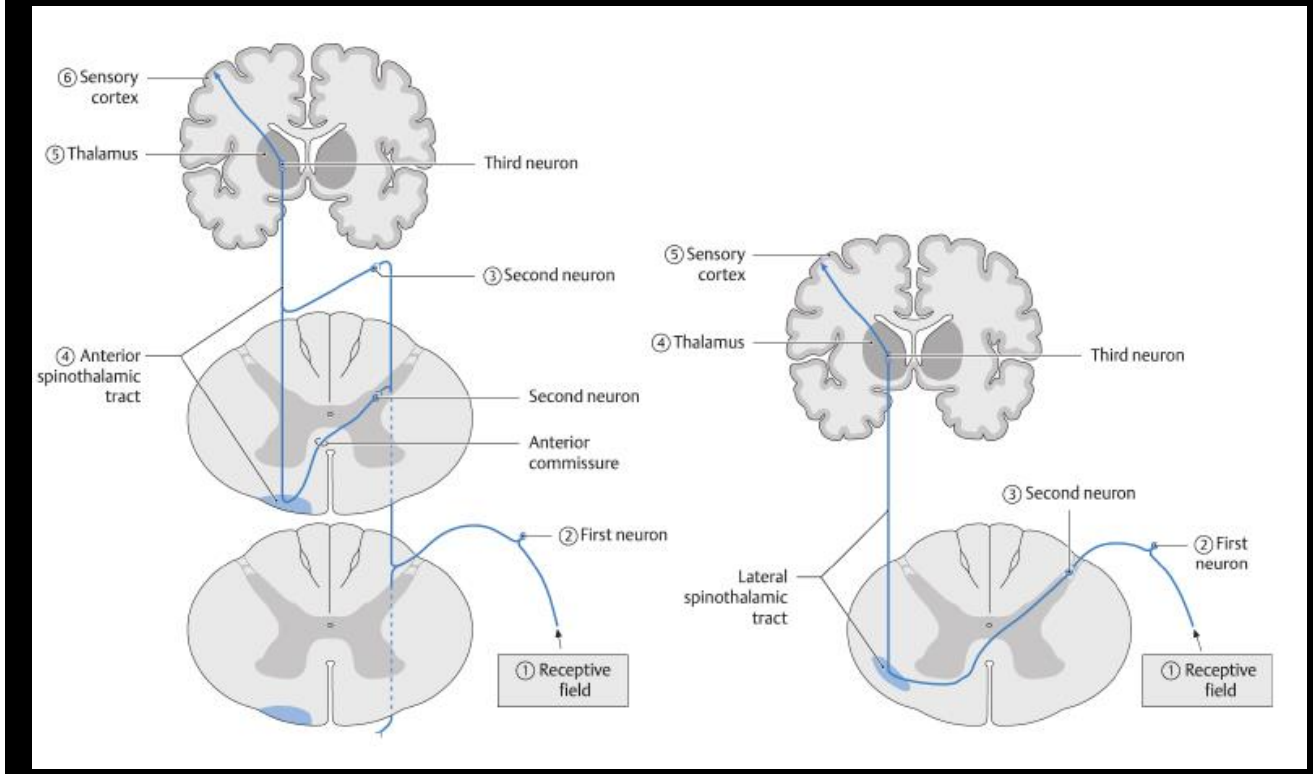
Dr Corentin DAULEAC
Neurochirurgie fonctionnelle, de la moelle épinière et des nerfs périphériques
Service du Pr MERTENS
HCL – Hôpital Neurologique Wertheimer – Lyon

Plan

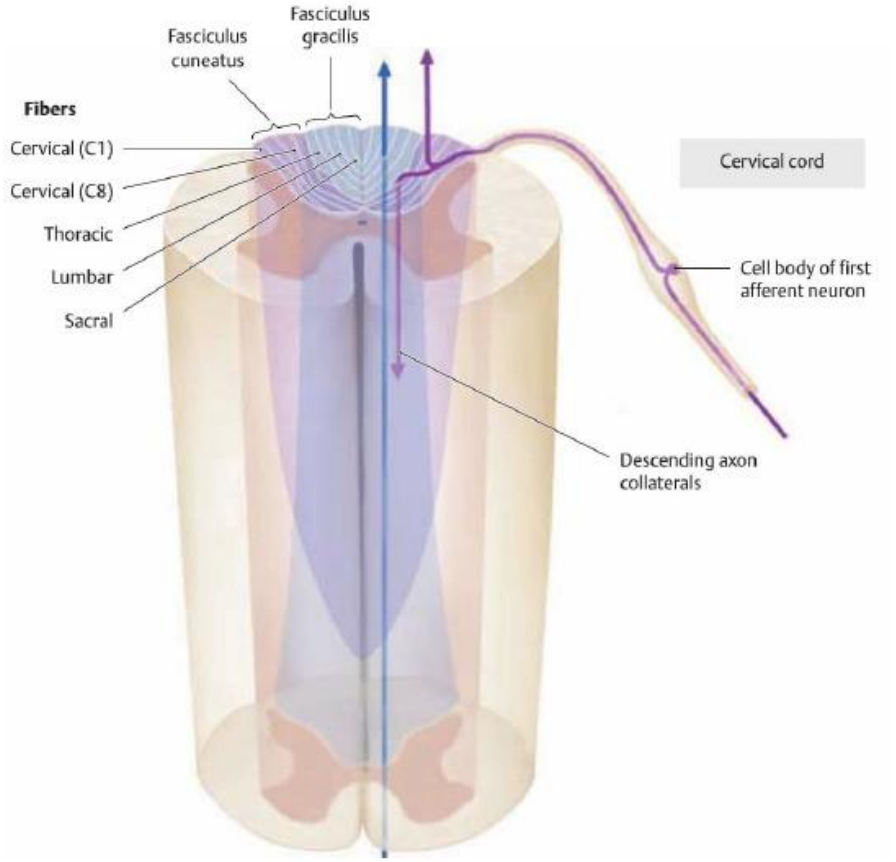
- 1. Anatomie des voies de la douleur
- 2. Théorie du « gate control » et application en neurochirurgie
- 3. Lésion médullaire et plexuelle: DREZotomie
- 4. Cordotomie
- 4. Thérapies intrathécales

