Non-Pharmacologic Management of Cancer Pain

Ivan Lesnik
OCT 2011

The views expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

NMCSD
Pain Medicine Center
“Restoration, Relief & Research”

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Disclosures

- The speaker has nothing to disclose.
- Exhibits coordinated through the Henry Jackson Foundation.
- Refreshments provided through the Henry Jackson Foundation.

Non Pharmoclogic Mangament of Cancer Pain

Not Considering

- Radiation Therapy
- Psychological Interventions
- Physical Therapy
- Occupational Therapy
- Alternative Medicine – acupuncture, aromatherapy, massage, music therapy, herbal medicine, meditation

Non Pharmoclogic Mangament of Cancer Pain

- Vertebroplasty and Kyphoplasty
- Neurolytic Techniques
- Intraspinal /Neuroaxial Techniques
- Plexus and Peripheral Nerve Blockade
- Neurosurgical procedures

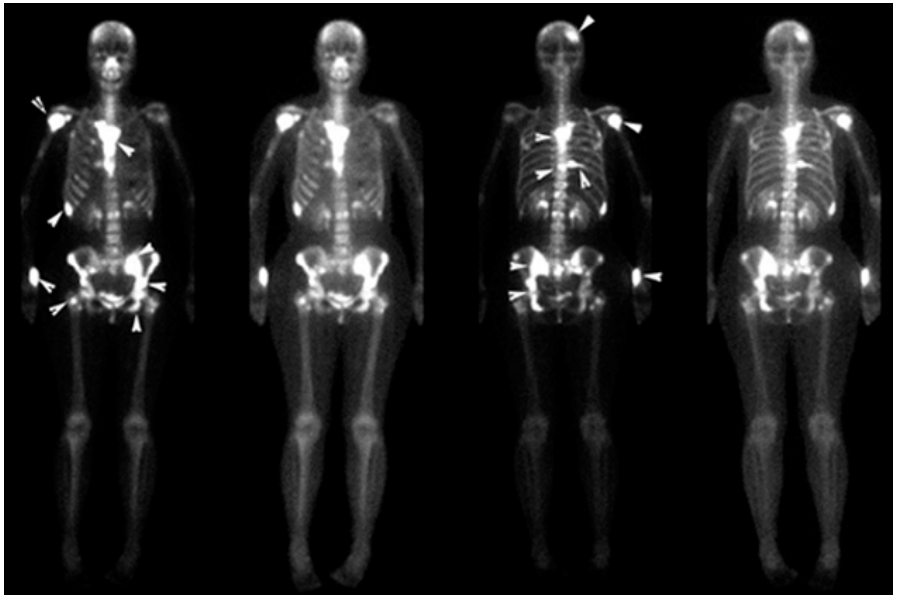
Non Pharmoclogic Mangament of Cancer Pain

- Clinical Case
  - 68 female- prior Fortune 500 CEO with widely metastatic breast CA
    - brain, multiple long bone and spine
  - Pain escalating
  - Patient requests supportive care only
  - Minimal response to prior XRT

- Palliative care service consulted
  - Ms04 300mg BID
  - Fentanyl lozenge for breakthrough
  - Pregabalin 100mg BID
  - Amitriptyline 30mg qHS
  - Dexamethasone 4 mg Q 6

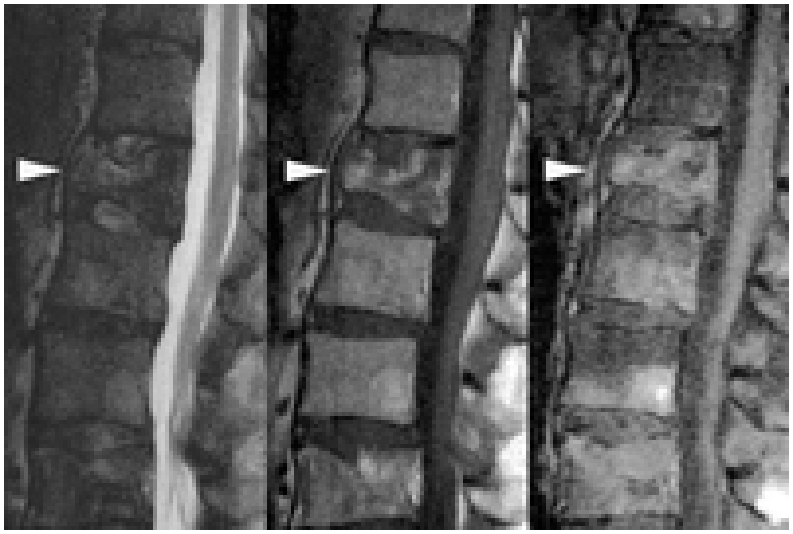
Non Pharmoclogic Mangament of Cancer Pain

- Clinical Case
  - 68 female- prior Fortune 500 CEO with widely metastatic breast CA
    - Brain, multiple long bone and spine
- Palliative care service consulted
  - Patient's pain well controlled however patient dissatisfied with ability to remain awake to communicate with family members.
  - Experiencing significant nausea and vomiting despite multitude of antiemetic's
  - Approached by family expressing concern about lack of ability to have any meaningful interaction with patient
  - Options?



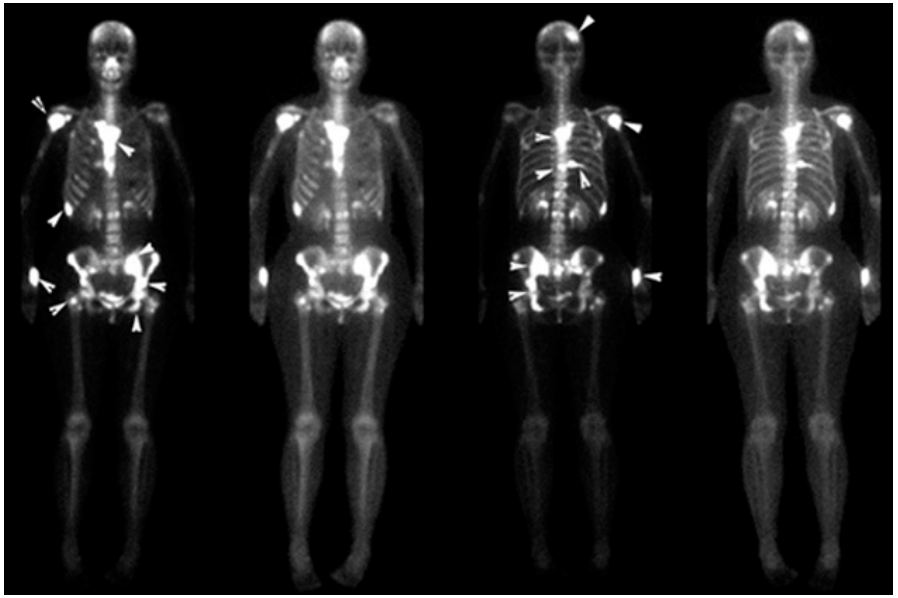
Non Pharmoclogic Mangament of Cancer Pain

- Clinical Case
  - 68 female- prior Fortune 500 CEO with widely metastatic breast CA
    - Brain, multiple long bone and spine
- Pain Medicine Service consulted
  - Thoracic compression fractures T7-8 highly symptomatic
  - Significant perineal pain component
  - Shoulder and wrist pain
  - Component of abdominal visceral pain
- Best approach?



Non Pharmoclogic Mangament of Cancer Pain

- Clinical Case
  - 68 female- prior Fortune 500 CEO with widely metastatic breast CA
    - Brain, pelvis, multiple long bone and spine
- Pain Medicine Service consulted
  - Thoracic compression fractures T7-8 highly symptomatic
  - Significant perineal pain component
  - Shoulder and wrist pain
  - Component of abdominal/pelvic visceral pain
- Best approach?



Non Pharmoclogic Mangament of Cancer Pain

- Vertebral augmentation techniques

  "*Thoracic compression fractures T7-8 highly symptomatic*"

- Vertebroplasty

- Kyphoplasty

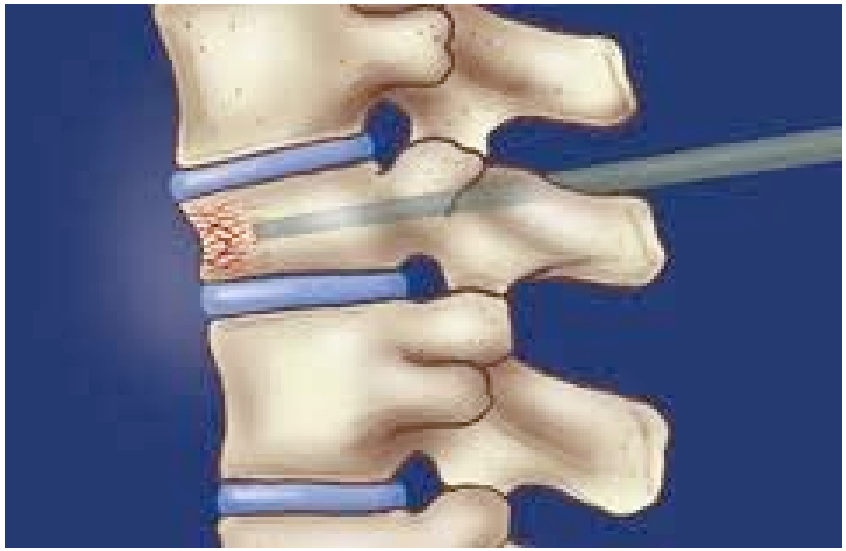
Non Pharmoclogic Mangament of Cancer Pain

- Vertebroplasty
  - First described by Galibert and Deramon 1987
  - Transpedicular injection of poly-methyl-methacrylate (PMMA)
  - Painful vertebral body hemangioma

Galibert P, Deramond H, Rosat P, Le Gars D: [Preliminary note on the treatment of vertebral angioma by percutaneous acrylic vertebroplasty]. Neurochirurgie 1987, 33:166-168.

Non Pharmoclogic Mangament of Cancer Pain

- Vertebroplasty
  - Percutaneous fixation of vertebral fracture elements
  - Generally transpediculate
  - Fluoroscopic guidance in prone position with sedation



Interventional radiologists treat vertebral fractures with vertebroplasty. (c) 2004, Society of Interv
Radiology, www.SIRweb.org

