MALATTIA DOLORE E RETE TERRITORIALE IL DIRITTO DEL PAZIENTE AD ESSERE CREDUTO

MILANO 23 > 24 MARZO 2017

AULA MAGNA · OSPEDALE NIGUARDA

DOLORE ONCOLOGICO CRONICO
Tecniche invasive algologiche

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Chronic Pain Syndromes Associated with Cancer Treatment
Chemotherapy-Related Pain Syndromes

- **Chemotherapy-Related Pain Syndromes**

Bony complications of long-term corticosteroids – Avascular necrosis – Vertebral compression fractures • Carpal tunnel syndrome • Chemotherapy-induced peripheral neuropathy • Raynaud's syndrome

- **Hormonal Therapy-Related Pain Syndromes**

Arthralgias • Dyspareunia • Gynecomastia • Myalgias • Osteoporotic compression fractures

- **Radiation-Related Pain Syndromes**

Chest wall syndrome • Cystitis • Enteritis and proctitis • Fistula formation • Lymphedema • Myelopathy • Osteoporosis Osteoradionecrosis and fractures • Painful secondary malignancies • Peripheral mononeuropathies • Plexopathies – brachial, sacral.

- **Stem Cell Transplant Mediated Graft Versus Host Disease •**

Arthralgias/myalgias • Dyspareunia, vaginal pain • Dysuria • Eye pain • Oral pain and reduced jaw motion • Paresthesias • Scleroderma-like skin changes

- **Surgical Pain Syndromes**

Lymphedema • Post-amputation phantom pain • Post-mastectomy pain • Post-radical neck dissection pain • Postsurgery pelvic floor pain • Post-thoractomy pain/frozen shoulder • Post-surgery extremity pain (e.g. sarcoma)

American Society of Clinical Oncology 2016.

Prevalence of pain

- In particular, pain prevalence was 64% in patients with metastatic, advanced or terminal phases of the disease, 59% in patients on anticancer treatment and 33% in patients after curative treatment.

ESMO Clinical Practice Guidelines 2011

Prevalence of pain

- The 10-15 % of patients do not get benefits from conventional therapies with opioids and non opioids.

Van den Beuken et al. Prevalence of pain in patient eith cancer: a sistematic reviewof the past 40 years. Ann. Oncol. 2007; 18: 1437-1449

Disciplines and Interventions for Chronic Pain

Disciplines	Examples of Possible Interventions	Strength of Evidence and Recommendation
Physical medicine and rehabilitation	Physical therapy, occupational therapy, recreational therapy, individualized exercise program, orthotics, ultrasound, heat/cold	Type: Evidence-based; benefits outweigh harms Evidence quality: Intermediate Strength of Recommendation: Moderate
Integrative Therapies	Massage, acupuncture, music	Type: Evidence-based; benefits outweigh harms Evidence quality: Low Strength of Recommendation: Weak
Interventional Therapies	Nerve blocks, neuraxial infusion (epidural/intrathecal), vertebroplasty/kyphoplasty	Type: Evidence-based; benefits outweigh harms Evidence quality: Intermediate Strength of Recommendation: Moderate
Psychological Approaches	Cognitive behavioral therapy, distraction, mindfulness, relaxation, guided imagery	Type: Evidence-based; benefits outweigh harms Evidence quality: Intermediate Strength of Recommendation: Moderate
Neurostimulatory	TENS, spinal cord stimulation, peripheral nerve stimulation, transcranial stimulation	Type: Evidence-based; benefits outweigh harms Evidence quality: Low Strength of Recommendation: Weak

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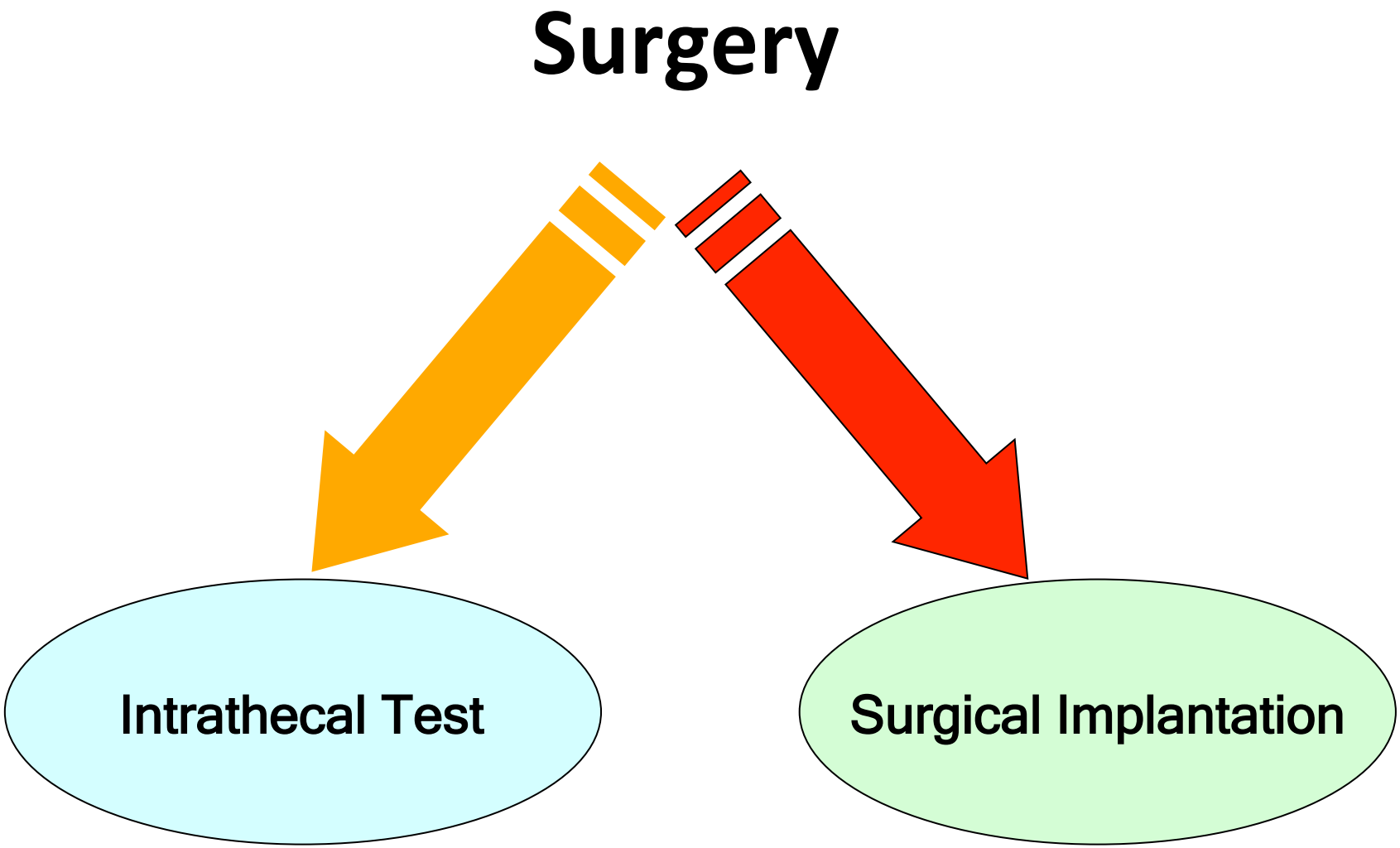
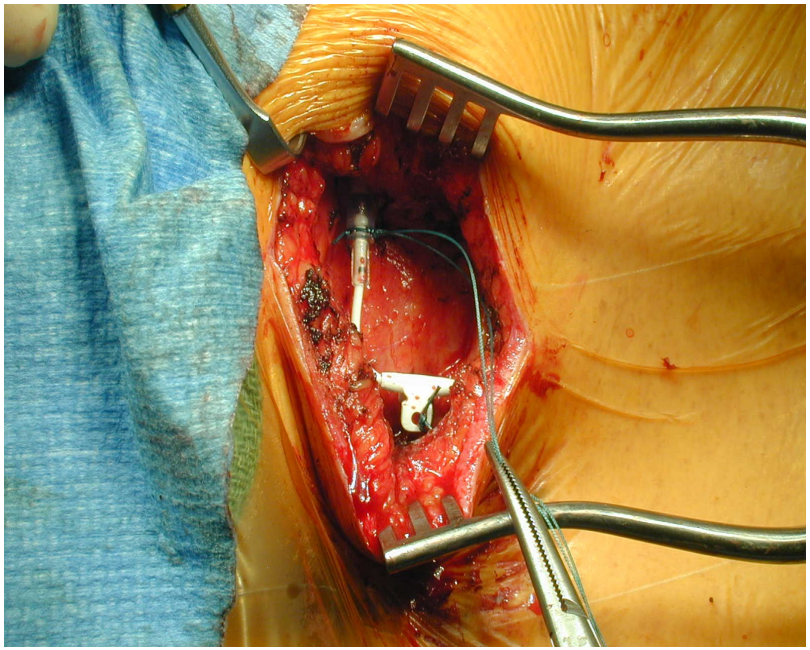
IMPLANTABLE DRUG DELIVERY SYSTEM