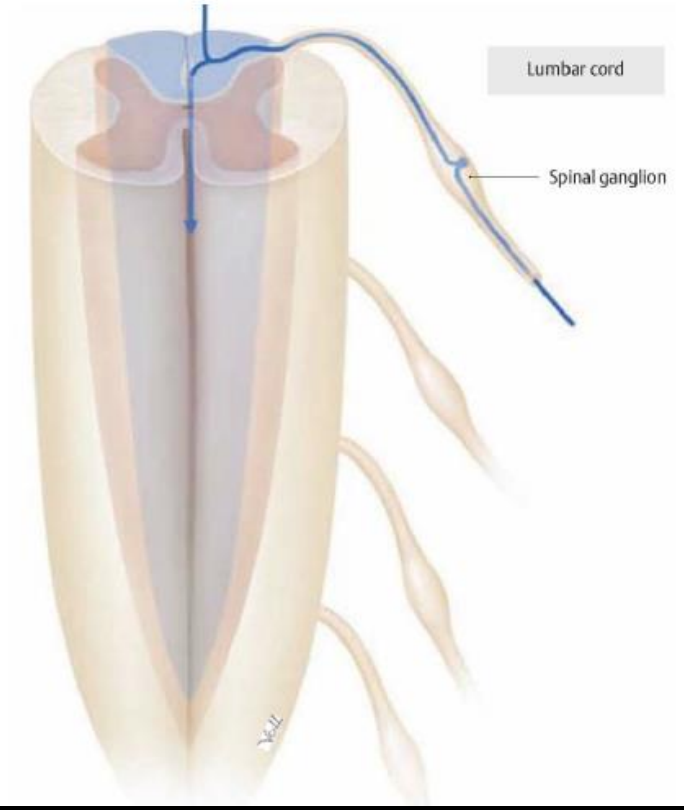
ANATOMIE - Spinothalamic pathway

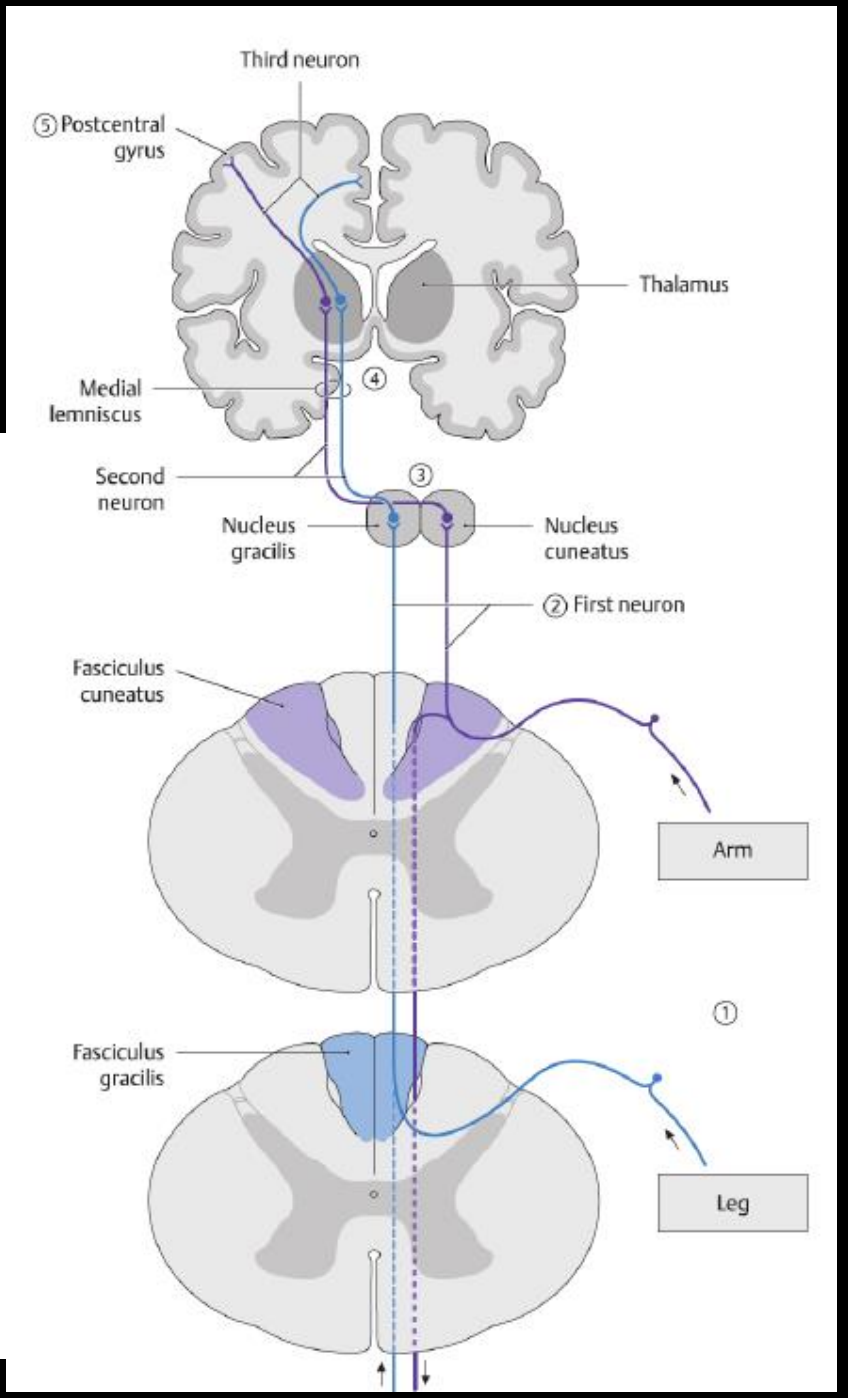


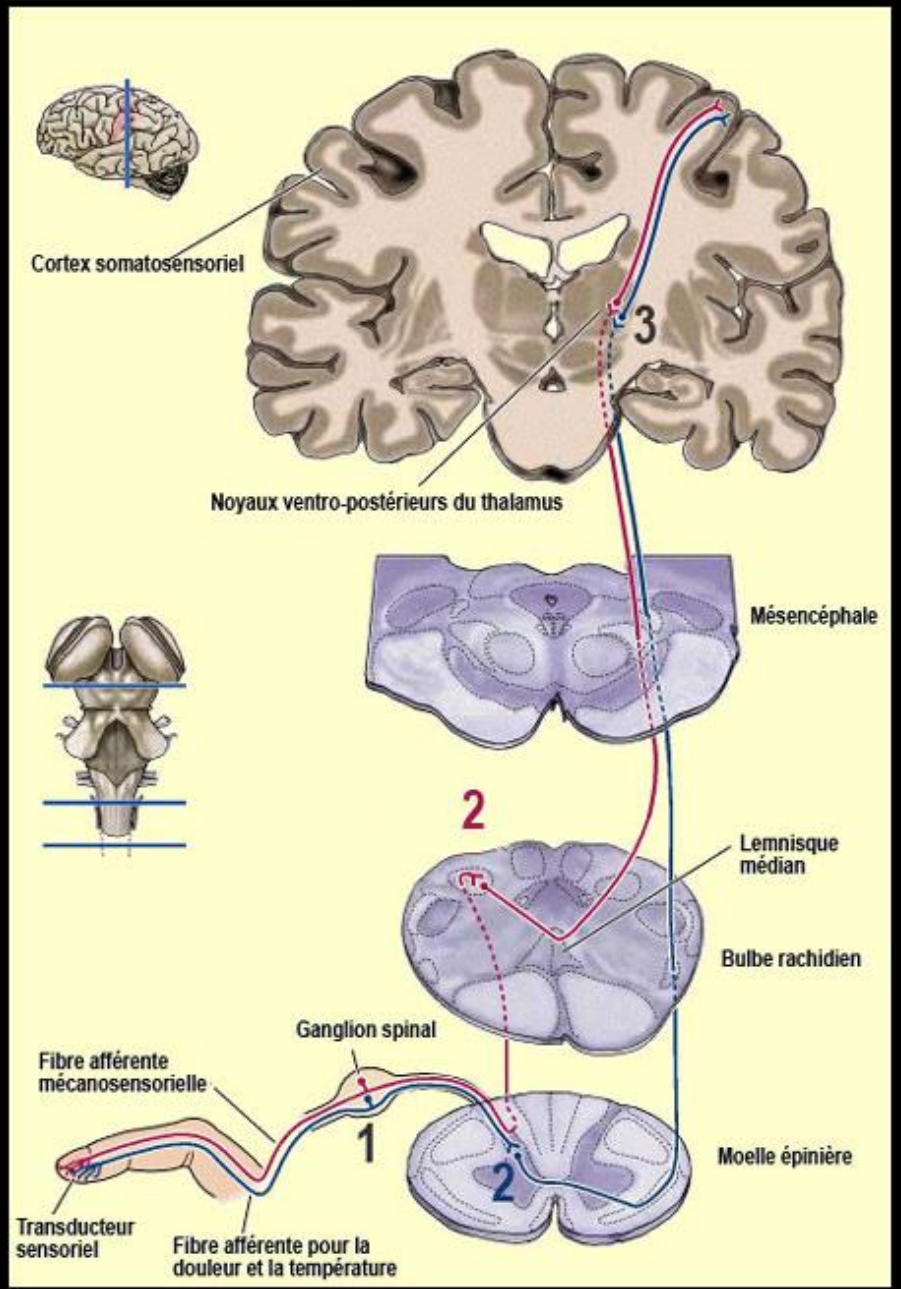


ANATOMIE - Cordonal pathway



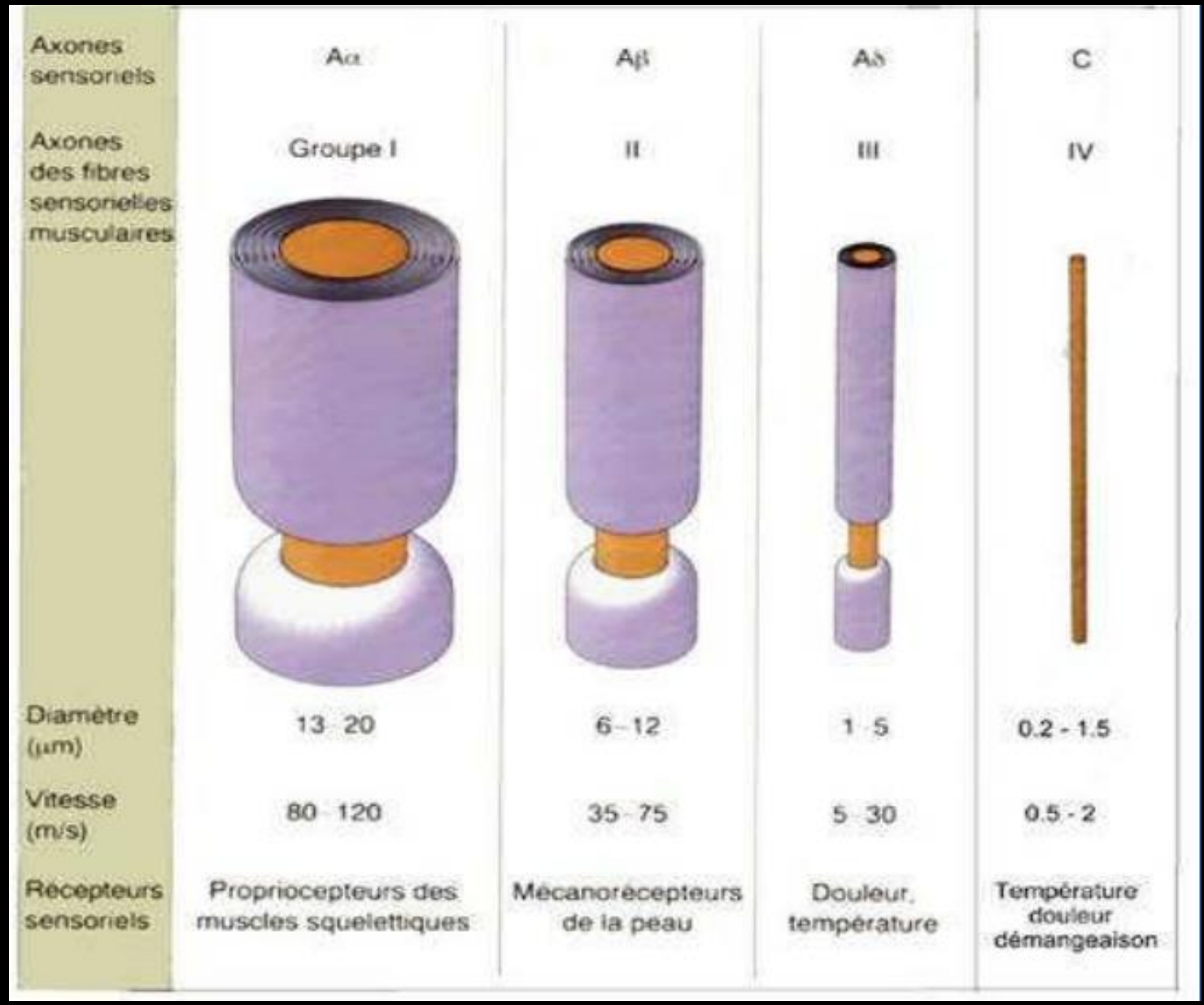




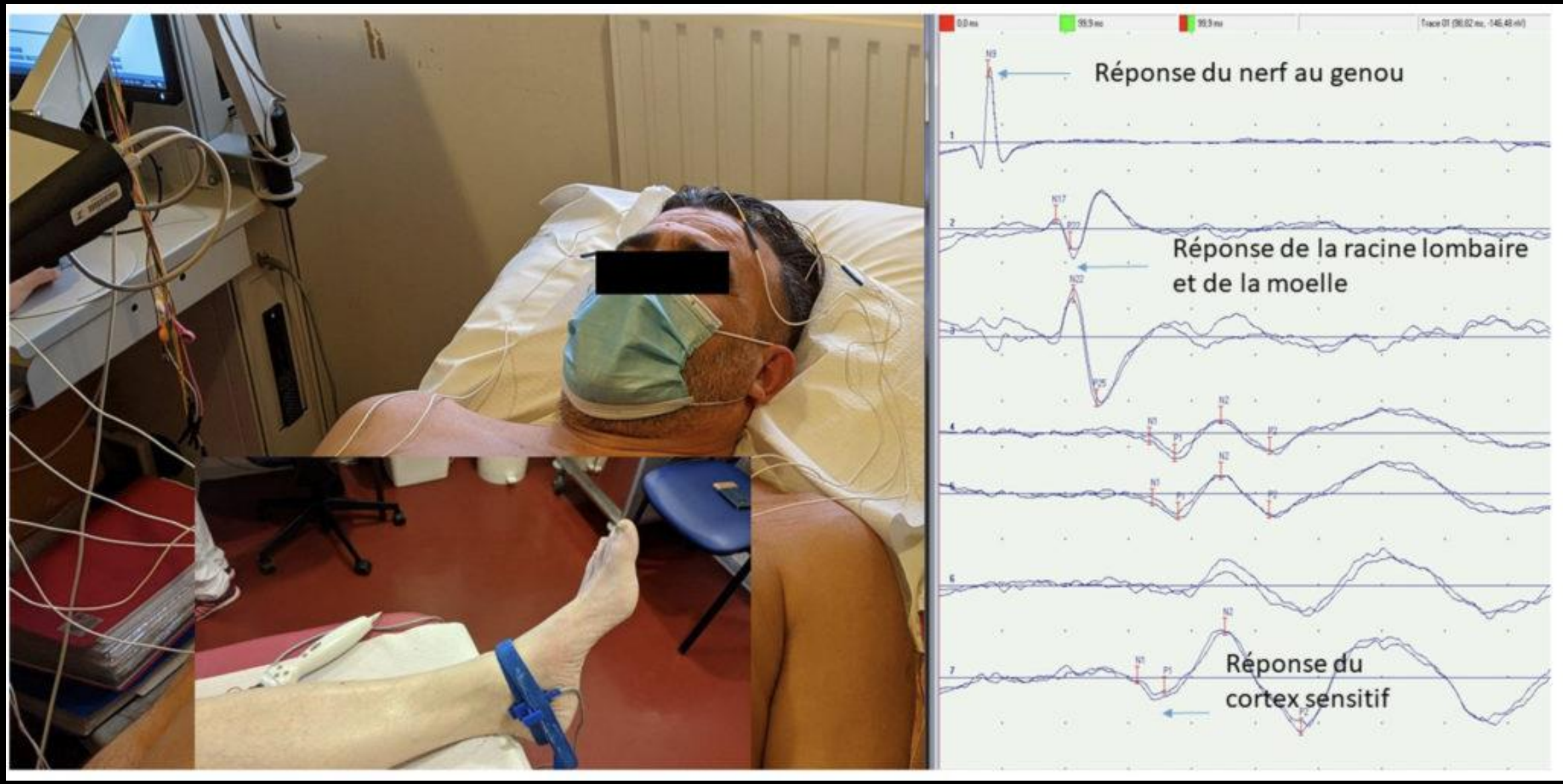

Cortex somatosensoriel
3
Noyaux ventro-postérieurs du thalamus
Mésencéphale
2
Lemnisque médian
Bulbe rachidien
Ganglion spinal
Fibre afférente mécanosensorielle
1
2
Moelle épinière
Transducteur sensoriel
Fibre afférente pour la douleur et la température

Neuroanatomie de la douleur

- Les fibres C - amyélinisées, vitesse de conduction = 1m/s - sont INEXCITABLES avec des impulsions de durée inférieure à 200 µs
- Les fibres Aδ – myélinisées, faible diamètre, conduction = 20m/s - sont INEXCITABLES aux stimulations d'une durée de moins de 10 µs
- Les fibres Aβ RESTENT EXCITABLES avec des impulsions de seulement 2 µs
- → 2 types de douleur:
- Lente, lancinante, diffuse
- Rapide, bien localisée, réflexe de retrait


Axones sensoriels
Aα
Aβ
Aδ
C
Axones des fibres sensorielles musculaires
Groupe I
II
III
IV
Diamètre (µm)
13 20
6 12
1 5
0.2 - 1.5
Vitesse (m/s)
80 120
35 75
5 30
0.5 - 2
Récepteurs sensoriels
Propriocepteurs des muscles squelettiques
Mécanorécepteurs de la peau
Douleur, température
Température douleur démangeaison

PES


Réponse du nerf au genou
Réponse de la racine lombaire et de la moelle
Réponse du cortex sensitif

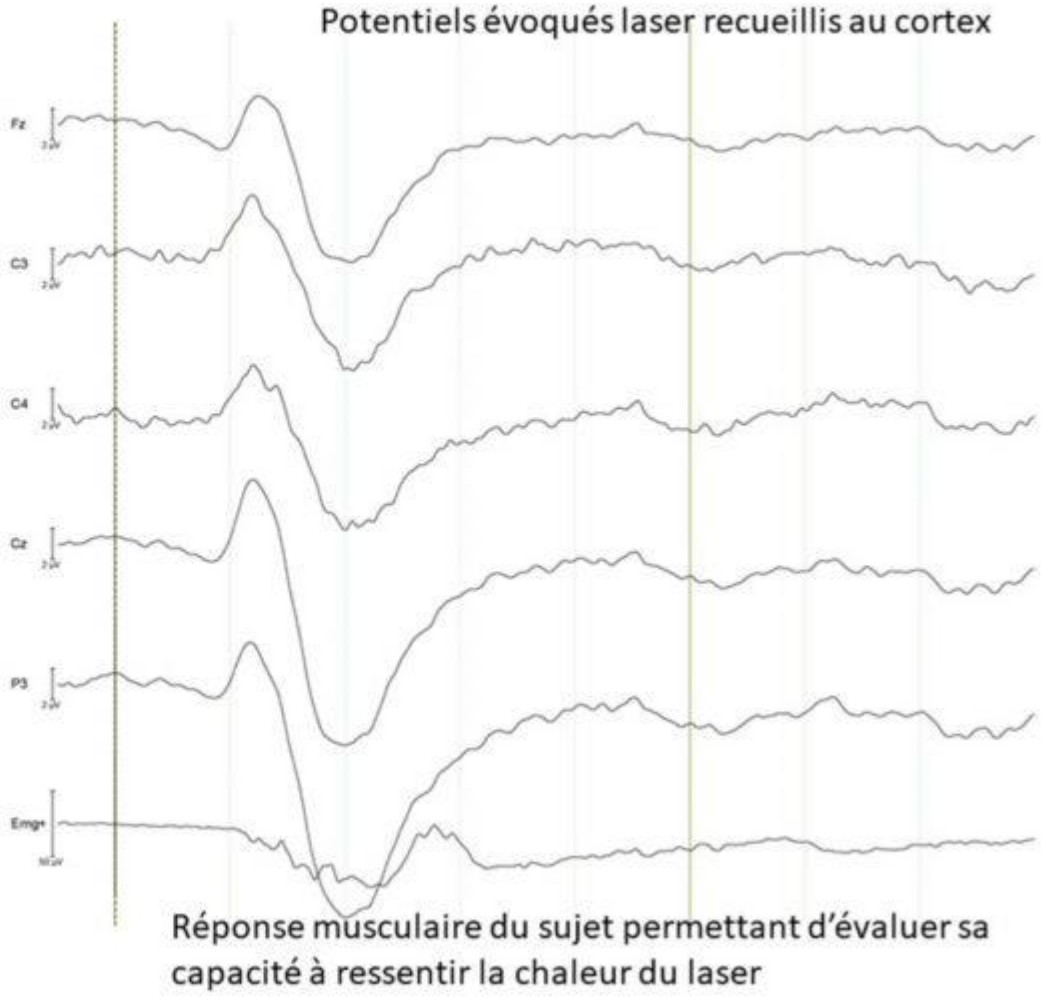
PEL

Neuropathies sensitives des petites fibres : intérêt des potentiels évoqués laser

Small fiber sensory neuropathies: Contribution of laser evoked potentials

C. Créac'h [a,*,b], P. Convers [a,b], F. Robert [a], J.-C. Antoine [a,c], J.-P. Camdessanche [a,c]

[a] Service de neurologie, CHU Saint-Étienne, hôpital Nord, 42055 Saint-Étienne, France
[b] Inserm U879, UCB Lyon 1, UJM, Saint-Étienne, France
[c] Inserm U842, UCB Lyon 1, UJM, Saint-Étienne, France



Contrôle segmentaire - Gate control

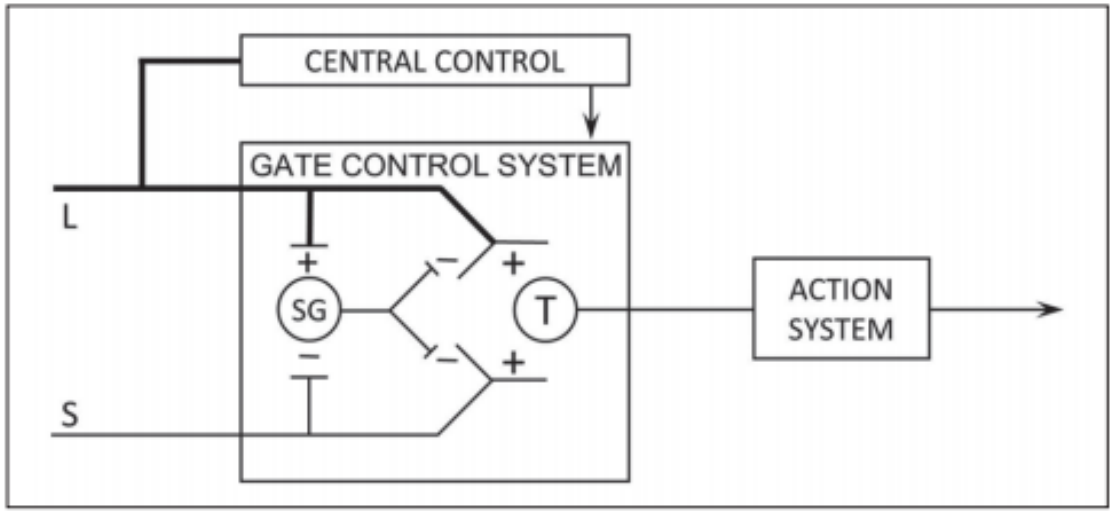


Figure 1) *A schematic illustration of the gate control theory of pain proposed by Melzack and Wall (1), demonstrating how the gating mechanism in the spinal dorsal horn modulates transmission of nerve impulses from afferent fibres to spinal cord transmission cells. The gating mechanism is affected by the relative activity in large- and small-diameter fibres, with the former inhibiting transmission (closing the gate) and the latter facilitating transmission (opening the gate). Notably, the spinal gating mechanism is also modulated by descending nerve impulses from the brain. The authors proposed that the spinal transmission cells activate an action system in the brain comprising regions that underlie the experience and behaviours characteristic of pain. Reproduced with permission from Melzack and Wall (1)*

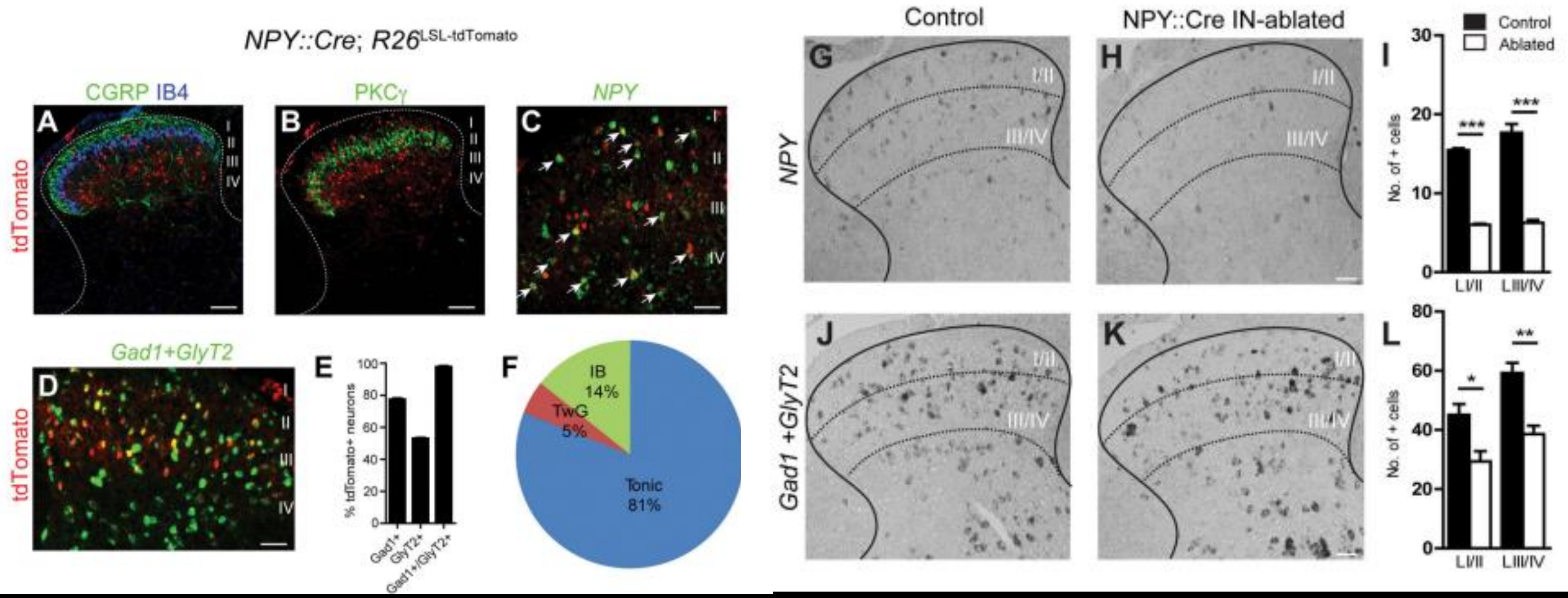
- Melzack and Wall, 1965

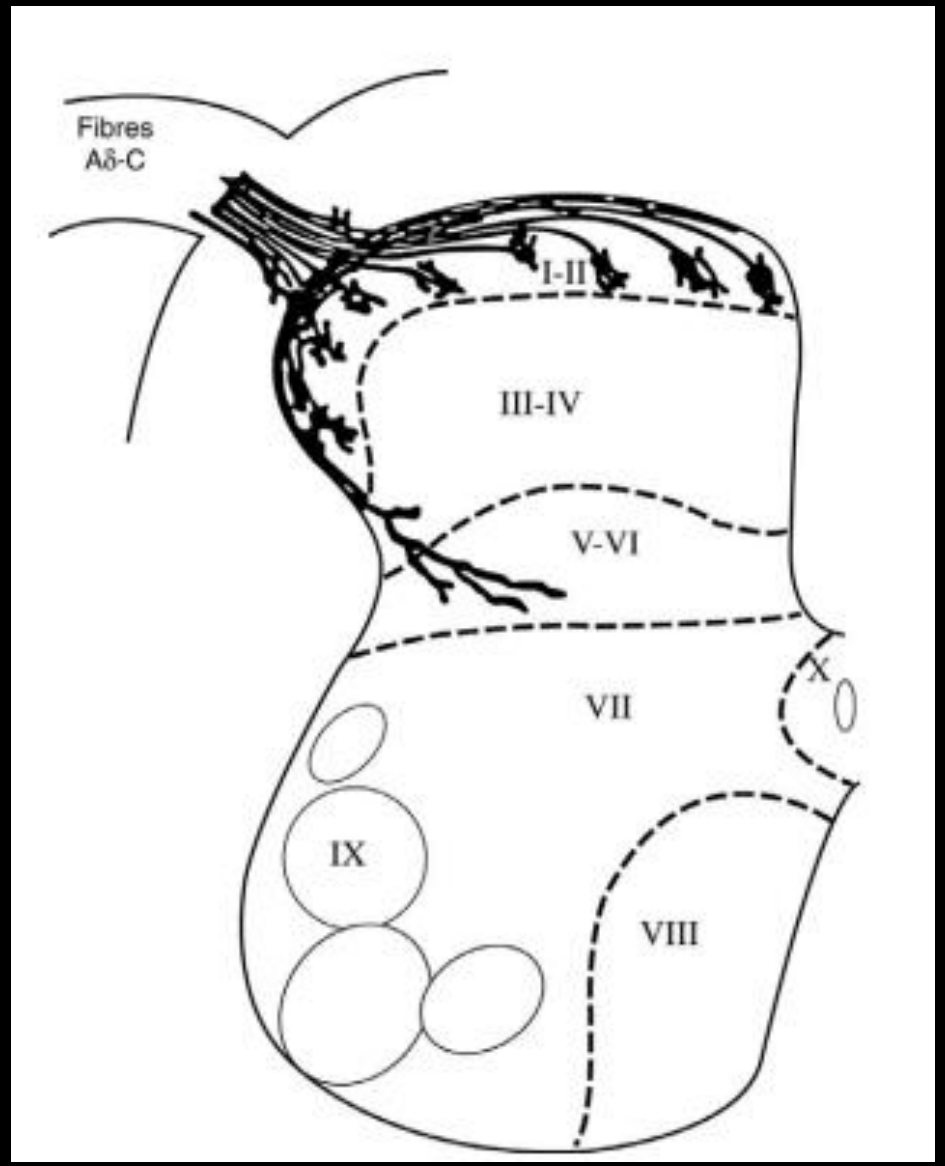
Published in final edited form as:
Science. 2015 October 30; 350(6260): 550–554. doi:10.1126/science.aac8653.

Gate control of mechanical itch by a subpopulation of spinal cord interneurons

Steeve Bourane[1,*], **Bo Duan**[2,*], **Stephanie C. Koch**[1], **Antoine Dalet**[1], **Olivier Britz**[1], **Lidia Garcia-Campmany**[1], **Euiseok Kim**[3], **Longzhen Cheng**[2,4], **Anirvan Ghosh**[3], **Qiufu Ma**[2,#], and **Martyn Goulding**[1,#]

[1]Molecular Neurobiology Laboratory, The Salk Institute for Biological Studies, 10010 North Torrey Pines Road, La Jolla, CA 92037, USA





Le contrôle central de la douleur

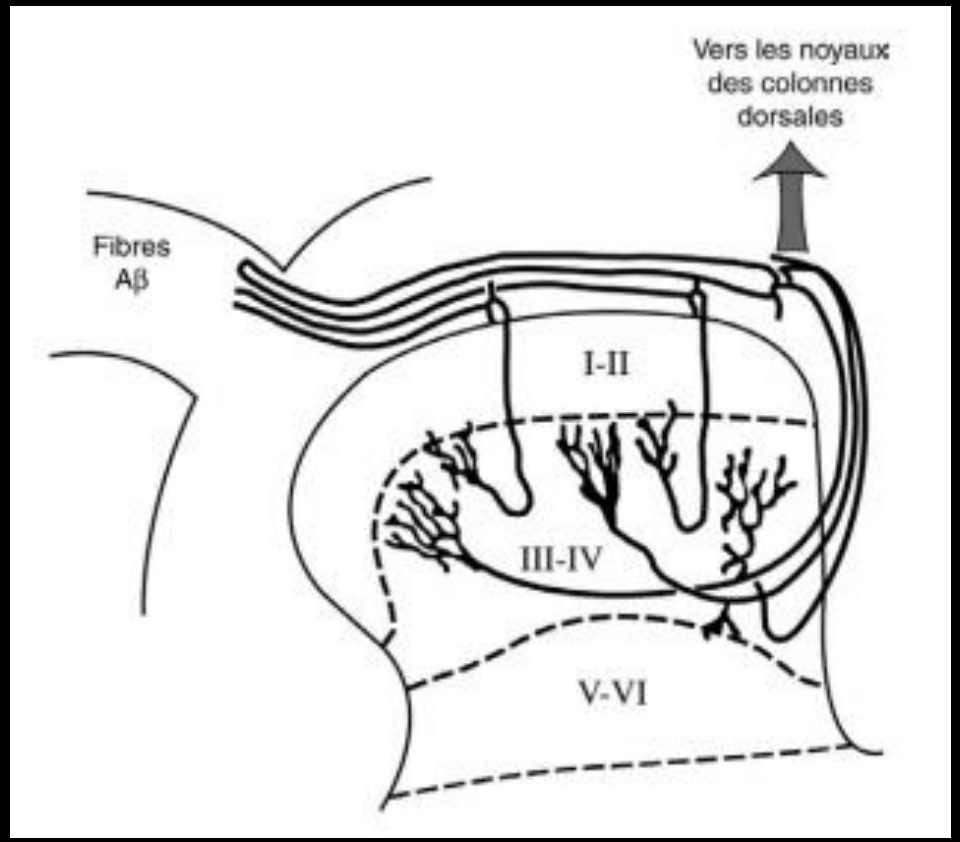
Central pain control ◇

Bernard Calvino *, Rose Marie Grilo [1]

Laboratoire de neurobiologie, CNRS UMR 7637, ESPCI, 10, rue Vauquelin, 75231 Paris cedex 05, France

Reçu le 20 septembre 2004 ; accepté le 10 novembre 2004

Disponible sur internet le 19 avril 2005



Gate control

- Rôle inhibiteur des fibres de gros diamètre (tactiles) sur les fibres de petit diamètre (nociceptives) au niveau des cellules convergentes (couche 5) via l'interneurone inhibiteur (SG) situé dans les couches 2 et 3.