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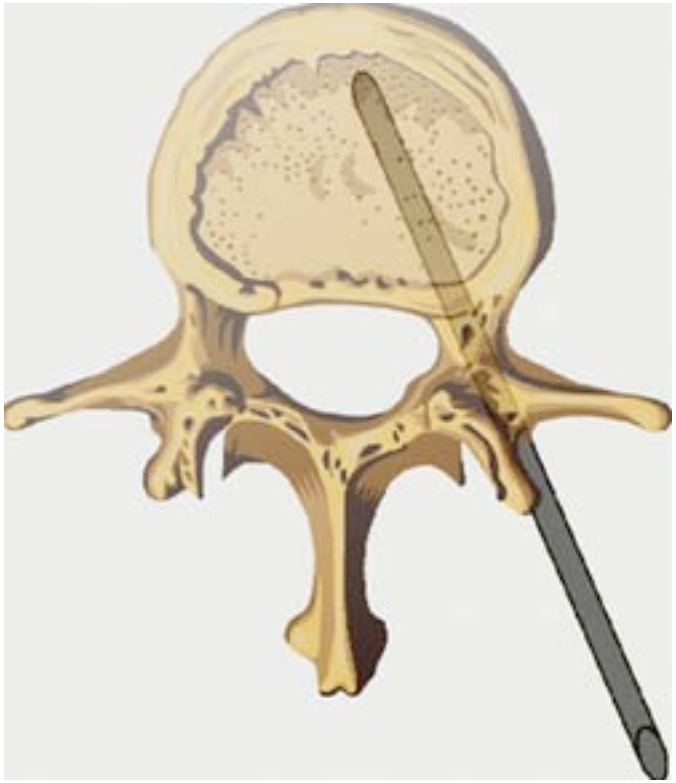
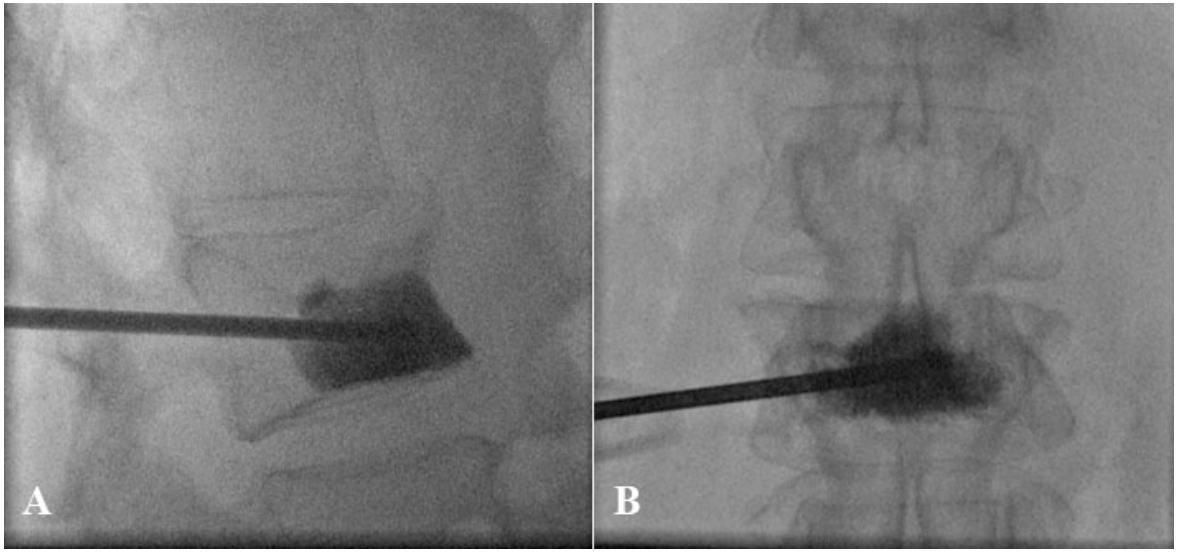
- Vertebroplasty





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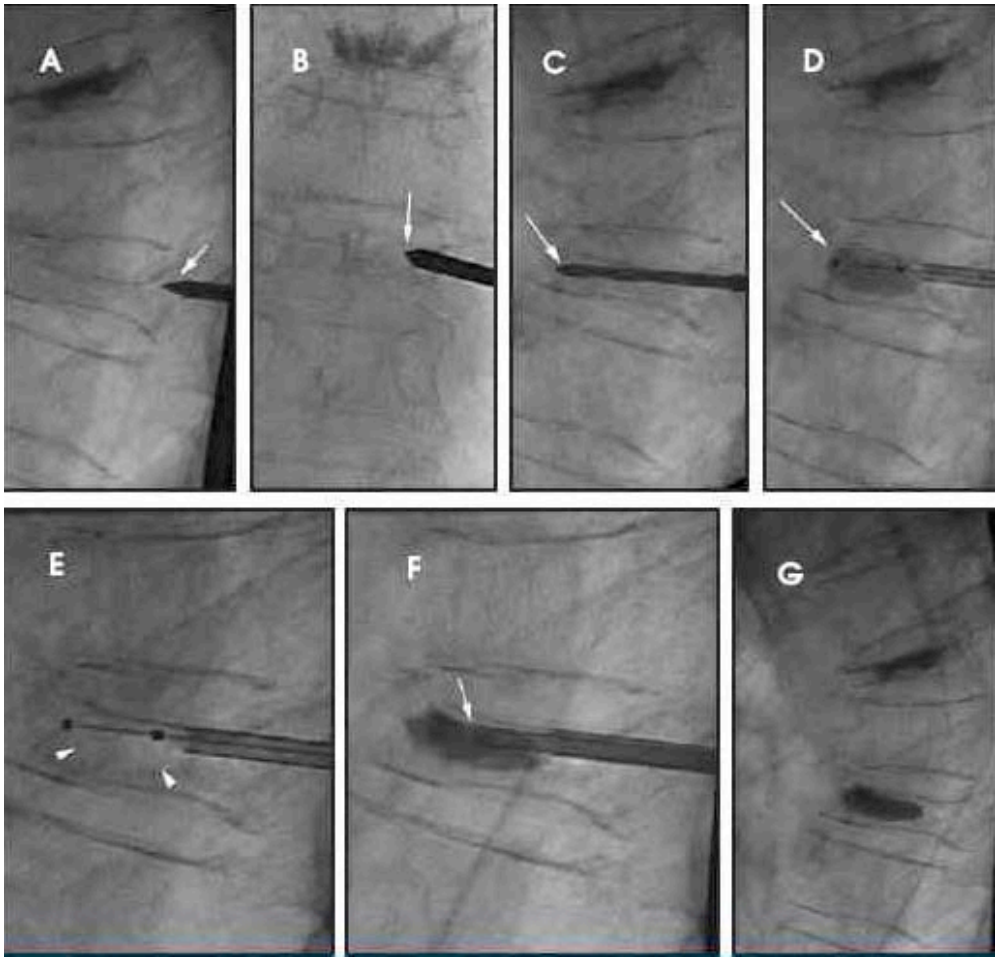
Kyphoplasty



Applied Radiology. 2008;37(12):10-24. © 2008 Anderson Publishing, Ltd.

Non Pharmoclogic Mangament of Cancer Pain

Kyphoplasty in the Treatment of Osteolytic Vertebral Compression Fractures as a Result of Multiple Myeloma

By S. Dudeney, I.H. Lieberman, M-K. Reinhardt, and M. Hussein

Purpose: **We prospectively evaluated the safety and efficacy of kyphoplasty in the treatment of osteolytic vertebral compression fractures resulting from multiple myeloma. The principle symptoms in multiple myeloma result from bone destruction, especially the spine. Kyphoplasty is a new technique that involves the introduction of inflatable bone tamps (IBT) into the vertebral body. The purpose of the IBT is to restore the vertebral body back toward its original height, while creating a cavity that can be filled with highly viscous bone cement.**

Patients and Methods: **Fifty-five consecutive kyphoplasty procedures were performed in 18 patients with osteolytic vertebral compression fractures resulting from multiple myeloma. Cement leakage and any complications were recorded. Early objective analysis was made by comparing preoperative and latest Short Form 36 Health Survey scores. Height restoration was estimated by measuring vertebral height on lateral radiographs.**

Results: **The mean age of patients was 63.5 years, mean duration of symptoms was 11 months, and mean follow-up was 7.4 months. There were no major complications related directly to use of this technique. On average, 34% of height lost at the time of fracture was restored. Asymptomatic cement leakage occurred at two (4%) of 55 levels. Significant improvement in SF36 scores occurred for Bodily Pain (23.2 to 55.4, *P* = .0008), Physical Function (21.3 to 50.6, *P* = .0010), Vitality (31.3 to 47.5, *P* = .010), and Social Functioning (40.6 to 64.8, *P* = .014).**

Conclusion: **Kyphoplasty was efficacious in the treatment of osteolytic vertebral compression fractures resulting from multiple myeloma. Kyphoplasty is associated with early clinical improvement of pain and function as well as some restoration of vertebral body height.**

J Clin Oncol 20:2382-2387. ***© 2002 by American Society of Clinical Oncology.***

Non Pharmoclogic Mangament of Cancer Pain

Kyphoplasty in the Treatment of Osteolytic Vertebral Compression Fractures as a Result of Multiple Myeloma

By S. Dudeney, I.H. Lieberman, M-K. Reinhardt, and M. Hussein

- 55 pts – osteolytic vertebral compression fxs secondary to multiple myeloma
- Mean symptom duration – 11 mo
- Significant improvement in:
  - SF36 scores occurred for Bodily Pain (23.2 to 55.4, $P = .0008$),
  - Physical Function (21.3 to 50.6, $P = .0010$), Vitality (31.3 to 47.5, $P = .010$)
  - Social Functioning (40.6 to 64.8 $P = .014$).
- 34% vertebral height restored

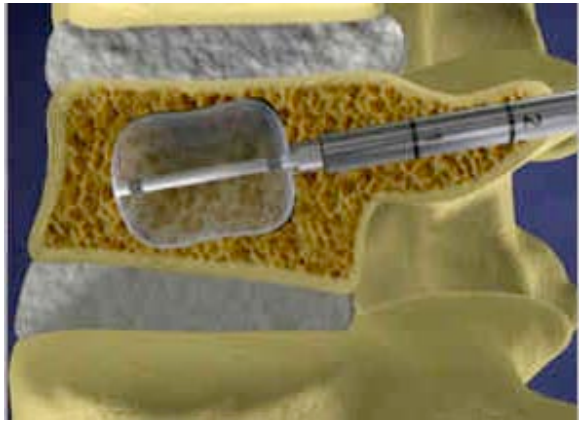
J Clin Oncol 2002;20(9):2382–7.

Non Pharmoclogic Mangament of Cancer Pain

Kyphoplasty in the Treatment of Osteolytic Vertebral Compression Fractures as a Result of Multiple Myeloma

By S. Dudeney, I.H. Lieberman, M-K. Reinhardt, and M. Hussein

- Effect durable to 7.4 months
- No major complications related to procedure
- Asymptomatic cement leakage 4%



J Clin Oncol 2002;20(9):2382–7.

Non Pharmoclogic Mangament of Cancer Pain

Percutaneous vertebroplasty and kyphoplasty for painful vertebral body fractures in cancer patients.
Fourney DR, Schomer DF, Nader R, et al. J Neurosurg. 2003

- 56 pts –vertebral compression fxs (multiple myeloma(21),other (35)
- 97 fractures tx – 65 VP/32 KP
- Mean symptom duration – 3.2 mo
- Marked or complete relief 84%
- VAS reductions significant up to 1 year
- Reduced opioid consumption at 1 mo
- Asymptomatic cement leakage 9.2 %

- Mean height restoration 42%
- No deaths or complication secondary to procedure

J Neurosurg. 2003 Jan;98(1 Suppl):21-30..

