Analgésie intrathécale dans les douleurs neuropathiques du cancer

Denis Dupoiron

Classification des douleurs neuropathiques en cancérologie

Evolution du Cancer

- Compression des racines
- Plexopathies
- compression/ infiltration des nerfs
- Compression médullaires
- Méningites carcinomateuses
- Neuropathies paranéoplasiques

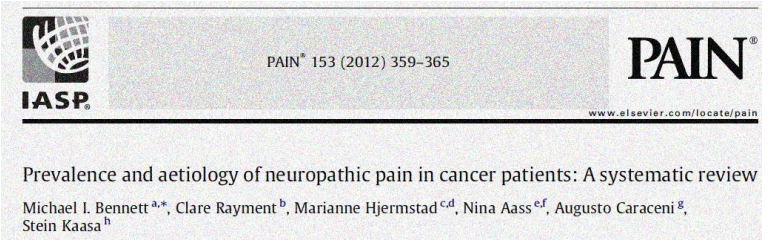
induites par le traitement

- Post chirurgicales
- Post radiothérapie
- Post chimiothérapies(CIPN)

associées au cancer

- Varicella Zoster Virus

Global Prevalence of Neuropathic Pain in cancer: Review of Published studies



- M . Bennet (2012) [1]:
  - 22 studies
  - 11063 patients
- Prevalence
  - ≈ 20 % of patients : pure neuropathic pain
  - ≈ 40 % of patients with Mixed pain
  - ≈ 40 à 60% of Patients with partial relief with standard treatment
- Etiology
  - reported in for 4 studies
  - 64% the pain was caused by cancer
  - 20% caused by a treatment of cancer
  - 3,5 % associated with cancer

- A Roberto (2015)[2] :
  - 29 studies
- Prevalence
  - 31.2 %
  - studies based in palliative care : 33.3%
  - Only thirteen studies reported the use of a diagnostic test (DN4)

1. Bennett MI, Rayment C, Hjermstad M, Aass N, Caraceni A, Kaasa S. Prevalence and aetiology of neuropathic pain in cancer patients: A systematic review. *Pain* 2012;153:359-365.
2. Roberto A, Deandrea S, Greco MT et al. Prevalence of neuropathic pain in cancer patients: Pooled estimates from a systematic review of published literature and results from a survey conducted in 50 italian palliative care centers. *J Pain Symptom Manage* 2016;51:1091-1102 e4.

Traitements

Orale

Antidépresseurs
- IRSNA
- Imipraminiques

Anticonvulsivants
- Anti-épileptiques 1ère et 2ème générations

Anesthésiques Inhibiteurs des récepteurs NMDA

Opioïdes forts

Locaux

ALR amino-amide bloquant des canaux sodique

ALR Agonistes TRPV1 issus du piment

Neuromodulation

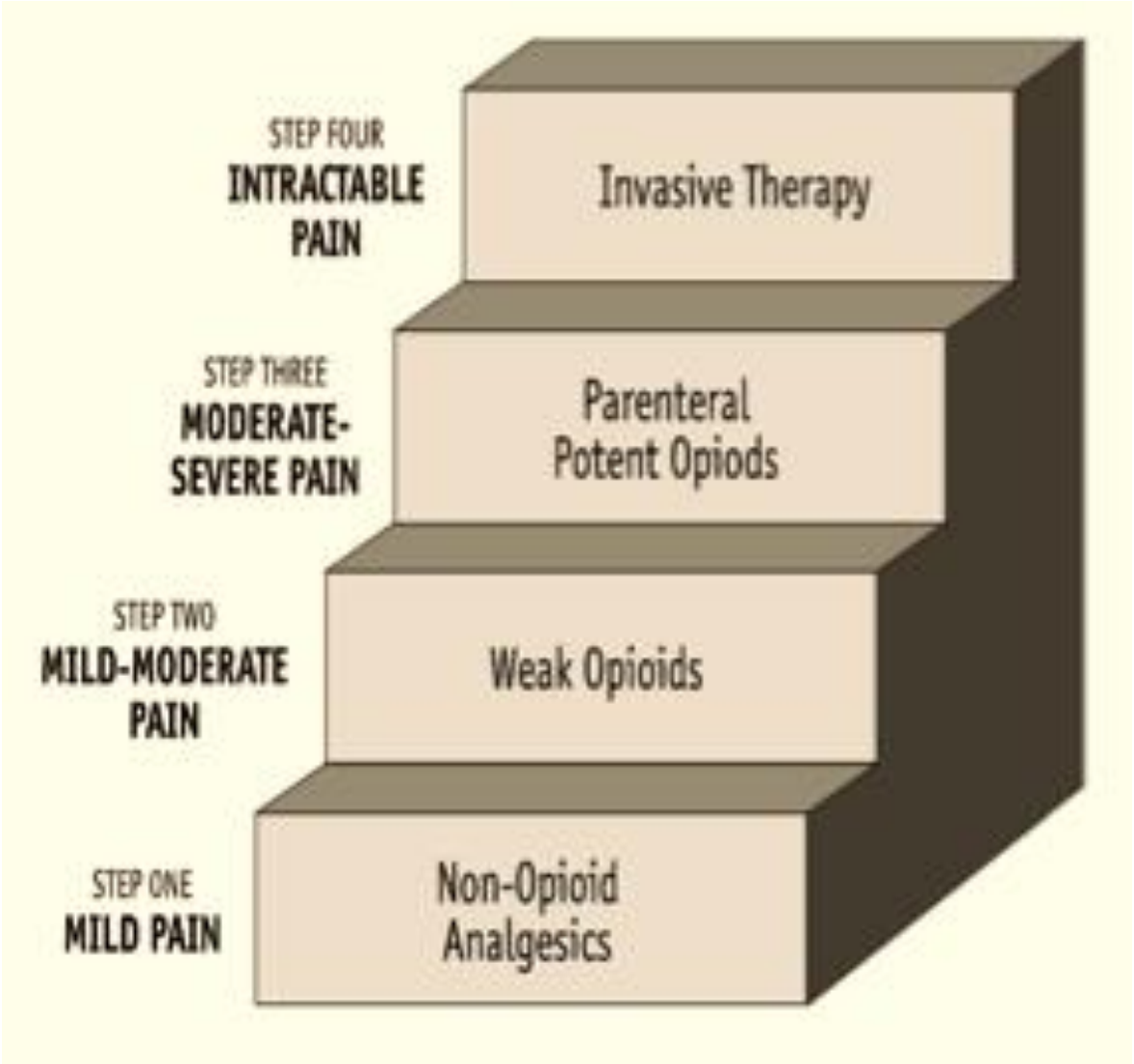
Stimulation médullaire

Blocs lytiques

Intrathecal

Douleurs réfractaires : Niveau IV ?

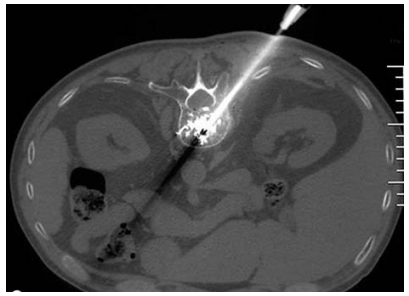
- **Douleurs réfractaires**
  - Persistantes malgré un TTT bien conduit
  - Respect de l'échelle
  - rotation des opioïdes
  - Doses > 300mg/j E.M.O.
- **Effets indésirables insupportables**
  - Somnolence
  - Constipation
  - nausées….
- **Prévalence**
  - Meuser :2001(1)
  - 15 % de douleurs rebelles
- **Proposition d'un niveau 4 ?**
  - Rafael Miguel 2000 (2)
  - Antalgie : techniques interventionnelles

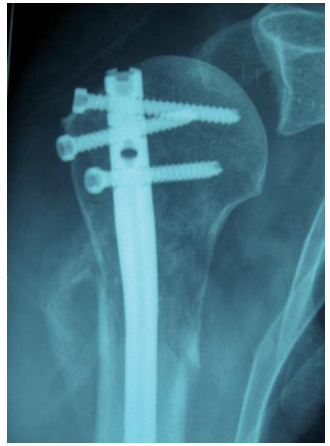


(1) Meuser T,, et al: Symptoms during cancer pain treatment following WHO-guidelines; a longitudinal follow-up study of symptom prevalence, severity and etiology. *Pain , 2001, 93 247-257*
(2) Rafael Miguel : Interventional treatment of cancer pain: The fourth step in the WHO analgesic ladder? *Cancer Control 7,2 :149-156,2000*

Techniques interventionnelles

- **Radiologie**
  - Alcoolisations
  - Radiofréquence
  - Cimentoplasties
- **Radiothérapie**
  - Métaboliques
  - Ciblées
- **Chirurgie**
  - Stabilisation
  - Décompression
  - Neurochirurgie
- **Analgésie spinale (2%) (1)**
  - Péridurales
  - Intrathécales





(1) Epidural and Intrathecal Analgesia Is Effective in Treating Refractory Cancer Pain
Allen W. Burton, Arun Rajagopal, Hemant N. Shah, MD,* Tito Mendoza, ,†Charles Cleeland,, Samuel J. Hassenbusch III,,‡ and James F. Arens,
Pain Medecine 2005, 3 , 2004 239 -247

Literature review

Table 3. Summary of recommendations for addressing pain in advanced cancer patients.

	Strength of evidence
Do	
1. Screen for pain	Strong
2. Assess the components of the pain (e.g. neuropathic, nociceptive, inflammatory)	Tentative
3. Agree upon a tailored pain management plan	
(a) Treat moderate or severe pain with a strong opioid, such as morphine	Strong
(b) Consider opioid switching	Moderate
(c) Consider epidural or intrathecal administration of opioids	Moderate
(d) Treat metastatic bone pain with radiotherapy and/or bisphosphonates	Strong
(e) Support patients to use self-management strategies	Strong
(f) Physiotherapy-based interventions	Tentative
(g) Non-pharmacological approaches, for example, music therapy	Tentative
4. Regularly review and evaluate cancer pain treatment outcomes	Moderate
Do not	
1. Routinely use oral paracetamol to treat moderate or severe pain in patients on strong opioids	Moderate
2. Routinely use weak opioids such as codeine	Moderate
3. Routinely use ketamine	Moderate
4. Routinely use intravenous lidocaine	Moderate
5. Use cannabis-based medicines	Strong
Don't know if there is benefit of	
1. Non-steroidal anti-inflammatory drugs	
2. Anti-convulsants, anti-depressants	
3. Corticosteroids	
4. Other anaesthetic interventions, such as coeliac plexus block and spinal cord stimulation	
5. Acupuncture, massage	
6. Transcutaneous electrical nerve stimulation	

Chapman EJ, Edwards Z, Boland JW, Maddocks M, Fettes L, Malia C, et al. Practice review: Evidence-based and effective management of pain in patients with advanced cancer. Palliat Med. 2020:269216319896955. Epub 2020/01/26. doi: 10.1177/0269216319896955. PubMed PMID: 31980005.

Les Règles de L'OMS

The WHO ladder conference 1986- 1996[1]

- Suivre les 3 étapes

The WHO 2019 guidelines update[2]

- L'echelle n'est plus utile en pratique clinique
- Aucune recommendation medicamenteuses sur les DN
- **Opioïdes en Première ligne**
- **Pas de place pour les traitements interventionnels**

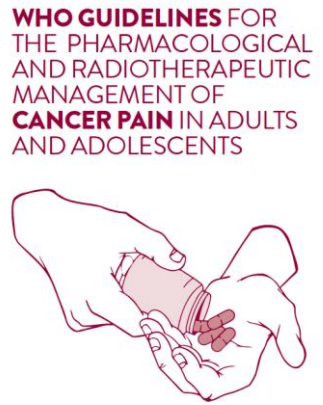


Figure A1.1. The three-step analgesic ladder

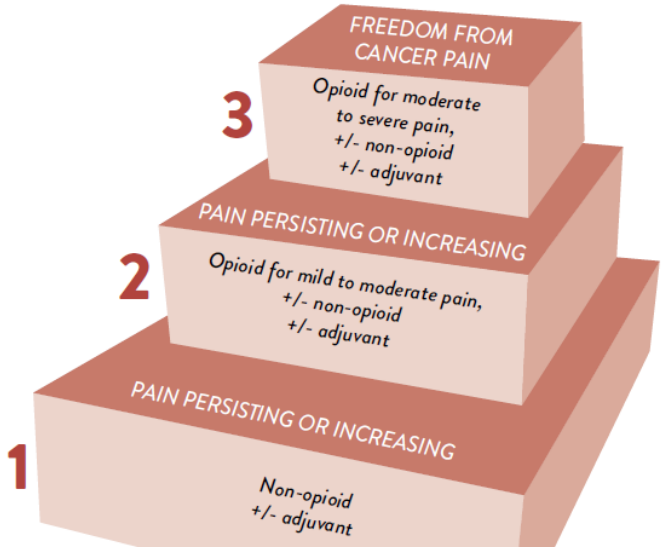


Figure from WHO Guidelines 2019.[2]