Stimulation médullaire

- **<u>Objectifs</u>** :
- Soulager la douleur tout en réduisant la consommation de médicaments et le besoin en ressources de soins de santé
- Améliorer la qualité de vie et augmenter la capacité d'accomplir des actes de la vie quotidienne
- Améliorer les symptômes de la dépression tout en soulageant la douleur

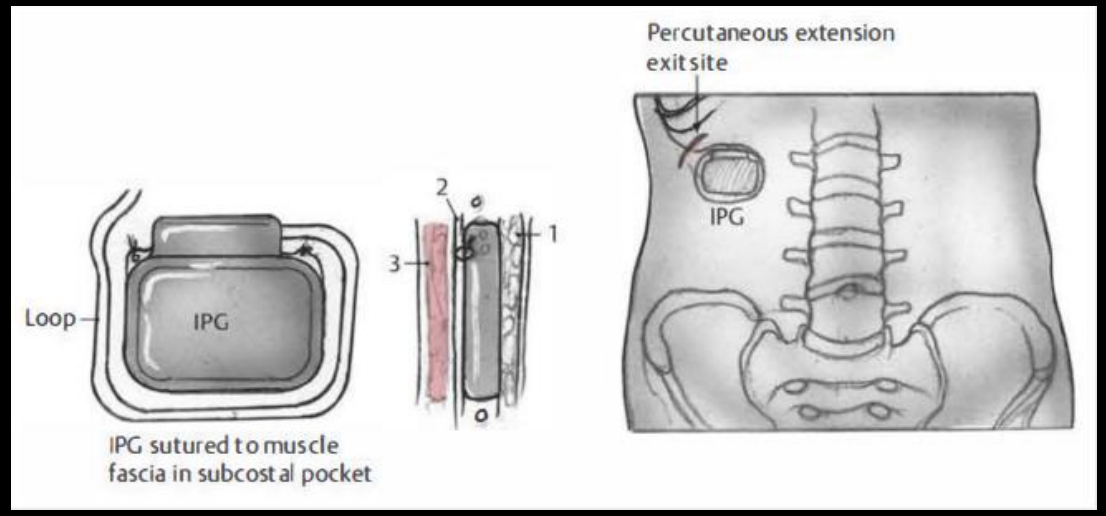
Stimulation médullaire

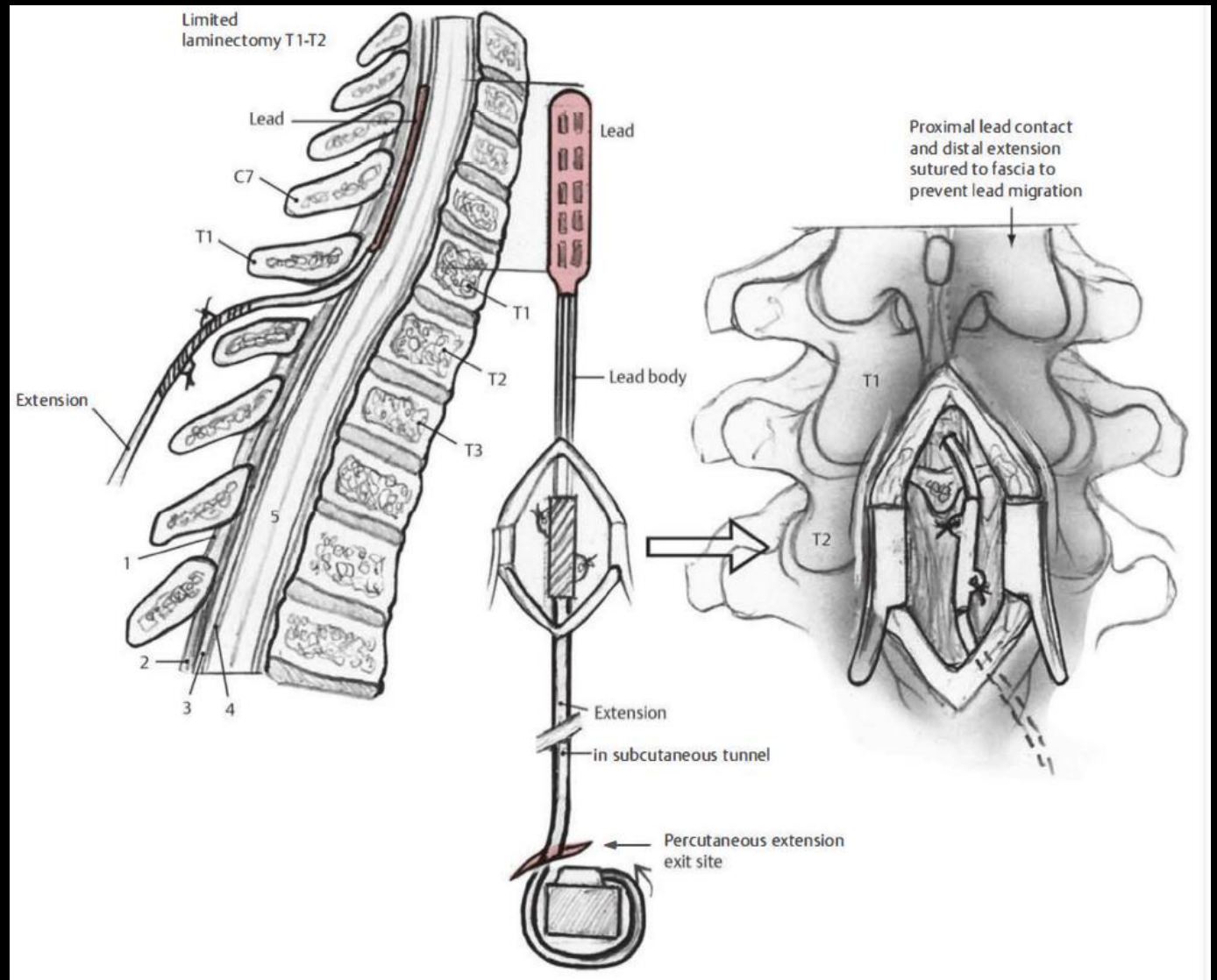
- **<u>Indications:</u>**
- Toute douleur neuropathique avérée
- Sans anomalie de la voie cordonale postérieure
- Chez un patient prêt psychologiquement pour cette PEC
- En échec thérapeutique de ttt précédemment bien conduits

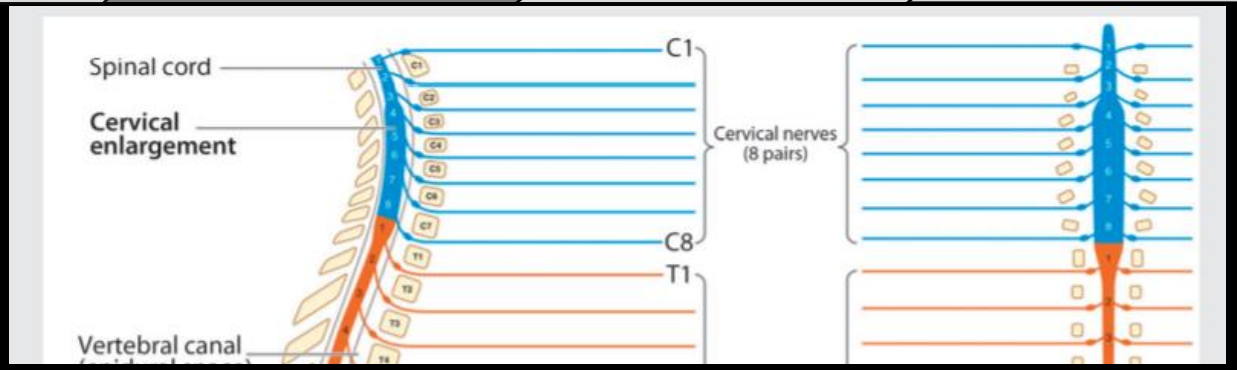
- Failed back surgery syndrome
- Complex regional pain syndrome (CRPS) I and II
- Douleur neuropathique périphérique
- Syndrome du membre fantôme (amputé)
- Névralgie post-herpétique

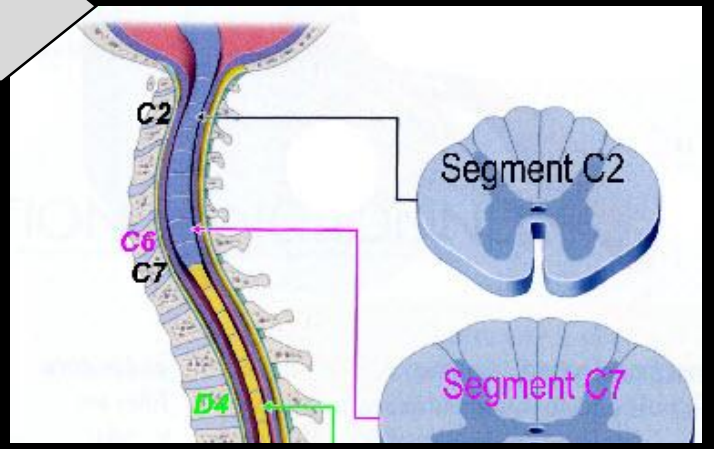
Stimulation médullaire

- **Techniques chirurgicales**
- open
- Per-cutané

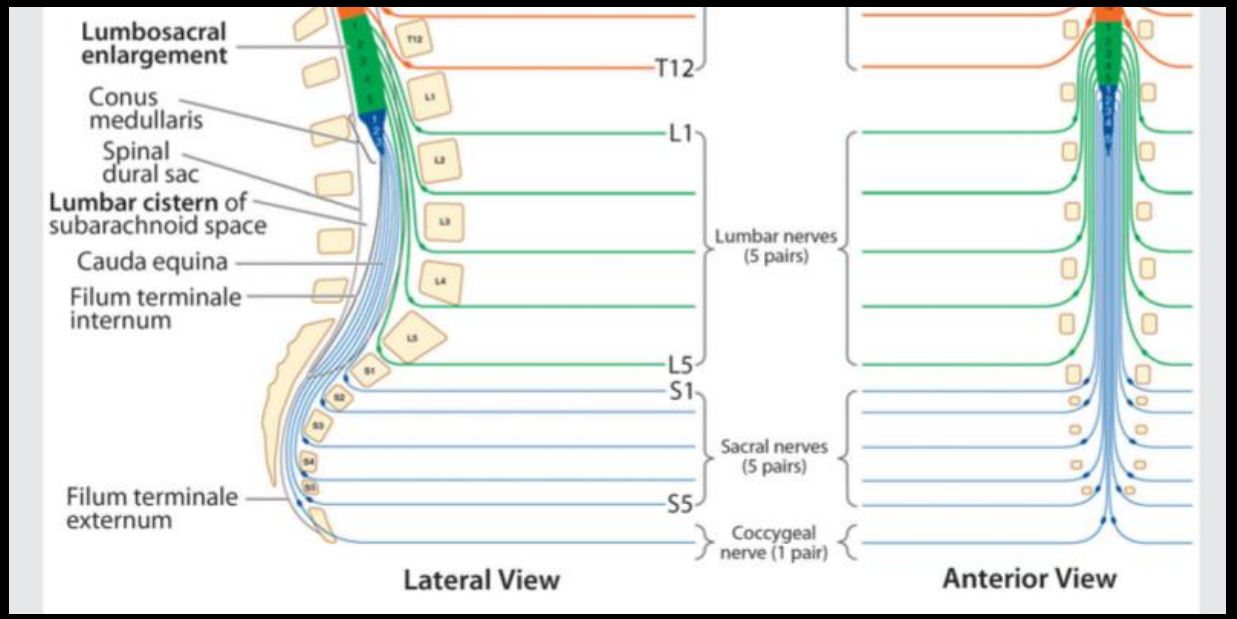


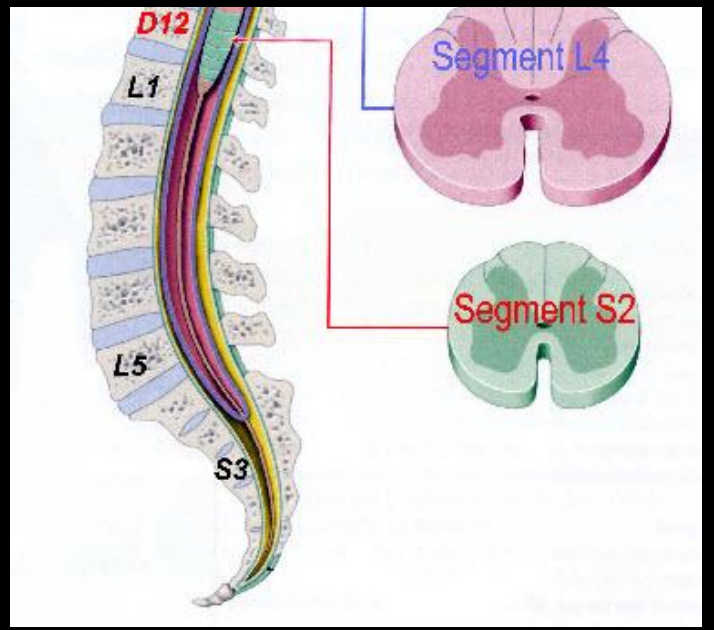






IMPORTANCE DE LA BONNE LOCALISATION DE L'ELECTRODE





Stimulation médullaire

Pain Physician 2016; 19:E33-E54 • ISSN 2150-1149

Systematic Review

Effectiveness of Spinal Cord Stimulation in Chronic Spinal Pain: A Systematic Review

Jay Grider, DO, PhD[1], Laxmaiah Manchikanti, MD[2], Alexios Carayannopoulos, DO, MPH[3], Manohar Lal Sharma, MD, FRCA, FFPMRCA[4], Carl C. Balog, MD[5], Michael E. Harned, MD[6] Vahid Grami, MD, MPH[7], Rafael Justiz, MD[8], Kent Nouri, MD[9], Salim M. Hayek, MD, PhD[10], Ricardo Vallejo, MD, PhD[11], and Paul J. Christo, MD[12]

- **Résultats**

Table 4. Results of published studies of effectiveness of spinal cord stimulation in failed back surgery syndrome.

Study	Study Characteristics	Methodological Quality Scoring	Patients	Pain Relief		Results	
				≤ 12 mos.	> 12 mos.	Short-term ≤ 12 mos.	Long-term > 12 mos.
Kapural et al (38,39)	RA, AC	Cochrane:8/12 IPM-QRB: 34/48	SCS = 81 HF10 = 90	55% vs. 80%	55% vs. 80%	P	P
North et al (13)	RA, AC	Cochrane: 7/12 IPM-QRB: 31/48	SCS = 29 Reoperation = 31	52% vs. 10%	52% vs. 10%	P	P
Kumar et al (18,86)	RA, AC	Cochrane: 9/12 IPM-QRB: 32/48	Total = 100 CMM = 48 SCS = 52	18% vs. 48%	18% vs. 48%	P	P
Schultz et al (77)	RA, AC	Cochrane: 7/12 IPM-QRB: 20/48	Manual = 40 Adaptive = 36 Total = 76	U	NA	U	NA
Perruchoud et al (78)	RA, AC	Cochrane: 7/12 IPM-QRB: 23/48	Total = 33 Sham vs HFSCS = 20	N	NA	N	NA
Schu et al (79)	RA, AC	Cochrane: 9/12 IPM-QRB: 24/48	20	P (burst)	NA	U	NA

RA = randomized; AC = Active-control; SCS = spinal cord stimulation; CMM = conventional medical management; vs = versus; P = positive; N = negative; NA = Not applicable; U = undetermined; HF10 = 10 kHz high frequency therapy; HFSCS = high frequency spinal cord stimulation

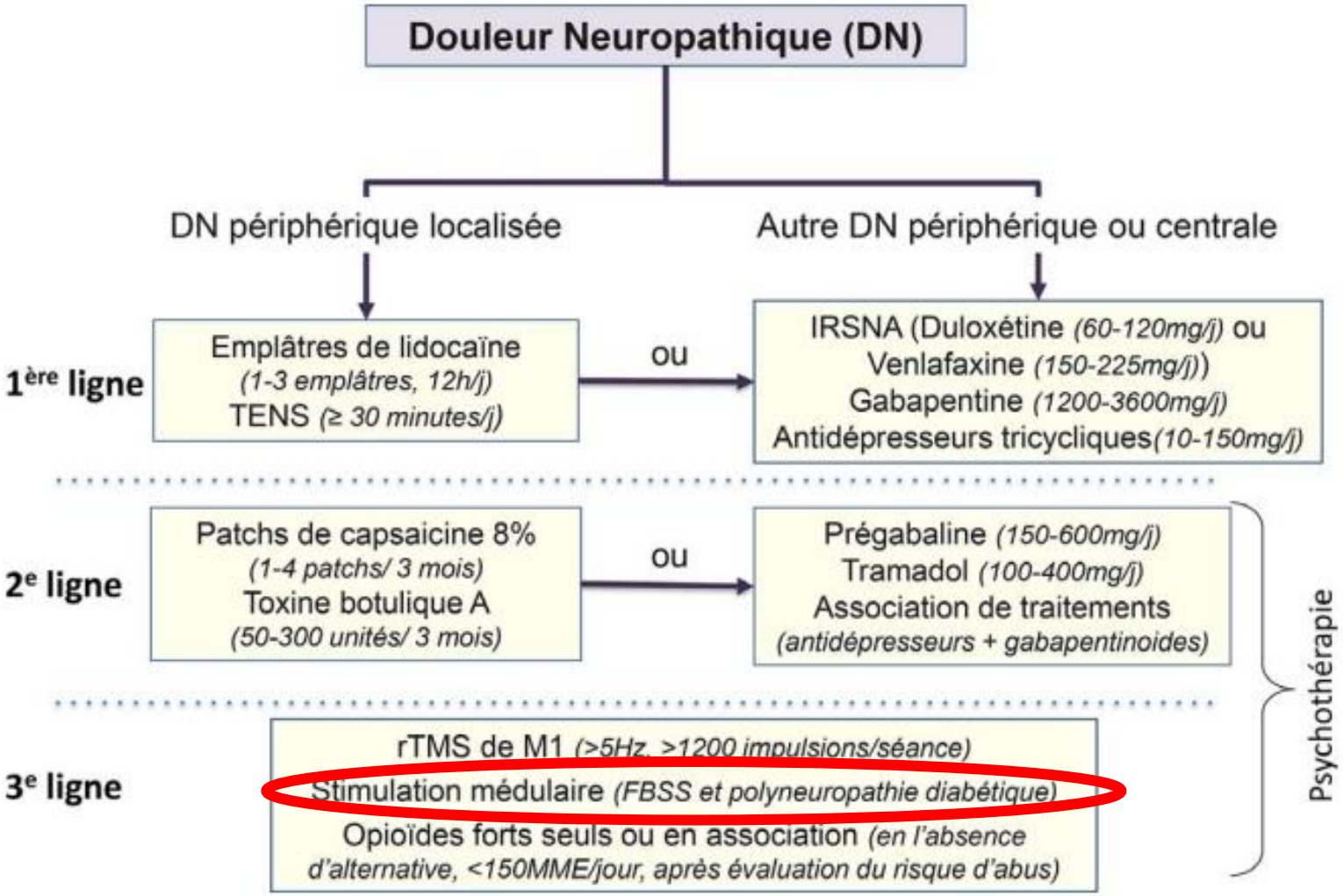


Fig. 1 Algorithme thérapeutique proposé pour la prise en charge de la douleur neuropathique de l'adulte. TENS : *transcutaneous electrical nerve stimulation* ; IRSNA : antidépresseur inhibiteur de recapture de la sérotonine et de la noradrénaline ; rTMS : *repetitive transcranial magnetic stimulation*