Non Pharmoclogic Mangament of Cancer Pain

Balloon kyphoplasty versus non-surgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: a multicentre, randomised controlled trial

*James Berenson, Robert Pflugmacher, Peter Jarzem, Jeffrey Zonder, Kenneth Schechtman, John B Tillman, Leonard Bastian, Talat Ashraf, Frank Vrionis, for the Cancer Patient Fracture Evaluation (CAFE) Investigators**

- Multicenter RCT
- 134 pts – 70 kyphoplasty / 64 non-surgical
- RDQ score kyphoplasty group changed from 17·6 at baseline to 9·1 at 1 month (mean –8·3 points, p<0·0001).
- RDQ control group changed from 18·2 to 18·0 (p=0·83)

Lancet Oncol 2011; 12: 225–35

Non Pharmoclogic Mangament of Cancer Pain

Balloon kyphoplasty versus non-surgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: a multicentre, randomised controlled trial

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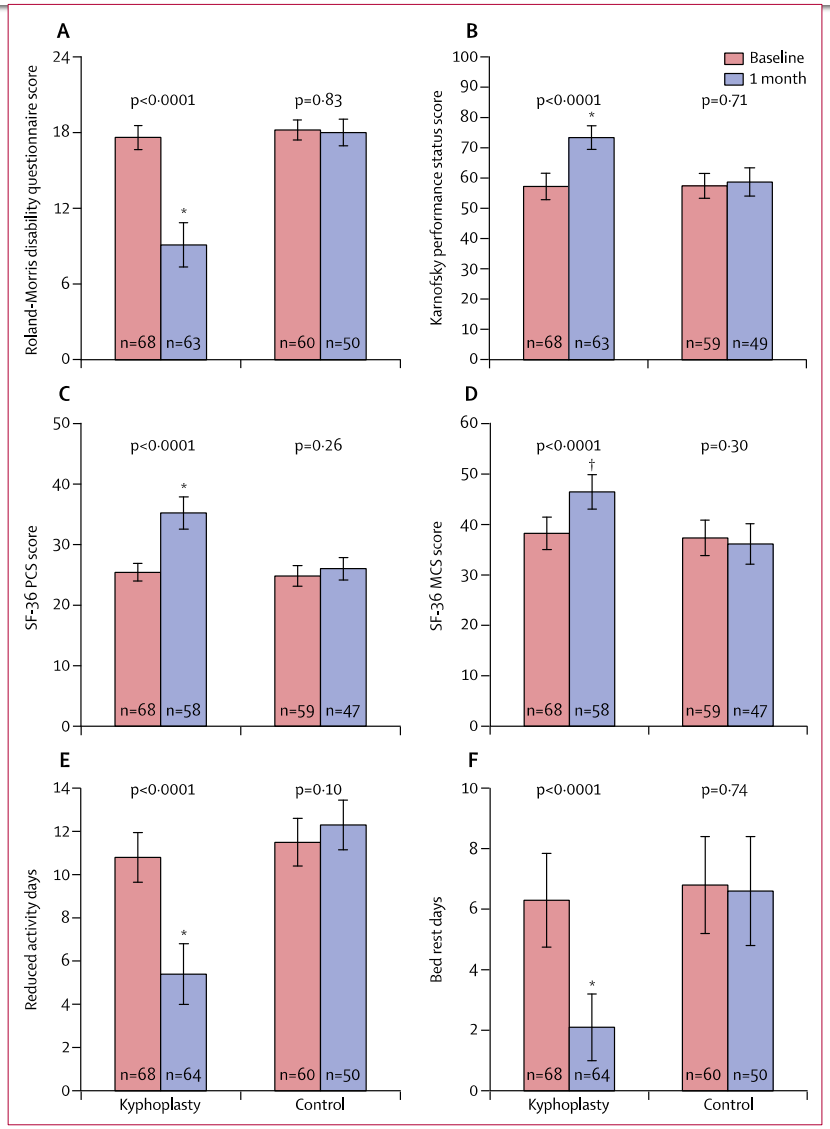
Lancet Oncol 2011; 12: 225–35



Non Pharmoclogic Mangament of Cancer Pain

- Vertebroplasty
  - Osteoporotic fx
  - RCT with sham
  - No difference noted at 1 mo
  - 1830 subjects screened to enroll 131 – suspicion of major selection bias in favor of non-responders
  - Absence of positive physical exam findings
  - Unclear volume of PMMA

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Vertebroplasty for Osteoporotic Spinal Fractures

David F. Kallmes, M.D., Bryan A. Comstock, M.S., Patrick J. Heagerty, Ph.D., Judith A. Turner, Ph.D., David J. Wilson, F.R.C.R., Terry H. Diamond, F.R.A.C.P., Richard Edwards, F.R.C.R., Leigh A. Gray, M.S., Lydia Stout, B.S., Sara Owen, M.Sc., William Hollingworth, Ph.D., Basavaraj Ghdoke, M.D., Deborah J. Annesley-Williams, F.R.C.R., Stuart H. Ralston, F.R.C.P., and Jeffrey G. Jarvik, M.D., M.P.H.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 6, 2009 VOL. 361 NO. 6

A Randomized Trial of Vertebroplasty for Painful Osteoporotic Vertebral Fractures

Rachelle Buchbinder, Ph.D., Richard H. Osborne, Ph.D., Peter R. Ebeling, M.D., John D. Wark, Ph.D., Peter Mitchell, M.Med., Chris Wriedt, M.B., B.S., Stephen Graves, D. Phil., Margaret P. Staples, Ph.D., and Bridie Murphy, B.Sc.

Non Pharmoclogic Mangament of Cancer Pain

- Neurolytic Techniques

  "Significant perineal pain component & Component of abdominal visceral pain"

■ These neural destructive procedures involve the use of chemical agents (alcohol 50–100% and phenol 6–10%), physical methods of heat (radiofrequency) and cold (cryoablation) and surgery

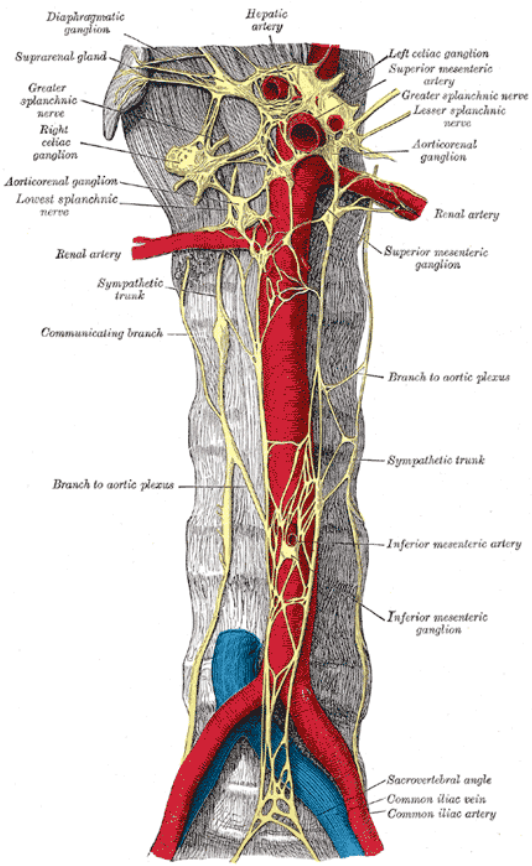
■Patients should be thoroughly informed about likely sensory deficits and possible complications – *post denervation neuralgia*

■ **In most cases, destructive procedures should first be simulated with local anesthetic to allow the patient to experience the sensory changes that may occur**

Non Pharmoclogic Mangament of Cancer Pain

- Neurolytic Techniques
  "Significant perineal pain component & Component of abdominal visceral pain"

- Celiac *Plexus* – mesh like neural complex carrying visceral afferents/efferents from pancreas, liver, biliary tract, renal pelvis, ureter, spleen, and bowel up to the first part of the transverse colon

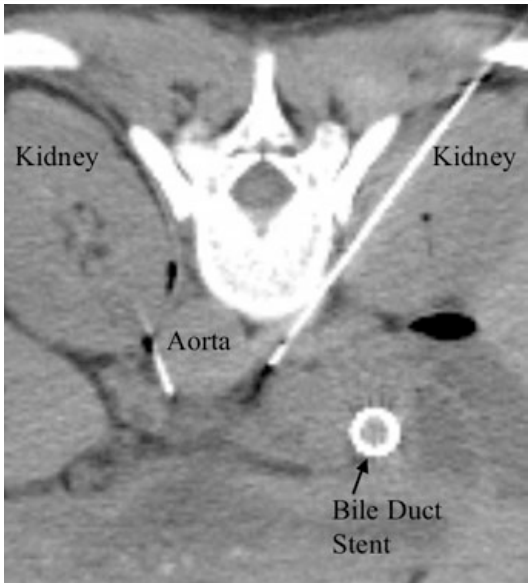


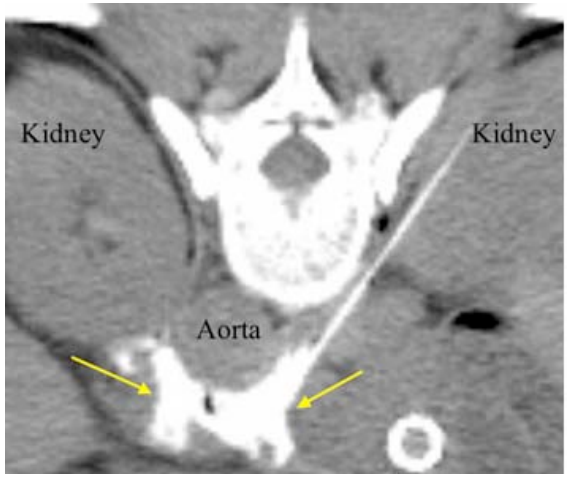
Non Pharmoclogic Mangament of Cancer Pain

- Neurolytic Techniques
  "Significant perineal pain component & Component of abdominal visceral pain"
- Celiac *Plexus* – *Neurolytic technique with either ETOH or Phenol performed after diagnostic block with local anesthetic*

- Most commonly utilized in Tx of pancreatic CA role in - gastric cancer, esophageal cancer, colorectal cancer, liver metastasis, gallbladder cancer and cholangiocarcinoma

  - Success better with earlier intervention
  - Helpful in addressing opioid toxicity- constipation
  - Hypotension and diarrhea not uncommon – temporary
  - Paraplegia after 4/ 2,730 celiac plexus blocks





Non Pharmoclogic Mangament of Cancer Pain

Celiac *Plexus* – *Neurolytic*

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Celiac *Plexus* – *Neurolytic*

- Wong et. al. - Single-blind RCT of 100 patients with pancreatic cancer
- Plexus ablation vs. pharmacological management with sham procedure

- Pain relief was better in the interventional
  - 53% reduction in NRS vs 27% in SAT
- Fewer episodes of moderate/severe pain in NCPB
  - 40% vs 14% in NCPB
- 20% required rescue NCBP in SAT group - ITT issue

- No effect on QOL or Survival

ORIGINAL CONTRIBUTION

Effect of Neurolytic Celiac Plexus Block on Pain Relief, Quality of Life, and Survival in Patients With Unresectable Pancreatic Cancer

A Randomized Controlled Trial

Gilbert Y. Wong, MD
Darrell R. Schroeder, MS
Paul E. Carns, MD
Jack L. Wilson, MD
David P. Martin, MD, PhD
Michelle O. Kinney, MD
Carlos B. Mantilla, MD, PhD
David O. Warner, MD

Context Pancreatic cancer is an aggressive tumor associated with high mortality. Optimal pain control may improve quality of life (QOL) for these patients.

Objective To test the hypothesis that neurolytic celiac plexus block (NCPB) vs opioids alone improves pain relief, QOL, and survival in patients with unresectable pancreatic cancer.

Design, Setting, and Patients Double-blind, randomized clinical trial conducted at Mayo Clinic, Rochester, Minn. Enrolled (October 1997 and January 2001) were 100 eligible patients with unresectable pancreatic cancer experiencing pain. Patients were followed up for at least 1 year or until death.

Intervention Patients were randomly assigned to receive either NCPB or systemic analgesic therapy alone with a sham injection. All patients could receive additional opioids managed by a clinician blinded to the treatment assignment.

Main Outcome Measures Pain intensity (0-10 numerical rating scale), QOL, opioid consumption and related adverse effects, and survival time were assessed weekly by a blinded observer.

Results Mean (SD) baseline pain was 4.4 (1.7) for NCPB vs 4.1 (1.8) for opioids alone. The first week after randomization, pain intensity and QOL scores were improved (pain intensity, $P \leq .01$ for both groups; QOL, $P < .001$ for both groups), with a larger decrease in pain for the NCPB group ($P = .005$). From repeated measures analysis, pain was also lower for NCPB over time ($P = .01$). However, opioid consumption ($P = .93$), frequency of opioid adverse effects (all $P > .10$), and QOL ($P = .46$) were not significantly different between groups. In the first 6 weeks, fewer NCPB patients reported moderate or severe pain (pain intensity rating of ≥5/10) vs opioid-only patients (14% vs 40%, $P = .005$). At 1 year, 16% of NCPB patients and 6% of opioid-only patients were alive. However, survival did not differ significantly between groups ($P = .26$, proportional hazards regression).

Conclusion Although NCPB improves pain relief in patients with pancreatic cancer vs optimized systemic analgesic therapy alone, it does not affect QOL or survival.