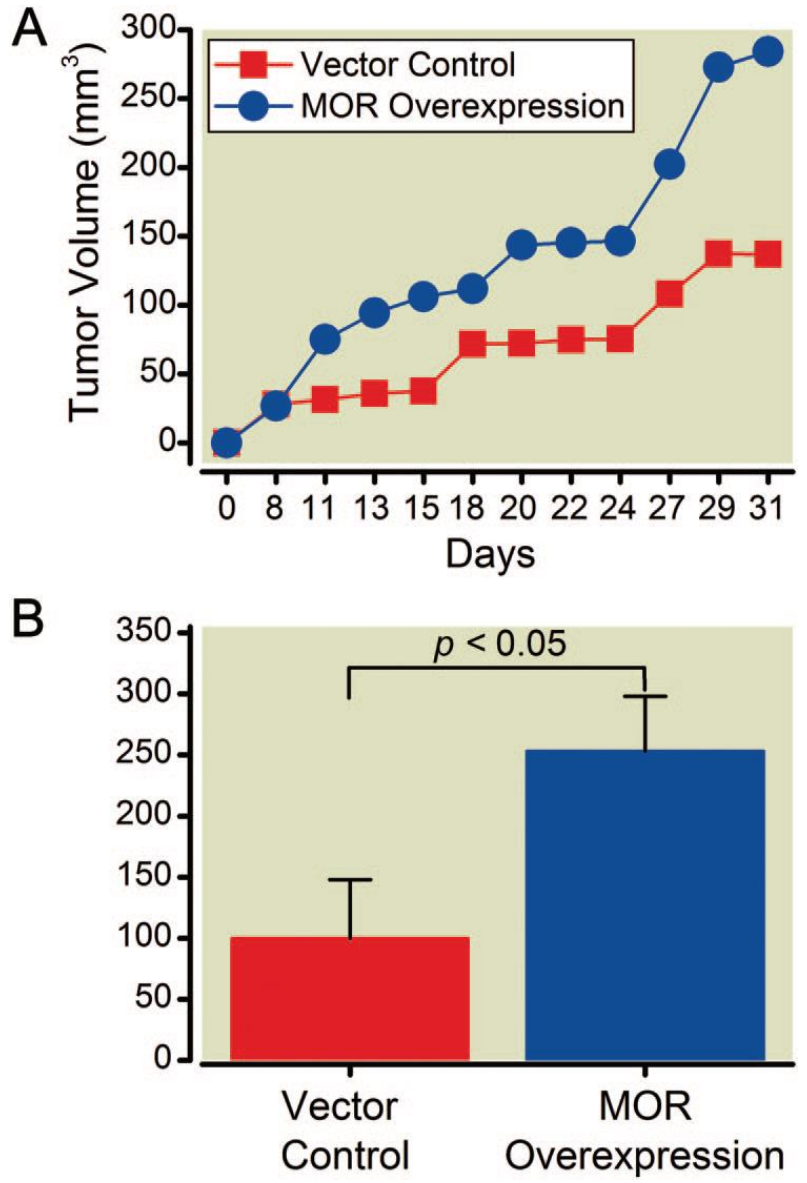
WHO, World Health Organization.
1. World Health Organization. WHO's Pain Ladder. 1986; 2. World Health Organization. WHO Guidelines for the pharmacological and radiotherapeutic management of cancer pain in adults and adolescents. 2019;

In Vitro

Overexpression of the μ-Opioid Receptor in Human Non-Small Cell Lung Cancer Promotes Akt and mTOR Activation, Tumor Growth, and Metastasis

Frances E. Lennon, Ph.D.,* Tamara Mirzapoiazova, M.D., Ph.D.,† Bolot Mambetsariev, Ph.D.,† Ravi Salgia, M.D., Ph.D.,‡ Jonathan Moss, M.D., Ph.D.,§ Patrick A. Singleton, Ph.D.‖

- Overexpression of μ-opioid receptors in a human non-small cell lung cancer cell line increased *in vitro* and *in vivo* measures of tumor growth and metastasis
- These findings further support the role of μ-opioid receptor activation in tumor progression, and suggest both therapeutic and diagnostic opportunities



Lennon, F.E., et al., Overexpression of the mu-opioid receptor in human non-small cell lung cancer promotes Akt and mTOR activation, tumor growth, and metastasis. Anesthesiology, 2012. 116(4): p. 857-67

HAUTE AUTORITÉ DE SANTÉ

Antalgie des douleurs rebelles et pratiques sédatives chez l'adulte : prise en charge médicamenteuse en situations palliatives jusqu'en fin de vie

2020

Indications

L'analgésie intrathécale est recommandée chez les patients en situation palliative ayant des douleurs rebelles, lorsqu'un syndrome douloureux n'est pas contrôlé par une équivalence de l'ordre de 300 mg de morphine *per os,* ou chez les patients présentant des effets indésirables graves des antalgiques (*accord d'experts*).

Dans certains cancers, notamment les cancers pelviens, du pancréas et le syndrome de Pancoast-Tobias, l'antalgie intrathécale doit être envisagée précocement dans l'optique d'améliorer la qualité de vie.

PACC 2016

INTRATHECAL THERAPY IN NEUROPATHIC AND NOCICEPTIVE PAIN STATES

Table 12. Cancer or Other Terminal Condition-Related Pain With Localized Nociceptive or Neuropathic Pain.

Line 1A	Ziconotide			Morphine		
Line 1B	Fentanyl			Morphine or fentanyl + bupivacaine		
Line 2	Hydromorphone	Hydromorphone + bupivacaine		Hydromorphone or fentanyl or morphine + clonidine	Morphine or hydromorphone or fentanyl + ziconotide	
Line 3	Hydromorphone or morphine or fentanyl + bupivacaine + clonidine	Ziconotide + bupivacaine		Ziconotide + clonidine	Hydromorphone or morphine or fentanyl + bupivacaine + ziconotide	Sufentanil
Line 4	Sufentanil + ziconotide	Sufentanil + bupivacaine	Baclofen	Sufentanil + clonidine	Bupivacaine + clonidine + ziconotide	Bupivacaine + clonidine
Line 5	Sufentanil + bupivacaine + clonidine					
Line 6	Opioid* + bupivacaine + clonidine + adjuvants†					

*Opioid (all known intrathecal opioids).
†Adjuvants include midazolam, ketamine, octreotide.

PACC 2024

The Polyanalgesic Consensus Conference (PACC)®: Updates on Clinical Pharmacology and Comorbidity Management in Intrathecal Drug Delivery for Cancer Pain

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Table 3. Cancer Pain Treatment in a Patient with Limited Life Expectancy.

Line 1	Morphine or hydromorphone ± bupivacaine		Fentanyl ± bupivacaine			
Line 2	Morphine or hydromorphone or fentanyl + low-dose ziconotide ± bupivacaine					
Line 3	Hydromorphone or morphine or fentanyl + clonidine ± bupivacaine	Ziconotide + bupivacaine	Ziconotide + clonidine		Clonidine as secondary or tertiary adjuvant	Sufentanil as primary or secondary (along with morphine or hydromorphone) opioid
Line 4	Opioid + ziconotide	Sufentanil + bupivacaine	Baclofen as secondary or tertiary adjuvant	Sufentanil + clonidine	Bupivacaine + clonidine + ziconotide	Bupivacaine + clonidine
Line 5	Refractory pain – consider complex regimen including combination of multiple drug classes					

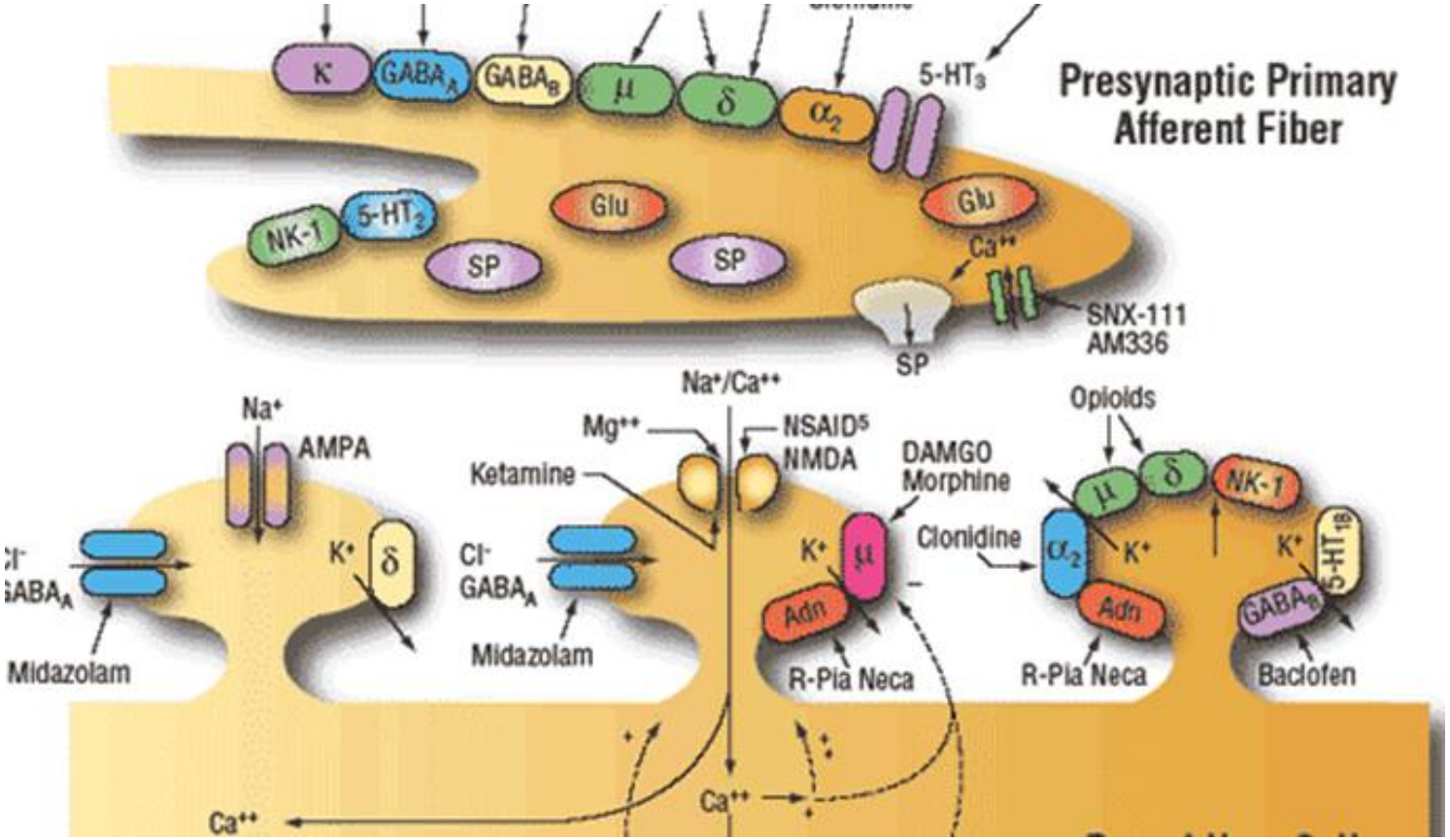
In a patient with limited life expectancy (<six months), aggressive dose titration is implemented to obtain satisfactory analgesia. Regimen selection also should be based on pain characteristics, catheter tip location, and the individual drug factors presented in Table 5.

Table 4. Chronic Cancer Pain Treatment With Favorable Prognosis (Six Months to Years).

Line 1	Morphine or hydromorphone or fentanyl ± bupivacaine		Ziconotide	
Line 2	Hydromorphone or morphine or fentanyl + bupivacaine + ziconotide		Hydromorphone or morphine or fentanyl + clonidine	
Line 3	Hydromorphone or morphine or fentanyl + bupivacaine + clonidine	Ziconotide + bupivacaine	Ziconotide + clonidine	Sufentanil
Line 4	Refractory pain – consider complex regimen including combination of multiple drug classes			

Emphasis is on attaining improvement in pain and function, while considering durability and safety of therapy for a long period. Regimen selection should also be based on the patient's condition and individual drug factors.

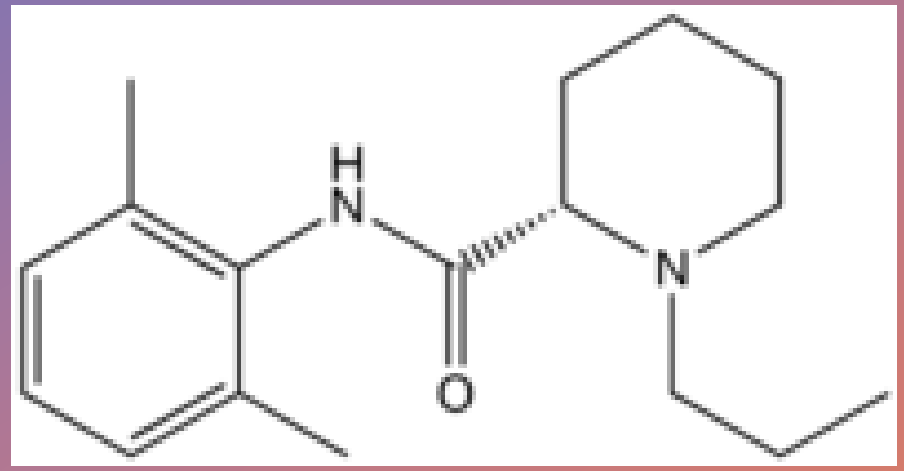
Modulation médullaire du signal nociceptif