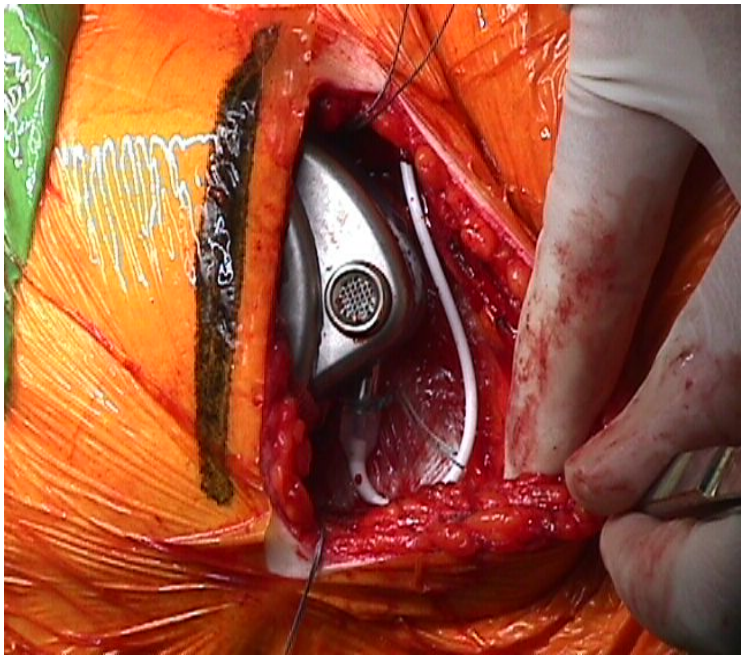
Neuroaxial infusion


Surgery
Intrathecal Test
Surgical Implantation

Surgical tecnique

Surgical tecnique





Drugs

- Local anesthetics (bupivacaine)
- Opioid (morphine, hydromorphone, fentanyl, sufentanil)
- Centrally acting muscle relaxant (baclofen)
- Calcium Channel Inhibitors (ziconotide)
- Other (clonidine, gabapentin, etc.)

Drugs

- Lipophilic agents are more likely to be taken up by the systemic circulation than hydrophilic agents, as they diffuse easier across cell layers. Hence, hydrophilic opioids such as morphine and hydromorphone are sometimes preferred over hydrophobic opioids as they can diffuse in the CSF and have a higher chance of reaching target areas in the superficial layers of the dorsal horn that may not be immediately adjacent to the catheter tip.

Bernards CM.. *Curr Opin Anaesthesiol 2004; 17:441-447*

Clinical results

- Excellent pain relief in 65-80% of selected patients improvements in activities of daily living a reduction in the side effects seen with oral / parenteral narcotics or tolerance and dependence.
- Less sedation and constipation compared with systemic drugs.
- Doses lower than those required with oral and intravenous methods, or the equivalent of 1/300 of an oral dose of morphine can often lead to an effective pain relief
- Patients switching from the administration of oral medication to the intrathecal have a better long-term relief of pain.

1. Winkelmuller M et al. *Journal of Neurosurgery* 1996;85:458-67
2. Penn R, Paice J. *J Neurosurg* 1987;67:182-6\
3. Paice J et al. *J Pain Symptom Manage* 1996;11:71-80 1997;14 (suppl. 3):S27-3
4. Follett K et al. *Pain* 1992;49:21-25
5. Gilmer-Hill H et al. *Surg Neurol* 1999; 51:6-11
6. Portenoy RK and Savage SR. *J Pain Symptom M*
7. Gianino. *Practical Pain Management* 1996:127-154
8. Krames ES. *J Pain Symptom Manage* 1996;11:333-352

Implantable Drug Delivery System

Original article

Annals of Oncology 16: 825–833, 2005
doi:10.1093/annonc/mdi156
Published online 7 April 2005

An implantable drug delivery system (IDDS) for refractory cancer pain provides sustained pain control, less drug-related toxicity, and possibly better survival compared with comprehensive medical management (CMM)

T. J. Smith[1*], P. J. Coyne[1], P. S. Staats[2], T. Deer[3], L. J. Stearns[4], R. L. Rauck[5], R. L. Boortz-Marx[6], E. Buchser[7], E. Català[8], D. A. Bryce[9], M. Cousins[10] & G. E. Pool[6] for the Implantable Drug Delivery Systems Study Group

At 4 weeks 67% pain reduction> 20% vs 36% of the conventional therapy At 6 months 32% of patients in the conventional therapy had survived vs 52% of implanted patients undergoing

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SPINAL CORD STIMULATION

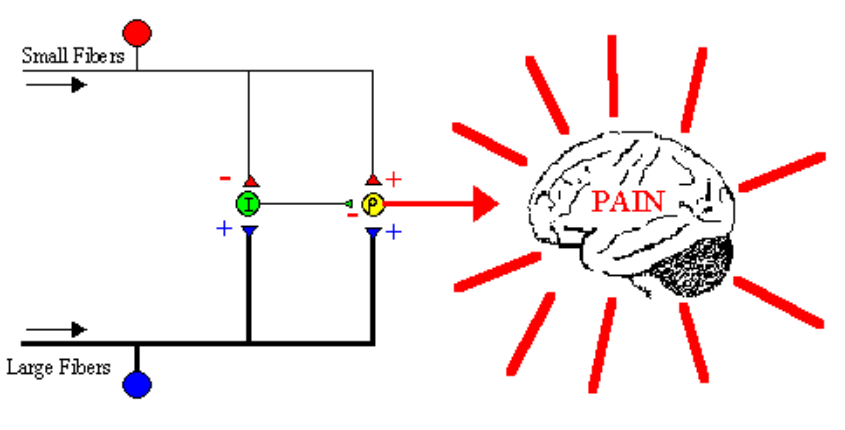
Spinal Cord Stimulation

Chronic cancer pain

- The 15-40% of cancer patients showed a chronic pain; the first available technology, not compatible with MRI, required for controls, reduced the use of SCS in these patients.

Curr Pain Headache Rep (2012) 16:343–349 DOI 10.1007/s11916-012-0276-9

Gate Control Theory



- Without any stimulation, both large and small nerve fibers are quiet and the inhibitory interneuron (I) blocks the signal in the projection neuron (P) that connects to the brain. The "gate is closed" and therefore *NO PAIN*.
- With pain stimulation, small nerve fibers become active. They activate the projection neurons (P) and BLOCK the inhibitory interneuron (I). Because activity of the inhibitory interneuron is blocked, it CANNOT block the output of the projection neuron that connects with the brain. The "gate is open", therefore, *PAIN.*
- With non-painful stimulation, large nerve fibers are activated primarily. This activates the projection neuron (P), BUT it ALSO activates the inhibitory interneuron (I) which then BLOCKS the signal in the projection neuron (P) that connects to the brain. The "gate is closed" and therefore *NO PAIN*.