JAMA. 2004;291:1092-1099 www.jama.com

PANCREATIC ADENOCARCINOMA is an aggressive tumor associated with high mortality. Up to 73% of patients are in pain at the time of diagnosis.[1] Thus, a major treatment focus is to optimize the quality of life (QOL) by managing symptoms, especially by providing adequate pain control.

The recommended approach to manage cancer pain uses systemic medications according to the World Health Organization analgesic ladder.[2] At times, systemic analgesics do not provide adequate pain relief, or doses are limited by opioid-related adverse effects.[3] In these circumstances, celiac plexus or splanchnic nerve blocks with neurolytic solutions may provide analgesia by interrupting visceral afferent pain transmission from the upper abdomen.[4] However, randomized clinical trials evaluating the efficacy of neurolytic celiac plexus block (NCPB) for pancreatic cancer pain have been limited by small sample sizes, lack of blinding, infrequent pain assessments, or lack of standardized delivery of systemic analgesic medications.[5-8] Indeed, the role of neurolytic blocks in the management of any type of cancer pain has not been firmly established by randomized, blinded clinical trials.

Lillemoe and colleagues[8] showed that patients with unresectable pancreatic cancer randomly assigned to receive in-

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Corresponding Author: Gilbert Y. Wong, MD, Mayo Clinic College of Medicine, Department of Anesthesiology, Division of Pain Medicine, 200 First St SW, Rochester, MN 55905 (wong.gilbert@mayo.edu).

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Wong GY, Schroeder DR, Carns PE, et al. Effect of neurolytic celiac plexus block on pain relief, quality of life, and survival in patients with unresectable pancreatic cancer: A randomized controlled trial. JAMA 2004;291:1092–9.

Non Pharmoclogic Mangament of Cancer Pain

- Celiac Plexus
- *Neurolytic*
- Yan et al 2007
- Meta-analysis of five RCTs -303 subjects
- Significantly improved pain relief vs pharmacological management
- WMD in VAS score was –0.60 (95% CI –0.82 to –0.37, P < 0.00001)
- Magnitude of VAS reduction minimal
- Reduced opioid consumption in NCPB group
- Reduction in constipation risk ≈50 %
- End points calculated at 8 weeks

Neurolytic Celiac Plexus Block for Pain Control in Unresectable Pancreatic Cancer

Brian M. Yan, M.D., F.R.C.P.C. and Robert P. Myers, M.D., F.R.C.P.C.
Division of Gastroenterology, Department of Medicine, University of Calgary, Calgary, Alberta, Canada

BACKGROUND: A major focus of palliation in patients with unresectable pancreatic cancer is pain control. The aim of this systematic review was to examine the efficacy and safety of neurolytic celiac plexus blockade (NCPB) compared with standard treatment in randomized controlled trials (RCTs) involving patients with unresectable pancreatic cancer.

METHODS: An electronic search was completed (1966 through August, 2005) for RCTs comparing NCPB *versus* control (standard treatment and/or sham NCPB) in patients with unresectable pancreatic cancer. The primary outcome was pain measured on a 10-point visual analogue scale (VAS). Secondary outcomes included opioid usage, adverse effects, quality of life (QOL), and survival. All outcomes were assessed at 2, 4, and 8 wk.

RESULTS: Five RCTs involving 302 patients (NCPB, N = 147; control, N = 155) met the inclusion criteria. Mean age was 61.0 ± 4.3 yr. Compared with control, NCPB was associated with lower VAS scores for pain at 2, 4, and 8 wk (weighted mean difference [WMD] −0.60, 95% CI −0.82 to −0.37). Opioid usage (in mg/d oral morphine) was also reduced at 2, 4, and 8 wk (WMD −85.9, 95% CI −144.0 to −27.9). NCPB was associated with a reduction in constipation (relative risk 0.67, 95% CI 0.49–0.91), but not other adverse events. No differences in survival were observed. QOL could not be adequately analyzed due to differences in outcome scales among studies.

CONCLUSIONS: In patients with unresectable pancreatic cancer, NCPB is associated with improved pain control, and reduced narcotic usage and constipation compared with standard treatment, albeit with minimal clinical significance.

(Am J Gastroenterol 2007;102:430–438)

Yan BM, Myers RP. Neurolytic celiac plexus block for pain control in unresectable pancreatic cancer. Am J Gastroenterol 2007;102(2):430–8.

Non Pharmoclogic Mangament of Cancer Pain

VOLUME 29 • NUMBER 28 • SEPTEMBER 10, 2011

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Randomized, Double-Blind, Controlled Trial of Early Endoscopic Ultrasound–Guided Celiac Plexus Neurolysis to Prevent Pain Progression in Patients With Newly Diagnosed, Painful, Inoperable Pancreatic Cancer

Jonathan M. Wyse, Marco Carone, Sarto C. Paquin, Mariana Usatii, and Anand V. Sahai

Jonathan M. Wyse, Sarto C. Paquin, Mariana Usatii, and Anand V. Sahai, Centre Hospitalier de l'Universite de Montreal, Hopital Saint Luc, Montreal, Quebec, Canada; and Marco Carone, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.

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Presented in part at Digestive Disease Week, May 30-June 4, 2009, Chicago, IL.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

Clinical Trials repository link available on JCO.org.

Corresponding author: Jonathan Wyse, MDCM, MSc, Centre Hospitalier de l'Universite de Montreal, Hopital Saint Luc, 1058 Rue Saint Denis, Montreal, Quebec H2X 3J4, Canada; e-mail: jonwyse@gmail.com.

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0732-183X/11/2926-3541/$20.00

DOI: 10.1200/JCO.2010.32.2750

A B S T R A C T

Purpose
Celiac plexus neurolysis (CPN) is currently used as salvage therapy for morphine-resistant pancreatic cancer pain. Endoscopic ultrasound–guided CPN (EUS-CPN) can be performed early, at the time of EUS. We hypothesized that early EUS-CPN would reduce pain and morphine consumption, increase quality of life (QOL), and prolong survival.

Patients and Methods
Patients were eligible if referred for EUS for suspected pancreatic cancer with related pain. If EUS and EUS-guided fine-needle aspiration cytology confirmed inoperable adenocarcinoma, patients were randomly assigned to early EUS-CPN or conventional pain management. Pain scores (7-point Likert scale), morphine equivalent consumption, and QOL scores (Digestive Disease Questionnaire-15) were assessed at 1 and 3 months.

Results
Five hundred eighty eligible patients were seen between April 2006 and December 2008. Ninety-six patients were randomly assigned (48 patients per study arm). Pain relief was greater in the EUS-CPN group at 1 month and significantly greater at 3 months (difference in mean percent change in pain score = −28.9 [95% CI, −67.0 to 2.8], $P = .09$, and −60.7 [95% CI, −86.6 to −25.5], $P = .01$, respectively). Morphine consumption was similar in both groups at 1 month (difference in mean change in morphine consumption = −1.0 [95% CI, −47.7 to 49.2], $P = .99$), but tended toward lower consumption at 3 months in the neurolysis group (difference in mean change in morphine consumption = −49.5 [95% CI, −127.5 to 7.0], $P = .10$). There was no effect on QOL or survival.

Conclusion
Early EUS-CPN reduces pain and may moderate morphine consumption in patients with painful, inoperable pancreatic adenocarcinoma. EUS-CPN can be considered in all such patients at the time of diagnostic and staging EUS.

J Clin Oncol 29:3541-3546. © 2011 by American Society of Clinical Oncology

Non Pharmoclogic Mangament of Cancer Pain

Randomized, Double-Blind, Controlled Trial of Early Endoscopic Ultrasound–Guided Celiac Plexus Neurolysis to Prevent Pain Progression in Patients With Newly Diagnosed, Painful, Inoperable Pancreatic Cancer

Jonathan M. Wyse, Marco Carone, Sarto C. Paquin, Mariana Usatii, and Anand V. Sahai

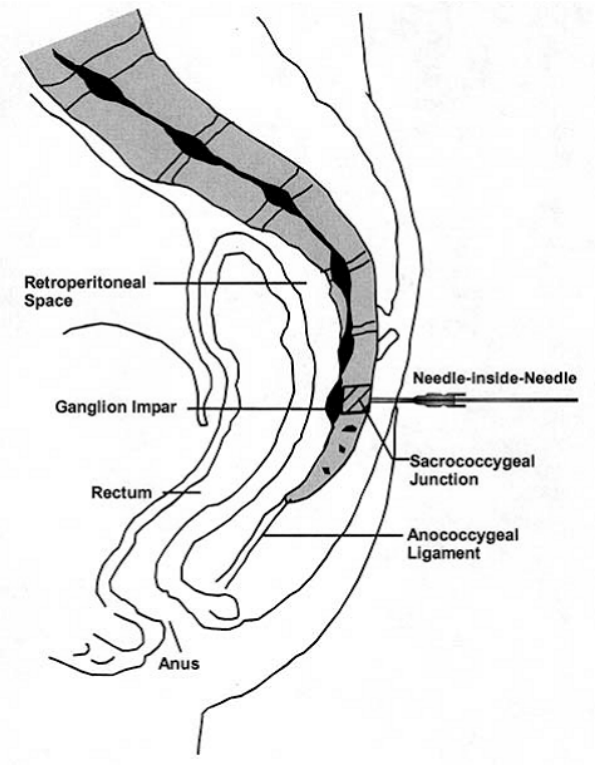
- Celiac Plexus -*Neurolysis*
- RCT - 96 subjects, 48 conventional pain management / 48 in early endoscopic ultrasound-guided celiac plexus neurolysis
- Likert scale, Opioid consumption, QOL, survival at 1 and 3 months
- Pain score change vs. control: -28.9% [95% CI -67.0 to 2.8] ***P=0.09*** at one month
- Pain score change vs. control: -60.7% [95% CI -86.6. to -25.5] ***P=0.01*** at 3 months
- No difference in opioid consumption, QOL or survival

Yan BM, Myers RP. Neurolytic celiac plexus block for pain control in unresectable pancreatic cancer. Am J Gastroenterol 2007;102(2):430–8.

Non Pharmoclogic Mangament of Cancer Pain

- Neurolytic Techniques
  "Significant perineal pain component"
- Ganglion Impar Block

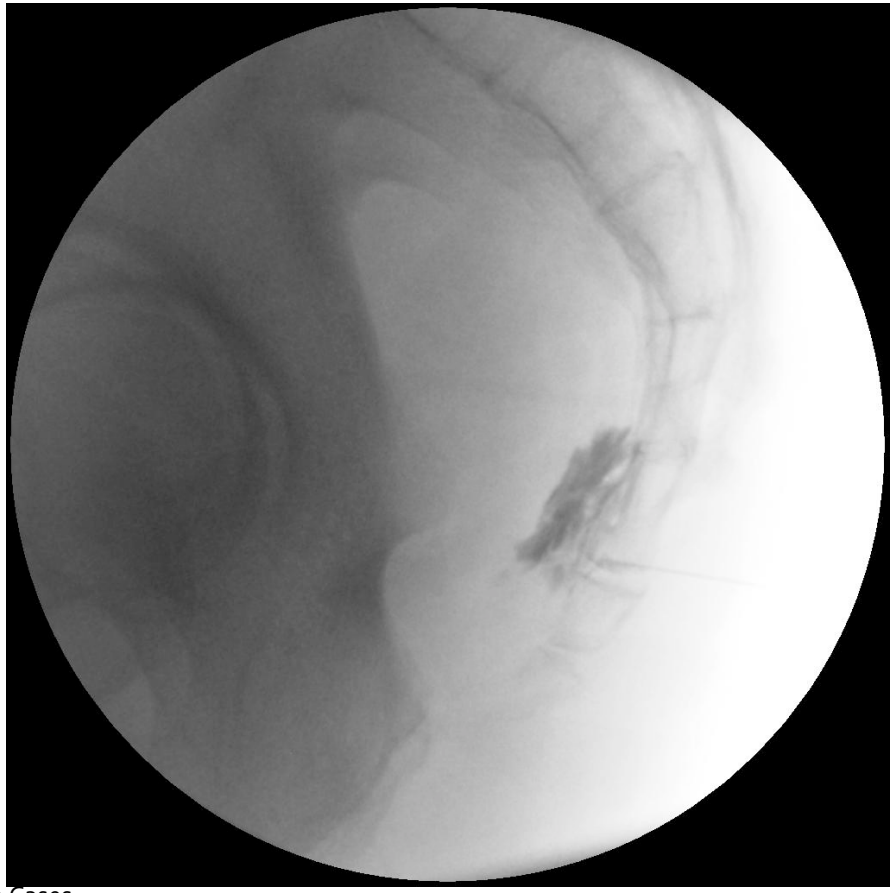
- Most inferior sympathetic ganglion
- Anterior to the sacrococcygeal junction
- Pain relief for cancers of the :
  - Pelvis and perineum
  - Abdomino- perineal resection for rectal cancer
  - Radiation proctitis



- Rabah E, Souyet H, Aguilera C, Neurolytic Elzo JJ. Block of the ganglion impar (walther) chronic radia- tion proctitis. Analgesia 2001;5(2):63–5.