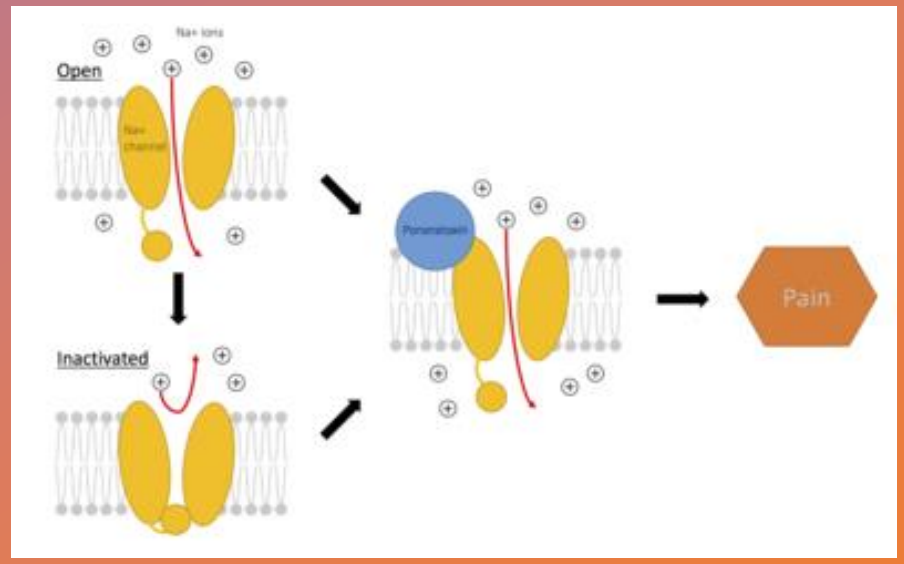


- **Pré synaptiques**
  - Morphiniques : μ et δ
  - α2 adrénergique : clonidine
  - GABA a :Midazolam
  - GABA b : Baclofène
  - Canaux Ca^{++} : ziconotide
- **Post synaptiques**
  - α2 adrénergique :Clonidine
  - GABA a : Midazolam
  - Morphinique : μ et δ
  - NMDA : Kétamine
  - Canaux sodiques : Anest. Locaux

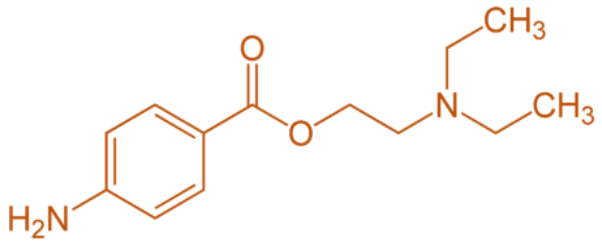
07/11/2024

Les Anesthésiques locaux





Les anesthésiques locaux mécanisme d'action



Blocage des canaux sodiques

- Agissent sur les douleurs nociceptives et neuropathiques

Action synergique avec les morphiniques

- Du pen 92 (1):
  - Péridural 61 patients
- Van Dongen(2) :
  - Intrathecal 17 patients

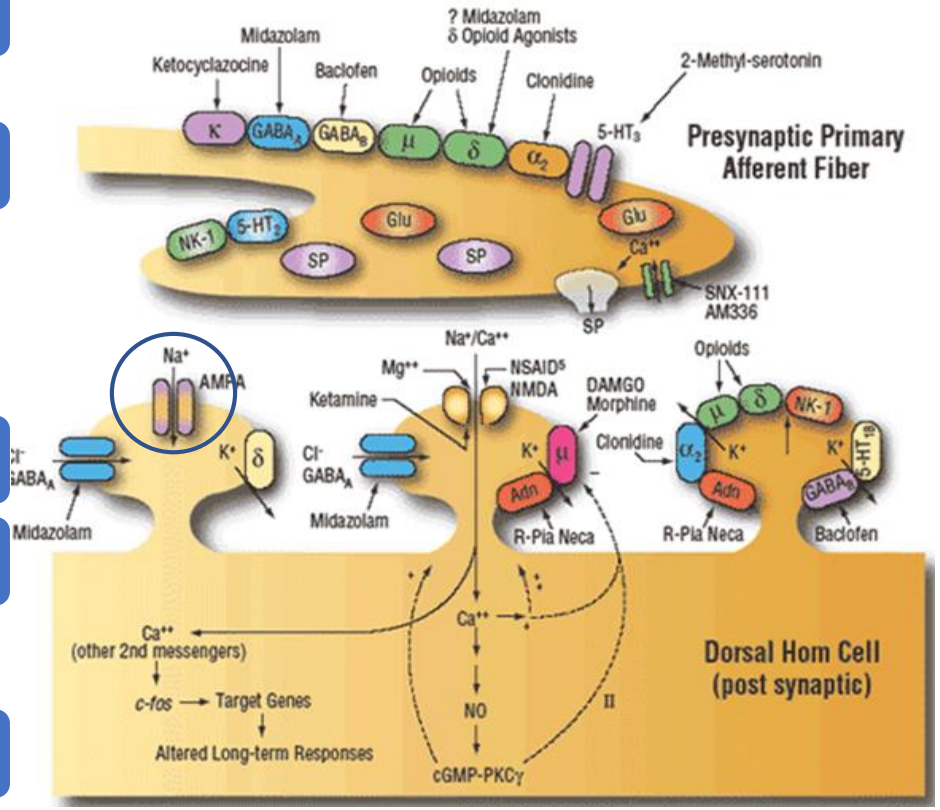
Nombreuses études cliniques

Action Rapide

- Péridurale ≈ 15mn
- Intrathécal ≈ 3mn

Stabilité des préparations

- >40 jours



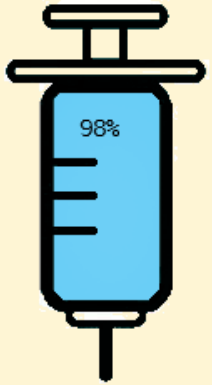
(1)Chronic epidural bupivacaine-opioid infusion in intractable cancer pain Stuart L. Du Pen 'Yaks,E',v an D. Kharasch d,' and Alexander W. Krembs b Pain, 49 (1992) 293- 300
(2)Long-term intrathecal infusion of morphine and morphine/bupivacaine mixtures in the treatment of cancer pain: a retrospective analysis of 51 casesR.T.M. Van Dongen, B. Pain, 55 (1993) 119-123

Problème des concentrations d'A.L. ?

Ropivacaïne : 10mg/ml

Produit	Dose /j	
Morphine 50mg/ml	8	mg/j
Naropeine 10mg/ml	18	mg/j
Prialt 100µg/ml	0,5	µg/j

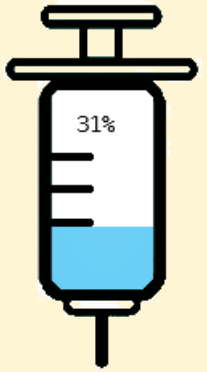
Durée min 12.5 jour



Bupivacaïne : 40mg/ml

Produit	Dose /j	
Bupivacaine 40mg/ml	18	mg/j
Morphine 50mg/ml	8	mg/j
Prialt 100µg/ml	0,5	µg/j

Durée min 21.74 jour



Intervalle de remplissage multiplié par 2ou 3 avec la bupivacaïne concentrée !

Bupivacaine en France

- ATU depuis juillet 2020
- Utilisation pour les doses élevées intrathécales
- Hospitalisation pour le Switch
- Monitoring
  - Respiratoire
  - Neuro
  - P.A
- Suivi jusqu'au 2eme remplissage
- Etude Medico Economique

Neuromodulation: Technology at the Neural Interface

Received: April 2, 2021 Revised: April 23, 2021 Accepted: May 17, 2021

(onlinelibrary.wiley.com) DOI: 10.1111/ner.13469

First Evaluation Switching From Ropivacaine to Highly Concentrated Bupivacaine in Intrathecal Mixtures for Cancer Pain

Florent Bienfait, MD[1]; Sabrina Jubier-Hamon, MD[1]; Valérie Seegers, MD[2]; Yves-Marie Pluchon, MD[3]; Nathalie Lebrec, MD[1]; Virginie Jaoul, MD[1]; François Boré, MD[1]; Thierry Delorme, MD[1]; Julien Robert, PharmD[4]; Martine Bellanger, PhD[5,6]; Jérémy Sorrieul, PharmD[4]; Denis Dupoiron, MD[1]

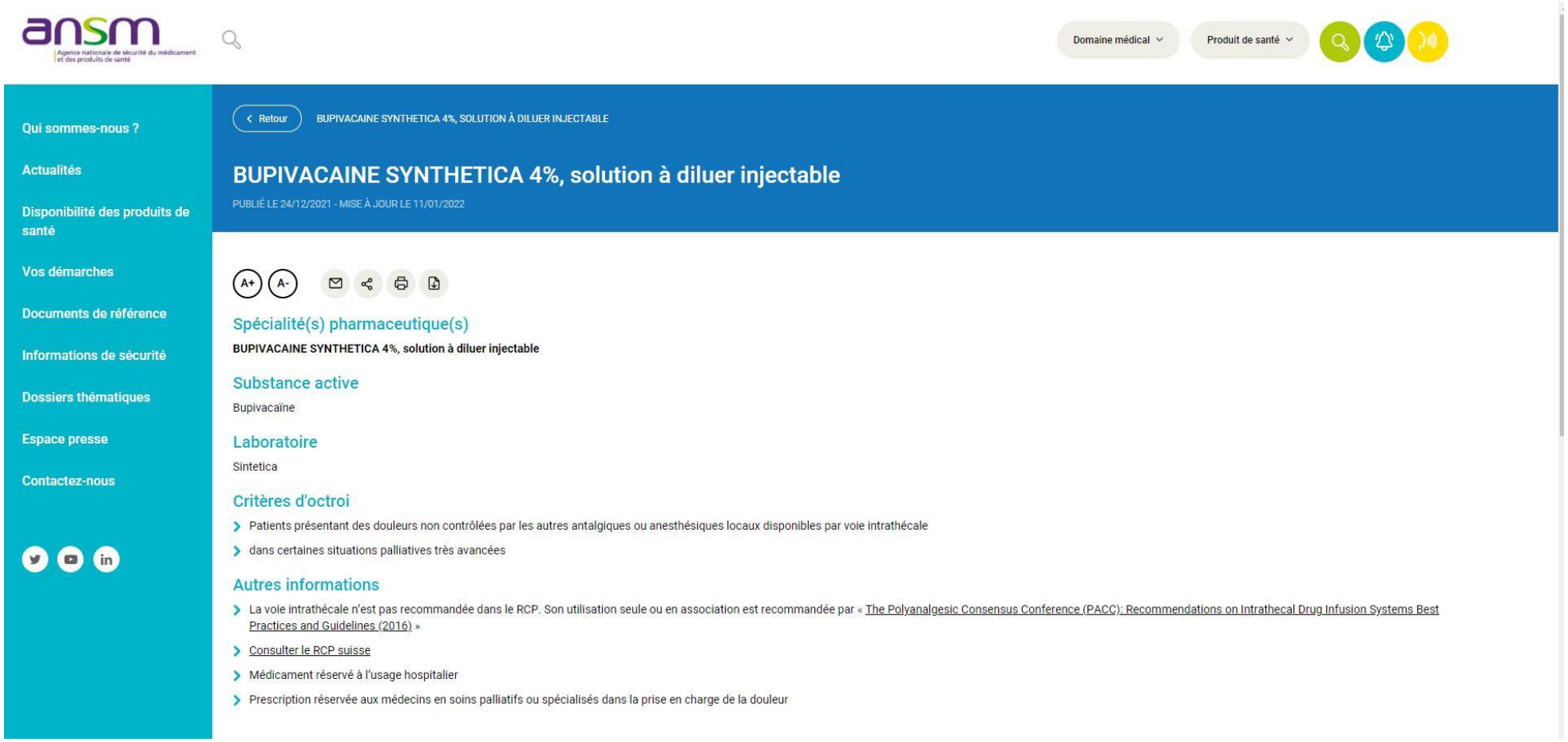
Robumix Resultats

- 14 Patients
- Mediane de suivi :
  - 76,5 Jours (43; 95)
- Diminution significative de la dose journalière de morphine
- Stabilité du Ziconotide
- Bon controle de la douleur

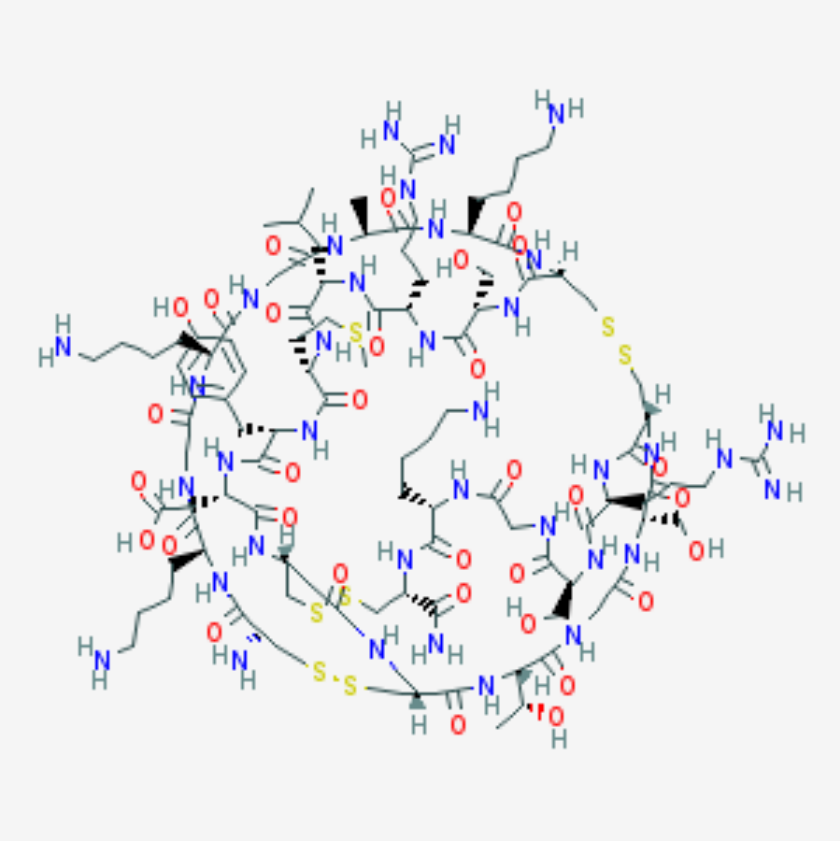
	Before Local anaesthetics Switch		At second refill after Switch		delta		
Drug	N	Med (IQR)	N	Med (IQR)	N	Med (IQR)	p-value
Morphine	14	17.8 (12.6;28.8)mg/d	12	16.5 (11.4;26) mg/d	12	-1.9 (-3.6;-0.5) mg/d	0.01
Ziconotide	14	3.2 (2.8;5.3)	12	16.5 (11.4;26) m	12	-0.1 (-0.6;0.4)	0.73
Ropivacaine	14	50.7 (46.7 ;58.4) mg/d	-	-	-	-	-
Bupivacaine	0	-	14	42.4 (29.9 ;50.0) mg/d	-	-	-