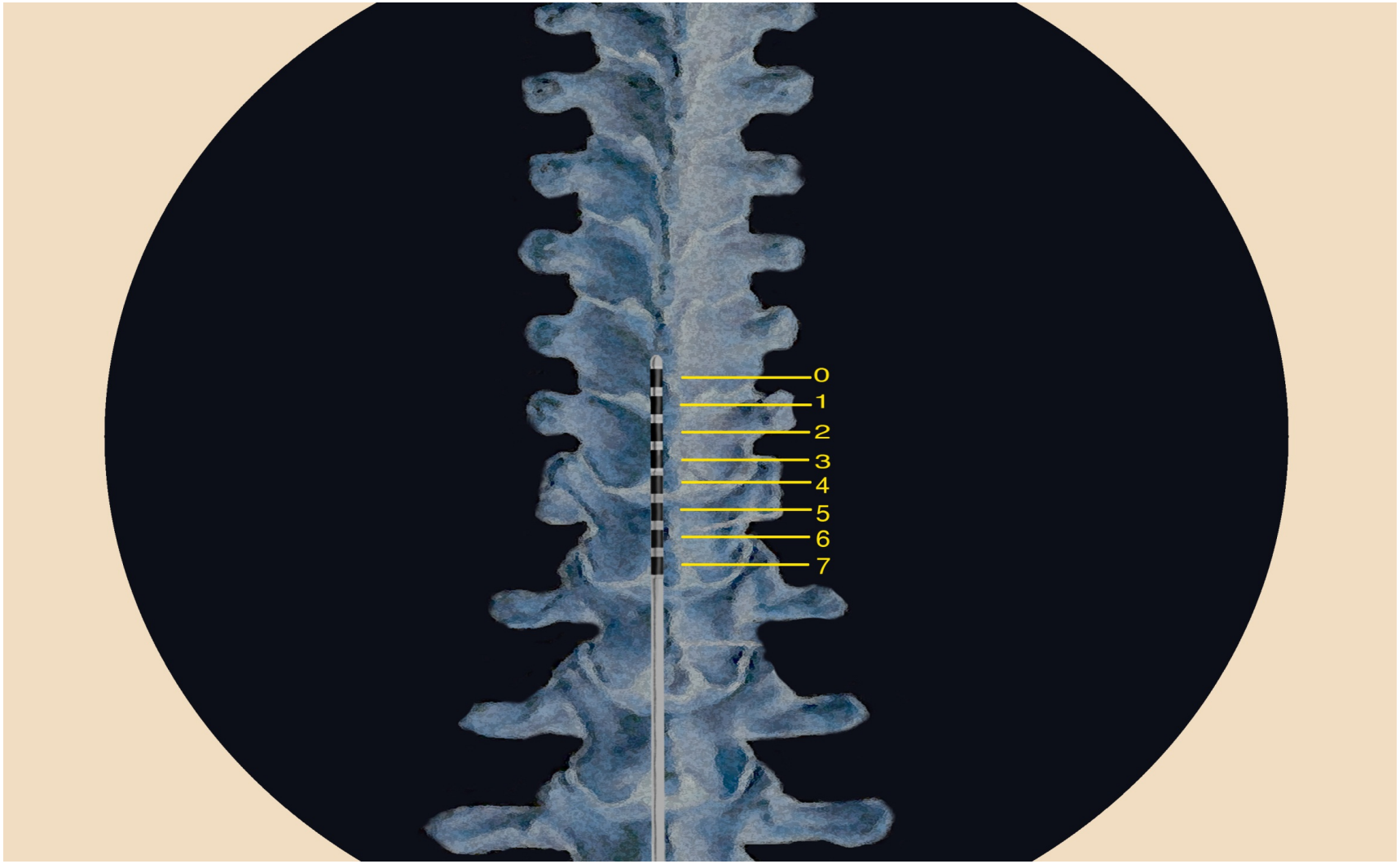
Melzack R, Wall PD. *Science* 1965;150:971-79

Electrode placement

- The positioning of the leads requires patient cooperation, in particular when they are used for percutaneous leads.
- The ideal position of the lead is in the posterior epidural space, on the same side of the median pain or in the case of bilateral pain.
- Bilateral pain often requires two leads.

Paresthetica coverage	Target
Upper Limb	**C3–C5**
Chest	**T1–T2**
Lower back eand lower limb	**T8–T9**
Foot	**T12–L1**

Surgical tecnique



Clinical indication

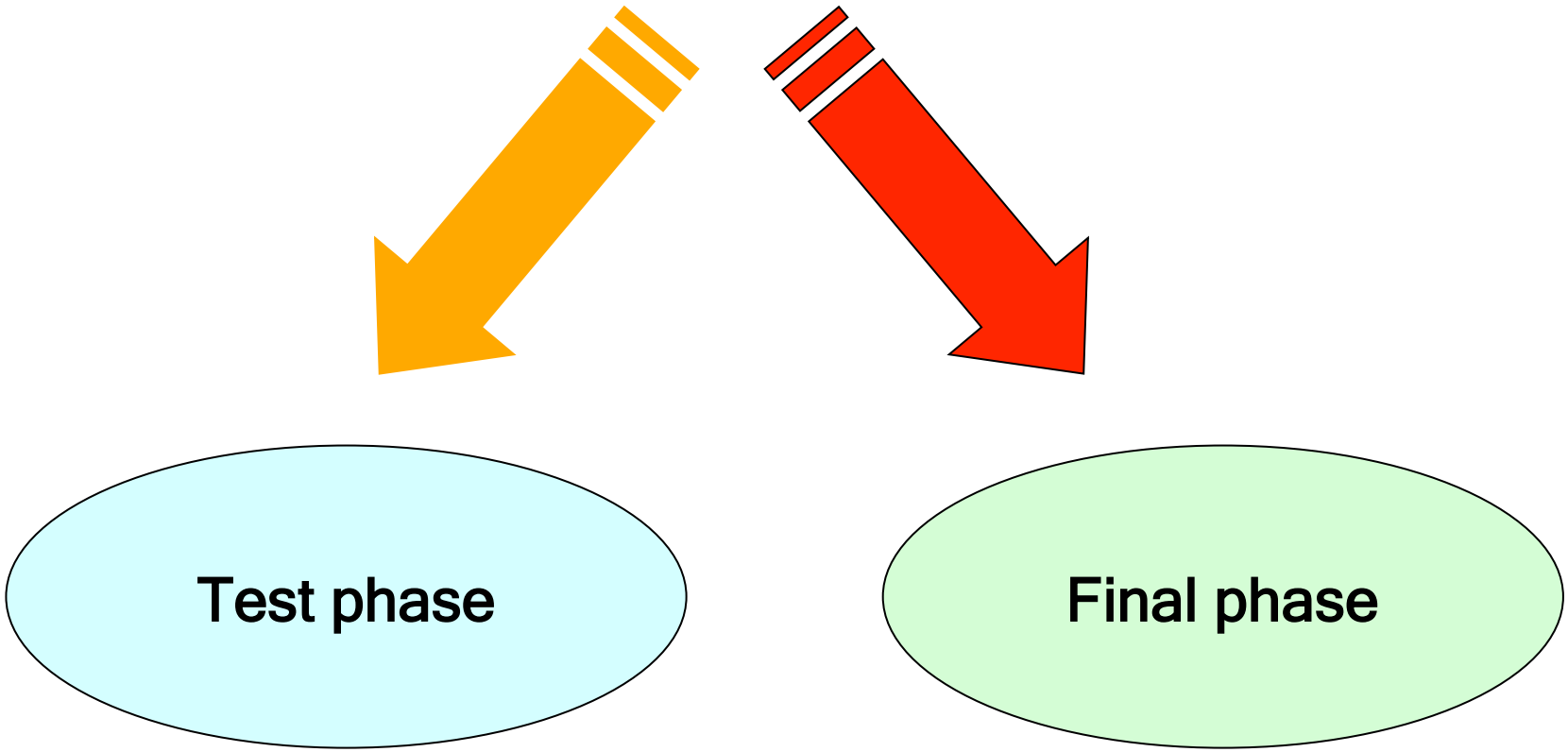
- Neuropathic pain in the limbs after surgery to the lumbar or cervical - FBSS
- Complex regional pain syndrome – CRPS Neuropathic pain secondary to nerve damage peripheral
- pain associated with vascular damage Peripheral Refractory angina pectoris
- Traumatic brachial plexopathy (partial) and post-irradiation

NICE Technology Appraisal guidance 159, 2008 e 2014
Consensus Document The British Pain Society's, 2009
EFNS guidelines on neurostimulation therapy for neuropathic pain, 2007