Douleur analg.
DOI 10.3166/dea-2020-0113

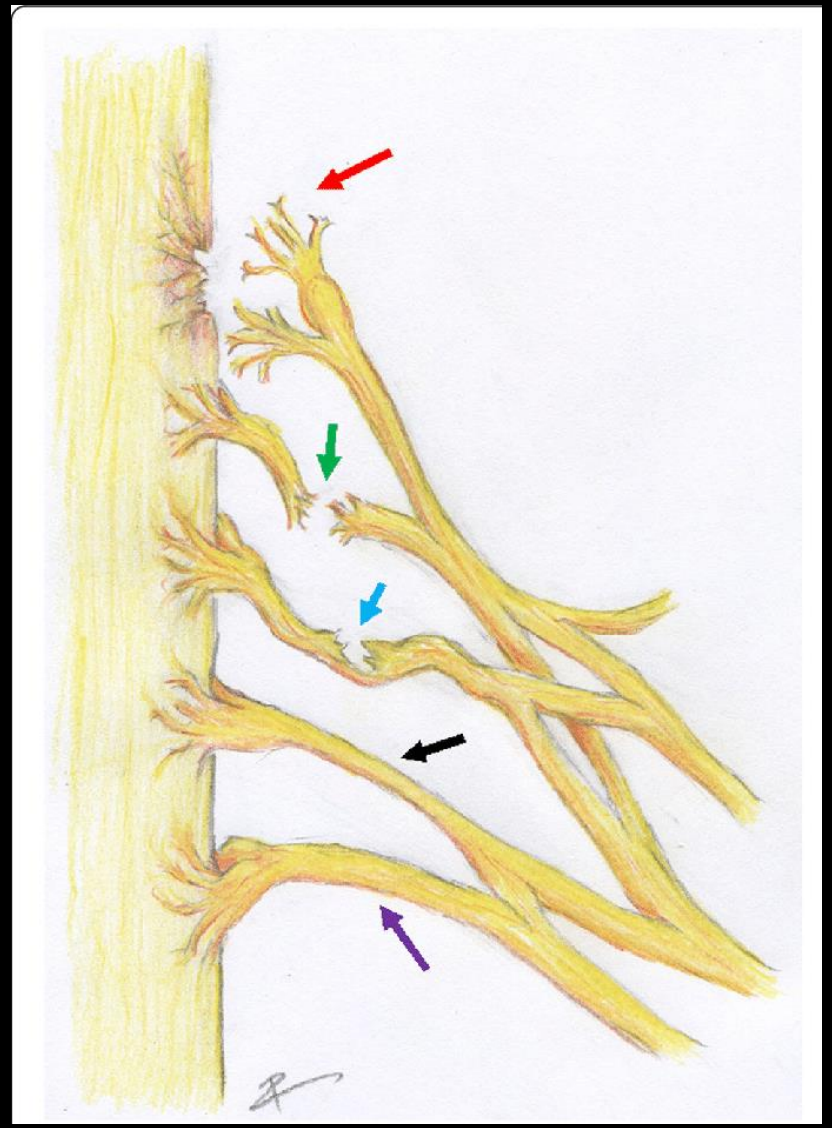
RECOMMANDATIONS / *RECOMMENDATIONS*

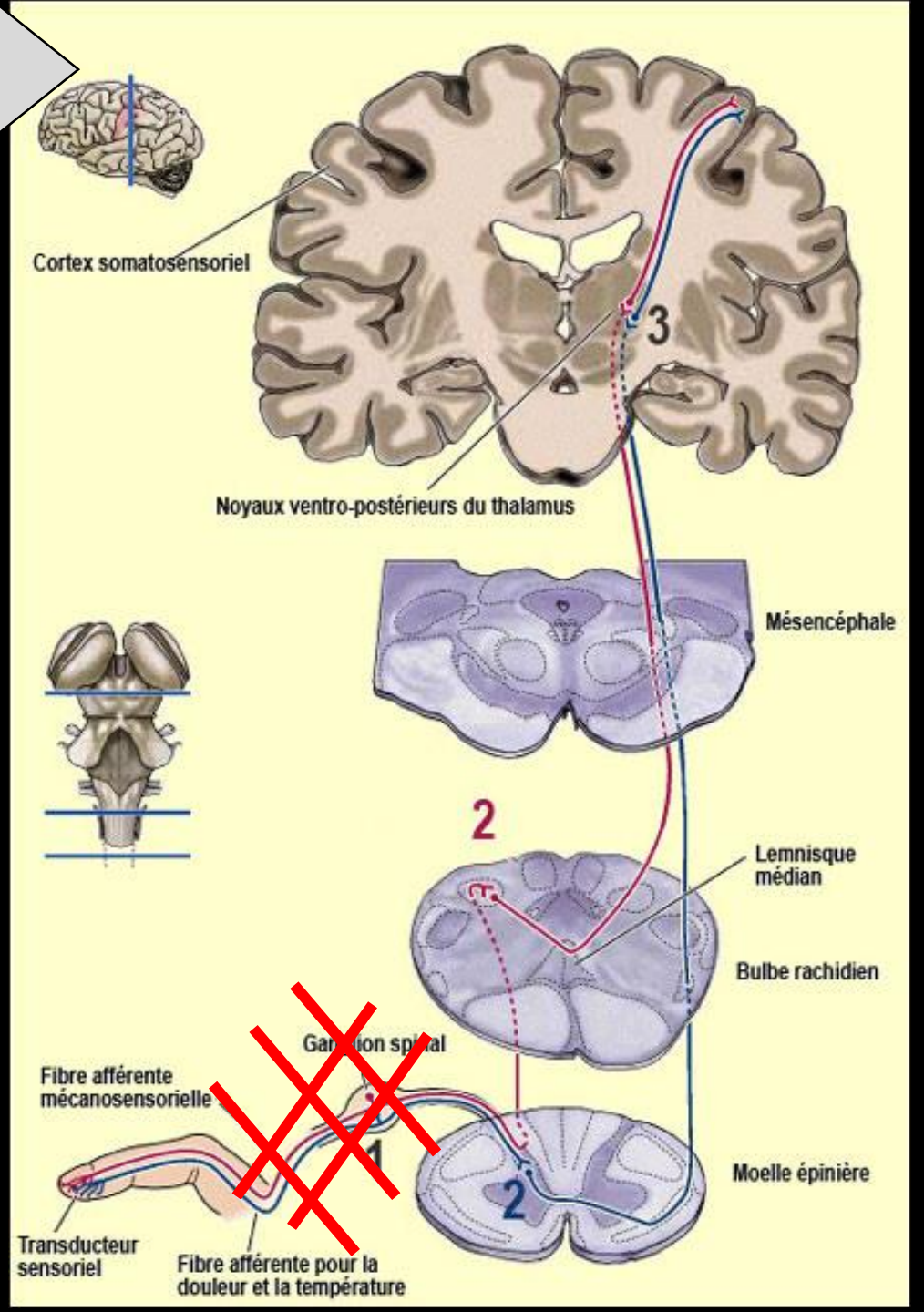
Traitements pharmacologiques et non pharmacologiques de la douleur neuropathique : une synthèse des recommandations françaises

Pharmacological and Non-Pharmacological Treatment for Neuropathic Pain: Short Form French Guidelines

X. Moisset · D. Bouhassira · J. Avez Couturier · H. Alchaar · S. Conradi · M.-H. Delmotte · M. Lantéri-Minet · J.-P. Lefaucheur · G. Mick · V. Piano · G. Pickering · E. Piquet · C. Regis · E. Salvat · N. Attal

Avulsion plexuelle



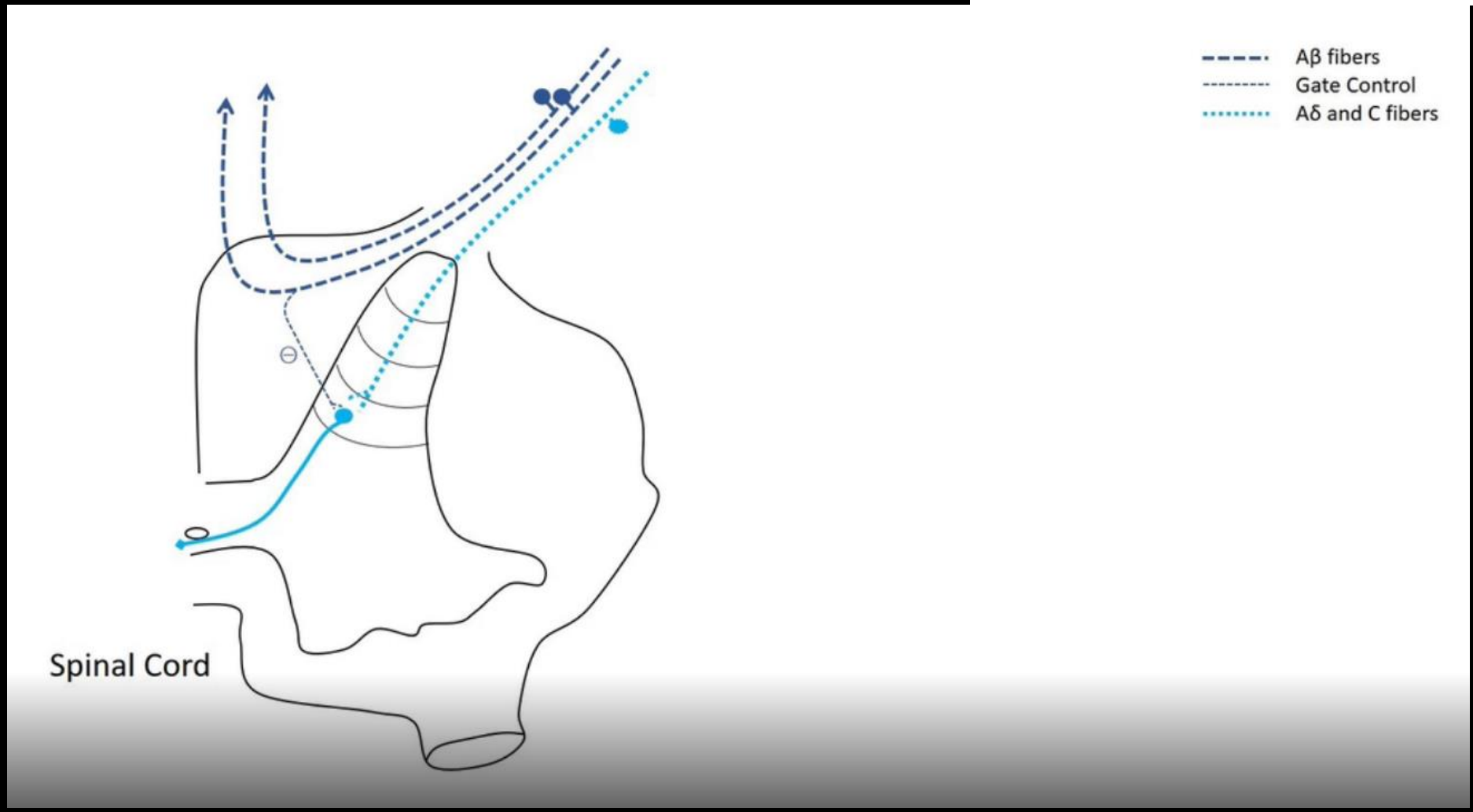


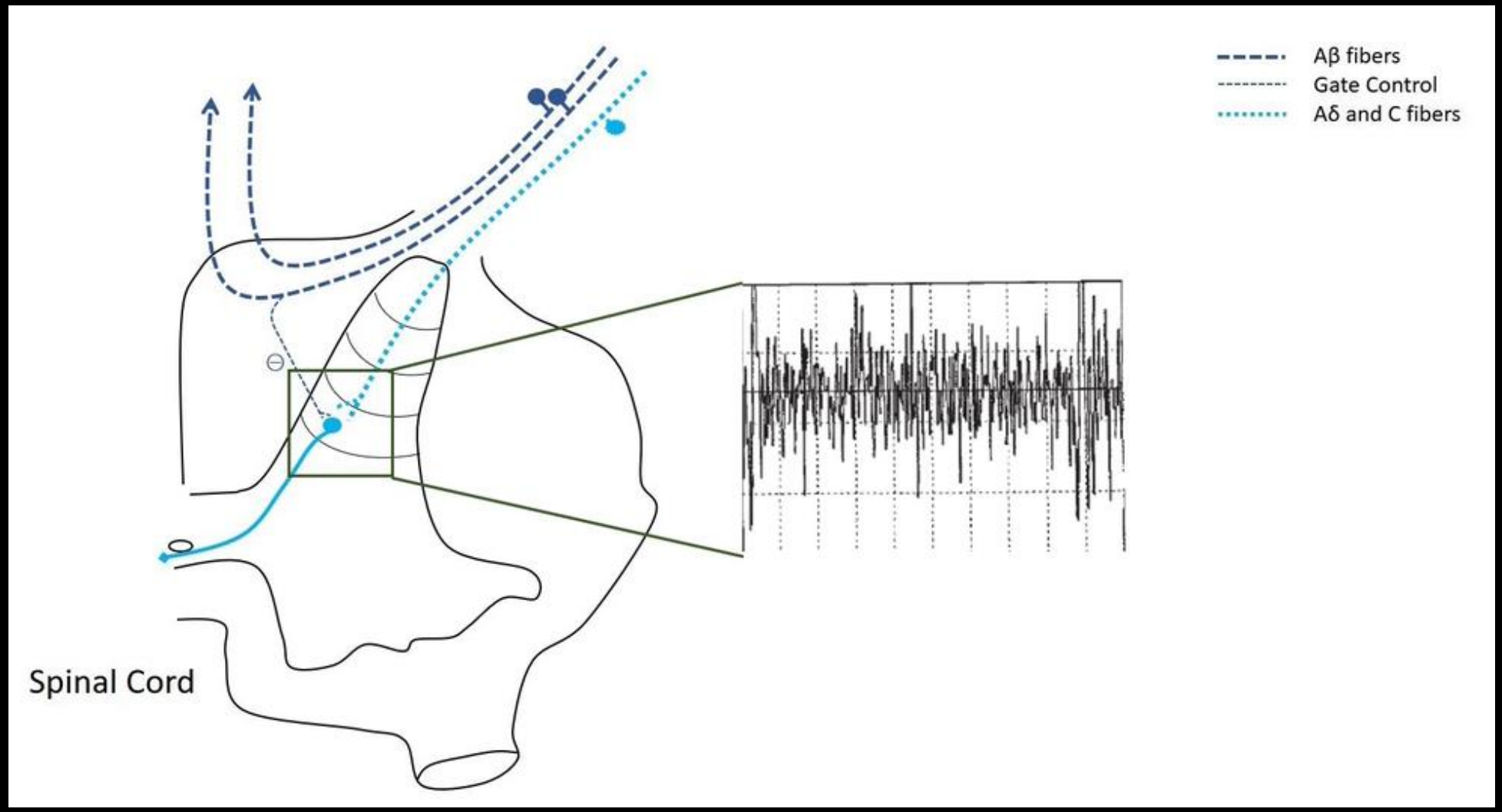
VIDEO ARTICLE

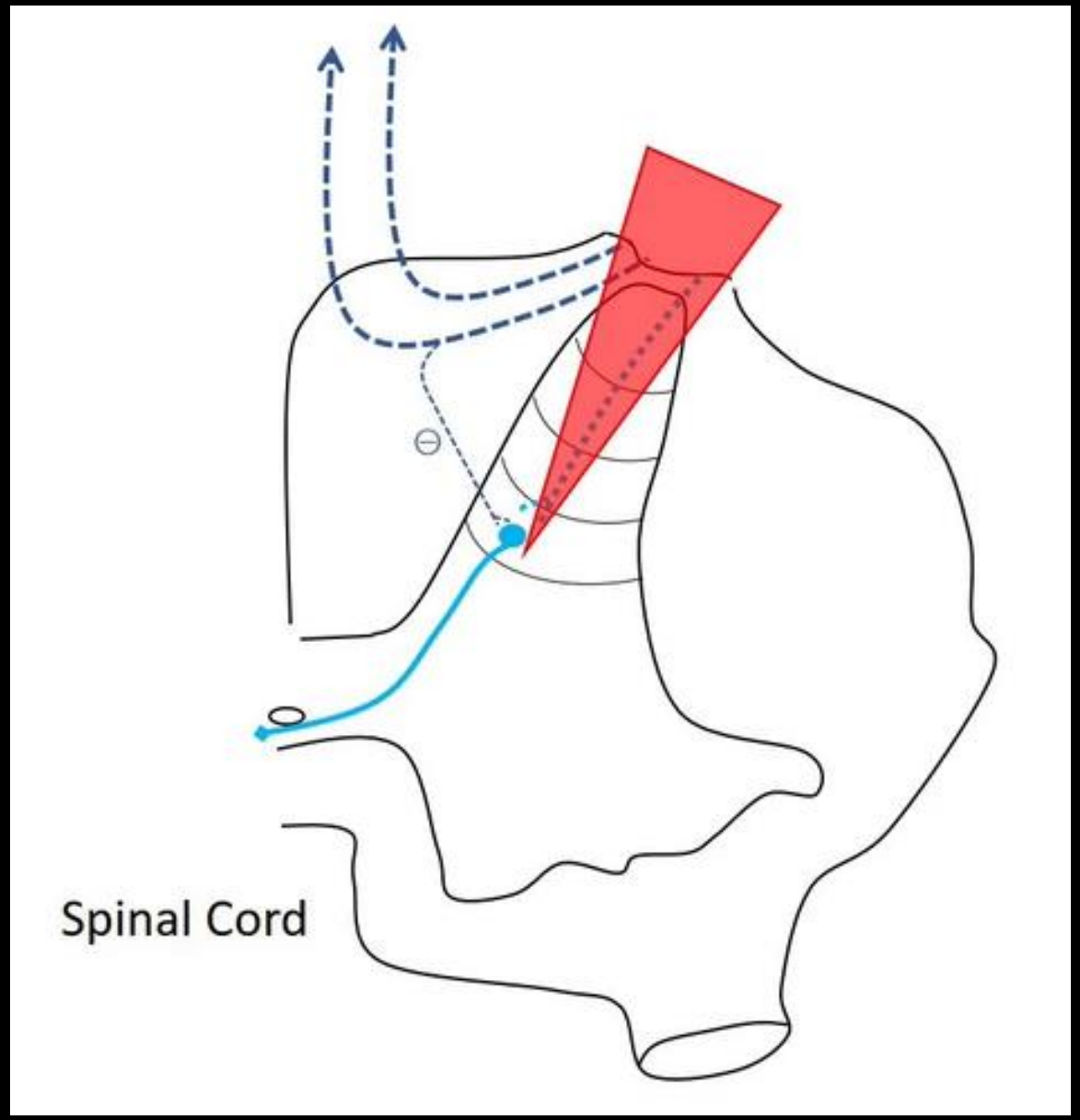
Check for updates

Microsurgical DREZotomy for Treatment of Brachial Plexus Avulsion Pain

Corentin Dauleac[1,2], Andrei Brinzeu[1,2,5], Inès Fenniri[1,2], Marc Sindou[4], Patrick Mertens[1-3]

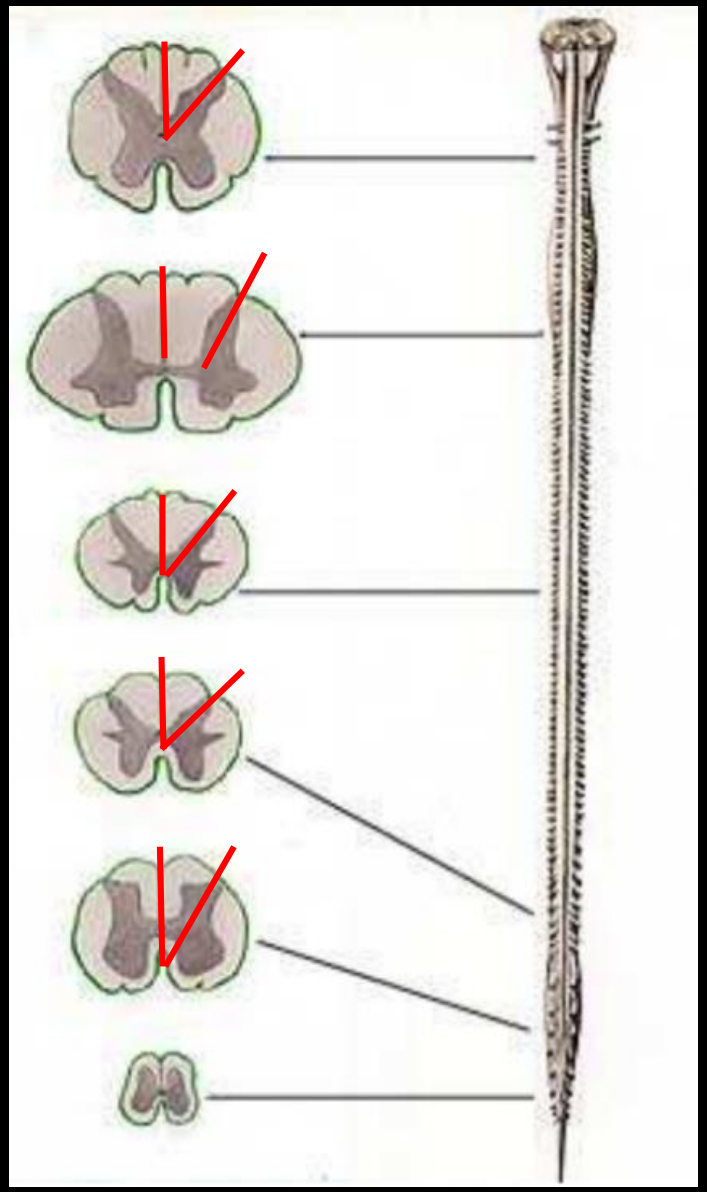



Aβ fibers
Gate Control
Aδ and C fibers
Spinal Cord


Spinal Cord

DREZotomie

- **Objectifs :**
- Interrompre préférentiellement les fibres nociceptives tout en préservant dans une certaine mesure les structures inhibitrices de la corne dorsale
- Détruire les neurones anormaux à l'intérieur de la corne dorsale, supposés être responsables de la douleur dite de désafférentation.