Non Pharmoclogic Mangament of Cancer Pain

- Neurolytic Techniques
  "Significant perineal pain component"
- Ganglion Impar Block
- Eker et al
  - Case report 3 patients
  - Recal Ca with perineal pain
  - Pre block VAS 8-9/10
  - VAS <3 - 6 mos post 4ml 6% Phenol



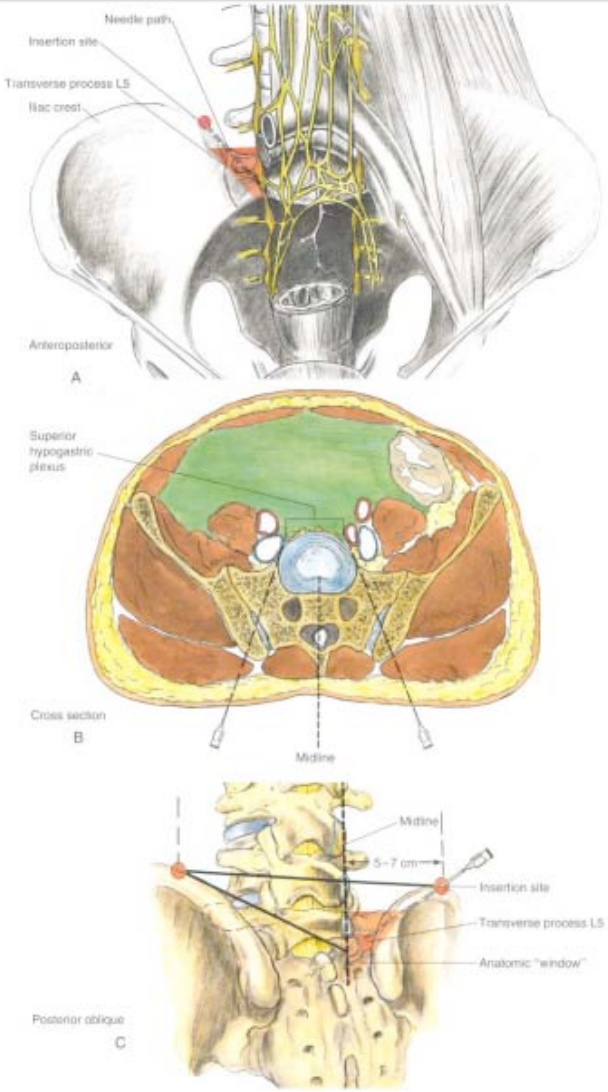
Transsacrococcygeal Approach to Ganglion Impar for Pelvic Cancer Pain: A Report of 3 Cases.
Eker, Evren H. M.D.; Cok, Oya Yalcin M.D.; Kocum, Aysu M.D.; Acil, Meltem M.D.; Turkoz, Ayda M.D.
Regional Anesthesia & Pain Medicine. 33(4):381-382, July/August 2008

Non Pharmoclogic Mangament of Cancer Pain

- Neurolytic Techniques
  "Significant perineal pain component"

- Superior Hypogastric Plexus Block
- Extension of aortic plexus – located anterior aspect of L5-S1

- Carries sympathetic afferents/efferents to and from the bladder, uterus, vagina, prostate, testes, urethra, descending colon and rectum.



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Non Pharmoclogic Mangament of Cancer Pain

- Neurolytic Techniques
  "Significant perineal pain component"

- Superior Hypogastric Plexus Block
- Carries afferent from the bladder, uterus, vagina, prostate, testes, urethra, descending colon and rectum

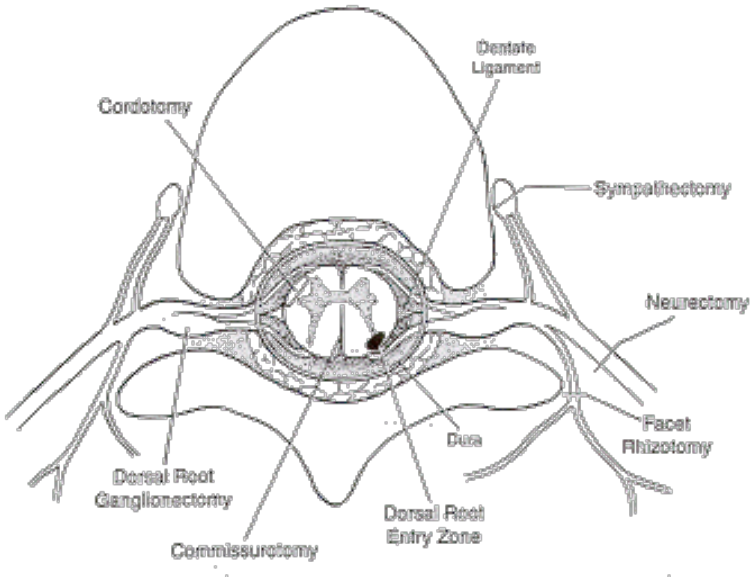
- May reduce pain associated with pelvic malignancy[1]. Posterior approach is commonest but an anterior approach has been described[2].

1)Plancarte R, de Leon-Casasola OA, El-Helaly M, Allende S, Lema MJ. Neurolytic superior hypogastric plexus block for chronic pelvic pain associated with cancer. Reg Anesth 1997;22:562–8.

1) Kanazi GE, Perkins FM, Thakur R, Dotson E. New technique for superior hypogastric plexus block. Region Anesth Pain Med 1999;24(5):473–6.

Non Pharmoclogic Mangament of Cancer Pain

- Neurolytic Techniques
  "Significant perineal pain component"
- Intrathecal & Spinal Nerve
  - Most often used in case of spinal nerve root or cauda equina tumor invasion – pelvic cancer
  - Utilizes baricity of either phenol (hyper) or ethanol (hypo) to localize
  - DREZ neurolysis intended for isolated segmental pain



Non Pharmoclogic Mangament of Cancer Pain

- Neuraxial Infusions
  - *"Thoracic compression fractures T7-8 highly symptomatic, Significant perineal pain component & component of abdominal visceral pain"*
- Intrathecal drug delivery systems
- Epidural infusion systems
- Percutaneous vs. implantable
- Intermittent -constant vs. programmable

Non Pharmoclogic Mangament of Cancer Pain

- Neuraxial Infusions
  - *"Thoracic compression fractures T7-8 highly symptomatic, Significant perineal pain component & component of abdominal visceral pain"*
  - Why?
    - Mixed pain components in multiple sites
    - Good evidence
    - Adverse effects of current pharmacology
      - Reversal of drowsiness associated with systemic opioids
      - Safety track record
      - May facilitate at home care

Non Pharmoclogic Mangament of Cancer Pain

- Implantable intrathecal drug delivery systems (IDDS)
- *"Thoracic compression fractures T7-8 highly symptomatic, Significant perineal pain component & component of abdominal visceral pain"*
  - Permits infusion of multitude of agents – primarily opioids and local anesthetics
  - May reduce motor, sensory and sympathetic effects associated with epidural based infusions
  - Generally life expectancy > 3 mo – cost effectiveness≈
  - No further identifiable surgical or medical correction indicated
  - Favorable pre-implantation response to IT trial

≈Mueller-Schwefe G, Hassenbusch SJ, Reig E. Cost effectiveness of intrathecal therapy for pain. Neuro- modulation 1999;2(2):77–87.

Non Pharmoclogic Mangament of Cancer Pain

- Implantable intrathecal drug delivery systems (IDDS)
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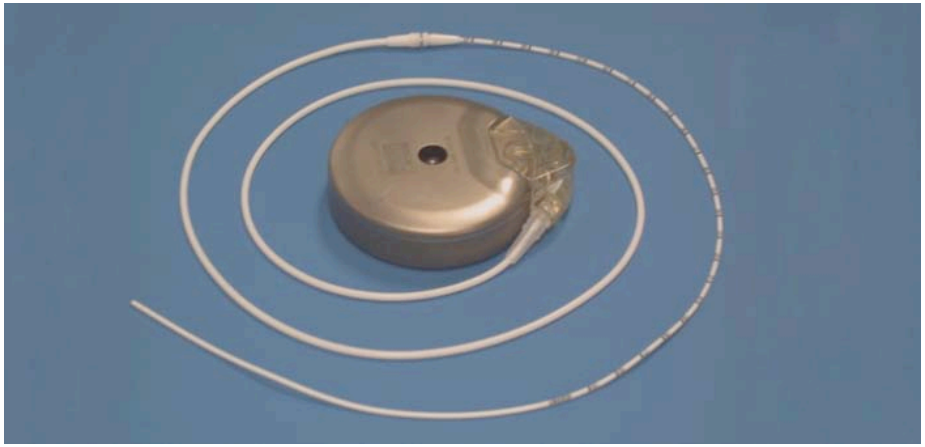

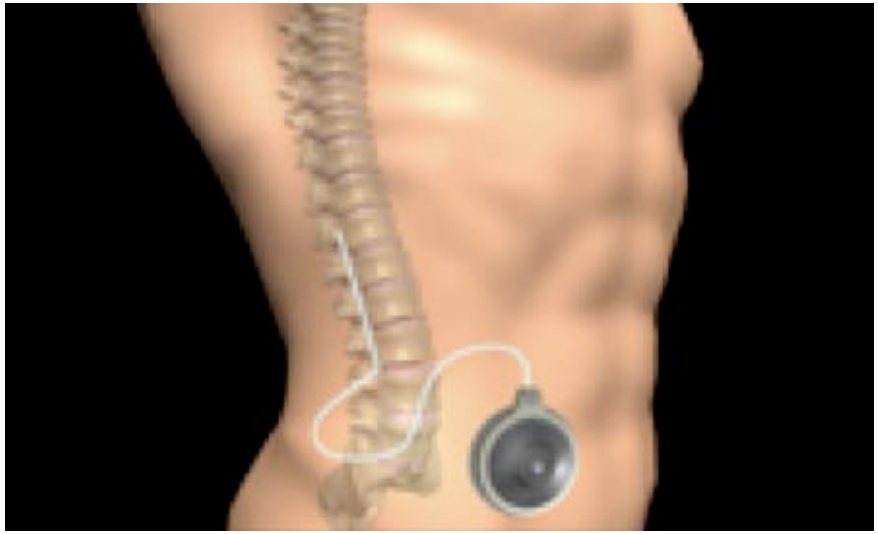

Non Pharmoclogic Mangament of Cancer Pain

- Implantable intrathecal drug delivery systems (IDDS)
  - *"Thoracic compression fractures T7-8 highly symptomatic, Significant perineal pain component & component of abdominal visceral pain"*
- Procedures carry a moderate level of minor adverse effects and a low level of serious adverse effects
- **Aftercare critical component of safety**