	Before the switch		After the switch : 2nd refill		delta		
	N	Med (IQR)	N	Med (IQR)	N	Med (IQR)	p-value
NRS	14	4 (2.5;5.8)	12	4 (2.8;5)	12	-0.5 (-1.2;0)	0.10

Finalement !


ansm
Agence nationale de sécurité du médicament et des produits de santé
Domaine médical
Produit de santé
Qui sommes-nous ?
Actualités
Disponibilité des produits de santé
Vos démarches
Documents de référence
Informations de sécurité
Dossiers thématiques
Espace presse
Contactez-nous
Retour
BUPIVACAINE SYNTHETICA 4%, SOLUTION À DILUER INJECTABLE
BUPIVACAINE SYNTHETICA 4%, solution à diluer injectable
PUBLIÉ LE 24/12/2021 - MISE À JOUR LE 11/01/2022
A+
A-
Spécialité(s) pharmaceutique(s)
BUPIVACAINE SYNTHETICA 4%, solution à diluer injectable
Substance active
Bupivacaïne
Laboratoire
Sintetica
Critères d'octroi
Patients présentant des douleurs non contrôlées par les autres antalgiques ou anesthésiques locaux disponibles par voie intrathécale
dans certaines situations palliatives très avancées
Autres informations
La voie intrathécale n'est pas recommandée dans le RCP. Son utilisation seule ou en association est recommandée par « The Polyanalgesic Consensus Conference (PACC): Recommendations on Intrathecal Drug Infusion Systems Best Practices and Guidelines (2016) »
Consulter le RCP suisse
Médicament réservé à l'usage hospitalier
Prescription réservée aux médecins en soins palliatifs ou spécialisés dans la prise en charge de la douleur

Le Ziconotide

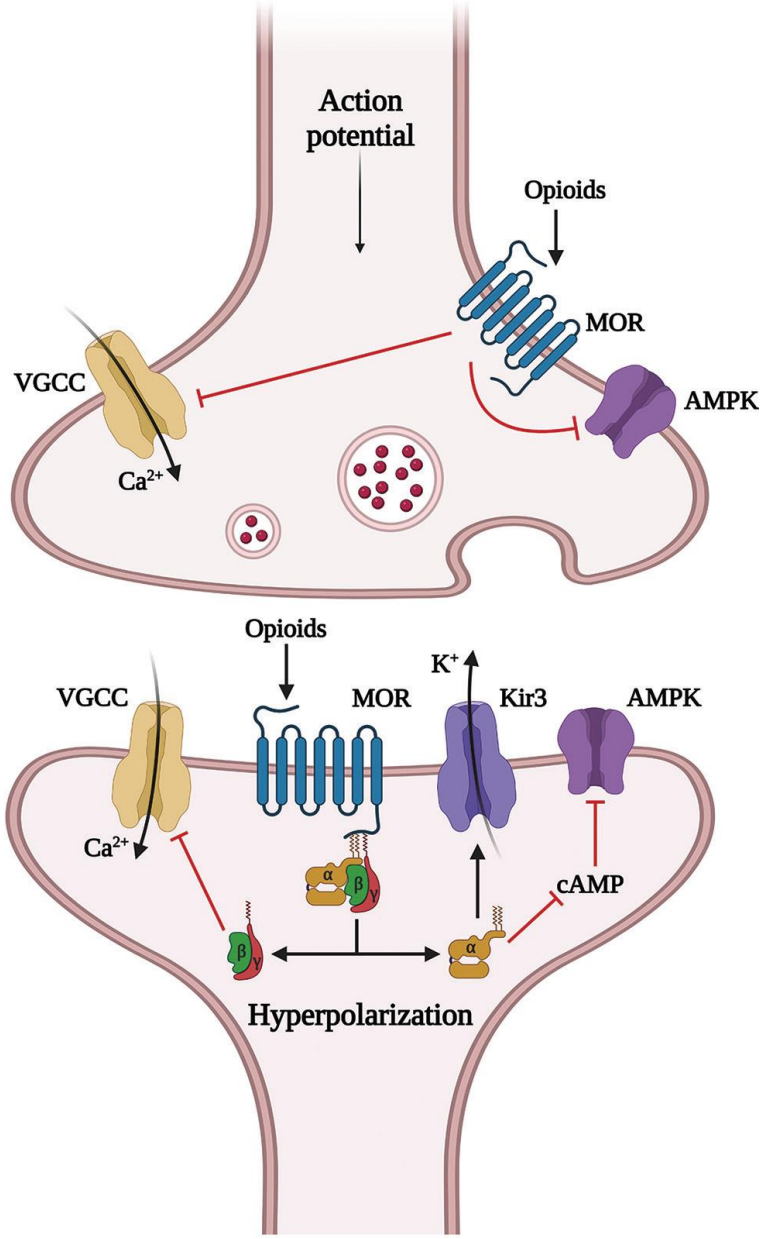


Ziconotide – opioids

- Presynaptic calcium channels trigger calcium-dependent transmitter release

- Ziconotide directly blocks presynaptic N-type calcium channels

- The opioid binds to the MOR in the presynaptic membrane and inhibits voltage-dependent calcium channel mediated by G Protein release*[1]



Ding R, Zhao Y, Li J, *et al.,* 2023, Basic and clinical insights of Mu (μ)-opioid receptor in cancer. *Gene Protein Dis*

Animal study for Morphine – Ziconotide

Pain 84 (2000) 271–281

PAIN

www.elsevier.nl/locate/pain

Interactions of intrathecally administered ziconotide, a selective blocker of neuronal N-type voltage-sensitive calcium channels, with morphine on nociception in rats

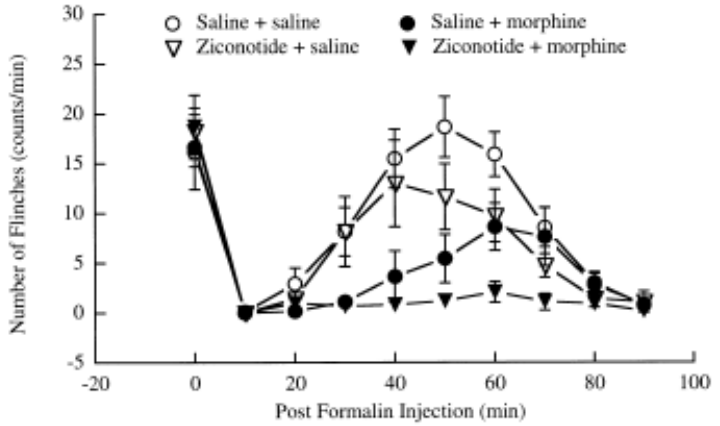
Yong-Xiang Wang*, Da Gao, Mark Pettus, Cora Phillips, S. Scott Bowersox

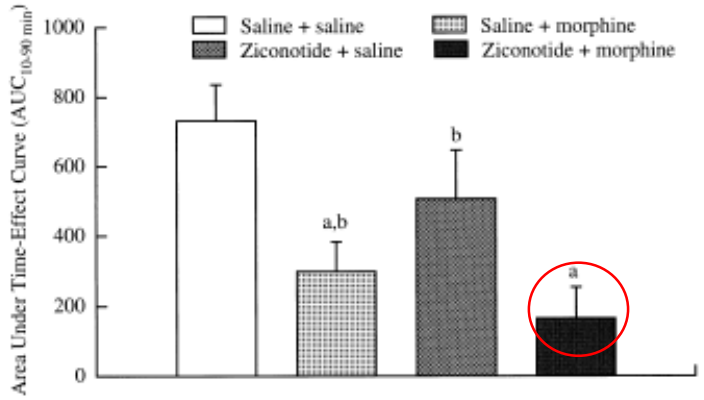
Department of Pharmacology, Elan Pharmaceuticals, 3760 Haven Avenue, Menlo Park, CA 94025, USA

Received 13 February 1999; received in revised form 16 June 1999; accepted 13 August 1999

Study performed on rats

Ziconotide is a selective, potent and reversible blocker of neuronal N-type voltage-sensitive calcium channels (VSCCs). Morphine is an agonist of μ-opioid receptors and inhibits N-type VSCC channels via a G-protein coupling mechanism. Both agents are antinociceptive when they are administered intrathecally (spinally). The present study investigated the acute and chronic (7-day) interactions of intrathecally administered ziconotide and morphine on nociception in several animal models of pain. In the acute study, intrathecal bolus injections of morphine and ziconotide alone produced dose-dependent inhibition of formalin-induced tonic flinch responses and withdrawal responses to paw pressure. The combination of ziconotide and morphine produced an additive inhibition of formalin-induced tonic flinch responses and a significant leftward shift of the morphine dose-response curve in the paw pressure test. After chronic (7-day) intrathecal infusion, ziconotide enhanced morphine analgesia in the formalin test. In contrast, chronic intrathecal morphine infusion produced tolerance to analgesia, but did not affect ziconotide antinociception. Antinociception produced by ziconotide alone was the same as that observed when the compound was co-administered with morphine to morphine-tolerant rats. In the hot-plate and tail immersion tests, chronic intrathecal infusion of morphine lead to rapid tolerance whereas ziconotide produced sustained analgesia with no loss of potency throughout the infusion period. Although ziconotide in combination with morphine produced an apparent synergistic analgesic effects during the initial phase of continuous infusion, it did not prevent morphine tolerance to analgesia. These results demonstrate that (1) acute intrathecal administrations of ziconotide and morphine produce additive or synergistic analgesic effects; (2) chronic intrathecal morphine infusion results in tolerance to analgesia but does not produce cross-tolerance to ziconotide; (3) chronic intrathecal ziconotide administration produces neither tolerance nor cross-tolerance to morphine analgesia; (4) intrathecal ziconotide does not prevent or reverse morphine tolerance. © 2000 International Association for the Study of Pain. Published by Elsevier Science B.V.

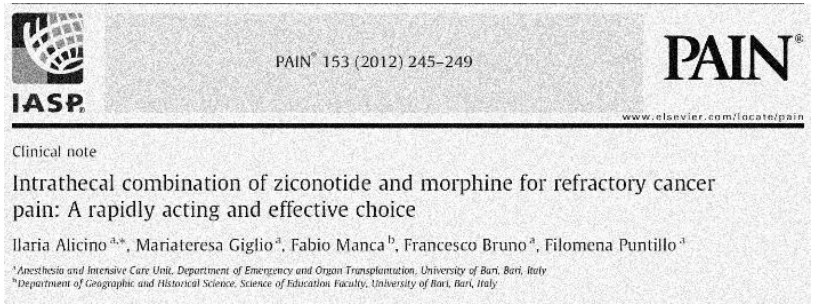




Association Morphine - Ziconotide is more efficient than Morphine or Ziconotide alone

Ziconotide in combination

- **Alicino (2012)**
- **Methodology**
  - **Prospective study**
  - Include 20 cancer Patients
  - Stable dose of IT morphine
  - Proceed to a progressive titration of Ziconotide
    - 2,4µg/d
- **Results**
  - Better pain Relief
    - Mean decrease of 62% at day 28
  - Only 4 Moderate AEs


PAIN® 153 (2012) 245–249

PAIN®

www.elsevier.com/locate/pain

Clinical note

Intrathecal combination of ziconotide and morphine for refractory cancer pain: A rapidly acting and effective choice

Ilaria Alicino [a,*], Mariateresa Giglio [a], Fabio Manca [b], Francesco Bruno [a], Filomena Puntillo [a]

[a] Anesthesia and Intensive Care Unit, Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy
[b] Department of Geographic and Historical Science, Science of Education Faculty, University of Bari, Bari, Italy

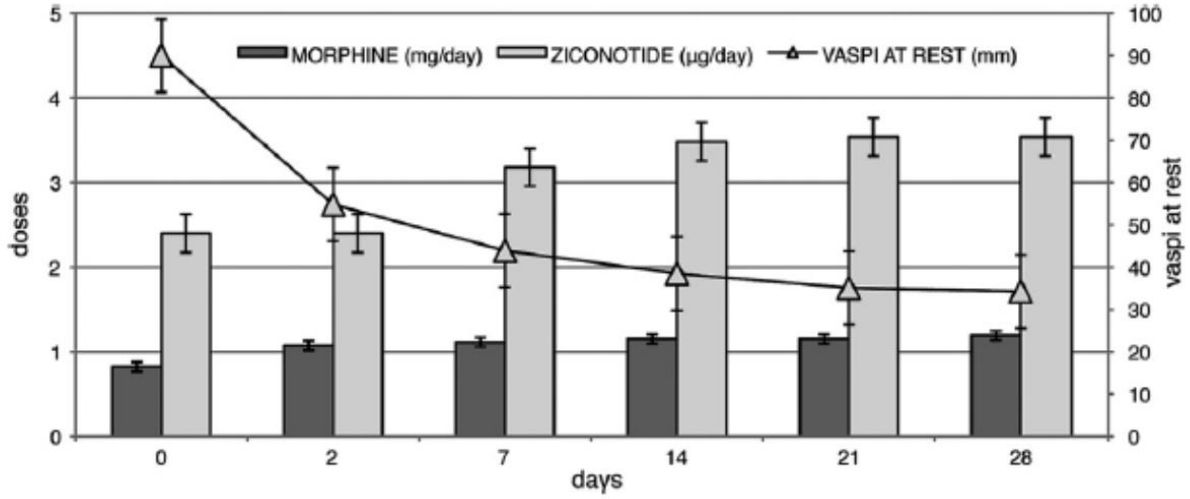
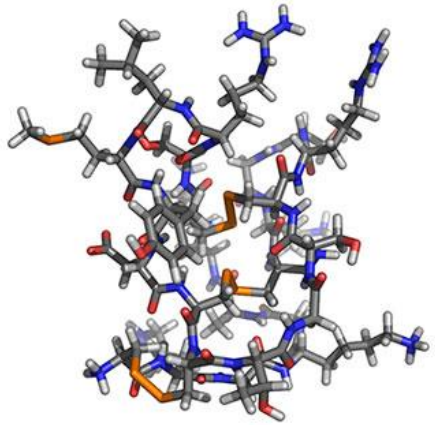


Fig. 1. Mean visual analogue scale of pain intensity (VASPI) score and mean doses of morphine (mg/day, filled bars) and ziconotide (µg/day, open bars) among patients at baseline, after 2 days, and weekly during treatment.