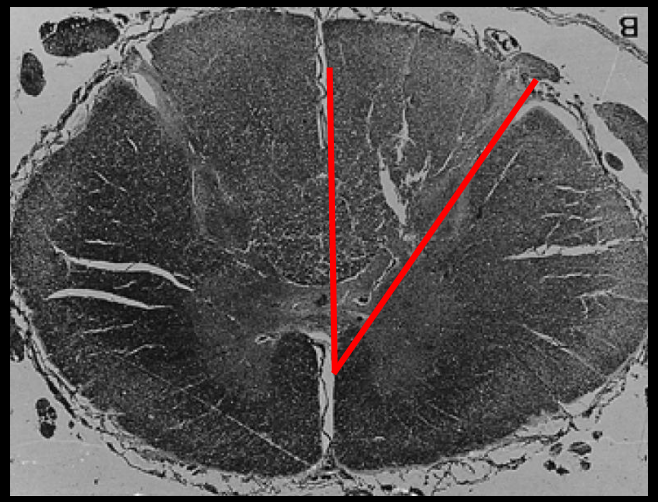


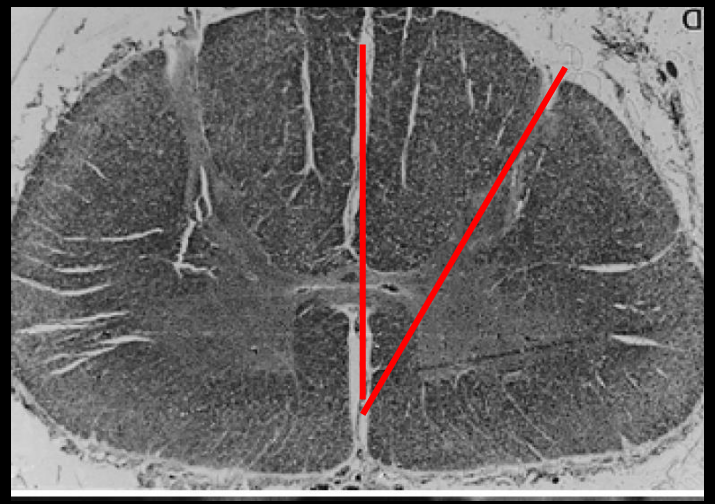
Surg Radiol Anat 22: 81-88

Radiological anatomy

Radiologic anatomy of the spinal dorsal horn at the cervical level (anatomic-MRI correlations)

P. Mertens[1], M. Guenot[4], M. Hermier[2], A. Jouvet[3], P. Tournut[2], J.L. Froment[2], M. Sindou[4] and J.P. Carret[1]





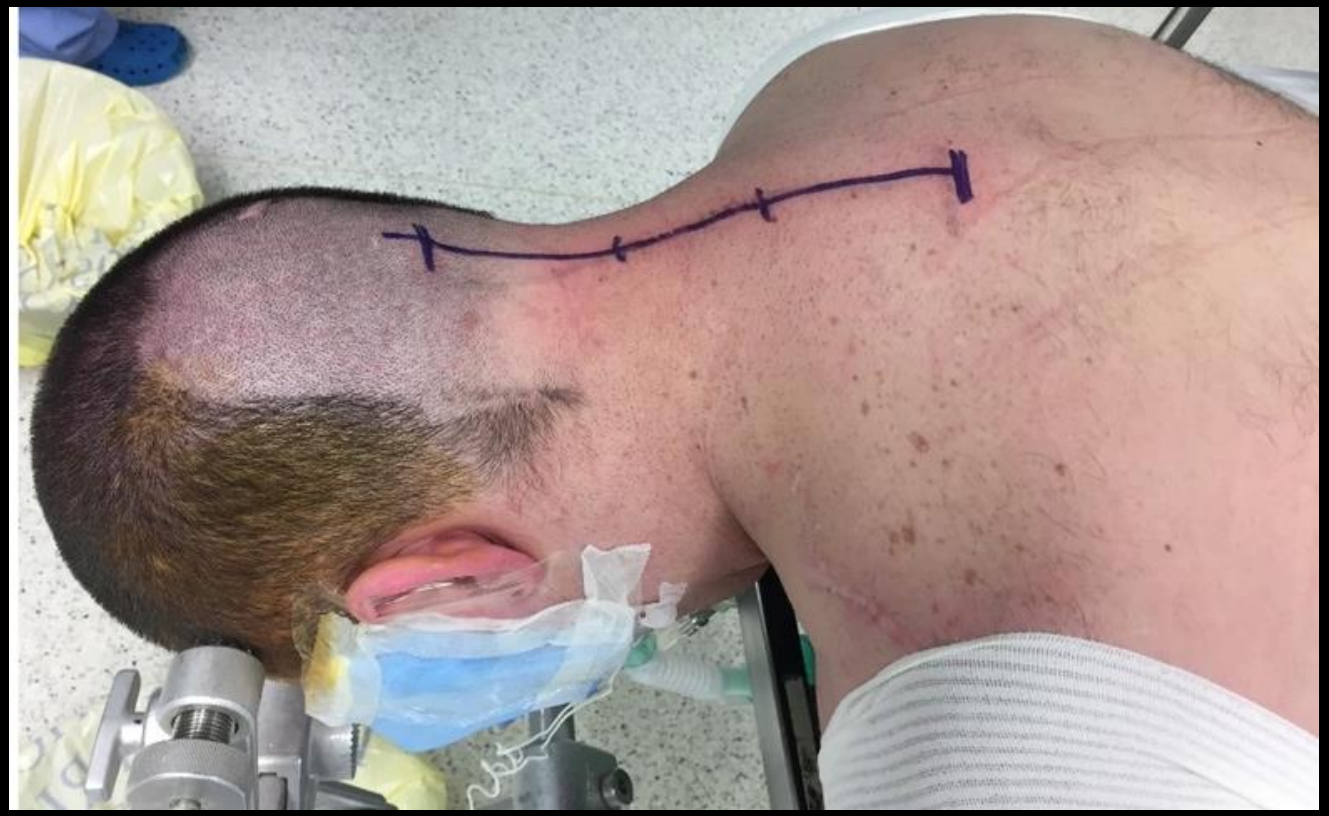
DREZotomie

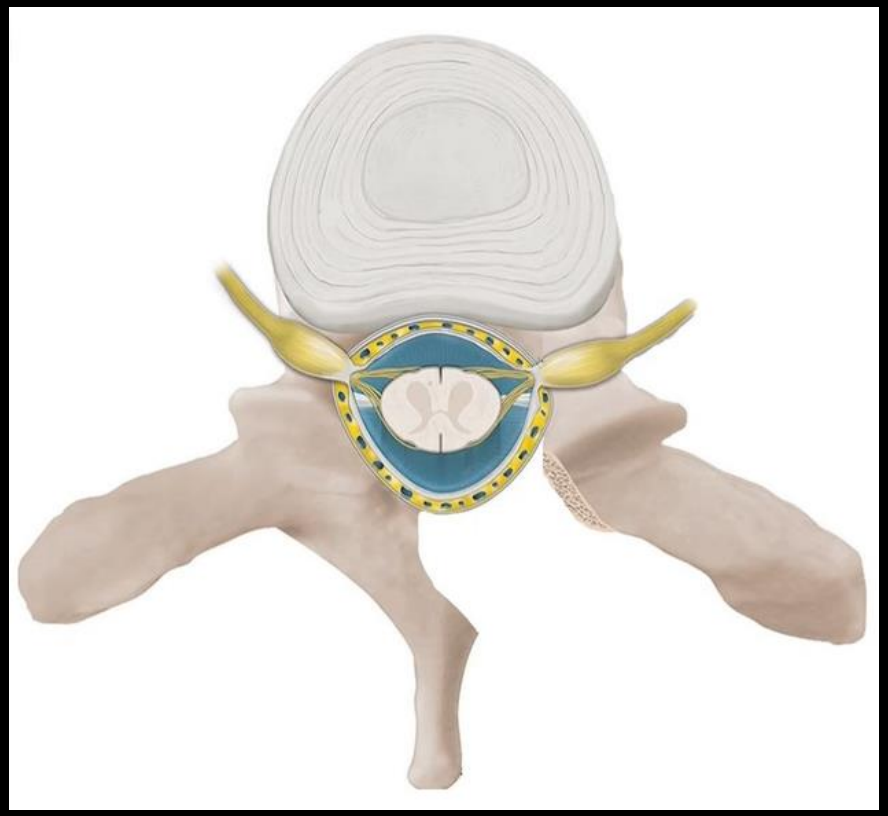
VIDEO ARTICLE

Check for updates

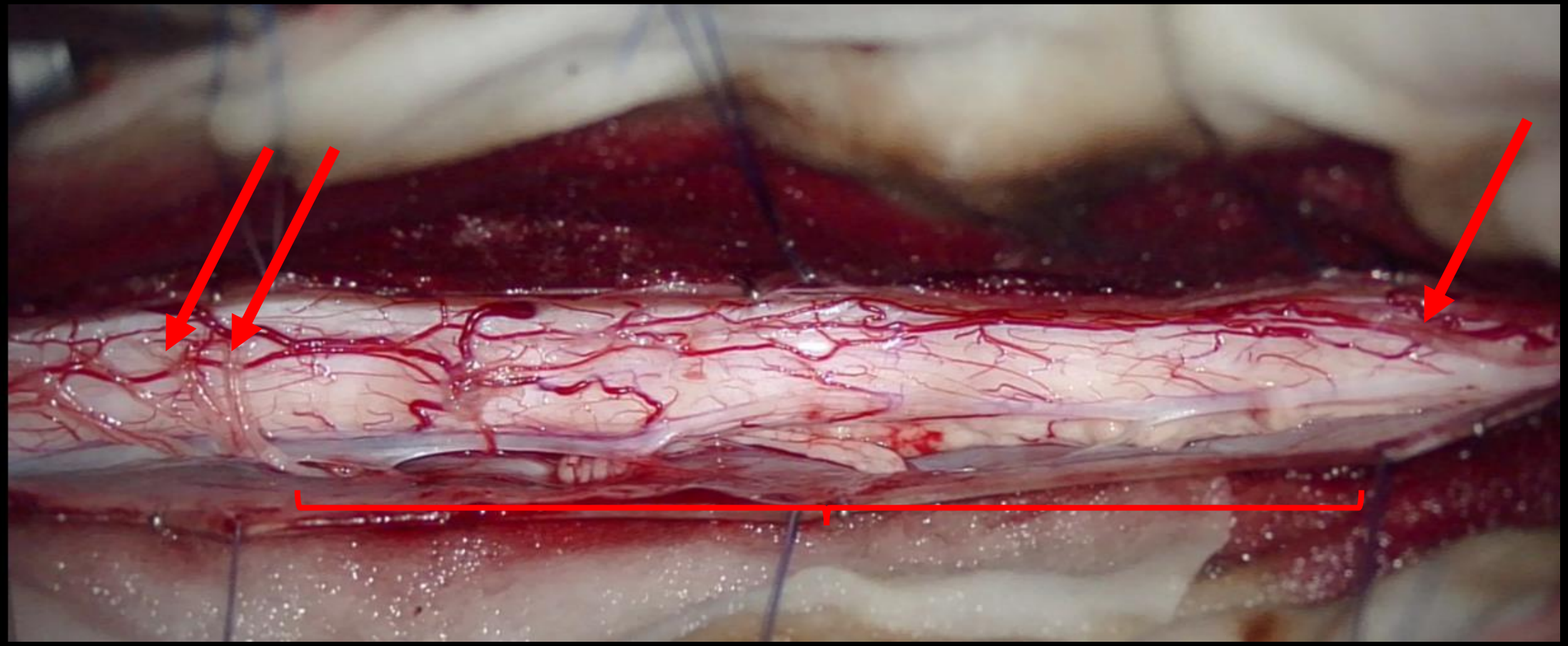
Microsurgical DREZotomy for Treatment of Brachial Plexus Avulsion Pain

Corentin Dauleac[1,2], Andrei Brinzeu[1,2,5], Inès Fenniri[1,2], Marc Sindou[4], Patrick Mertens[1-3]