Non Pharmoclogic Mangament of Cancer Pain

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

By Thomas J. Smith, Peter S. Staats, Timothy Deer, Lisa J. Stearns, Richard L. Rauck, Richard L. Boortz-Marx, Eric Buchser, Elena Català, David A. Bryce, Patrick J. Coyne, and George E. Pool for the Implantable Drug Delivery Systems Study Group

Purpose: **Implantable intrathecal drug delivery systems (IDDSs) have been used to manage refractory cancer pain, but there are no randomized clinical trial (RCT) data comparing them with comprehensive medical management (CMM).**

Patients and Methods: **We enrolled 202 patients on an RCT of CMM versus IDDS plus CMM. Entry criteria included unrelieved pain (visual analog scale [VAS] pain scores ≥ 5 on a 0 to 10 scale). Clinical success was defined as ≥ 20% reduction in VAS scores, or equal scores with ≥ 20% reduction in toxicity. The main outcome measure was pain control combined with change of toxicity, as measured by the National Cancer Institute Common Toxicity Criteria, 4 weeks after randomization.**

Results: **Sixty of 71 IDDS patients (84.5%) achieved clinical success compared with 51 of 72 CMM patients (70.8%, *P* = .05). IDDS patients more often achieved ≥ 20% reduction in both pain VAS and toxicity (57.7% [41 of 71] *v* 37.5% [27 of 72], *P* = .02). The mean CMM VAS score fell from 7.81 to 4.76 (39% reduction); for the IDDS group, the scores fell from 7.57 to 3.67 (52% reduction, *P* = .055). The mean CMM toxicity scores fell from 6.36 to 5.27 (17% reduction); for the IDDS group, the toxicity scores fell from 7.22 to 3.59 (50% reduction, *P* = .004). The IDDS group had significant reductions in fatigue and depressed level of consciousness (*P* < .05). IDDS patients had improved survival, with 53.9% alive at 6 months compared with 37.2% of the CMM group (*P* = .06).**

Conclusion: **IDDSs improved clinical success in pain control, reduced pain, significantly relieved common drug toxicities, and improved survival in patients with refractory cancer pain.**

J Clin Oncol 20:4040-4049. ***© 2002 by American Society of Clinical Oncology.***

Non Pharmcologic Mangament of Cancer Pain

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Smith TJ, Coyne PJ, Staats PS, et al, J Clin Oncol

- 202 patient RCT Multicenter
- Comprehensive medical management vs IDDS
- Unrelieved pain VAS > 5 with > 200 mg/d oral morphine
- Patients could be included if toxic opioid effects < 200mg
- Life expectancy > 3 mo
- Study end points > 20 reduction in VAS and toxicity
- Secondary measures – Brief pain inventory, SF-12,Health survey and care giver QOL, resource use and survival
- 60/71 IDDS > 20% reduction in VAS vs. 51/71 CMM

Non Pharmoclogic Mangament of Cancer Pain

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Table 4. Clinical Success and Failure of the Two Arms

Criteria	IDDS		CMM		
	No.*	%	No.*	%	*P*
VAS pain reduced by ≥ 20% regardless of increased toxicity, or equal VAS with ≥ 20% reduction in toxicity	60/71	84.5	51/72	70.8	.05
Both pain and toxicity reduced by ≥ 20%	41/71	57.7	27/72	37.5	.02
Neither pain nor toxicity reduced by ≥ 20%	8/71	11.3	17/72	23.6	.05

*No. of patients/total no. of patients.

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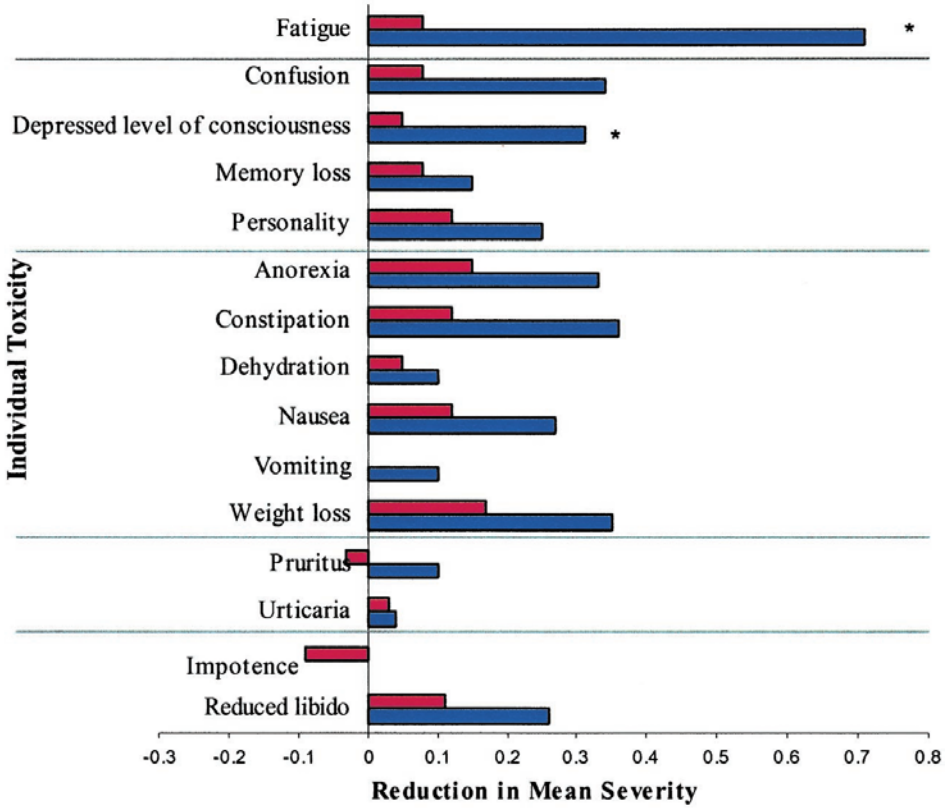

Fig 2. Reduction in individual toxicities from baseline to 4-week follow-up. *$P < .05$.

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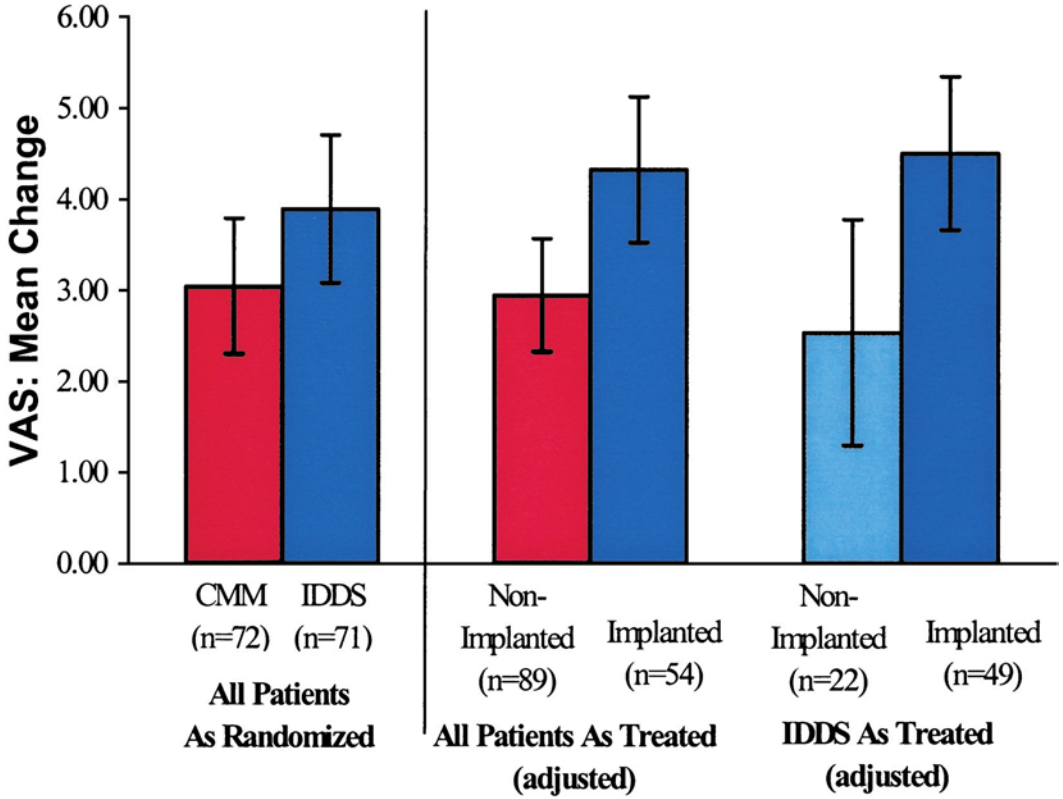

Fig 3. Reduction in VAS pain score from baseline to 4 weeks (as randomized and as treated). In the analysis of all patients as treated, the difference between nonimplanted and implanted is significant ($P = .007$). Error bars are ± 2 SE.

Non Pharmoclogic Mangament of Cancer Pain

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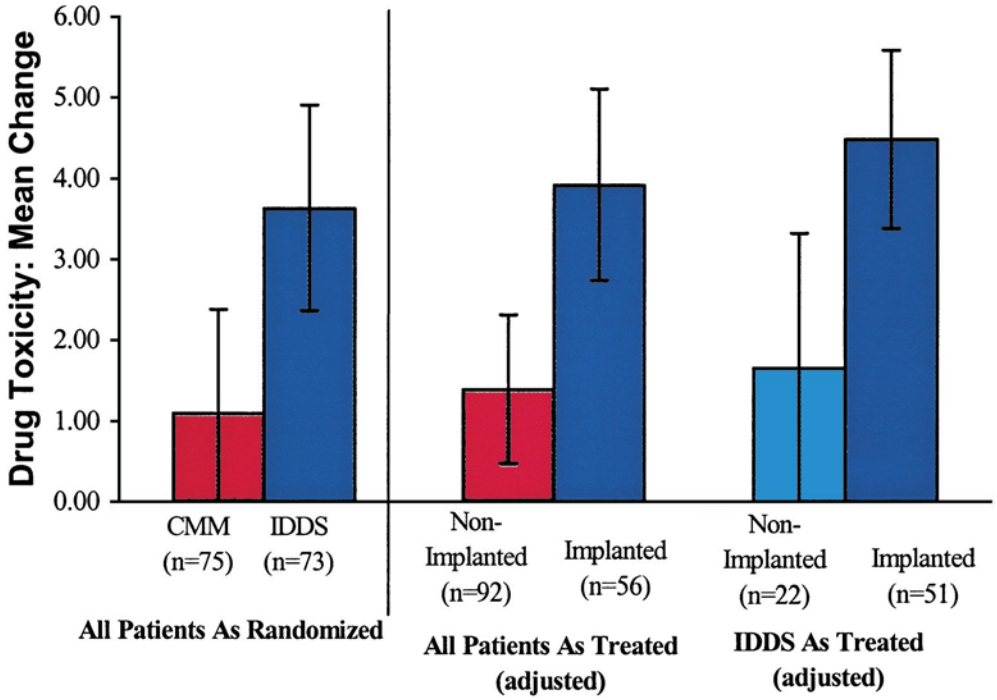

Fig 4. Reduction in toxicity from baseline to 4 weeks (as randomized and as treated). In the analysis of all patients as treated, the difference between nonimplanted and implanted is significant ($P = .008$). Error bars are ± 2 SE.