Alicino, I., et al., *Intrathecal combination of ziconotide and morphine for refractory cancer pain: a rapidly acting and effective choice.* Pain, 2012. **153**(1): p. 245-9.

Daily practice of Ziconotide challenging to use in oncology ?



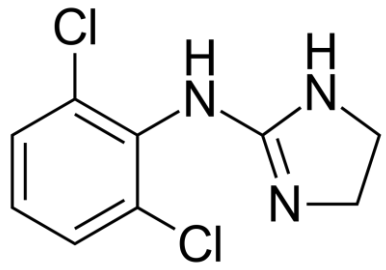
- **Cancer patients**
  - High level of pain and short life expectancy
  - Need of Low introduction level dosage and slow titration to prevent AEs

- **Ziconotide Introduction in first line for all patients**
  - Low level introduction: 0.5µg/day
  - **Sytematic dosage of all mixture**
- **Slow titration**
  - Never more than 0.5 µg/d per week
- **Ziconotide always in combination[1-2]**
  - Evidences of Synergic effect With Morphine
  - Decrease AEs rate

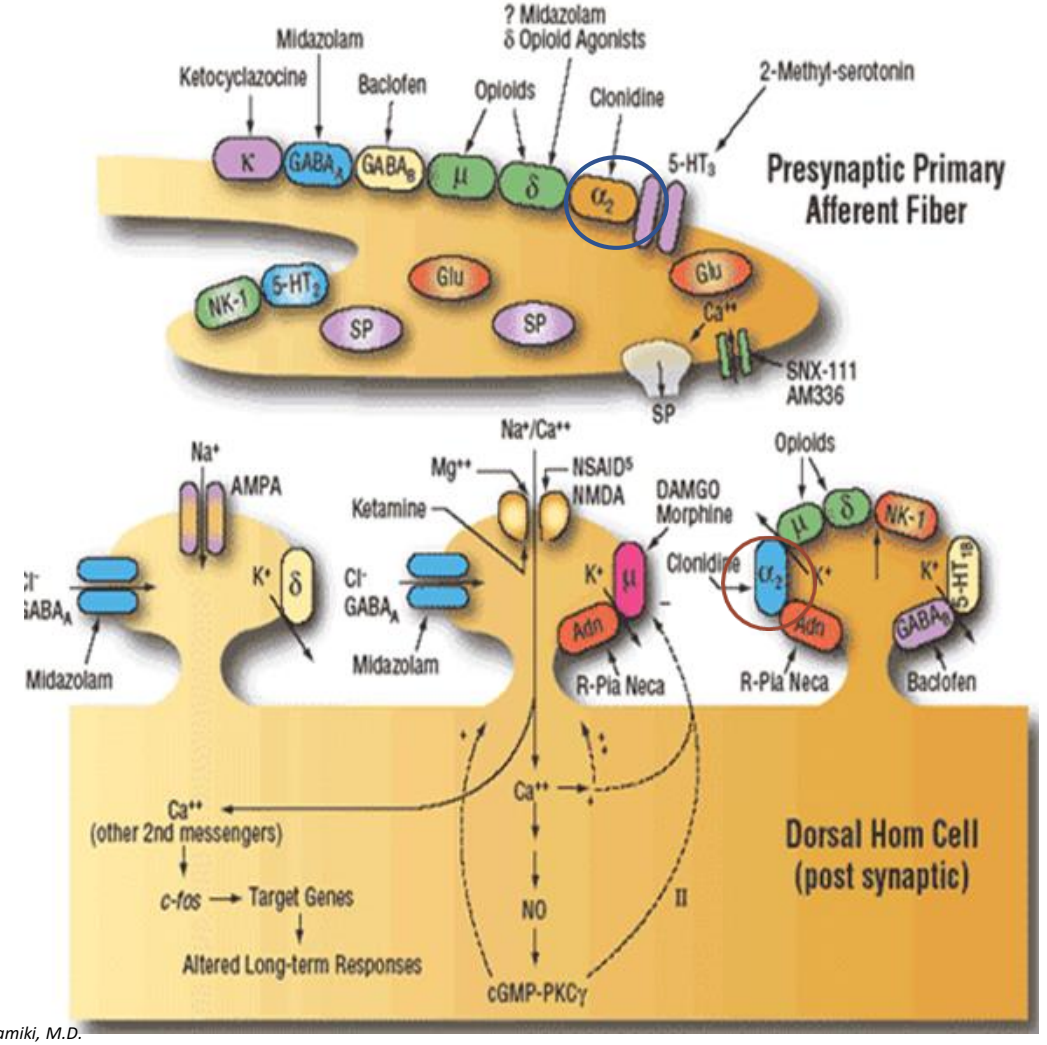
Use ziconotide in first line to be useful in 2nd line

1 - Alicino, I., et al., *Intrathecal combination of ziconotide and morphine for refractory cancer pain: a rapidly acting and effective choice.* Pain, 2012. **153**(1): p. 245-9.
2- Dupoiron, D., et al., *Ziconotide adverse events in patients with cancer pain: a multicenter observational study of a slow titration, multidrug protocol.* Pain Physician, 2012. **15**(5): p. 395-403

Clonidine



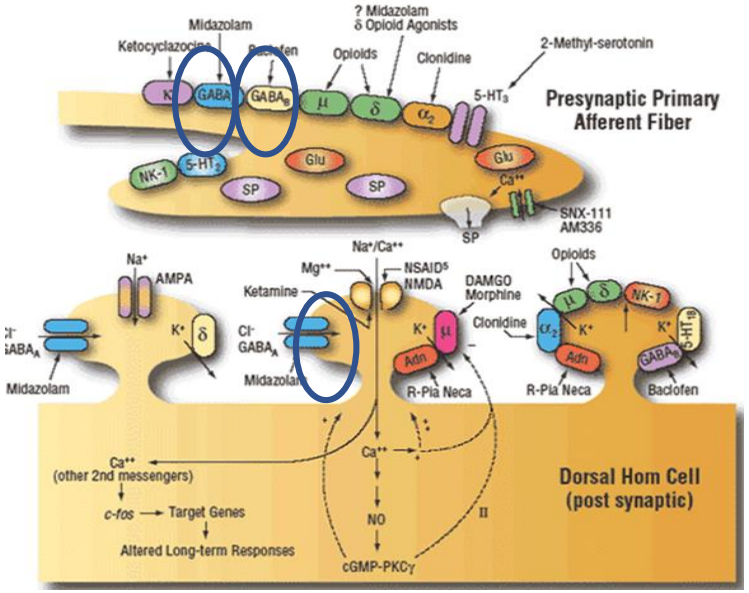
- Agoniste α2 adrénergique
- Très lipophile
  - Action rapide
- Récepteurs Pré et post synaptiques
- Diminue la sécrétion de la substance P(1)
- Très active sur les douleurs neuropathiques(2)
- Peu d'effets secondaires
- Non approuvée FDA
- Etudes cliniques
  - Ackerman (2003)
    - 10 patients
    - Doses élevées : 100- 500 µg/j
- Doses utilisables :
  - intrathécal : 10 – 100 µg / 24 h
  - Péridural : 100 – 300 µg / 24 h

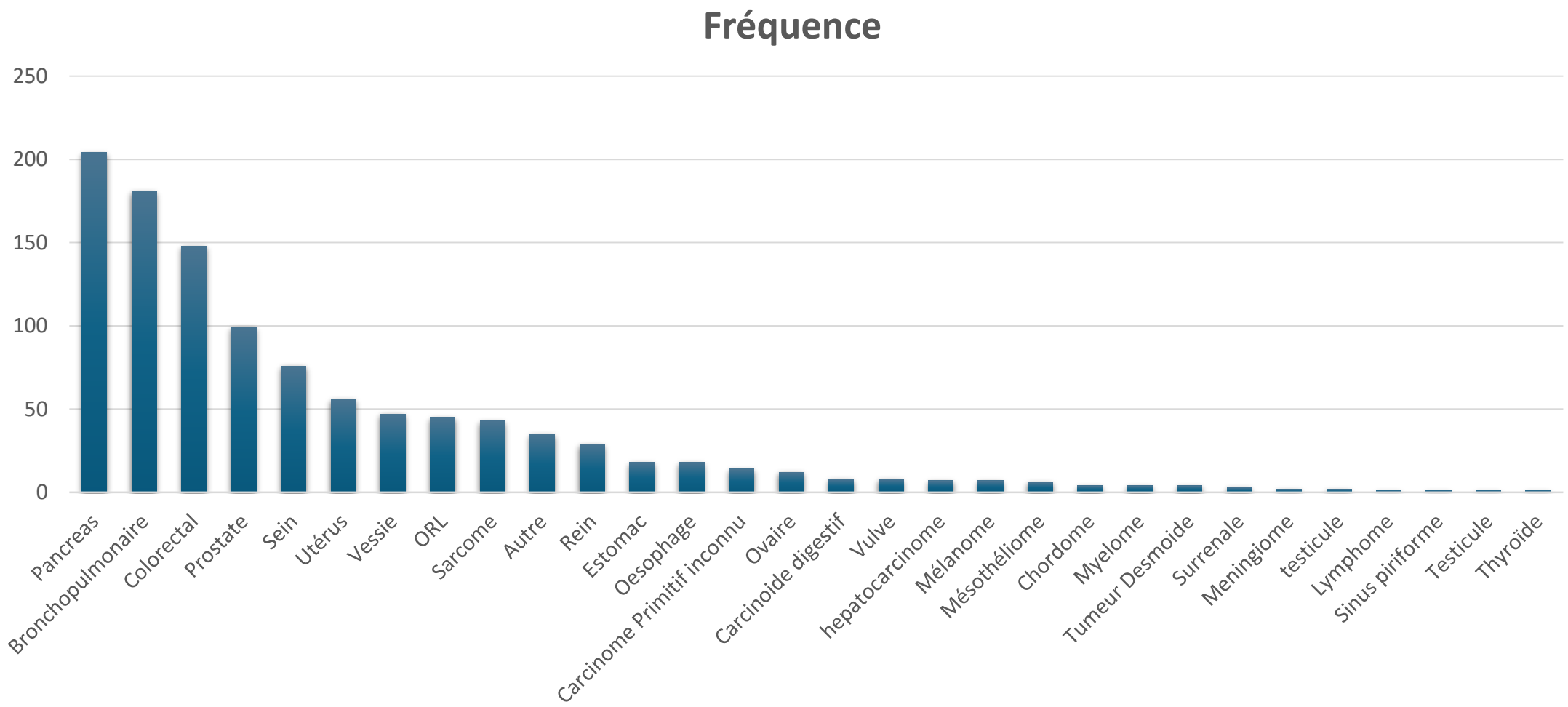


(1)Alternative intrathecal agents for the treatment of pain.
Hassenbusch SJ, Garber J, Buchser E, Du Pen S.Neuromodulation 1999;2:85–91.
(2)Antihyperalgesic and Side Effects of Intrathecal Clonidine and Tizanidine in a Rat Model of Neuropathic Pain
Tomoyuki Kawamata, M.D., Keiichi Omote, M.D.,† Hiroki Yamamoto, M.D.,‡ Masaki Toriyabe, M.D.,‡ Kohsuke Wada, M.D.,§ Akiyoshi Namiki, M.D.*
(3)Long-term outcomes during treatment of chronic pain with intrathecal clonidine or clonidine/opioid combinations.
Ackerman LL, Follett KA, RosenquistRW. *J Pain Symptom Manage* 2003; 26:668-677

Agonistes des Récepteurs GABA

- Midazolam
  - Agoniste des récepteurs GABA A
  - Potentialise l'effet des morphiniques + AL
  - Toxicité animale non retrouvée chez l'homme
  - Etudes observationnelles
  - Doses : 2- 7mg/j
- Baclofène
  - Agoniste des récepteurs GABA B
  - Très utilisée dans la spasticité
  - Effet sur les douleurs neuropathiques
  - Pas d'étude en cancérologie
  - Difficulté d'utilisation avec d'autres traitements
    - Sevrage