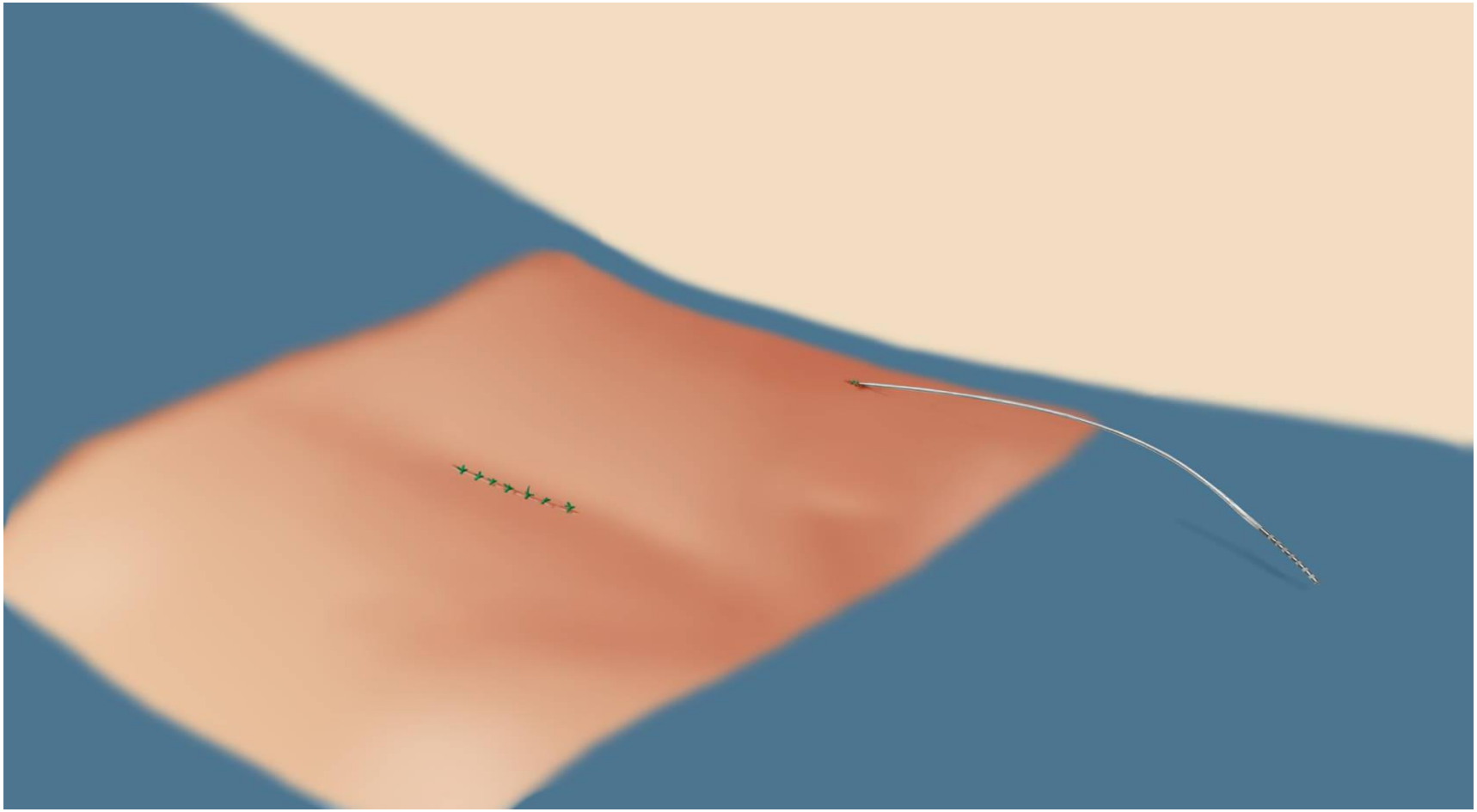
Clinical indication

- Post amputation pain
- Axial pain following spinal surgery
- Intercostal neuralgia (eg. Post thoracotomy or post-herpetic neuropathy)
- Pain associated with partial spinal cord injury
- Other peripheral neuropathic pain syndromes (eg. Post-traumatic) diabetic neuropathy