Non Pharmoclogic Mangament of Cancer Pain

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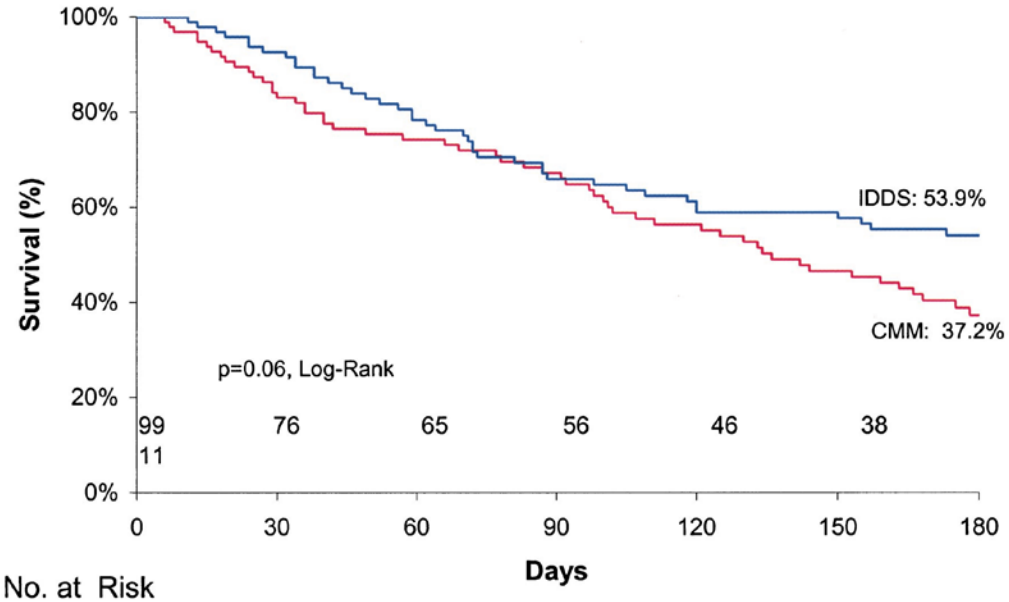

No. at Risk

CMM	99	76	65	56	46	48	11
IDDS	101	86	70	57	50	49	18

Percentage of surviving patients

CMM	6.6%	24.6%	33.9%	34.8%	39.5%	45.5%
IDDS	72.1%	78.6%	79.0%	84.0%	83.7%	83.3%

Non Pharmoclogic Mangament of Cancer Pain

- Neuraxial Infusions
  - *"Thoracic compression fractures T7-8 highly symptomatic, Significant perineal pain component & component of abdominal visceral pain"*
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Non Pharmoclogic Mangament of Cancer Pain

- Neuraxial Infusions
  - *"Thoracic compression fractures T7-8 highly symptomatic, Significant perineal pain component & component of abdominal visceral pain"*
  - Epidural infusion systems
    - Generally for briefer periods
    - Often tunneled to reduce displacement issues and infection risk
    - Requires higher volumes with more systemic effect
    - Not as convenient for home care
    - Trend away from epidural infusions towards intrathecal lines both externalized and internalized

- Baker L, Lee M, Regnard C, Crack L, Callin S. Evolv- ing spinal analgesia practice in palliative care. Palliat Med 2004;18:507–15.

Non Pharmoclogic Mangament of Cancer Pain

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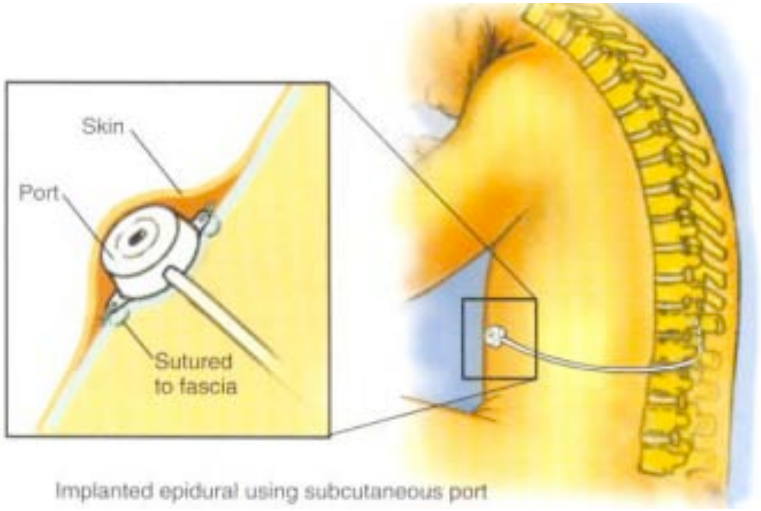
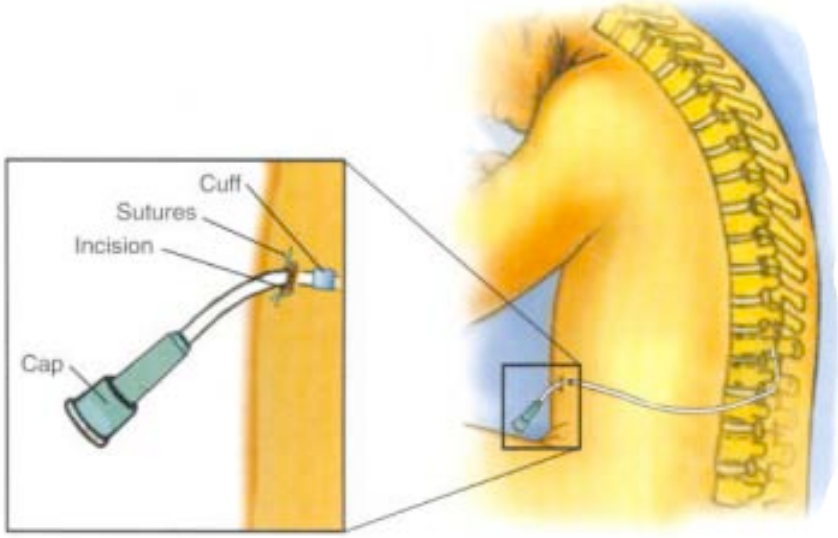


Implanted epidural using subcutaneous port



Implanted epidural using percutaneous silastic catheter (DuPen catheter)

Non Pharmoclogic Mangament of Cancer Pain

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Non Pharmoclogic Mangament of Cancer Pain

- Continuous regional techniques

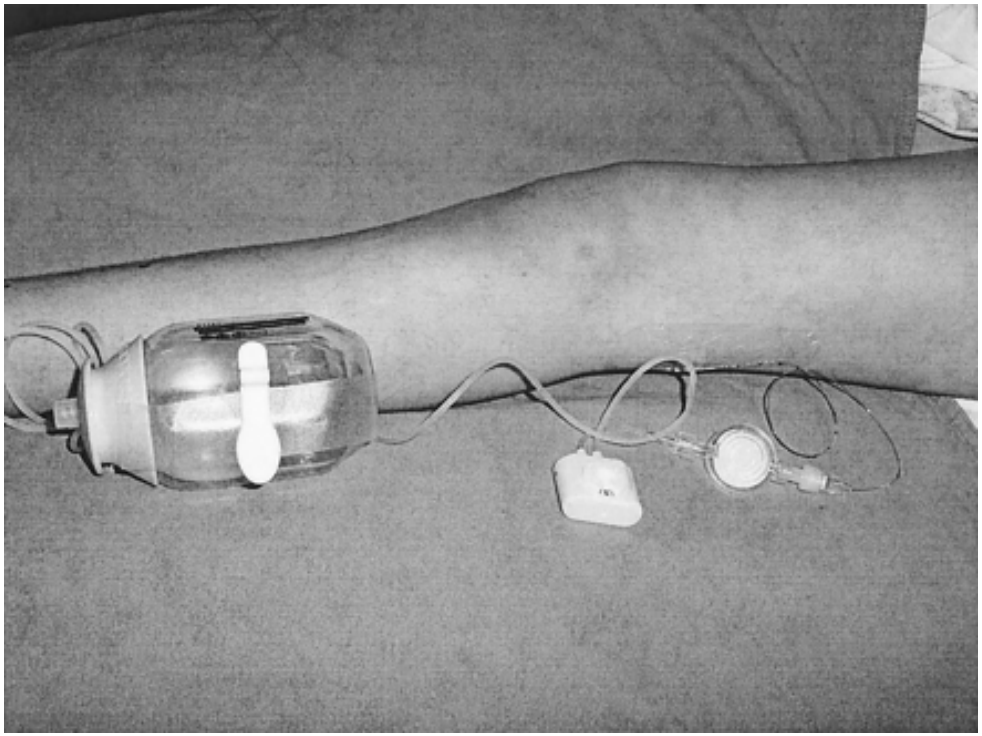
  "Shoulder and wrist pain & Significant perineal pain component & component of abdominal visceral pain"

  - Peripheral Nerve Blockade
    - Limited role in cancer pain management
    - Potential role to address pathologic fractures not responsive to conservative care - i.e. rib or long bone fracture
    - Literature supports use in some pediatric cancer pain settings

Non Pharmoclogic Mangament of Cancer Pain

- Continuous regional techniques

  "Shoulder and wrist pain & Significant perineal pain component & component of abdominal visceral pain"



Non Pharmoclogic Mangament of Cancer Pain

- Continuous regional techniques

  "Shoulder and wrist pain & Significant perineal pain component & component of abdominal visceral pain"

  - Vranken et. al. – case series of six Pancoast syndrome patients with severe neuropathic pain
  - Continuous brachial plexus catheter
  - Non responsive to maximal medical management
  - Marked improvement in VAS, QOL and Functional health
  - No noted complications
  - Infusions continued until patients expired

Vranken JH, Zuurmond WW, de Lange JJ. Continuous brachial plexus block as treatment for the Pan- coast syndrome. Clin J Pain 2000;16(4):327–33.

Non Pharmoclogic Mangament of Cancer Pain

- Continuous regional techniques

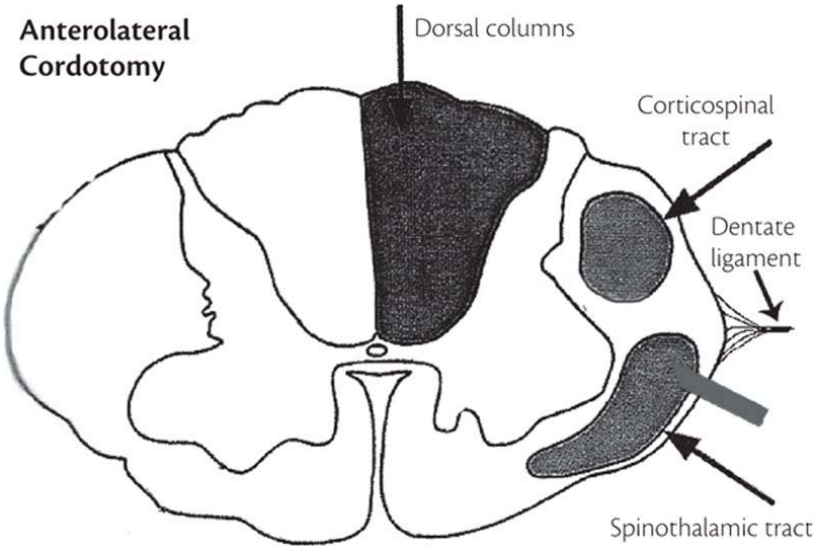
Pacenta et. al. – Tunneled femoral nerve block for palliative care of metastatic osteosarcoma
Breakthrough pain despite optimized medical management
0.2 % Ropivacaine and 4 µg/ml – 10 cc hr
Patient died in comfort 88 days later with catheter infusing

Pacenta et al. Continious tunneled femoral nerve block for palliative care of a patient with metastatic osteosarcome. Anaesth Intensive Care. 2010 May; 38 (3):563-565

Non Pharmoclogic Mangament of Cancer Pain

Neurosurgical Palliative Techniques

- Anterolateral Cordotomy
  - Interruption of ascending spinothalamic tract – contralateral to pain site
  - Reduced sensation to touch, temperate and pain
  - Both percutaneous and open approaches
  - 80% immediate pain relief
  - 1/3 with return of pain in 6-12 mo
  - Painful dysethesias 5%



Crul BJP, Blok LM, Van Egmond J, Van Dongen RTM. The present role of percutaneous cervical cordotomy for the treatment of cancer pain. J Headache Pain 2005;6(1):24–9.