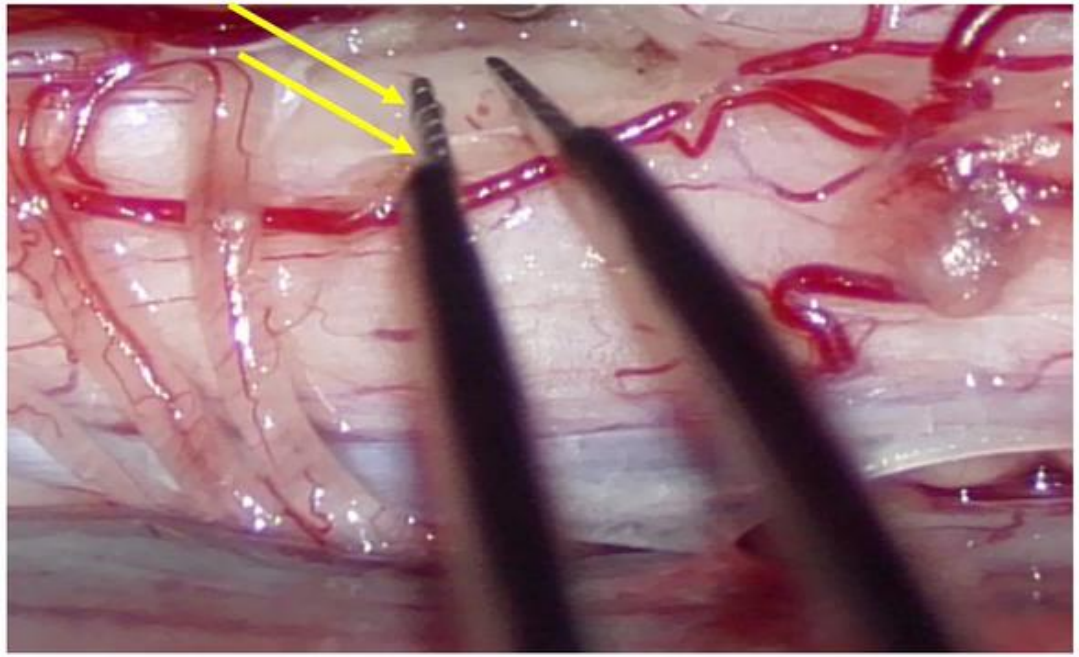


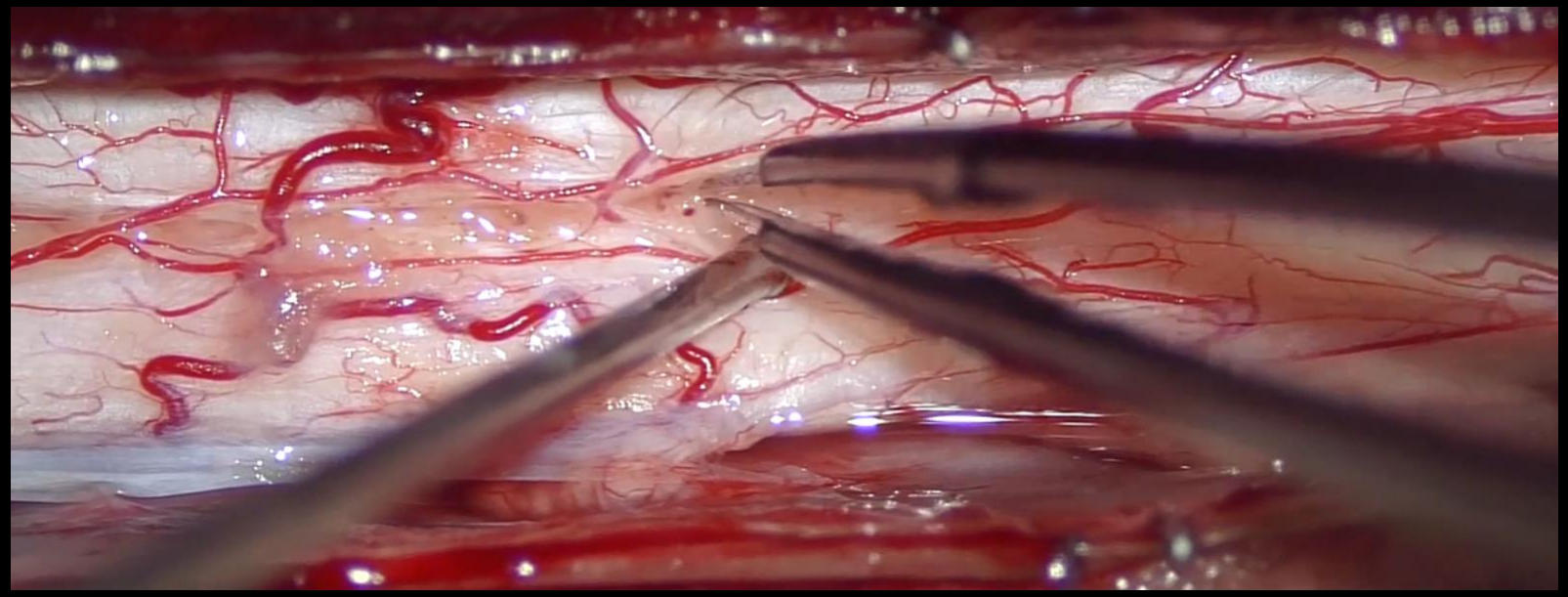


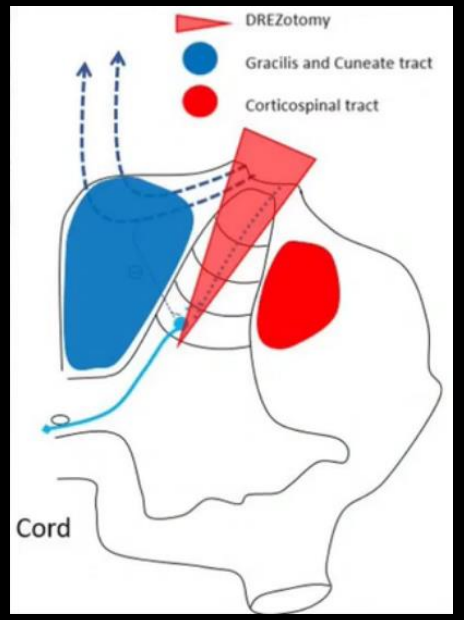
DREZotomie

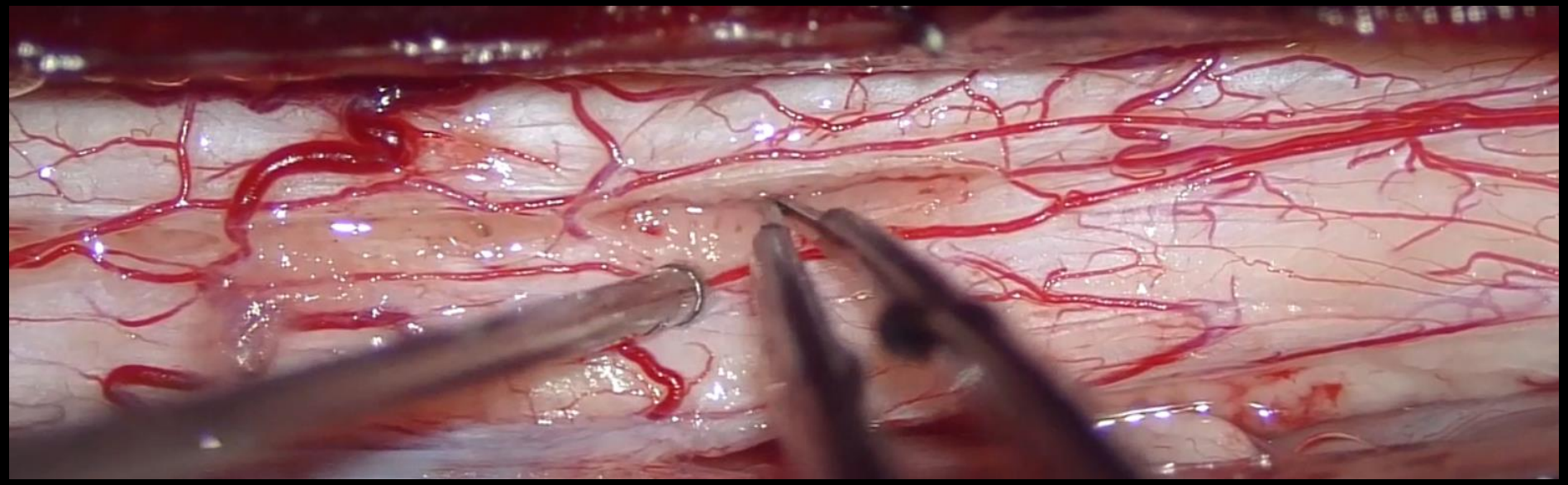


Micro instruments






DREZotomy
Gracilis and Cuneate tract
Corticospinal tract
Cord



DREZotomie

- **Indications :**

- **lésions du plexus**, notamment l'avulsion, au niveau brachial ou plus rarement lombo-sacré.
- **douleurs segmentaires** après lésions de la moelle épinière (surtout au niveau du conus medullaris). Douleurs résultant de lésions des nerfs périphériques, mais uniquement lorsque les principales composantes sont de type paroxystique et/ou allodynique, après échec de la SCS.
- **douleurs circonscrites** dues à une lésion cancéreuse bien limitée topographiquement, comme par exemple dans l'apex thoracique. Syndrome de Pancoast-Tobias
- spasticité invalidante sévère, notamment associée à une à la douleur

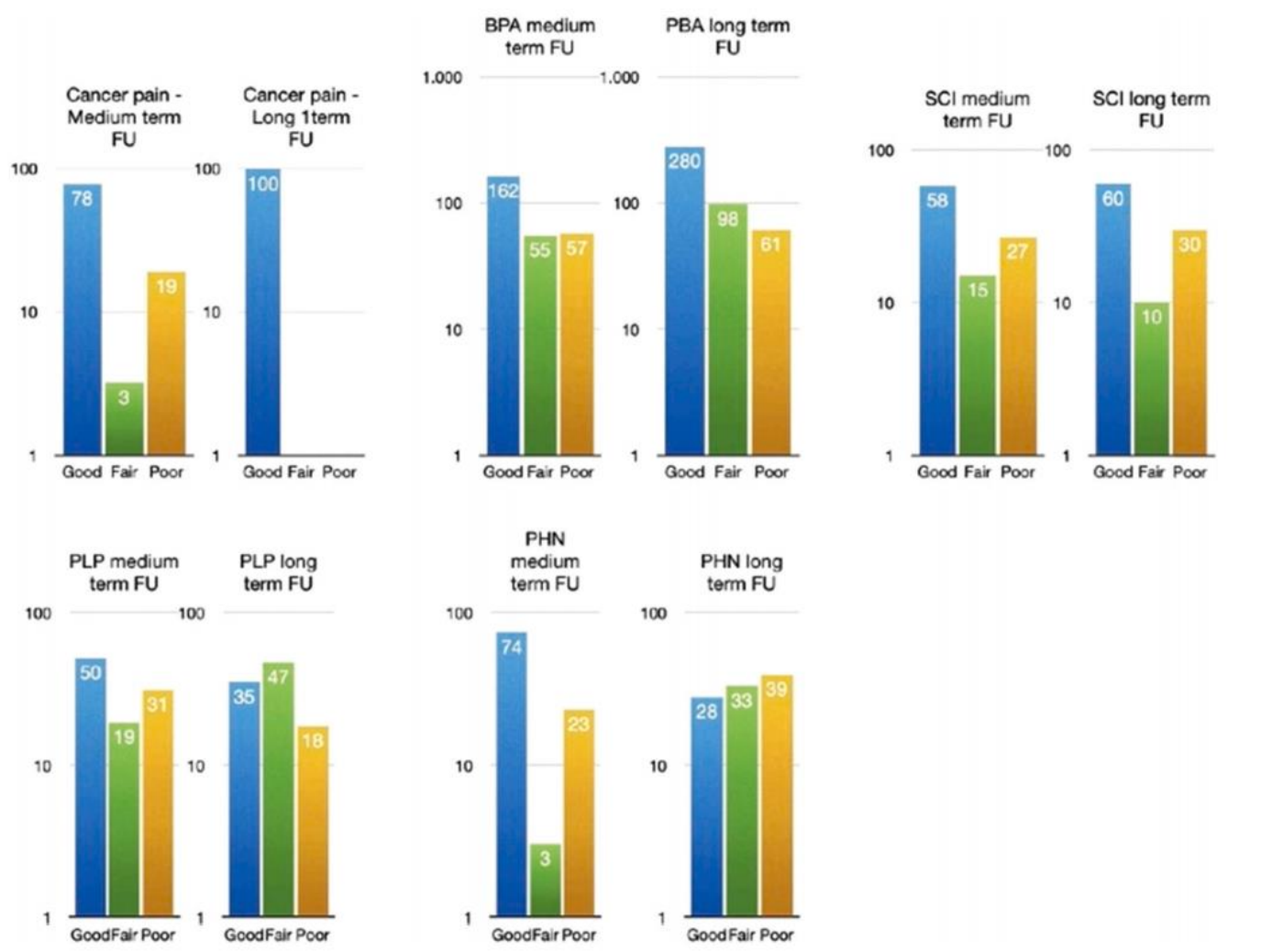
DREZotomie

- **Résultats**

Table 6
Clinical outcome evaluation by Sindou [9].

Outcome	Clinical characteristics and drug intake evaluation
Good	- pain reduction of more than 75% - VAS < 3 - no need of analgesic drugs
Fair	- pain reduction between 75% and 50% - VAS < 5 - residual need of moderate doses of analgesic drugs
Poor	- pain reduction lower than 50% - VAS between 3 and 6 with paroxysms higher than 6 - need of high doses of analgesic drugs

DREZotomie – résultats



Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Review Article

Long term results of Dorsal Root Entry Zone (DREZ) lesions for the treatment of intractable pain: A systematic review of the literature on 1242 cases

Lorenzo Mongardi [a,1,*], Jacopo Visani [a,1], Giorgio Mantovani [a], Costanza Vitali [b], Luca Ricciardi [c], Flavio Giordano [d], Michele Alessandro Cavallo [a,e], Giorgio Lofrese [f], Marcello D'andrea [f], Paul Roblot [g], Pasquale De Bonis [a,e], Alba Scerrati [a,e]

- Medium term < 3 ans
- Long term > 3 ans

DREZ – résultats

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Review Article

Long term results of Dorsal Root Entry Zone (DREZ) lesions for the treatment of intractable pain: A systematic review of the literature on 1242 cases

Lorenzo Mongardi[a,1,*], Jacopo Visani[a,1], Giorgio Mantovani[a], Costanza Vitali[b], Luca Ricciardi[c], Flavio Giordano[d], Michele Alessandro Cavallo[a,e], Giorgio Lofrese[f], Marcello D'andrea[f], Paul Roblot[g], Pasquale De Bonis[a,e], Alba Scerrati[a,e]

Table 7
Clinical outcome for each indication,.

Surgical indication	No. papers	No. patients evaluated	Good Outcome	Fair Outcome	Poor Outcome	Dead/lost during the follow up
Cancer Pain/post radiation	13	130 (10.19%)	98 (75.4%)	4 (3.1%)	24 (18.4%)	4 (3.1%)
Brachial plexus avulsion	25	717 (56,23%)	436 (60,80%)	150 (20,92%)	118 (16,45%)	13 (1,83%)
Spinal cord injury	15	301 (23,61%)	168 (55.8%)	35 (11.6%)	82 (27.3%)	16 (5.3%)
Phantom limb pain	8	49 (3,85%)	22 (44.9%)	14 (28.6%)	13 (26.5%)	–
Post herpetic neuralgia	9	78 (6.12%)	40 (51.2%)	14 (18%)	24 (30.8%)	–
Total	46	1275	764	217	261	33

Table 8
Medium (< 3 years) and long term (> 3 years) follow up outcome evaluation for single indication.

	Medium term follow-up				Long term follow-up			
Indication	Patients	Good	Fair	Poor	Patients	Good	Fair	Poor
Cancer pain	125	97 (77.6%)	4 (3.2%)	24 (19.2%)	1	1 (100%)	0	0
PBA	274	162 (59.1%)	55 (20.1%)	57 (20.8%)	439	280 (63,78%)	98 (22,32%)	61 (13,9%)
SCI	132	76 (57.6%)	20 (15.1%)	36 (27.3%)	153	92 (60.2%)	15 (9.8%)	46 (30%)
PLP	32	16 (50%)	6 (18.7%)	10 (31.3%)	17	6 (35.3%)	8 (47%)	3 (17.7%)
PHN	39	29 (74.4%)	1 (2.6%)	9 (23%)	39	11 (28.2%)	13 (33.3%)	15 (38.5%)
TOT	602				649			

DREZ – résultats

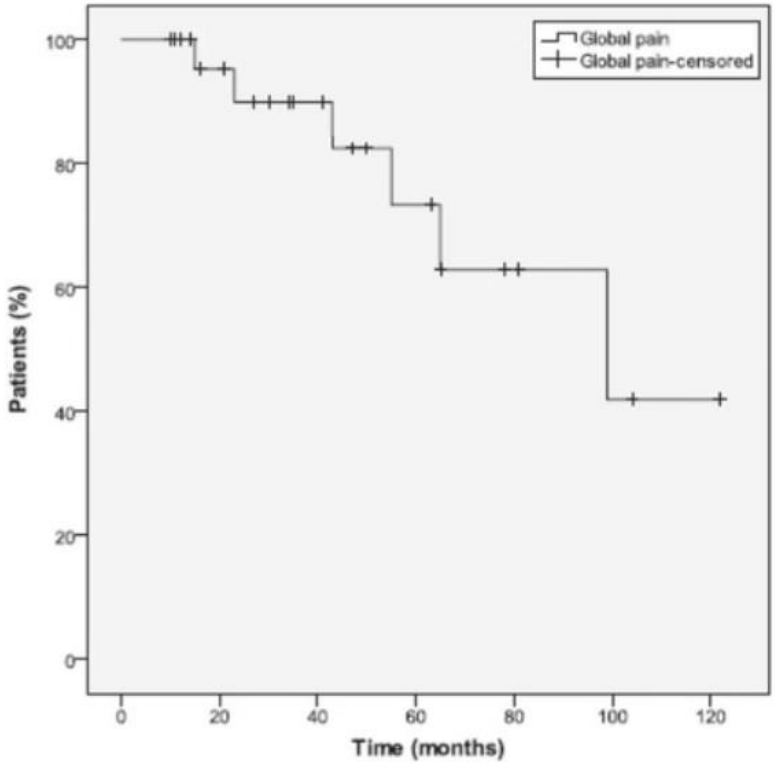
IASP
PAIN® 152 (2011) 1923–1930
PAIN®
www.elsevier.com/locate/pain

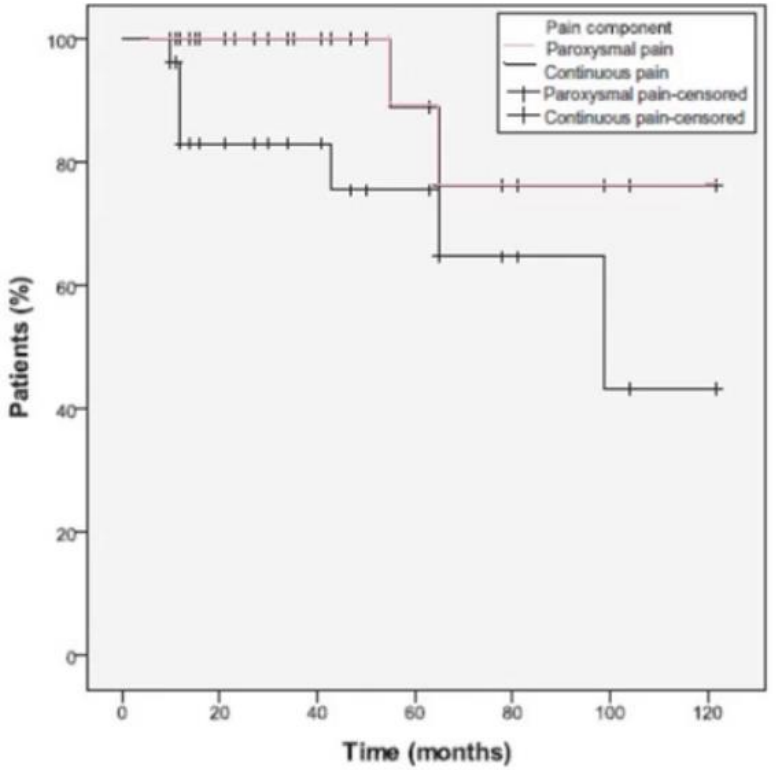
Clinical note

Dorsal root entry zone lesioning for pain after brachial plexus avulsion: Results with special emphasis on differential effects on the paroxysmal versus the continuous components. A prospective study in a 29-patient consecutive series

Faycal Aichaoui [a,*], Patrick Mertens [a,b], Marc Sindou [a]

[a] Department of Neurosurgery, P. Wertheimer Neurological Hospital, Hospices Civils de Lyon, Université Lyon 1, Lyon, France
[b] Institut National de la Sante et de la Recherche Medicale (INSERM U8), Lyon, France



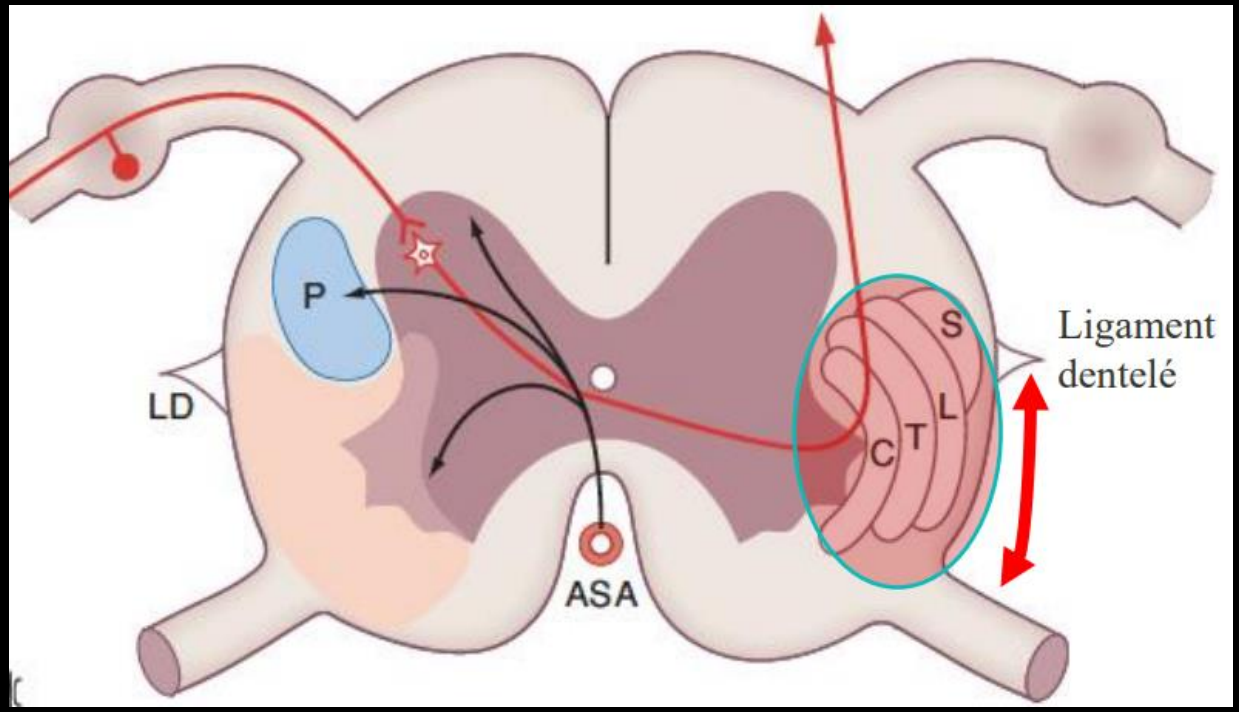


Pain was controled with or without any additional nonopioid drugs in 75-80%

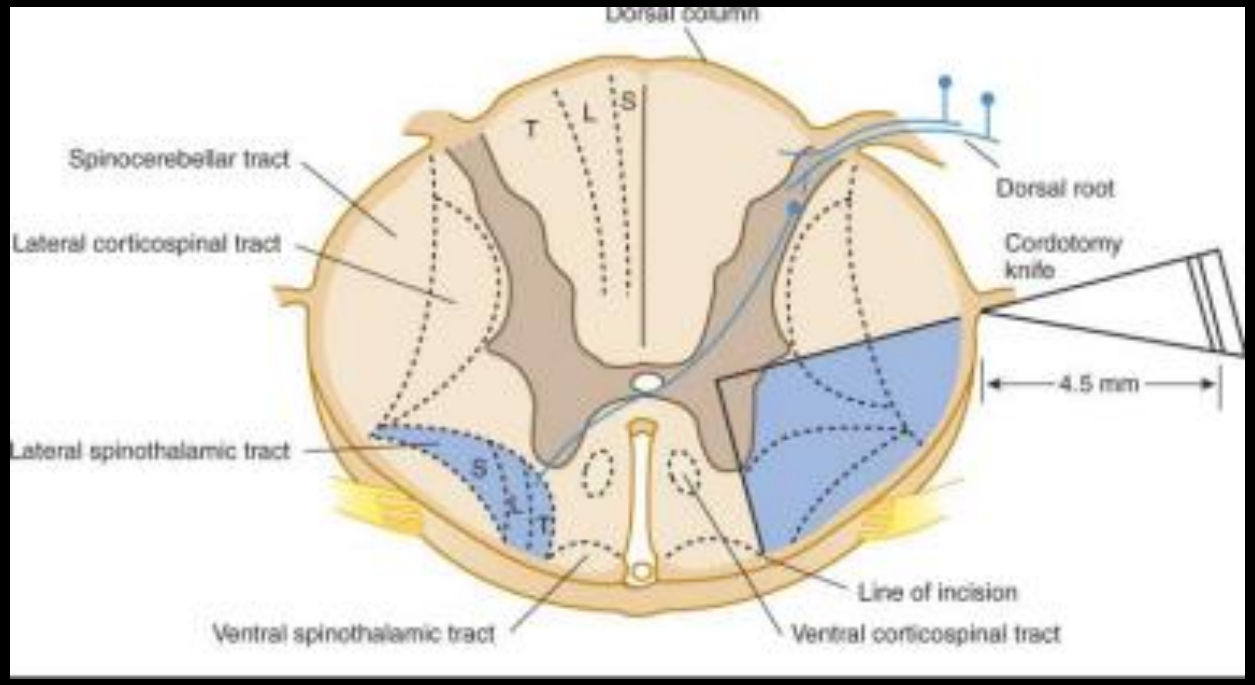
Aichaoui et al. Pain, 2011.