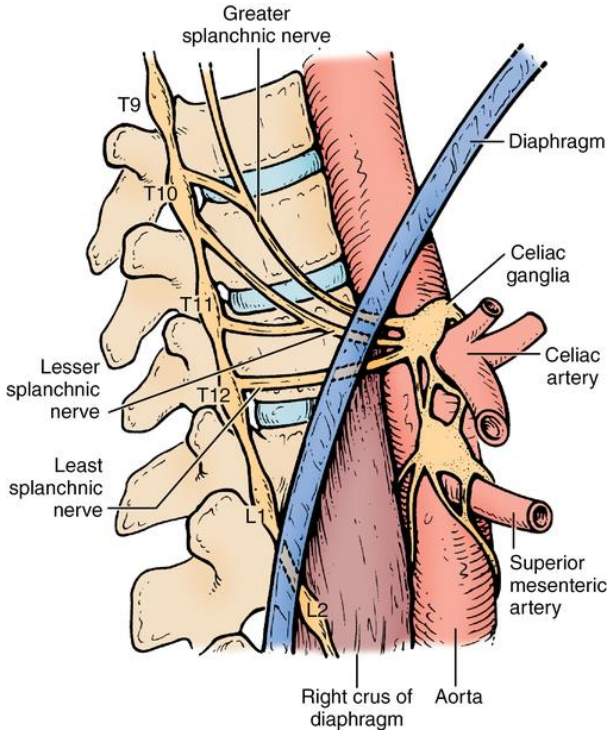
Cancer du Pancréas : 1ère Indication

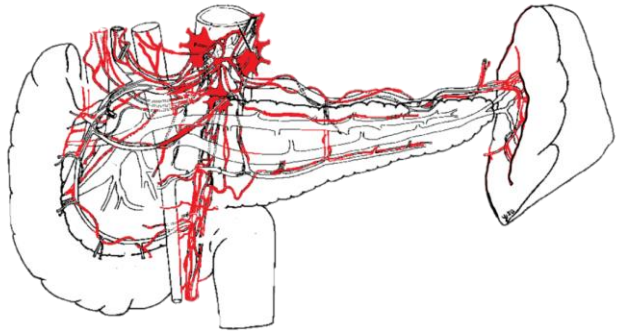
N = 1084

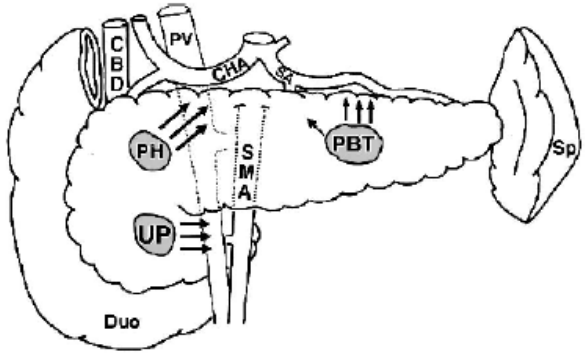
07/11/2024

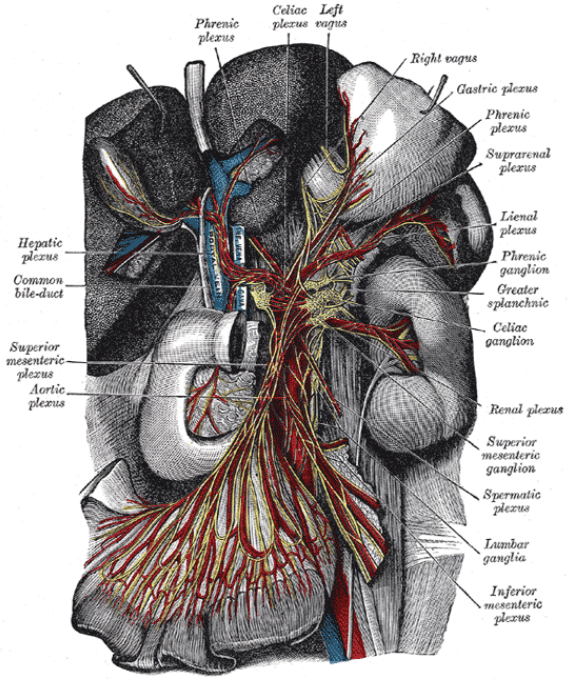
Facteurs anatomiques

- 10- Yi SQ, Miwa K, Ohta T, Kayahara M, Kitagawa H, Tanaka A, Shimokawa T, Akita K, Tanaka S. Innervation of the pancreas from the perspective of perineural invasion of pancreatic cancer. Pancreas. 2003 Oct;27(3):225-9.









Etude de suivi des patients implantés pour Cancer pancréatique

Intrathecal Drug Delivery Systems for Refractory Pancreatic Cancer Pain: Observational Follow-up Study Over an 11-Year Period in a Comprehensive Cancer Center

Gabriel Carvajal, MD,* Denis Dupoiron, MD,* Valerie Seegers, MD,† Nathalie Lebrec, MD,*
François Boré, MD,* Pierre-Yves Dubois, MD,* Damien Leblanc, MD,*
Thierry Delorme, MD,* and Sabrina Jubier-Hamon, MD*

Contexte et objectifs

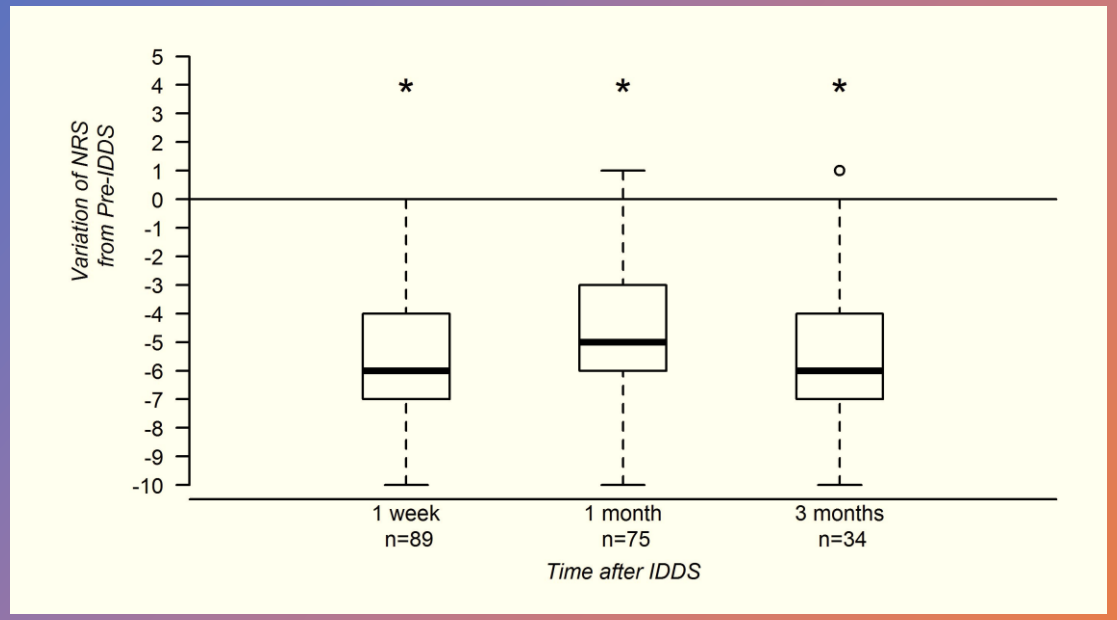
- Manque de données spécifiques dans les cancers du Pancréas
- Obtenir les données de suivi de ces patients

Critères d'évaluation

- Evaluation de la douleur
  - avant /après IT
- Survie globale
- Données d'implantation
  - Type de pompe
  - Niveau du cathéter
  - Complications chirurgicales

Carvajal, G., Dupoiron, D et al., *Intrathecal Drug Delivery Systems for Refractory Pancreatic Cancer Pain: Observational Follow-up Study Over an 11-Year Period in a Comprehensive Cancer Center.* Anesth Analg, 2018. **126**(6): p. 2038-2046.

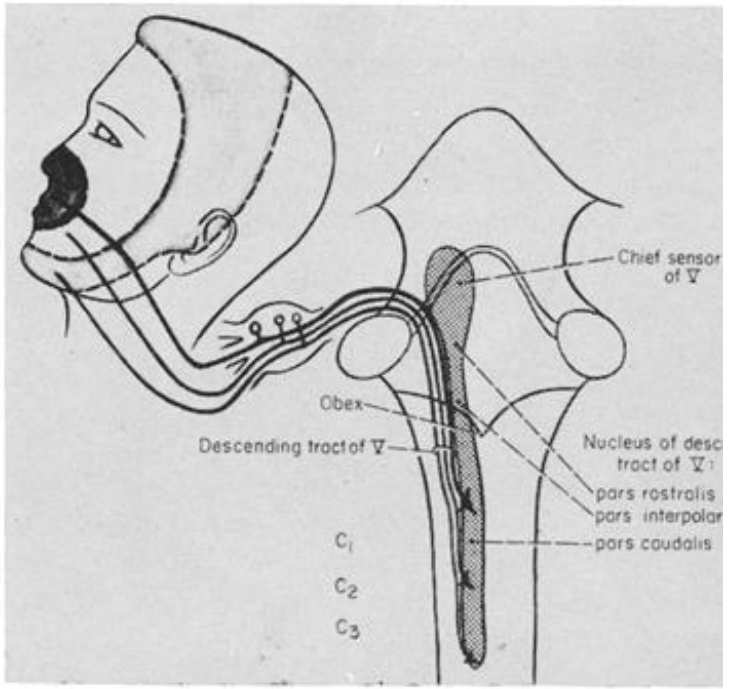
RESULTATS : PAIN FOLLOW UP

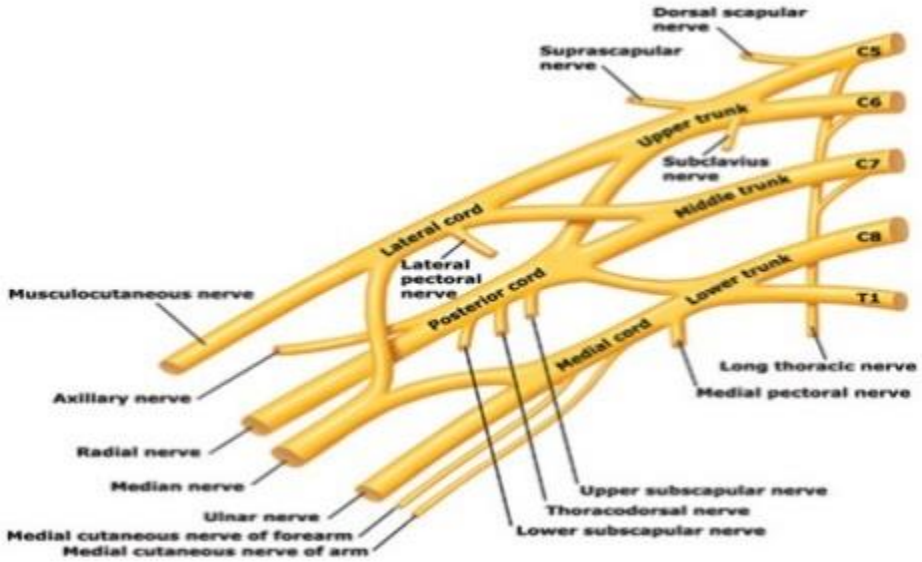


- **Significant statistical difference between preimplantation (0- 10 : NRS)**
  - **after 1 week**
    - median, −6 [IQR, −7 to −4]; P < .001
  - **after 1 month**
    - median, −5[IQR, −6 to −3]; P < .001),
  - **after 3 months**
    - median, −6 [IQR,−7 to −4]; P < .001
- **Seventy patients (78.7%) had an NRS ≤3** after 1 week
- **At least 50% reduction from basal pain** score was possible in 77 patients (86.5%) after 1 week
- Pre surgical use of IV ketamine was not significantly associated with better pain scores

Targets for HNC pain

- **Targets for interventional treatments**
  - **Head**
    - Trigeminal nerve for most head area
    - Synapse level C1 – C2 – C3
  - **Neck**
    - Brachial Plexus
    - Spinal level
      - C5 – T1





Taren, J.A. and E.A. Kahn, *Anatomic pathways related to pain in face and neck.* J Neurosurg, 1962. **19**: p. 116-21.

Regional Anesthesia & Pain Medicine

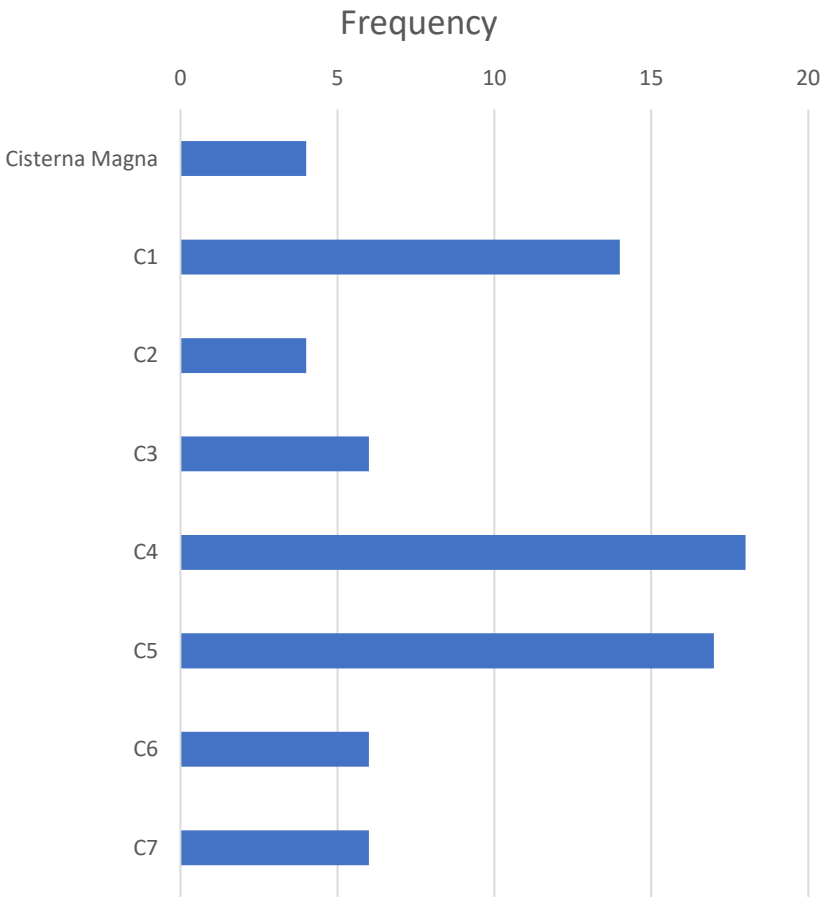
Intrathecal cervical analgesia for cancer pain: a 12-year follow-up study in a comprehensive cancer center

Denis Dupoiron [1], Florent Bienfait,[1] Gabriel Carvajal,[2] Valerie Seegers,[3] Thomas Douillard,[1] Sabrina Jubier-Hamon,[1] Thierry Delorme,[1] Arthur Julienne,[1] Yves Marie Pluchon,[4] Nicolas Ribault,[5] Edmond Nader,[5] Nathalie Lebrec[1]

CERVical IntraTHecal (CERVITH) Study

Dupoiron, D., et al., *Intrathecal cervical analgesia for cancer pain: a 12-year follow-up study in a comprehensive cancer center.* Reg Anesth Pain Med, 2023.