Non Pharmoclogic Mangament of Cancer Pain

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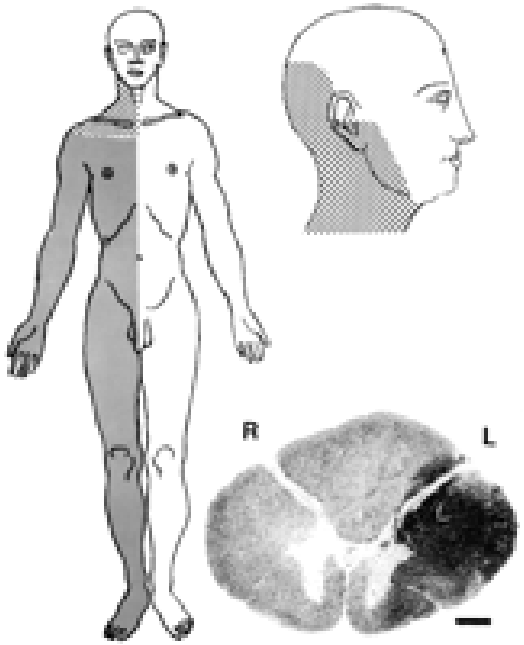

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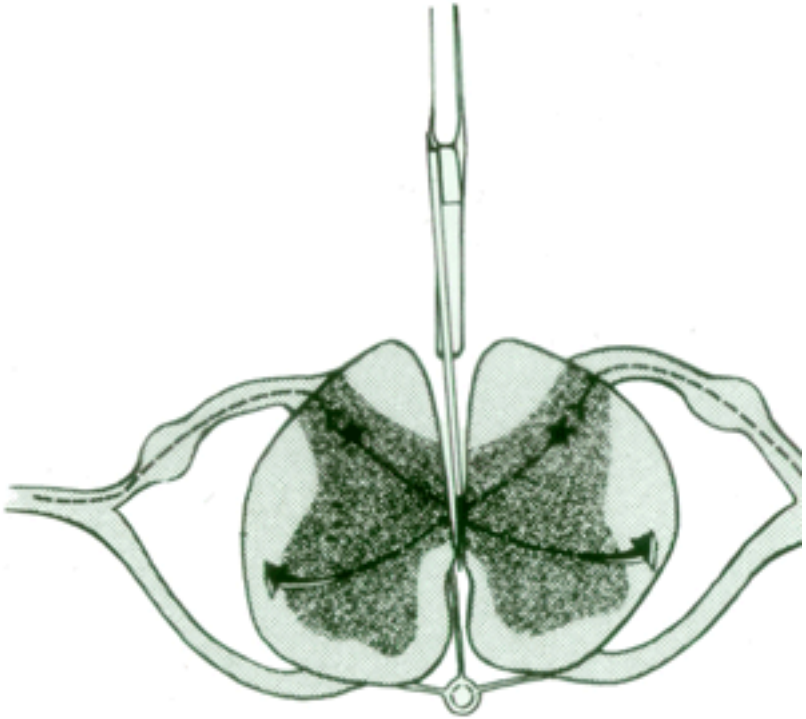
Non Pharmoclogic Mangament of Cancer Pain

Neurosurgical Palliative Techniques

- Midline Myelotomy
  - Lesion in dorsal cord midline in attempt to divide crossing spinothalamic fibers – bilateral pain
  - Midline lesion made fromT10- conus
  - Pelvic and visceral cancer pain
  - Similar concerns as Cordotomy
  - Rarely used



Gildenberg PL. Myelotomy through the years. Stereot Funct Neuros 1991;77:169–71.

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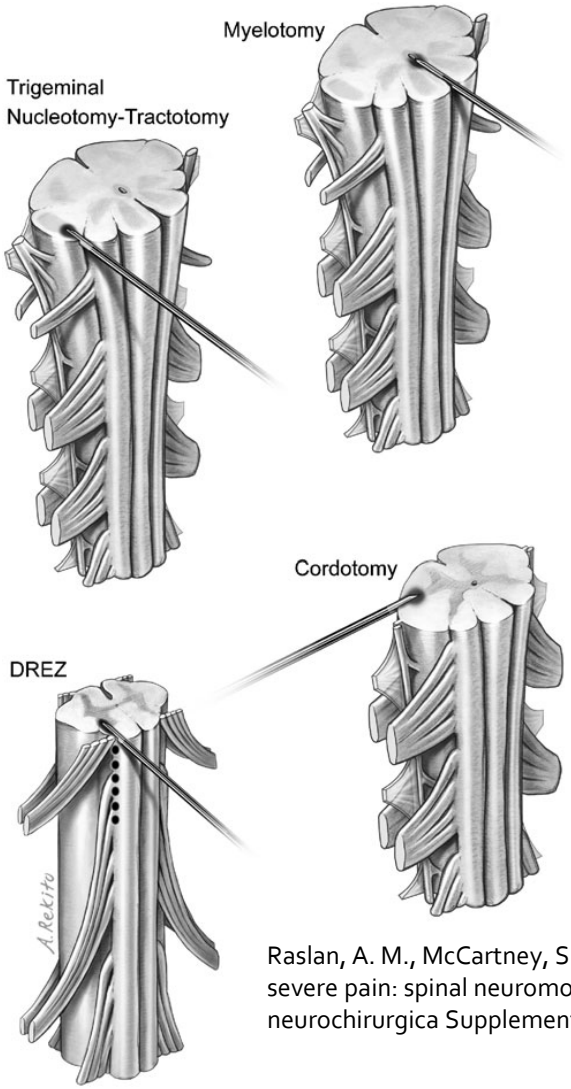
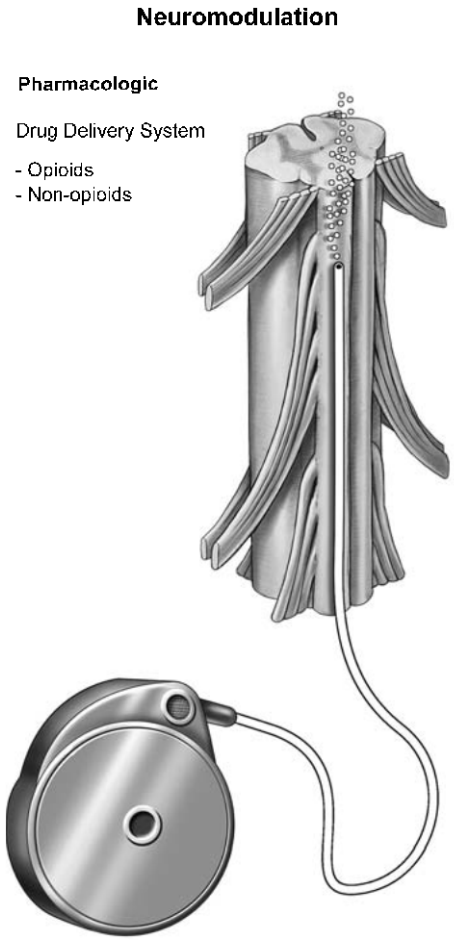
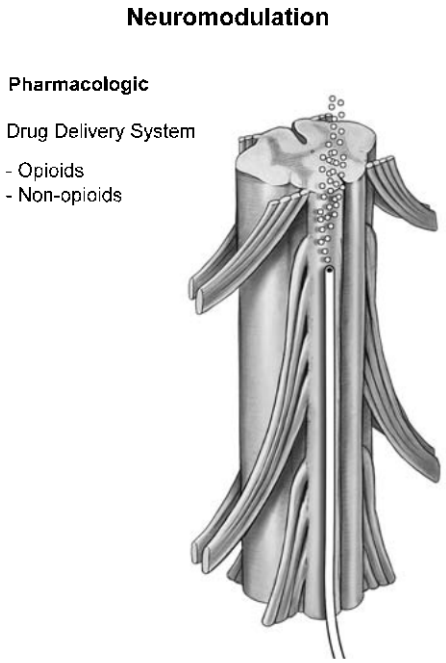


Raslan, A. M., McCartney, S., & Burchiel, K. J. (2007). Management of chronic severe pain: spinal neuromodulatory and neuroablative approaches Acta neurochirurgica Supplement, 97(Pt 1), 33–41.

Non Pharmoclogic Mangament of Cancer Pain





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Non Pharmoclogic Mangament of Cancer Pain

. Transcutaneous electrical nerve stimulation- TENS

- TENS is a noninvasive form of electrical stimulation
- No formal guidelines on the use of TENS in cancer patients.
- Only two RCTs evaluating TENS use in cancer-related pain have been identified [23,24]

- Cochrane review 2008 – included above 3 RCTs (64pts)
- Heterogeneous study populations, methodology and outcome measures - unable to provide meta-analysis
- Studies likely underpowered

- The effectiveness of TENS remains inconclusive -Yet some patients may find it beneficial

Robb K, Newham D, Williams JE. Transcutaneous electrical nerve stimulation vs transcutaneous spinal electroanalagesia for chronic pain associated with breast cancer treatments. J Pain Symptom Manag 2007;33(4):410–19.

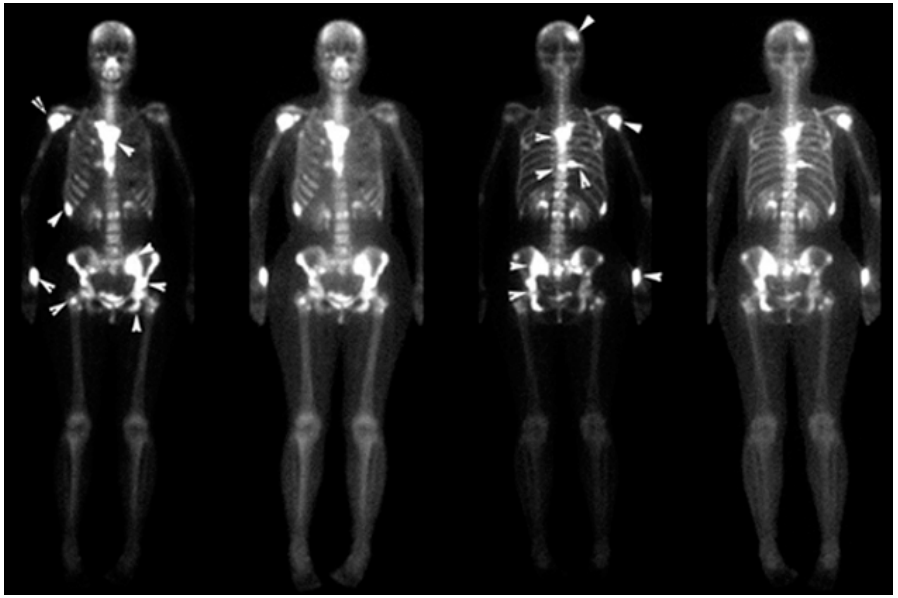
Gadsby JG, Franks A, Jarvis P, Dewhurst F. Acupuncture-like transcutaneous electrical nerve stimulation within palliative care. Complement Ther Med 1997;5:13–18.

Robb KA, Bennett MI, Johnson MI, Simpson KJ, Oxberry SG. Transcutaneous electric nerve stimula- tion (TENS) for cancer pain in adults. Cochrane Data- base Syst Rev 2008;(3):CD006276. DOI: 10.1002/ 14651858.CD006276.

Non Pharmoclogic Mangament of Cancer Pain

"You gotta be kidding! Your back *still* hurts?!"

Non Pharmoclogic Mangament of Cancer Pain

- Objectives:
- Basic understanding for role of:
  - Vertebral augmentation
  - Neurolysis techniques
  - Prolonged continuous regional
  - Implantable drug delivery systems

In pain management of cancer patients