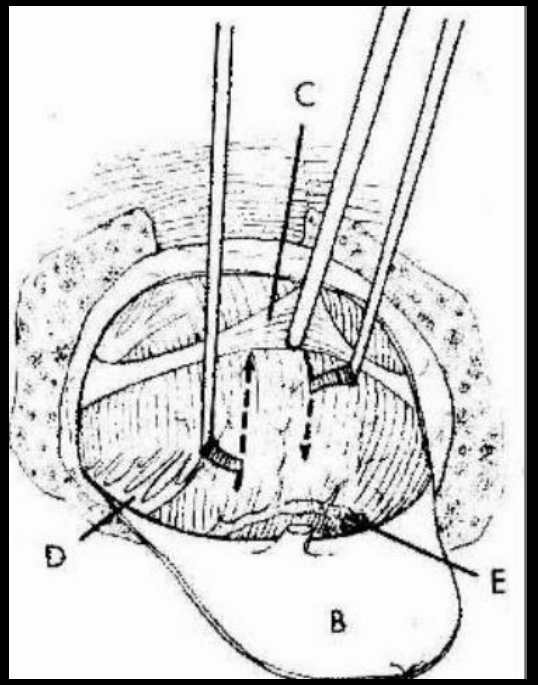
Cordotomie

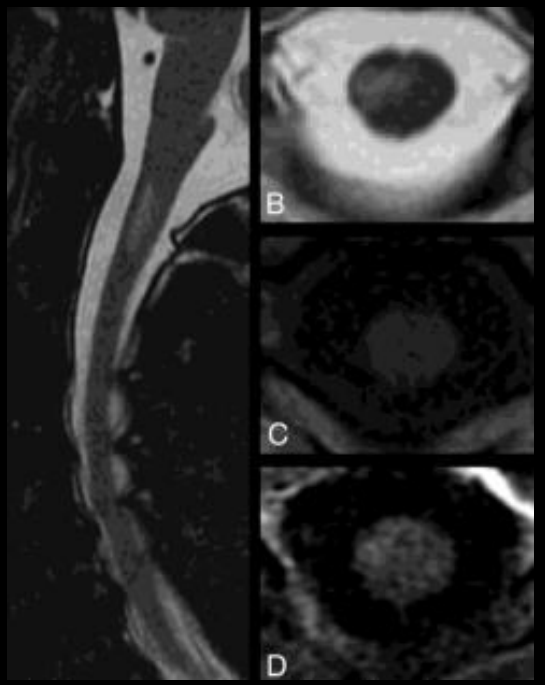
- Interruption de la voie nociceptive au niveau du faisceau spinothalamique dans le cordon antérolatéral à l'origine d'une anesthésie thermoalgique controlatérale



- Technique
  - Percutanée vs chirurgicale
  - Cervicale haute vs thoracique haute







- Résultats
- Efficacité à long terme : 6 mois 75%

  1 an 40%

TABLE 1. Mean, median, minimum, maximum, and standard deviation values of Karnofsky Performance Scale and visual analog scale scores[a]

Cordotomy	Preoperative		Postoperative		*P* value
	Mean ± SD	Median (range)	Mean ± SD	Median (range)	
VAS	7.61 ± 0.61	8 (5–9)	1.29 ± 2.21	0 (0–10)	<0.001
KPS	45.2 ± 14.4	40 (10–80)	65.7 ± 13.4	70 (20–100)	<0.001

 +

- Sous AL chez patient en mauvais EG
- Sous AG technique simple et rapide
- Couvre large territoire
- Réduction des opioïdes
- Suivi simple
- Non couteux

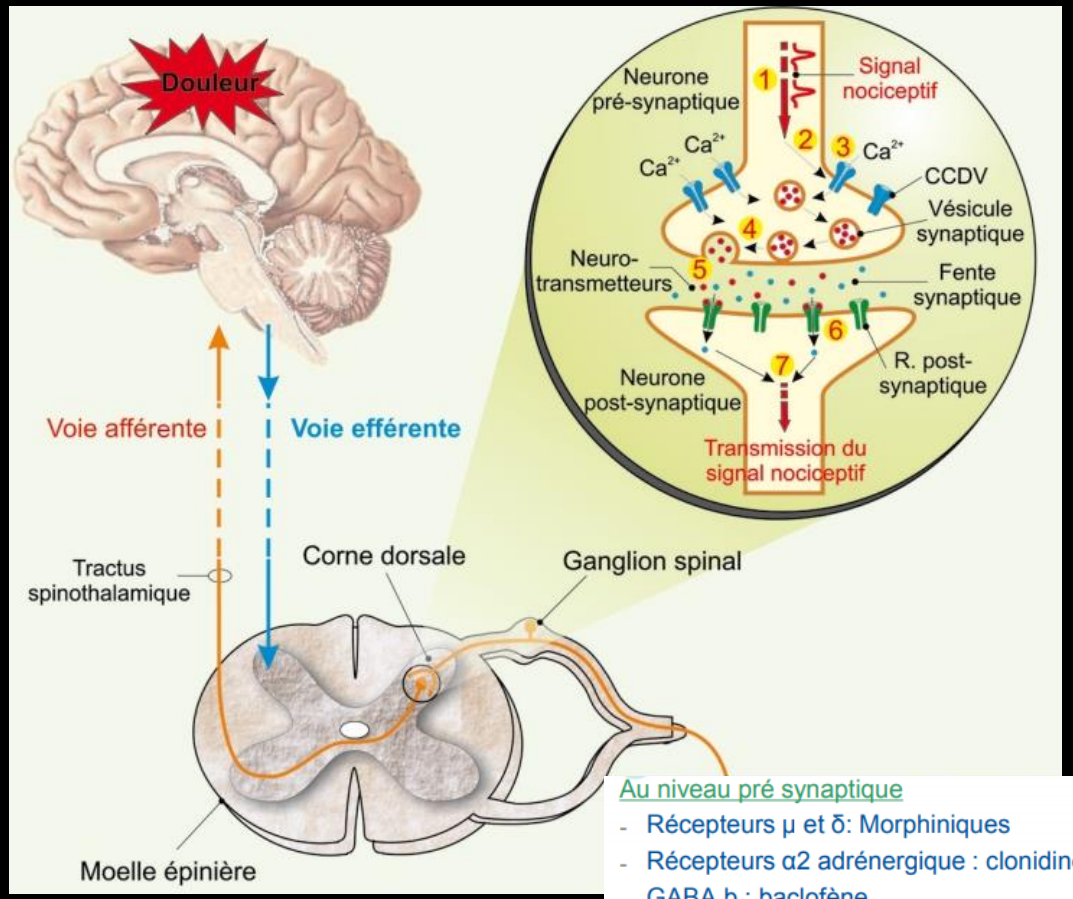
 -

- Technique délicate AL
- Effets temporaires (6 à 18 mois)
- Seulement pour douleur unilatérale
- Induit thermo-analgesie
- Peut induire douleurs neuropathiques secondaires (dysthesies)

Médications intrathécales

- **<u>Principe</u>**

- Distribuer les antalgiques au plus près des récepteurs médullaires pour :
  - diminuer les doses des analgésiques administrés par voie systémique (per os : 300mg → Iv : 100mg → péridural : 10 mg → IT : 1mg)
  - diminuer les effets secondaires liés aux traitements par voie systémique

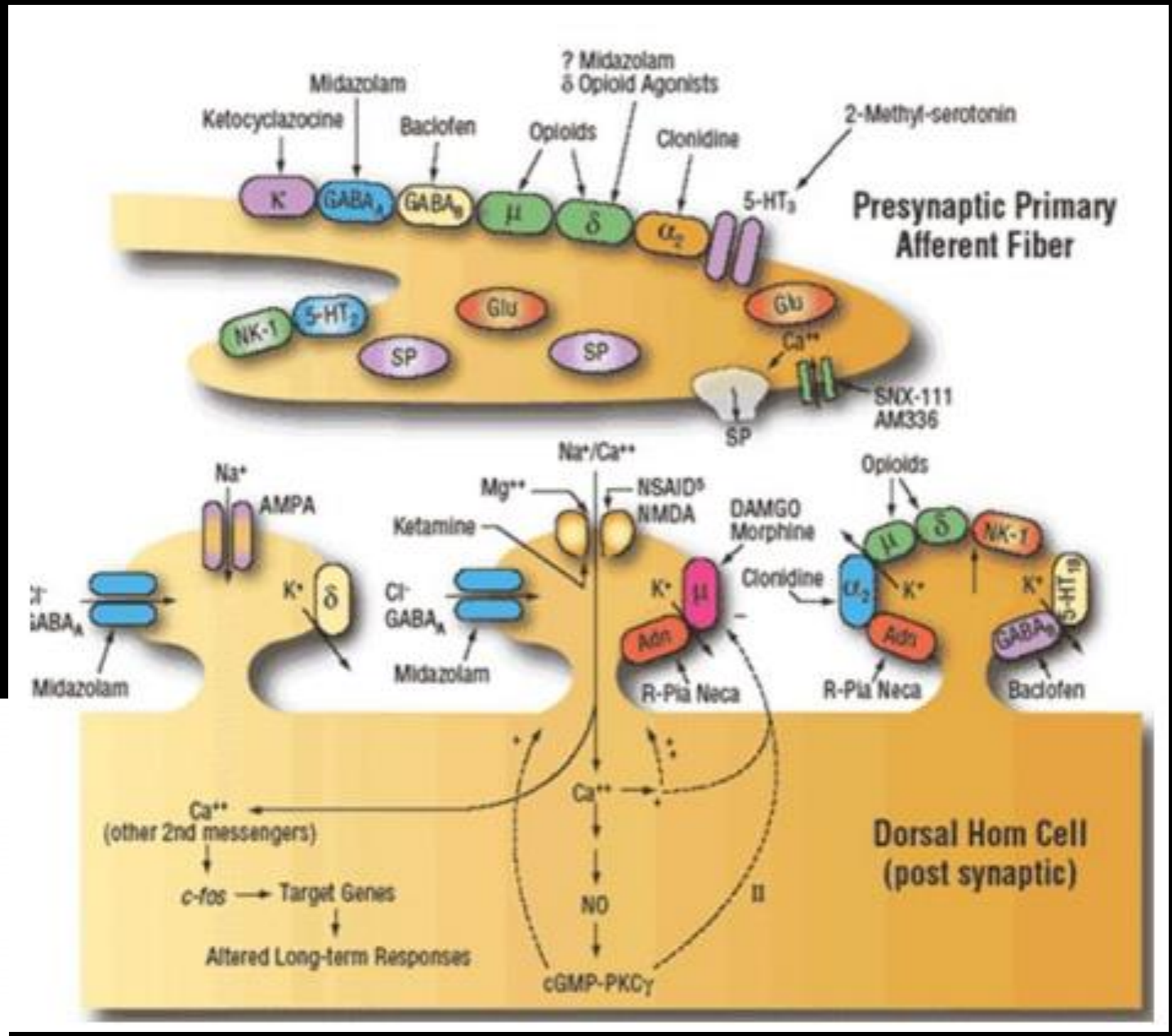


Au niveau pré synaptique

- Récepteurs μ et δ: Morphiniques
- Récepteurs α2 adrénergique : clonidine
- GABA b : baclofène
- Canaux calciques : ziconotide

Au niveau post synaptique

- Récepteurs μ et δ: Morphiniques
- Récepteurs α2 adrénergique : clonidine
- NMDA : kétamine
- Canaux sodiques : Anesthésiques Locaux



Médications intrathécales

- **Indications:**
- Avant tout : validation en RCP +++
- Douleurs nociceptives de cancer (EdV > 3 mois)
  - Chroniques, réfractaires
- Douleurs neuropathiques secondaires à un traumatisme médullaire, avec atteinte des cordons postérieurs

Review Article on Pain Therapy

Page 1 of 10

Narrative review of intrathecal drug delivery (IDD): indications, devices and potential complications

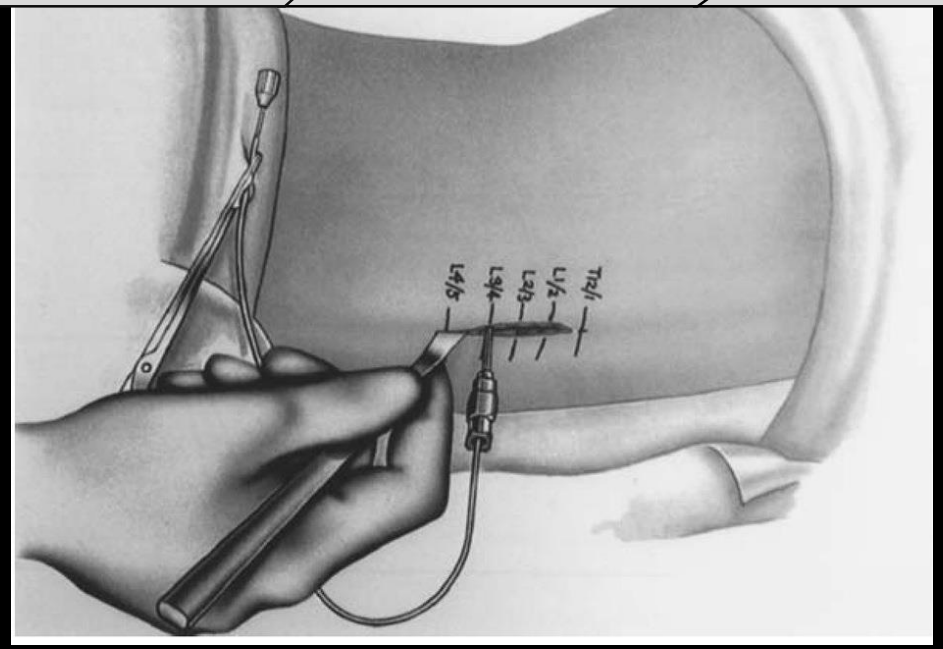
Michele Antonio Capozza, Silvia Triarico, Stefano Mastrangelo, Giorgio Attinà, Palma Maurizi, Antonio Ruggiero

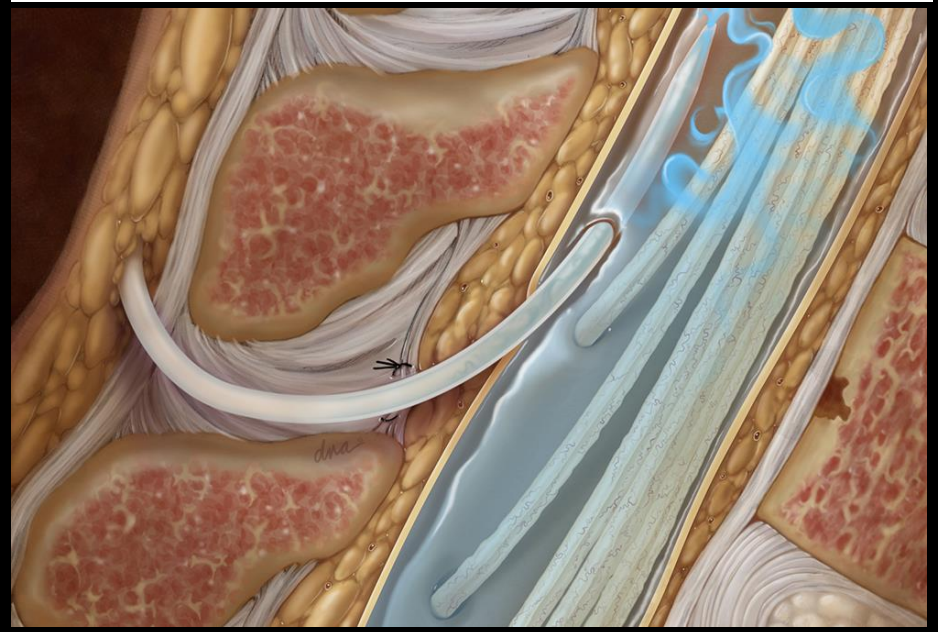
Table 1 Disease indications for IDD (modified by PACC) (2)

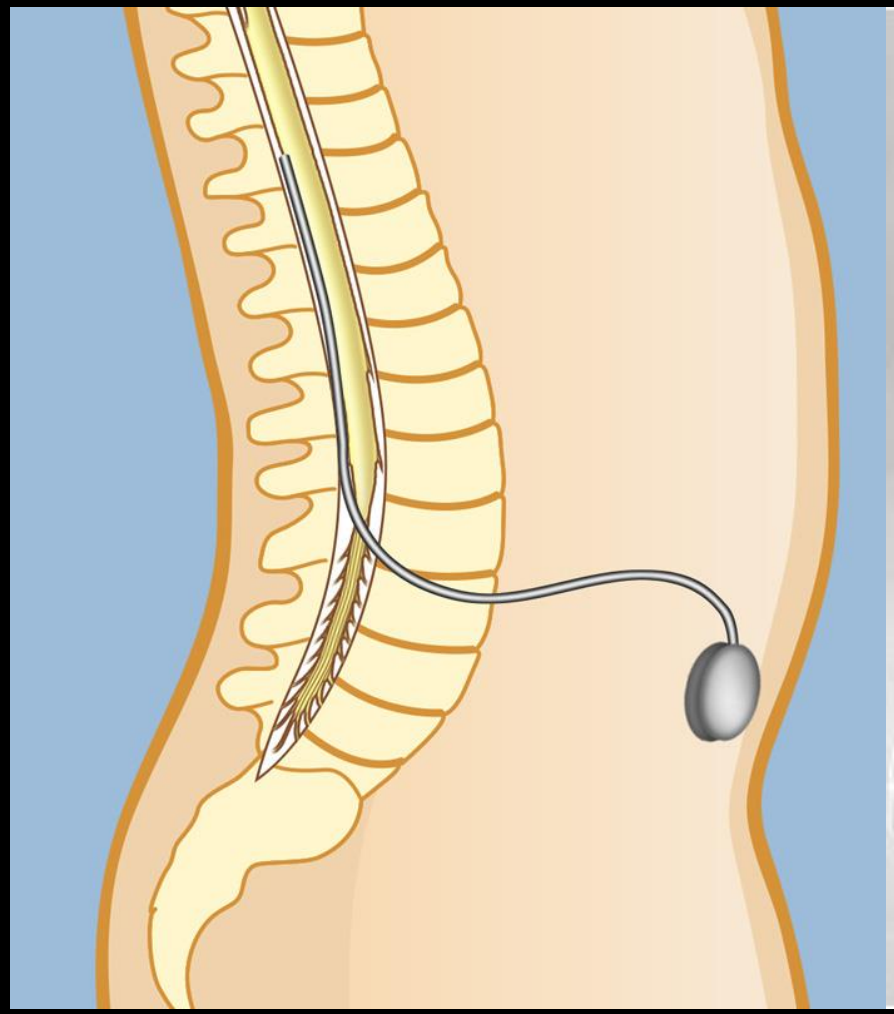
Axial neck or back pain (not a surgical candidate)
Multiple compression fractures
Discogenic pain
Spinal stenosis
Diffuse multiple-level spondylosis
Failed back surgery syndrome
Abdominal/pelvic pain
Visceral
Somatic
Extremity pain
Radicular pain
Joint pain
Complex regional pain syndrome
Trunk pain
Postherpetic neuralgia
Post-thoracotomy syndromes
Cancer pain, direct invasion and chemotherapy-related
Analgesic efficacy with systemic opioid delivery complicated by intolerable side effects

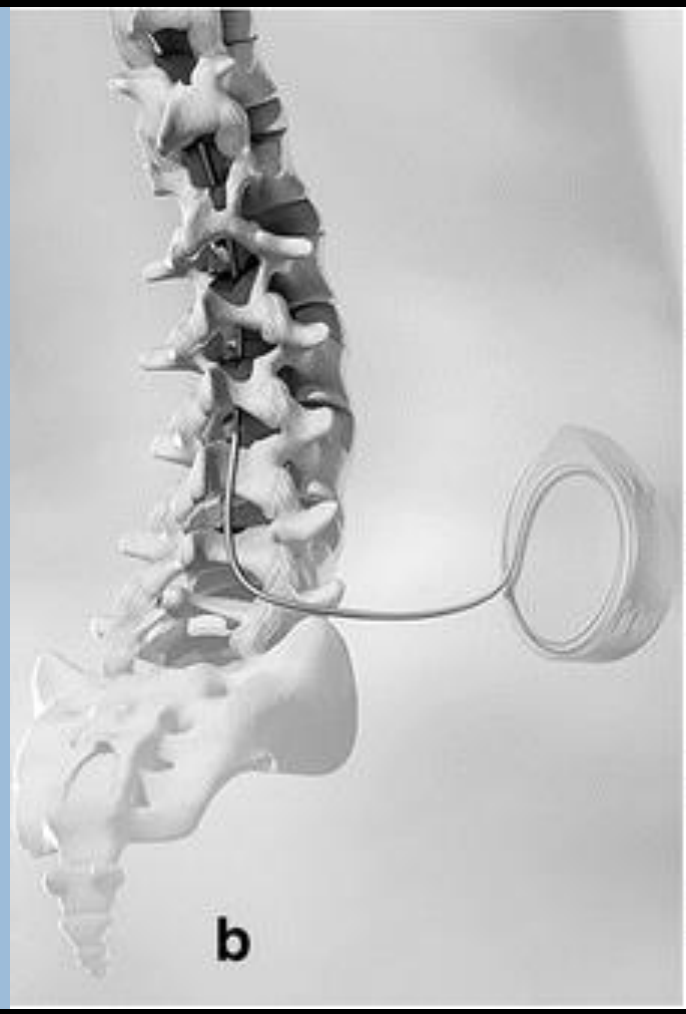
IDD, intrathecal drug delivery; PACC, Polyanalgesic Consensus Conference.