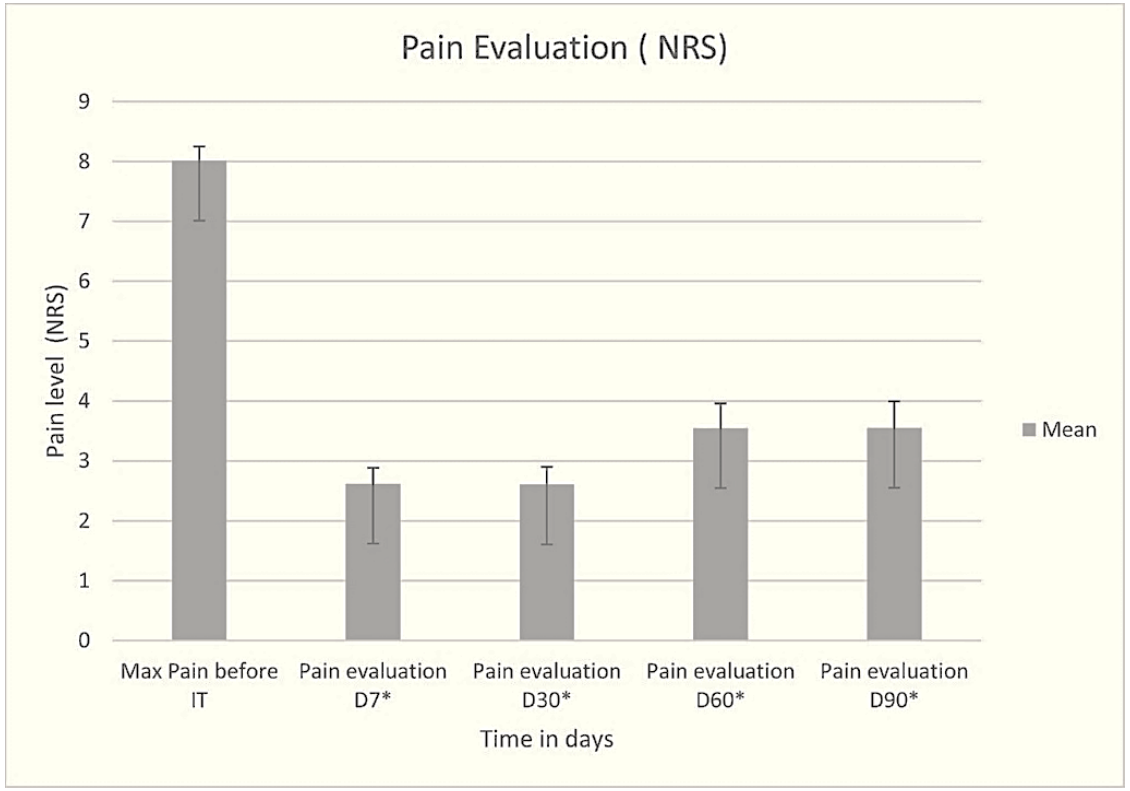
Procedural results



- **Devices**
  - 86 Implantable pumps
  - 12 Subcutaneous ports connected to an External pump
  - No implantation failure
- **Location**
  - For Head Pain
    - Cisternal
    - C1 – C2- C3
  - For Cervical Pain
    - C4- C5 – C6 - C7

Pain evaluation

- Mean Pain score before implantation
- Significant decrease after implantation
  - - 67 % at D7
  - - 67% at D30
  - - 56.7 % at D60 and D 90



Intrathecal Drugs DATA

- Mixtures prepared by our compounding pharmacy
- Systematic assay for each component since 2013
- No Serious AEs observed elsewhere, specifically with Ziconotide

	Mean Introduction dosage	Max Dosage
morphine	**1.42±0.24 mg/d**	**42.6 mg/d,**
ropivacaine	**5.8±0.4 mg/d,**	**76.8 mg/d**
Ziconotide	**0.34±0.02 μg/d.**	**15.39 μg/d**
Bupivacaine		**51.5 mg/day**

SCS sur les cancers évolutifs ?

Neuromodulation: Technology at the Neural Interface

Received: March 4, 2021 Revised: April 12, 2021 Accepted: May 4, 2021

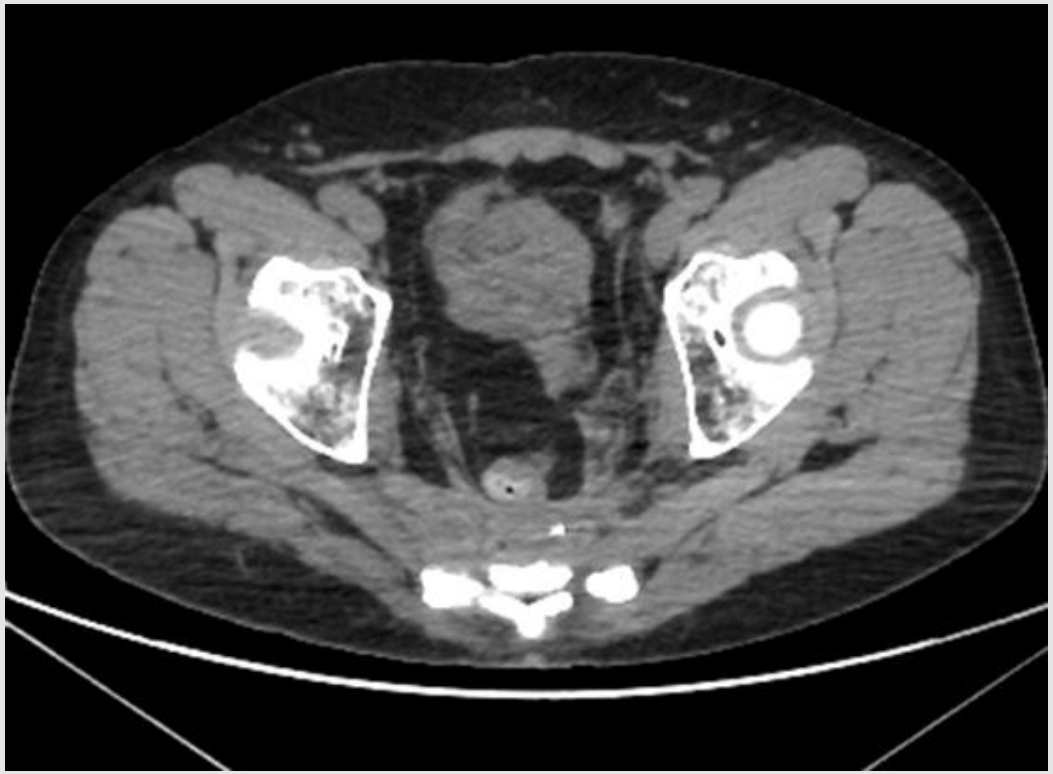
(onlinelibrary.wiley.com) DOI: 10.1111/ner.13464

Dura Fistula: A Rare Complication of Simultaneous Placement of Neurostimulation Leads and an Intrathecal Catheter

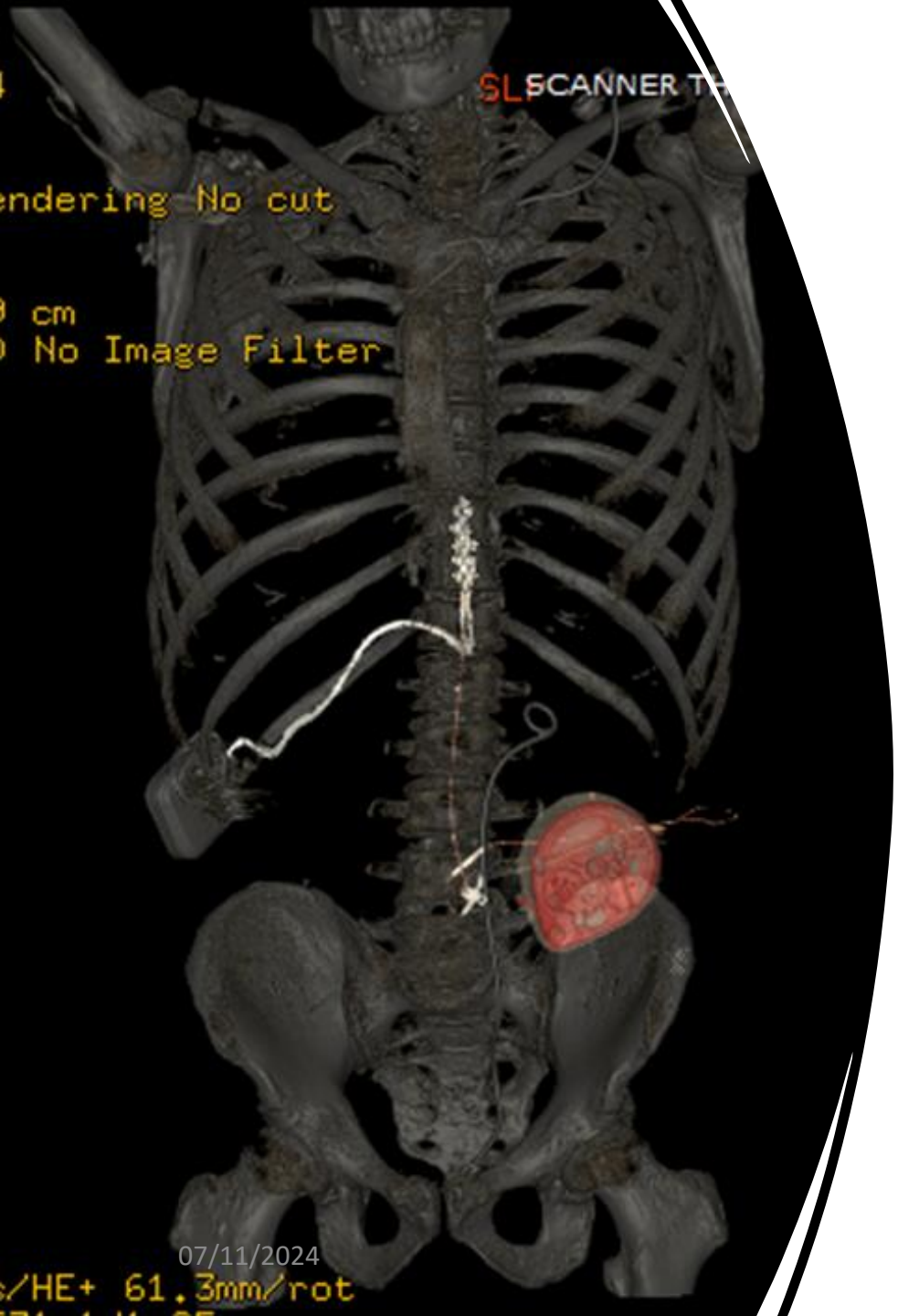
Denis Dupoiron, MD[1]; Timothy Deer, MD[2]

- Male 53 years old
  - Dignosed in 2014
  - Neo adjuvant radio – chemotherapy
  - Surgery
- Pulmonary recurrence in 2016
- Local recurrence in 2018
  - Stomia and palliative radiotherapy for pain

Douleur et Traitement par SCS



- Douleur :
  - Sciatalgie Droite
  - Douleur pelvienne nociceptive
  - ADP
- traitements:
  - Fentanyl patch 400µg/h
  - Oxynorm 80 mg
  - Abstral 100 µg
  - Gabapentine 600 X 3/j
  - Stéroïdes
- Neurostimulation
  - Sortie avec plus d’opioïdes



Indication IT treatment

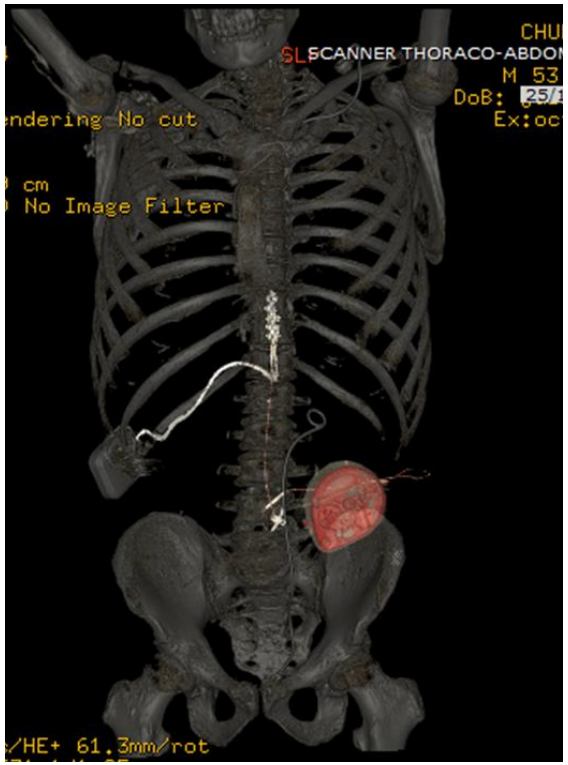
- Tip lying behind T10 2019
- Progressive titration
- Pain relief after one week
- Chemotherapy resumed