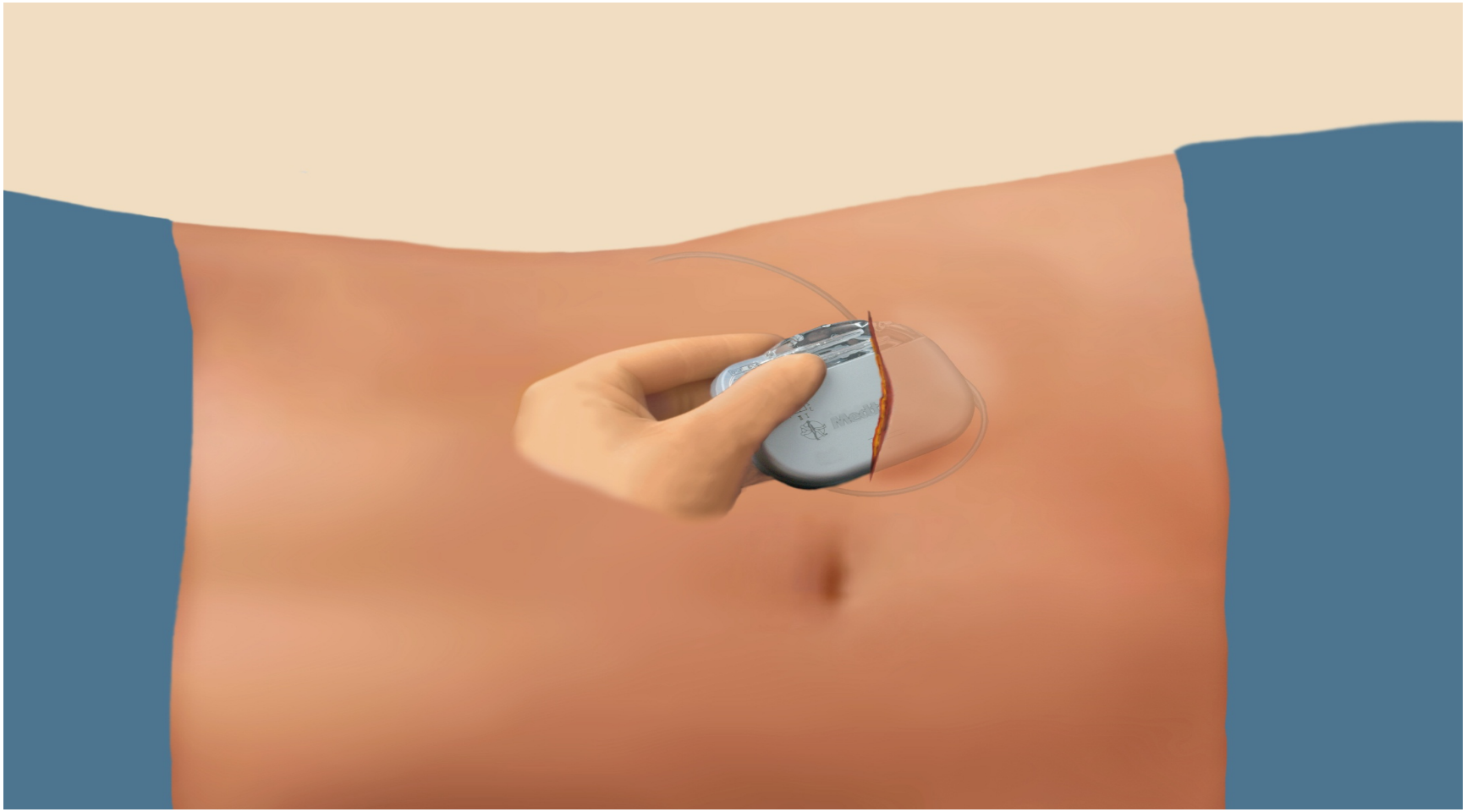
Surgery



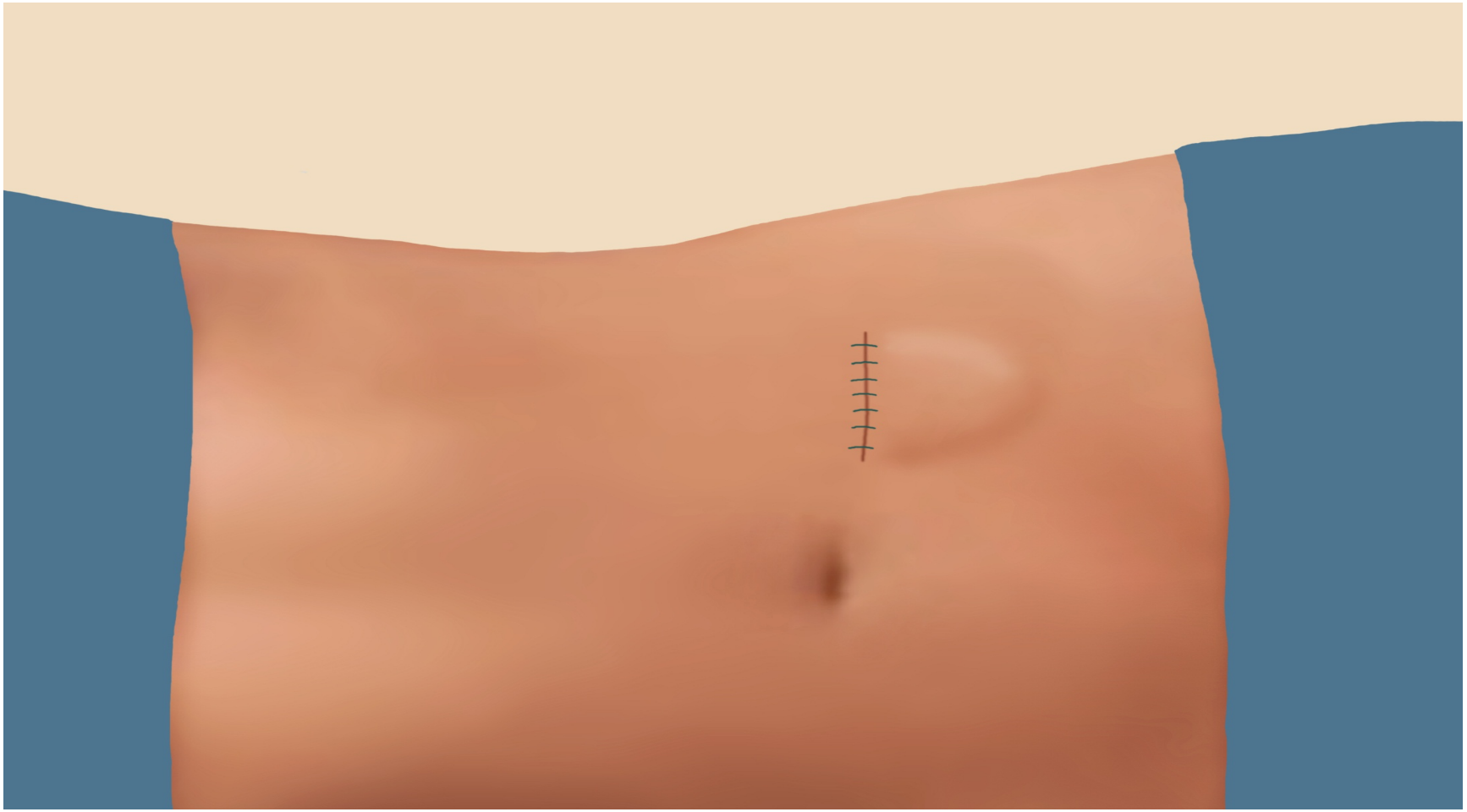
Surgical tecnique



Surgical tecnique



Surgical tecnique



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VERTEBROPLASTY WITH SPINAL TUMOR ABLATION RADIOFREQUENCY

Incidence

Bone Metastases: A large, underserved patient group

Metastatic Bone Disease is prevalent in many types of cancer

Cancer	Five-Year World Prevalence[1]	Incidence of bone metastases in cancers[2]	Median Survival (Months) [2,3]
Myeloma	144.000	70% - 95%	6 - 54
Renal	480.000	20% - 25%	6
Melanoma	533.000	14% - 45%	6
Thyroid	475.000	60%	48
Lung	1.394.000	30% - 40%	6
Breast	3.860.000	65% - 75%	19 - 25
Prostate	1.555.000	65% - 75%	12 - 53

1 Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2000: Cancer incidence, mortality and prevalence worldwide, version 1.0. IARC CancerBase No. 5, Lyon, IARCPress, 2001 Available at: http://www.dep.iarc.fr/globocan/cdrom.htm. Accessed February 26, 2004.
2 Coleman RE. Metastatic bone disease: clinical features, pathophysiology and treatment strategies. Cancer Treat Rev 2001:27:165-176
3 Coleman RE. Skeletal complications of malignancy. Cancer 1997:80 (suppl):1588-1594

Nature of spine metastases

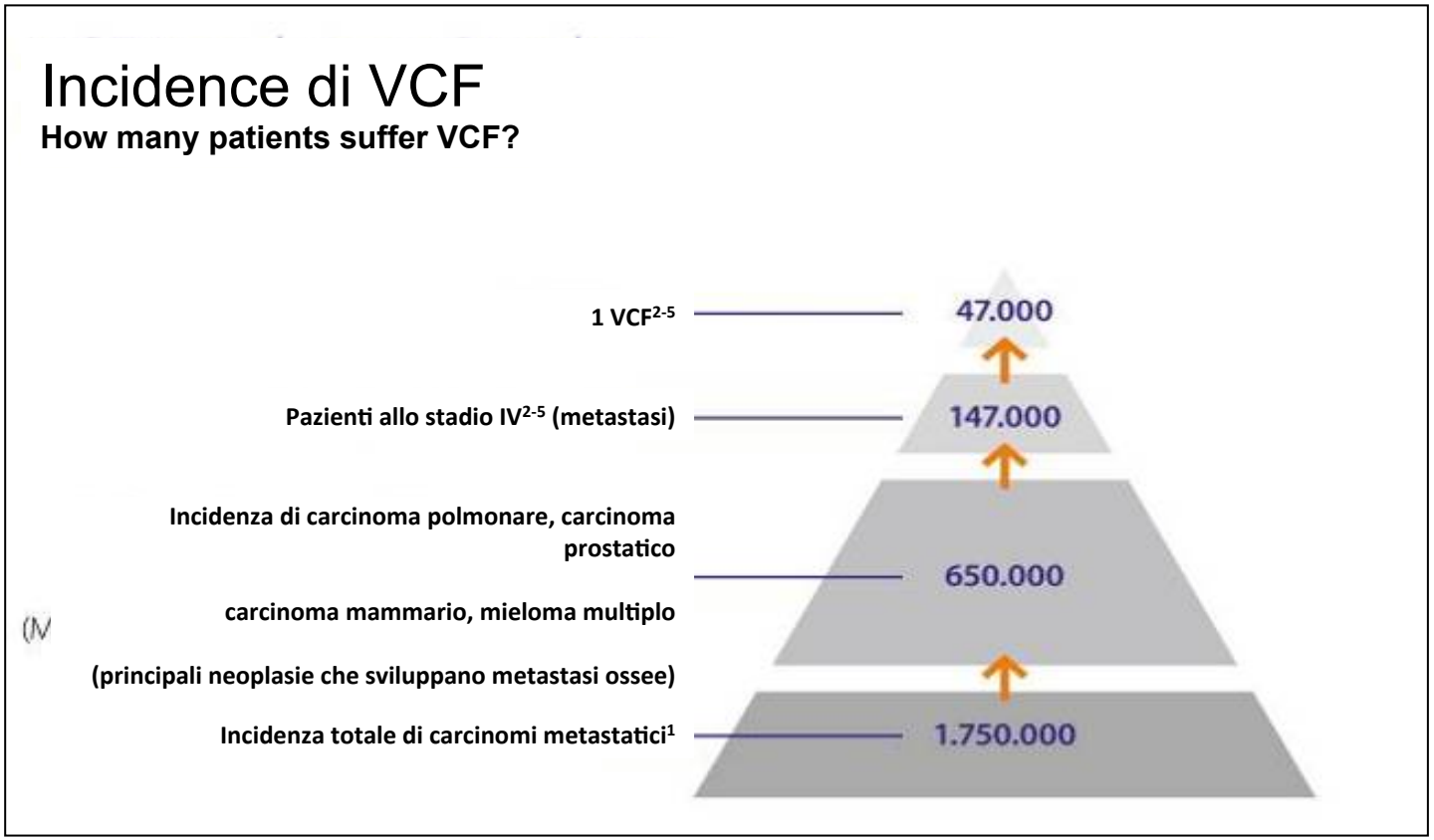
Nature of Spine Metastases

Type and Extent of Lesion	Number of Cases	Percent of Cases
Osteoblastic	45	8,0%
Osteolytic	**399**	**70,9%**
Mixed	**119**	**21,1%**
Involving 1 Vertebra	77	13,4%
Involving > 1 Vertebra	**486**	**86,3%**
Lesion of entire Vertebra	81	14,4%
Lesion of Vertebral Body	252	44,8%
Lesion of Posterior Arch	228	40,5%