Technique chirurgicale









Morphine

- Actif sur les canaux μ et delta pré et post synaptiques
- Dépresseur respiratoire
- Mais antidote (Naloxone)
- Effets stables dans le temps (1/2 vie IT : 73 et 140 min)
- Effet en 5-10 min
- Mais dépendance
- Et risque de diminution de l'effet antalgique avec le temps
- Surveillance de l'apparition d'effets secondaires

REVIEW

Check for updates

A safety review of approved intrathecal analgesics for chronic pain management

Alan Chalil[a,*], Michael D. Staudt [b,c,*], Tessa A. Harland[d,*], Elizabeth M. Leimer[e], Ravneet Bhullar[f] and Charles E. Argoff[g]

[a]Department of Clinical Neurological Sciences, London Health Sciences Centre, Western University, London, Ontario, Canada; [b]Department of Neurosurgery, Oakland University William Beaumont School of Medicine, Rochester, Michigan, USA; [c]Michigan Head and Spine Institute, Southfield, Michigan, USA; [d]Department of Neurosurgery, Albany Medical College, Albany, New York, USA; [e]Department of Anesthesiology & Perioperative Medicine, Oregon Health and Science University, Portland, Oregon, USA; [f]Department of Anesthesiology, Albany Medical College, Albany, New York, USA; [g]Department of Neurology, Albany Medical College, Albany, New York

Table 1. Drug summary: morphine.

Drug Name	Morphine
Phase	FDA Approved
Indication	Chronic refractory cancer and non-cancer pain
Mechanism of action	μ-opioid receptor agonist
Routes of administration	Intrathecal
Chemical Structure	$C_{17}H_{19}NO_3$
Randomized Controlled Trials	Smith TJ et al. Randomized clinical trial of an implantable drug delivery system compared with comprehensive medical management for refractory cancer pain: impact on pain, drug-related toxicity, and survival. *J Clin Oncol.* 1 October 2002;20 [19]:4040–9. Raphael JH et al. Randomized, double-blind controlled trial by dose reduction of implanted intrathecal morphine delivery in chronic non-cancer pain. *BMJ Open.* 31 July 2013;3 [7]:e003061.

ZICONOTIDE (Prialt)

Table 2. Drug summary: ziconotide.

Drug Name	Ziconotide
Phase	FDA Approved
Indication	Chronic refractory cancer and non-cancer pain
Mechanism of action	Non-opioid calcium channel antagonist
Routes of administration	Intrathecal
Chemical Structure	$C_{102}H_{172}N_{36}O_{32}S_7$
Randomized Controlled Trials	Staats PS et al. Intrathecal ziconotide in the treatment of refractory pain in patients with cancer or AIDS: a randomized controlled trial. *JAMA*. 7 January 2004;291 [1]:63–70 Wallace MS et al. Intrathecal ziconotide in the treatment of chronic nonmalignant pain: a randomized, double-blind, placebo-controlled clinical trial. *Neuromodulation*. 2006 Apr;9 [2]:75–86. Rauck RL et al. A randomized, double-blind, placebo-controlled study of intrathecal ziconotide in adults with severe chronic pain. *J Pain Symptom Manage*. 2006 May;31 [5]:393–406.

- Actif sur les canaux calciques
- Non dépresseur respiratoire
- Effets stables dans le temps
- Demi vie 4h30, pic de perfusion à 5 h
- Pas de toxicité à long terme connue
- Dégradé par les peptidases
- Début à 0,5µg/jour et réadaptation en fonction de l'efficacité et des effets secondaires.
- La dose peut être augmentée par paliers de 0,5µg tous les 3 à 15 jours jusqu'à une dose palier de 1,5 à 2,1µg/J (dose maximale 21µg/j).
- Surveillance de l'apparition d'effets secondaires (Neuro psychiatriques essentiellement)
- L'augmentation lente par posologies faibles a permis de réduire de manière significative les effets secondaires importants et fréquents (89%) observés dans les débuts d'utilisation.

	Morphine	Ropivacaïne Bupivacaïne	Ziconotide
Posologie initiale	Entre 1/50 et 1/100 par rapport à l'IV en mg/jour	6 à 8 mg/jour	0,25 à 0,50 µg/jour
Effets secondaires	• Détresse respiratoire • Rétention Aigue Urinaire : RAU • Œdèmes MI	• RAU • hypoTA • peu de bloc moteur • si bloc ou clonie des membres inférieurs: augmentation trop brutale	• Neuropsy: vertiges, hallucinations, confusion, syndrome dépressif, agressivité
Incrémentation	Quotidienne	Quotidienne	Toutes les 48 à 72H
Stabilité à 30 jours	excellente	excellente	-1%/ jour

Pain Medicine, 20(4), 2019, 784–798
doi: 10.1093/pm/pny132
Advance Access Publication Date: 22 August 2018
Review Article
OXFORD

Intrathecal Therapy for Chronic Pain: A Review of Morphine and Ziconotide as Firstline Options

Timothy R. Deer, MD,* Jason E. Pope, MD,† Michael C. Hanes, MD,‡ and Gladstone C. McDowell II, MD§

*The Center for Pain Relief, Spine and Nerve Centers of The Virginias, Charleston, West Virginia; †Thrive Clinic, Santa Rosa, California; ‡Jacksonville Spine Center, Jacksonville, Florida; §Integrated Pain Solutions, Columbus, Ohio, USA

Correspondence to: Timothy R. Deer, MD, The Center for Pain Relief, The Spine and Nerve Center of the Virginias, 400 Court Street, Ste 100, Charleston, WV, USA 25301. Tel: 304-347-6120; Fax: 304-347-6126; E-mail: doctdeer@aol.com.

Table 6. Advantages and disadvantages/considerations for IT morphine and ziconotide

	Morphine	Ziconotide
Advantages	Extensive safety and efficacy profile for systemic administration Tolerability likely in oral opioid–experienced patients	Efficacy demonstrated in randomized placebo-controlled studies No tolerance or withdrawal; may be discontinued abruptly No harmful effects of overdose No reported cases of granulomas
Disadvantages/ considerations	Risk of serious AEs (e.g., respiratory depression, granulomas) Tolerance may necessitate dose increases; should not be withdrawn abruptly Development of opioid-induced hyperalgesia	Contraindicated in patients with a history of psychosis Risk of neurologic AEs (e.g., dizziness, confused state) May cause elevations in creatinine kinase

AE = adverse event; CNS = central nervous system; IT = intrathecal.

Pain Medicine, 20(4), 2019, 784–798
doi: 10.1093/pm/pny132
Advance Access Publication Date: 22 August 2018
Review Article

Intrathecal Therapy for Chronic Pain: A Review of Morphine and Ziconotide as Firstline Options

Timothy R. Deer, MD,* Jason E. Pope, MD,† Michael C. Hanes, MD,‡ and Gladstone C. McDowell II, MD§

*The Center for Pain Relief, Spine and Nerve Centers of The Virginias, Charleston, West Virginia; †Thrive Clinic, Santa Rosa, California; ‡Jacksonville Spine Center, Jacksonville, Florida; §Integrated Pain Solutions, Columbus, Ohio, USA

Correspondence to: Timothy R. Deer, MD, The Center for Pain Relief, The Spine and Nerve Center of the Virginias, 400 Court Street, Ste 100, Charleston, WV, USA 25301. Tel: 304-347-6120; Fax: 304-347-6126; E-mail: doctdeer@aol.com.

Table 2. PACC 2016 recommendations for use of IT opioids and ziconotide in cancer and noncancer pain [9,40]

Statement	USPSTF Evidence Level*	USPSTF Recommendation Grade†	PACC Consensus Level‡
IT therapy with opioids should be utilized for active cancer-related pain	I	A	Strong
IT therapy with ziconotide should be utilized for active cancer-related pain	I	A	Strong
IT therapy with opioids should be utilized for active noncancer pain	III	B	Strong
IT therapy with ziconotide should be utilized for active noncancer pain	I	A	Strong

Figure adapted with permission from: Deer et al, The Polyanalgesic Consensus Conference (PACC): Recommendations on intrathecal drug infusion systems best practices and guidelines. Neuromodulation 2017;20(2):96–132 [9]. Additional data reprinted from: Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: A review of the process. Am J Prev Med 2001;20(3 Suppl):21–35 [40].

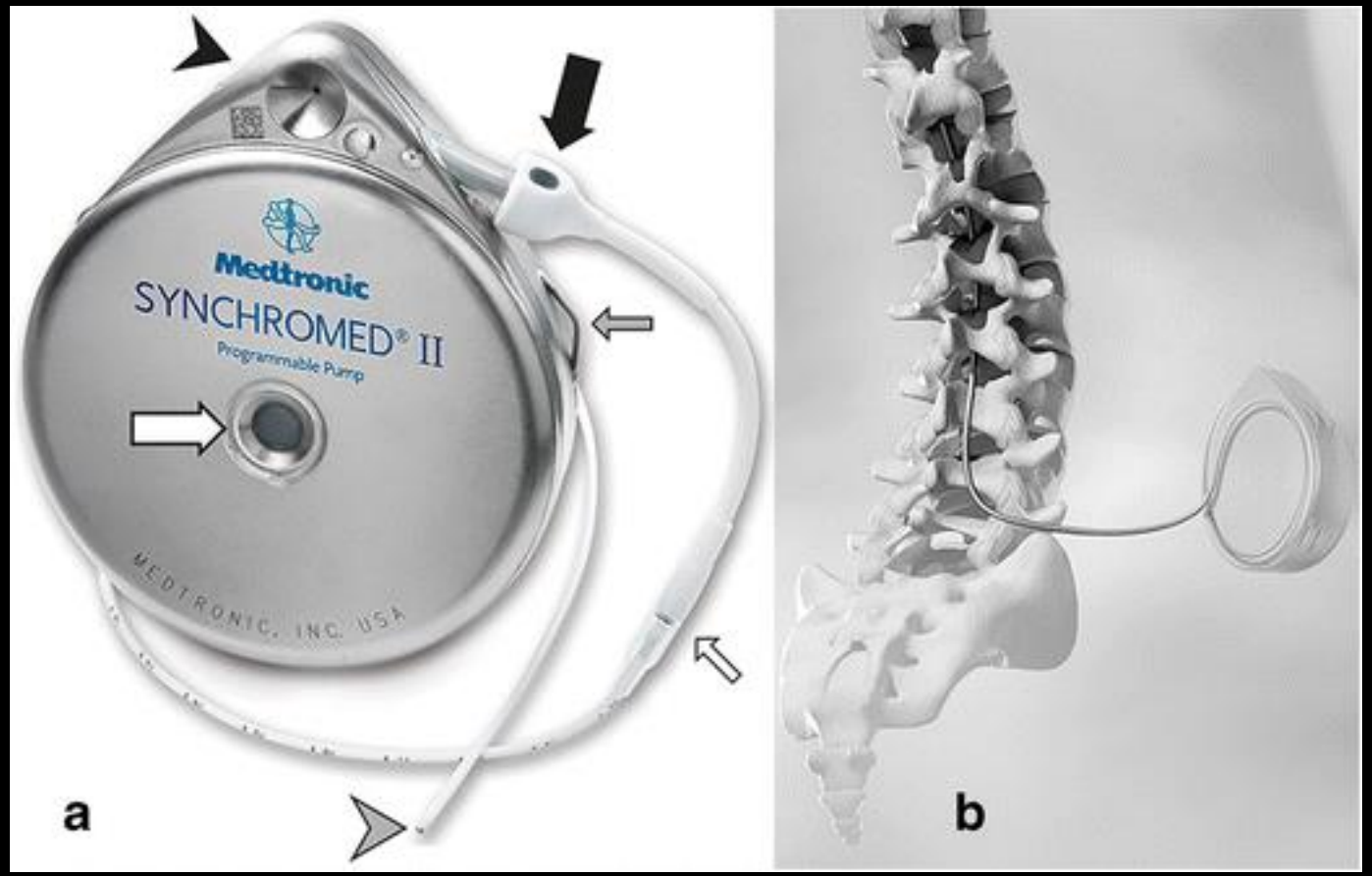
IT = intrathecal; PACC = Polyanalgesic Consensus Conference; USPSTF = United States Preventive Services Task Force.

*Evidence grades: I, at least one controlled and randomized clinical trial, properly designed; II-1, well-designed, controlled, nonrandomized clinical trials; II-2, cohort or case studies and well-designed controls, preferably multicenter; II-3, multiple series compared over time, with or without intervention and surprising results in noncontrolled experiences; III, clinical experience–based opinions, descriptive studies, clinical observations, or reports of expert committees.

†Recommendation grades: A, extremely recommendable (good evidence that the measure is effective and benefits outweigh the harms); B, recommendable (at least moderate evidence that the measure is effective and benefits exceed harms); C, neither recommendable nor inadvisable (at least moderate evidence that the measure is effective, but benefits are similar to harms and a general recommendation cannot be justified); D, inadvisable (at least moderate evidence that the measure is ineffective or that the harms exceed the benefits); I, insufficient, low-quality, or contradictory evidence (the balance between benefit and harms cannot be determined).

‡Level of consensus among members of the PACC: strong, >80% consensus; moderate, 50% to 79% consensus; weak, <49% consensus.

Complications



- 1. Mécaniques
- 2. Médicamenteuses
  - Sur-dosage
  - Sous dosage
- 3. Infectieuses

Résultats

- D’après les recommandations SFAR-SFETD,
- « toutes les études rapportent des résultats positifs, avec une réduction des scores de douleurs.
- 4 études sur 13 montrent une amélioration de la qualité de vie,
- 4 une amélioration fonctionnelle,
- 8 la diminution des traitements systémiques
- 2 une diminution du nombre des consultations ».

Résultats : Pain and **Cancer** (morphine IT)

Pain Medicine, 20(4), 2019, 784–798
doi: 10.1093/pm/pny132
Advance Access Publication Date: 22 August 2018
Review Article

Intrathecal Therapy for Chronic Pain: A Review of Morphine and Ziconotide as Firstline Options

Timothy R. Deer, MD,* Jason E. Pope, MD,† Michael C. Hanes, MD,‡ and Gladstone C. McDowell II, MD§

*The Center for Pain Relief, Spine and Nerve Centers of The Virginias, Charleston, West Virginia; †Thrive Clinic, Santa Rosa, California; ‡Jacksonville Spine Center, Jacksonville, Florida; §Integrated Pain Solutions, Columbus, Ohio, USA

Correspondence to: Timothy R. Deer, MD, The Center for Pain Relief, The Spine and Nerve Center of the Virginias, 400 Court Street, Ste 100, Charleston, WV, USA 25301. Tel: 304-347-6120; Fax: 304-347-6126; E-mail: doctdeer@aol.com.

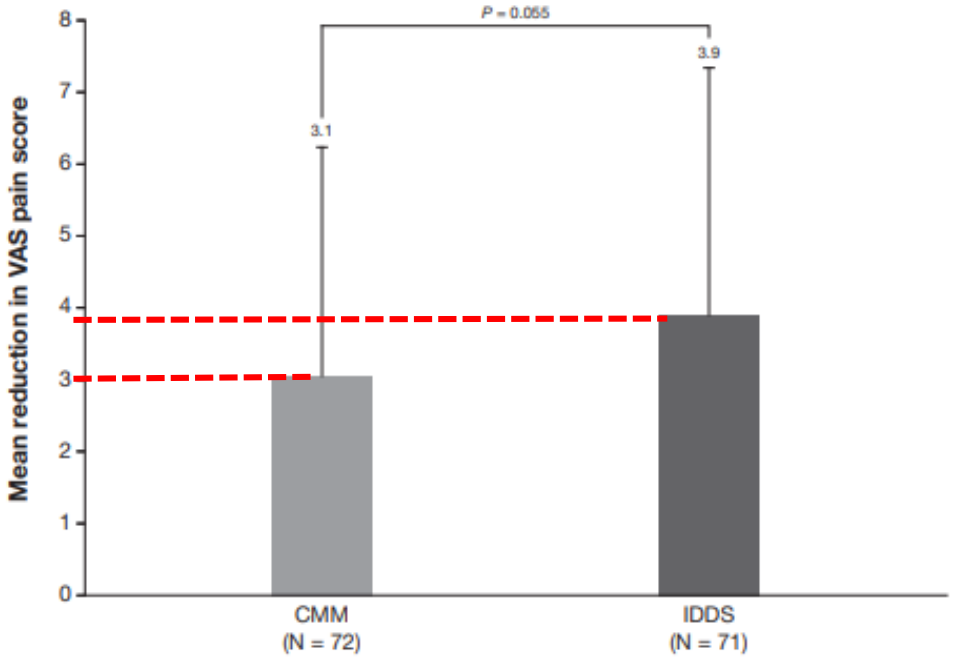


Figure 1. Pain reduction with intrathecal (IT) opioids as the first agent in pump in patients with cancer pain [29]. Patients with cancer pain received comprehensive medical management (CMM; all pain therapy except spinally administered medications, cordotomy, or other similar neurosurgical interventions) or IT morphine or hydromorphone therapy for four weeks. After four weeks of treatment, patients who received IT opioids had a nonsignificantly greater reduction in pain, as measured on a continuous visual analog scale ranging from 0 (no pain) to 10 (worst pain imaginable), than those who received CMM. Figure created with data from: Smith TJ, Staats PS, Deer T, et al. Randomized clinical trial of an implantable drug delivery system compared with comprehensive medical management for refractory cancer pain: Impact on pain, drug-related toxicity, and survival. J Clin Oncol 2002;20(19):4040–9 [29]. CMM = comprehensive medical management; IDDS = implantable drug delivery system; VAS = visual analog scale.

Résultats (morphine)

- Depuis les premiers essais cliniques chez l'homme à la fin des années 1970, de nombreux travaux ont été publiés pour évaluer l'analgésie intrathécale en cancérologie.
- Un seul essai multicentrique randomisé a mis en évidence une diminution de plus de 20 % de la douleur à un mois chez 84,5% des patients dans le groupe traité par un dispositif intrathécal contre 70 % dans le groupe témoin. Cette étude retrouve également une diminution de 50 % de l'indice de toxicité du traitement antalgique dans le groupe intrathécal par rapport au groupe témoin.

Si l’on résume …

Intérêt des PES +++

Après échec des techniques médicales bien tenues

- Douleurs lombaires + radiculaires post arthrodèse : SCS
- Douleurs radiculaires : SCS
- Douleurs sur SC injury (ischémie médullaire) : SCS, DREZ, Ziconotide IT
- Douleurs du membre fantôme : SCS, DREZ
- Douleurs sur Avulsion plexus : DREZ
- Douleurs post-zostériennes : SCS, DREZ
- Douleurs cancéreuses localisées (Pancoast Tobias) : DREZ
- Douleurs cancéreuses diffuses : Morphine IT
- Douleurs cancéreuses unilatérales : Cordotomie
- Douleurs AIDS : Ziconotide IT