évolution

- Soulagement pendant 5 mois
- En quelques jours recrudescence de la douleur
- Augmentation des dosages
  - Morphine 30mg/d
  - Naropeine 60mg/d
  - Prialt 5µg/d
- Mode séquentiel : aucun effet

- Imagerie

Imagery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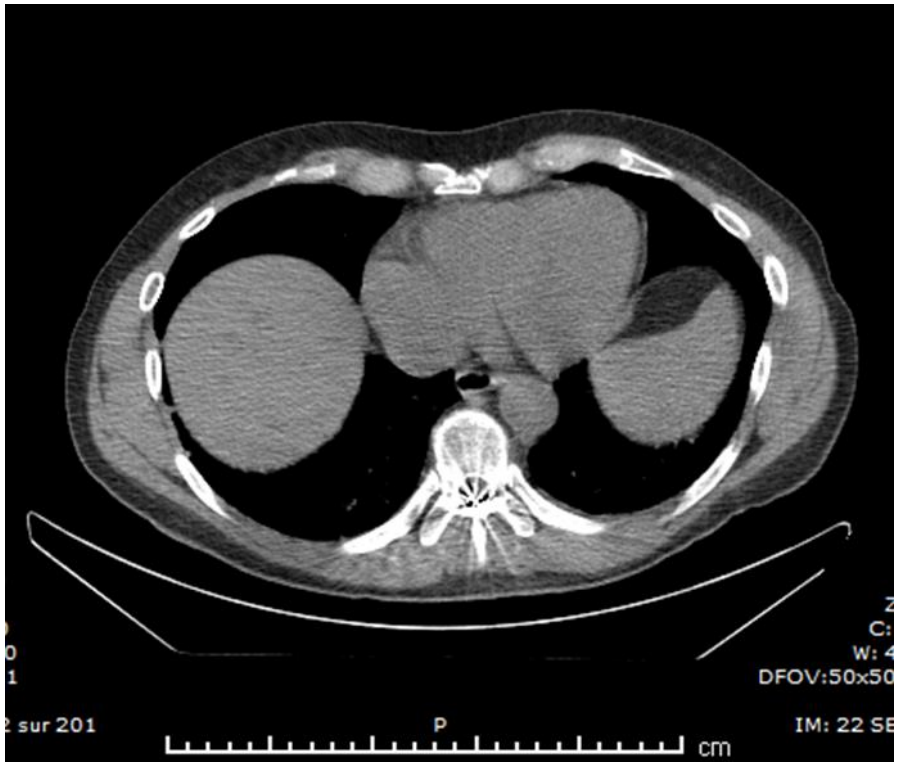
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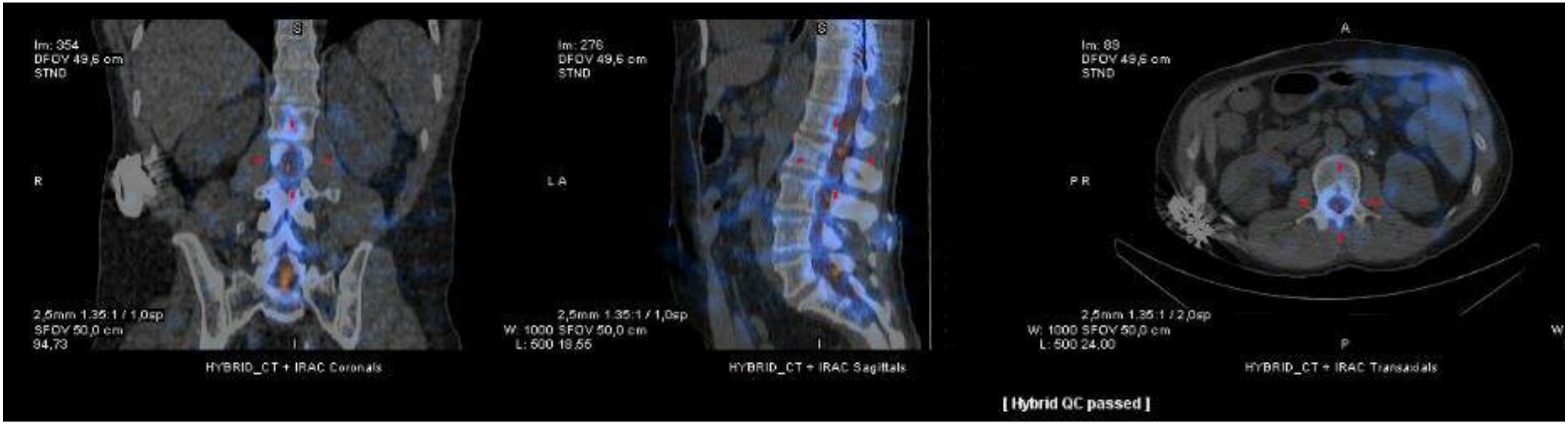
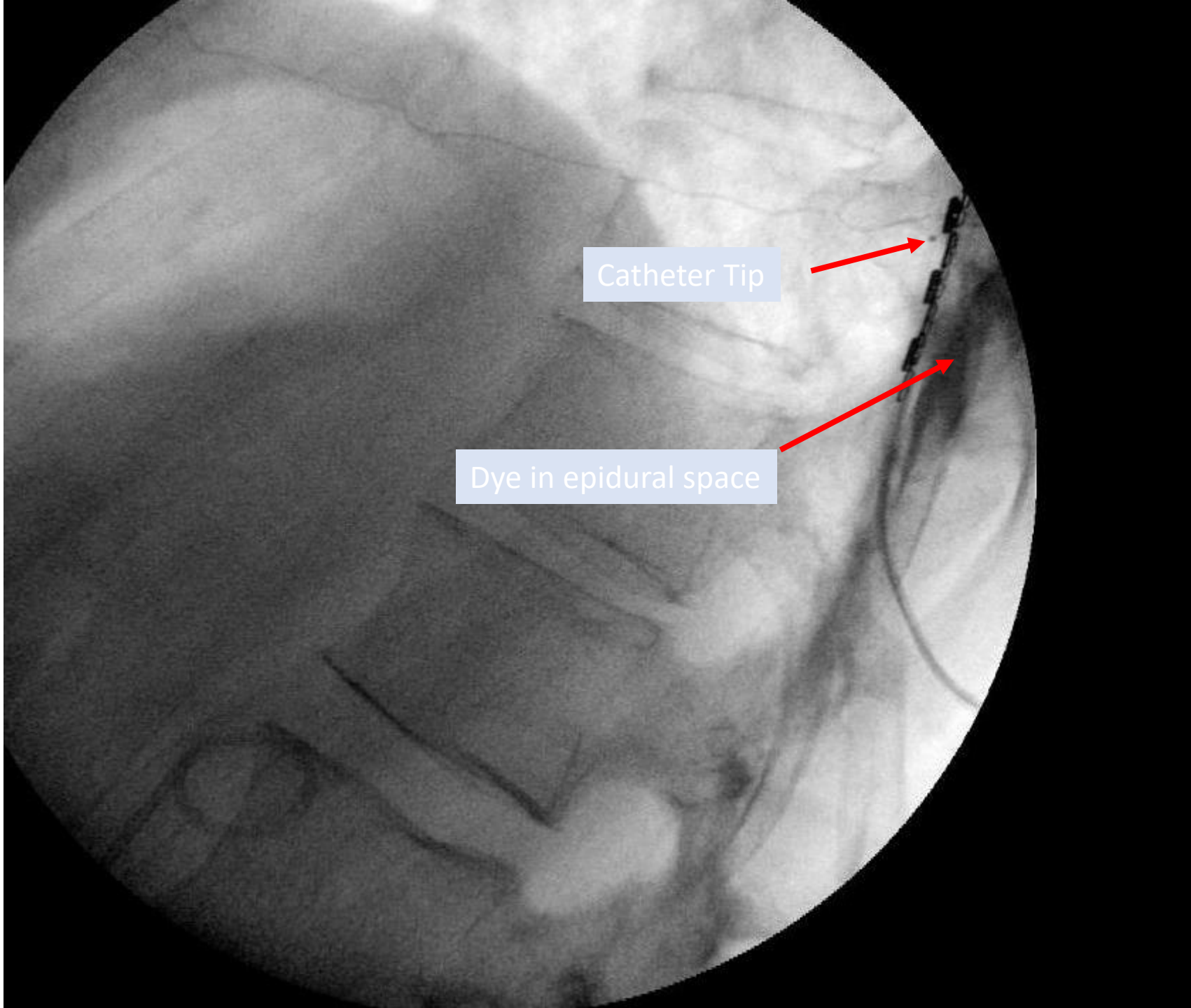
Imagery


Im: 354
DFOV 49,6 cm
STND
S
R
I
2,5mm 1.35:1 / 1,0sp
SFOV 50,0 cm
94,73
HYBRID_CT + IRAC Coronals
Im: 276
DFOV 49,6 cm
STND
S
LA
I
2,5mm 1.35:1 / 1,0sp
W: 1000 SFOV 50,0 cm
L: 500 18,55
HYBRID_CT + IRAC Sagittals
Im: 89
DFOV 49,6 cm
STND
A
P R
P
2,5mm 1.35:1 / 2,0sp
W: 1000 SFOV 50,0 cm
L: 500 24,00
HYBRID_CT + IRAC Transaxials
[Hybrid QC passed]

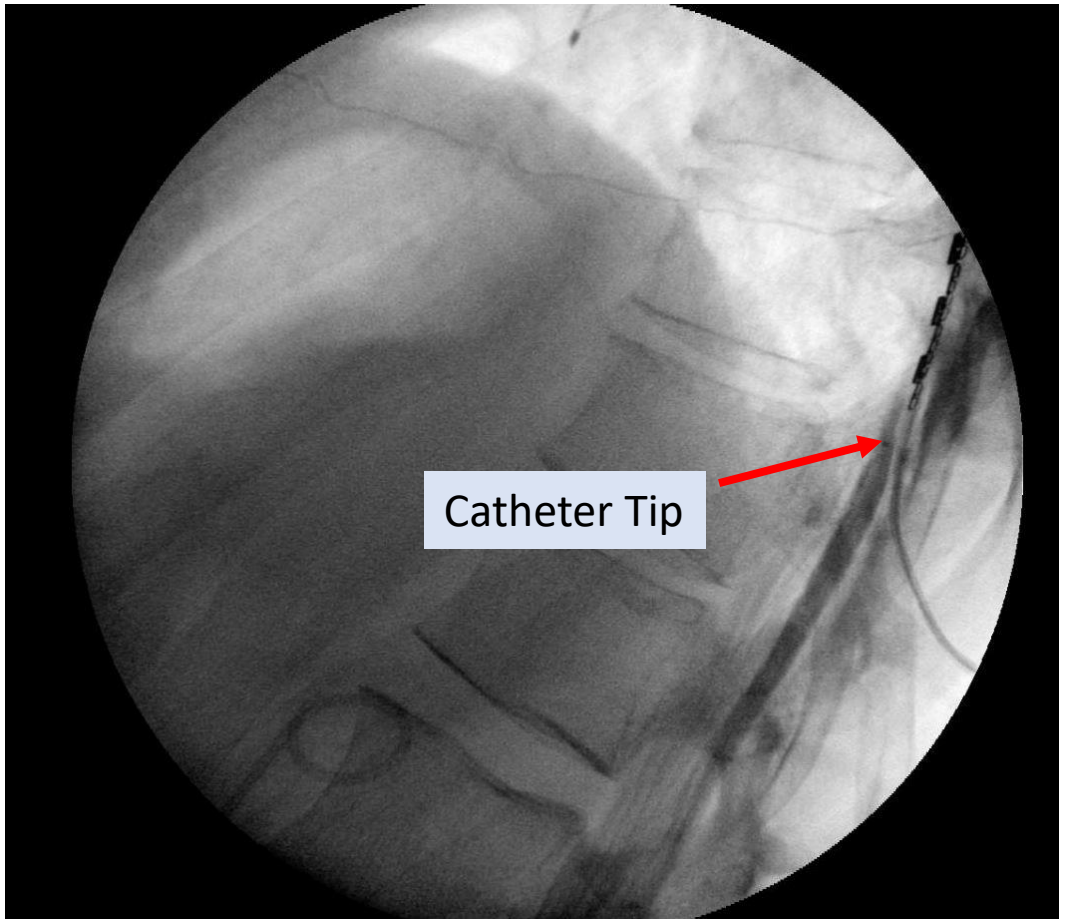
Fluoroscopy

- Indicates a dura Fistula
- show leaks with the dye moving behind the spinal space into the epidural space and behind the neurostimulation leads
-



Traitement

Demande neurochirurgiens	• Fermeture de fistule parait impossible
Déplacement du cathéter	• En dessous des électrodes • Normalisation de la diffusion



Evolution

- Après une semaine
  - Reprise de la douleur
  - Radio : élargissement de la fistule
- Demande de fin de vie
  - Décision de sédation terminale

Take Home message

- **Pourquoi l'intrathécal dans les DN du Cancer. ?**
  - Douleurs souvent mixtes
  - Utilisable et efficace quel que soit la localisation
  - Non ablative
  - Recommandée
- **Problèmes**
  - Diffusion de la technique
  - Patients vus tard dans l'évolution
  - Attention à la SCS ?