Metastatic Spinal Metastases are commonly osteolytic and affect multiple vertebrae.
- 600 cases of spinal metastases were reviewed of which 563 had characteristics of bone lesions
- Examined according to clinical characteristics, type of primary tumor, site of lesion, and survival
- Active treatment occured in all but 7 of the cases

Constans, JP. et al. Spinal metastases with neurological manifestations. J. Neurosurg 1983

Incidence of Vertebral Compressione Fractures in cancer patients (Western Europe)



GLOBOCAN (WE)

Hortobagy et al, "Efficacy of Pamidronate in reducing skeletal event in patients with breast cancer and lytic bone metastases", NEJM, Vol. 335, No. 24, pagg. 1785-1791

Rubens et al, "Bone Metastases", Clinical Oncology, 1995, pagg. 6433-665

Berruti et al, "Incidence of Skeletal Complications in Patients with Bone Metastatic Prostate Cancer and Hormone Refractory Disease", The Journal of Urology, Vol. 164, 0ct. 2000, pagg. 1248-1253

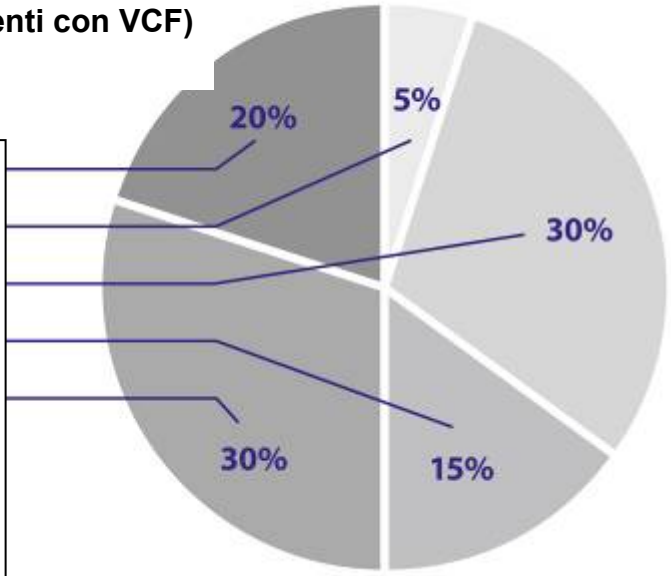
Brinker et al, "Failure of oral pamidronate to reduce skeletal morbidity in multiple myeloma: a double-blind placebo controlled trial", British Journal of Haematology, 1998, V.101, pagg. 280-286

Incidence of Vertebral Compressione Fractures in cancer patients (Western Europe)

Incidence of VCF

Number of patients with VCF (% di pazienti con VCF)

Altri carcinomi	9400
Carcinoma mammario	2350
Carcinoma polmonare	14100
Carcinoma prostatico	7050
Mieloma	14100
Totale	47000
Tumori primari	3000



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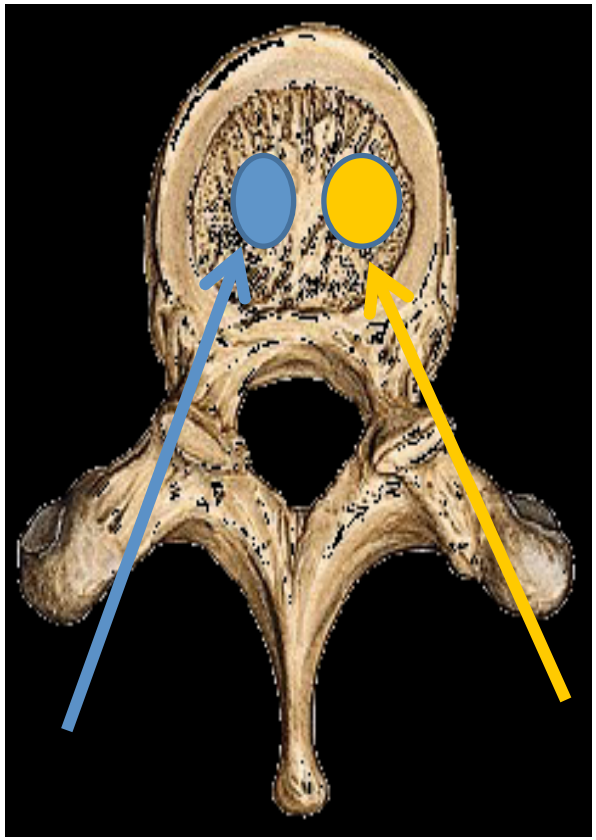
Classification vertebral fractures

Kyphoplasty: clinical indications

- Fracture >30%
- Lower risk of cement leakage
- Restore vertebral body height
- Approach bipeduncolare

Kyphoplasty: approach bipeduncolare

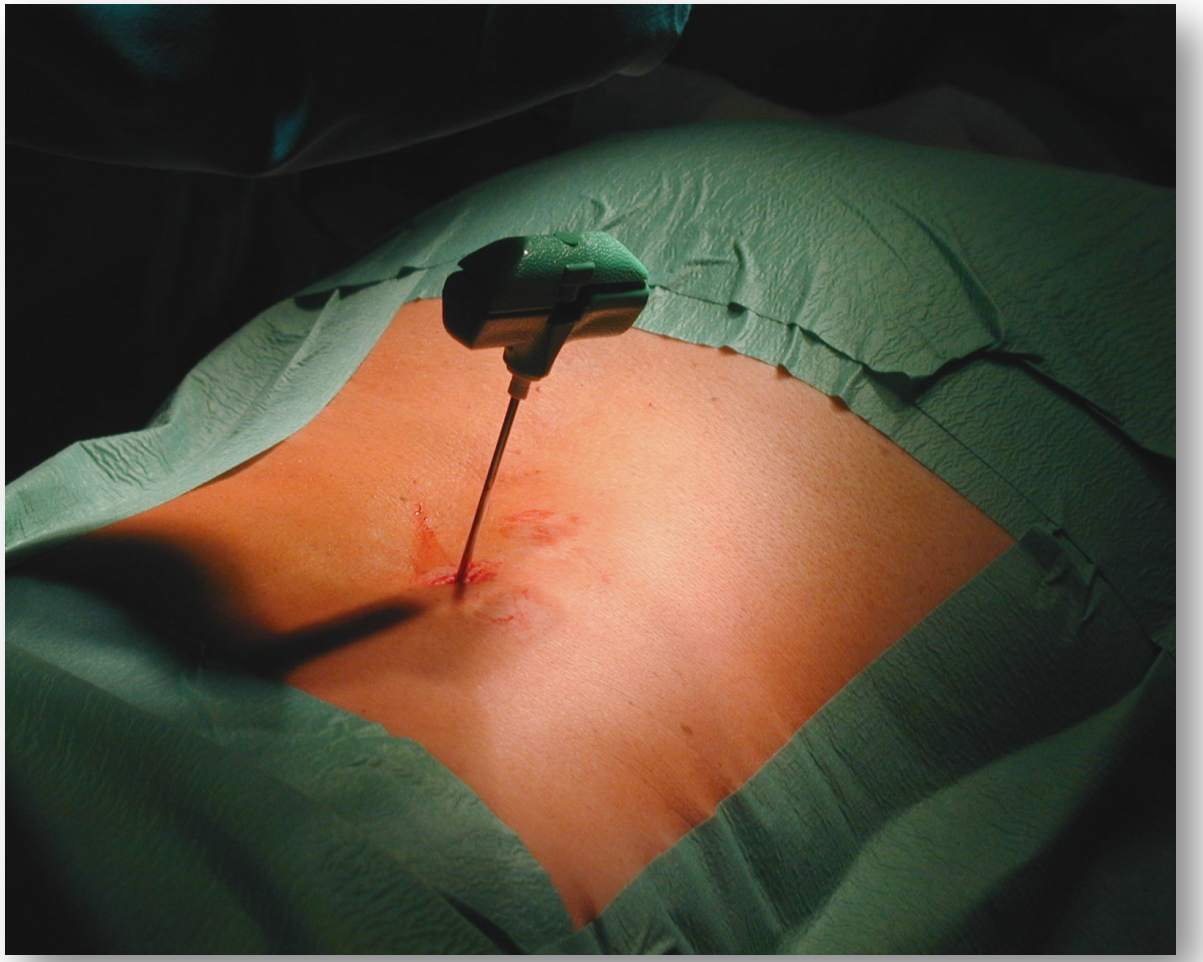


Kyphoplasty: approach bipeduncolare

Vertebroplasty: clinical indications

- Fracture < 30%
- Injection of high pressure cement into the vertebral body
- Approach monopeduncolare
- Packaging of the cement storage space through the use of an osteotome

Vertebroplasty: approach monopeduncolare



Vertebroplasty: approach monopeduncolare

Spinal **T**umor **A**blation **R**adiofrequency

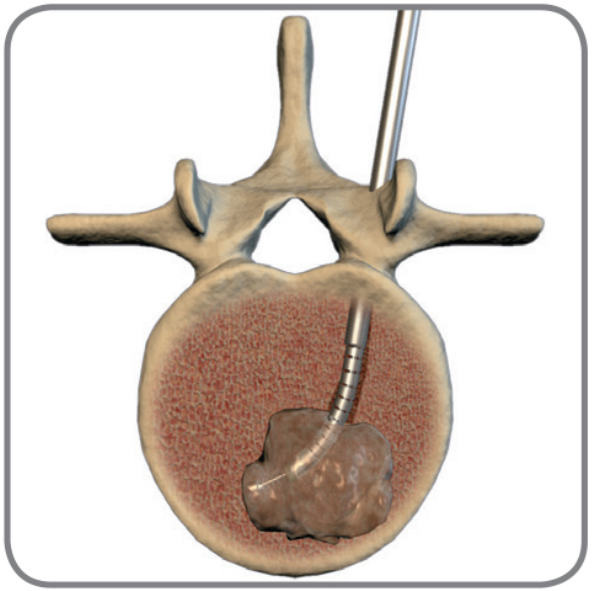
S.T.A.R.

SPINAL

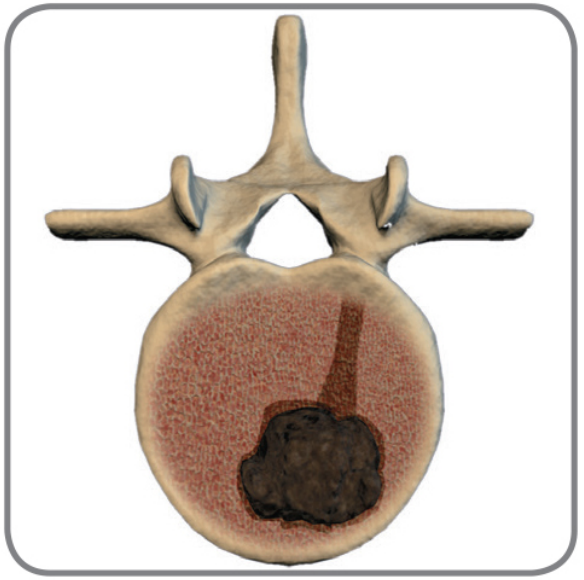
TUMOR

ABLATION

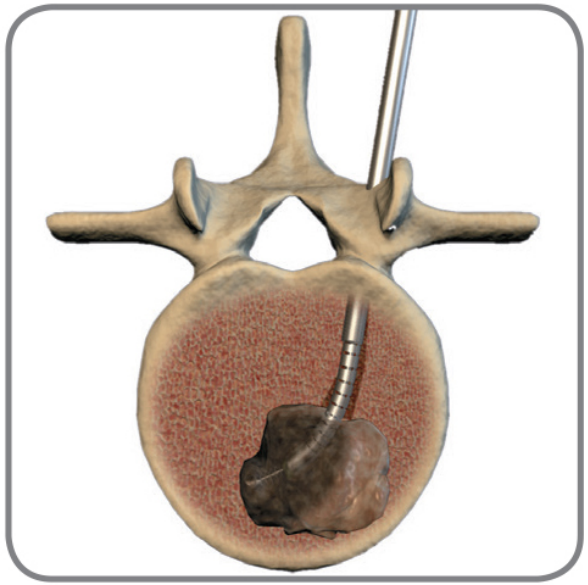
RADIOFREQUENCY



Device placed



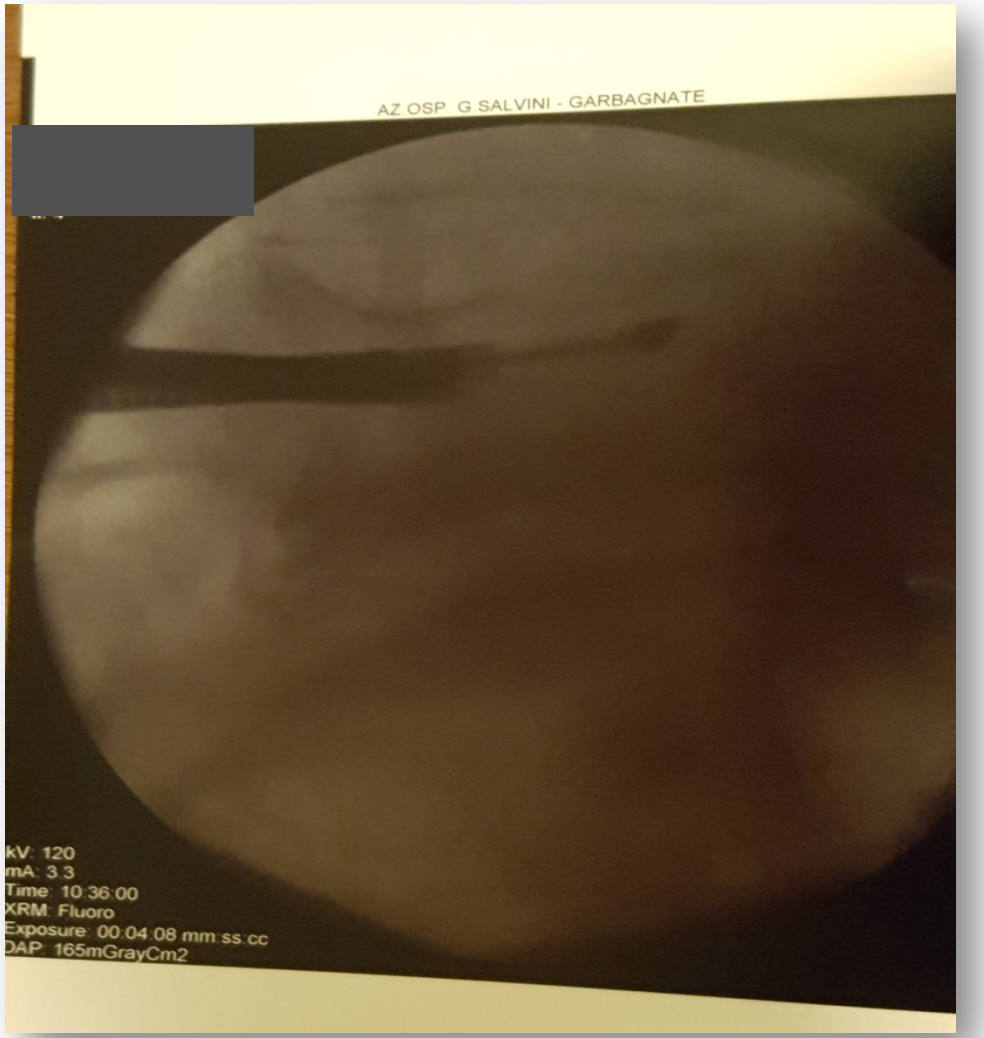
Tumor ablated

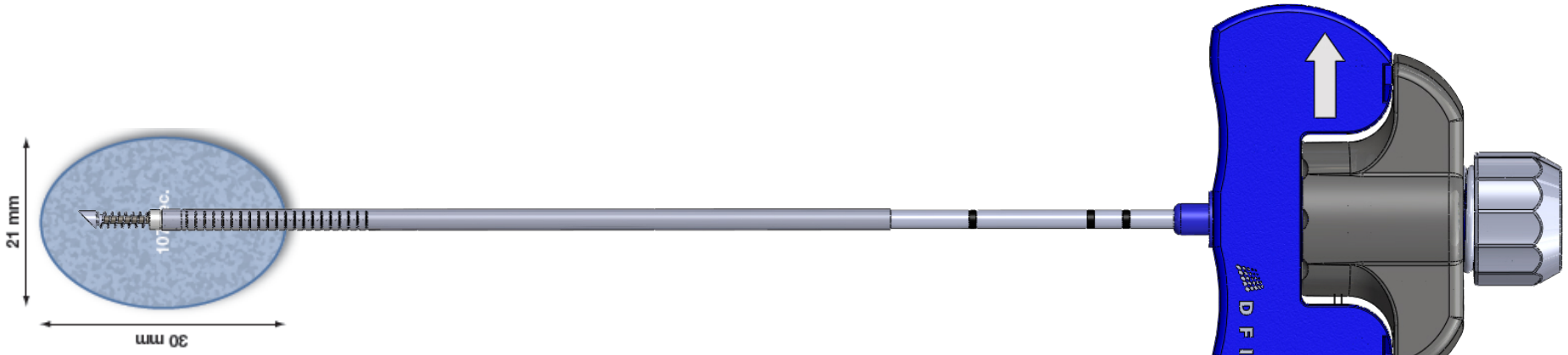


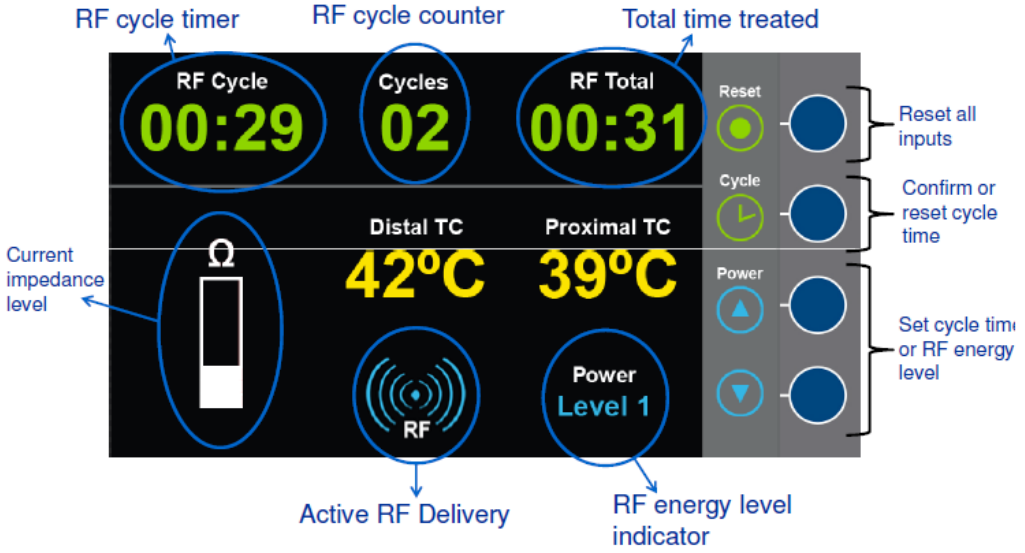
RF energy delivered

Tumor ablated + augmented

S.T.A.R.


AZ OSP. G.SALVINI - GARBAGNATE
[redacted]
kV: 120
mA: 3.3
Time: 10:36:00
XRM: Fluoro
Exposure: 00:04:08 mm:ss.cc
DAP: 165mGrayCm2


21 mm
30 mm
DEFINE


RF cycle timer
RF cycle counter
Total time treated
RF Cycle
00:29
Cycles
02
RF Total
00:31
Reset
Cycle
Power
Reset all inputs
Confirm or reset cycle time
Set cycle tim or RF energy level
Distal TC
Proximal TC
42°C
39°C
Current impedance level
Ω
RF
Power
Level 1
Active RF Delivery
RF energy level indicator

Patient selection

1. Patients selection for ablation

Patients may be offered focal ablative therapy (radio-frequency ablation [RFA] [75] or cryoablation) for painful metastases when 3 factors are present. First, a patient reports moderate or severe pain, typically ≥ 4 of 10 for worst pain in a 24-hour period. Second, a patient's local pain is limited to 1 or 2 sites and the patient's pain is associated with a corresponding abnormality evident with cross-sectional imaging. Third, treatment of the patient's painful metastatic lesion must be amenable to the use of ablative devices. Lesions that amenable to ablative therapy are typically osteolytic or mixed osteolytic/osteoblastic in nature or otherwise composed of soft tissue [76]. Exclusion of patients from focal ablative therapy usually occurs when

doi:10.1016/j.clon.2010.10.003

Can Radiotherapy be Combined with Radiofrequency Ablation in the Management of Symptomatic Osteolytic Skeletal Metastasis?

Published studies reveal that few data exist on the association between RFA and radiation therapy for the clinical management of skeletal metastases [2]. We hypothesise that radiation therapy and RFA may work synergistically by balancing each other's shortcomings. Radiation therapy is dependent on oxygen for cytotoxicity and is thought to be deficient in killing centrally located tumour cells that are often hypoxic. Conversely, RFA is dependent on the conduction of heat that dissipates with distance from the electrode tip, resulting in decreased efficacy around the tumour edge. Here we report the results from a non-consecutive case series of 11 patients suffering from painful osteolytic skeletal metastases and receiving a combination of RFA and radiation

Contraindications

- Vertebra plana
- Fracture of the back wall
- Coagulopathy
- Invasion of the medullary space
- PM or other device
- Inability to prone position (COPD)
- Proximity to the spinal cord

Complication

- Leakage of cement
- New fractures
- Pulmonary embolism

	TUMOR CONTROL (LOCAL)	PAIN RELIEF	RECOVERY/REGAIN OF STABILITY	SKELETAL RELATED EVENTS
Resezione chirurgica	☑	☐	☑	☑
Chemioterapia	☑	☐	☐	☐
Radioterapia	☑	☑	☐	☐
Radionuclidi	☐	☑	☐	☐
Bifosfonati/D-Mab	☐	☑	☐	☑
Cemento	☐	☑	☑	☑
Radioablazione	☑	☑	☑	☑

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CELIAC PLEXUS BLOCK

Celiac plexus block

- It prevein the transmission of pain to the central nervous system.
- Duration from 3 to 6 months.
- Repeatable bat less effective than two months.

MCGreevy et al. The effectiveness of repeat celiac plexus neurolysisfor pancreatic cancer: a pilot study. Pain Practice 2012; 13:89-95

Patients selection

- Visceral Pain
  (upper abdomen cancer)

- Non oncologic pain
  (pancreatitis)

Interventional Pain Treatments for Cancer Pain Paul J. Christo and Danesh Mazloomdoost*Department of Anesthesiology & Critical Care Medicine, Division of Pain Medicine, The Johns Hopkins University School*

of Medicine, Baltimore, Maryland, USA

Ischia, *et al. 2000. Celiac block for the treatment* of pancreatic pain. *Curr. Rev. Pain. 4: 127–133.*

Celiac plexus block: disputes

- Better efficacy compared to use of oppioids.
- Choise of method.
- Indication for celiac plexus block despite the risk of paraplegia.

Serdar Erdine Istanbul University Istanbul Faculty of Medicine, Department of Algology, Prof., M. D.

Celiac plexus block: aims

- Pain relief.
- Reducing use of oppioids.
- Better quality of life (QoL).

*Arcidiacono PG et al. Celiac plexus Block dor pancreatic cancer pain in adults. Cochrane Database Syst Rev 2011;CDOO7519.DOI:10.002/14651858.CD007519.pub2

Wong GY et al. Effect of neurolitic celiac plexus block on pain relief,QOL, and survival in patients with unresectable pancreatic cancer: a randomized controlled trial. JAMA 2004; 291:1092-1099

Celiac plexus block: controindication

- Use of anticoagulants.
- Coagulopathy.
- Bowel obstruction.
- Calcification of the aorta.
- Neoplastic infiltration of the celiac region.

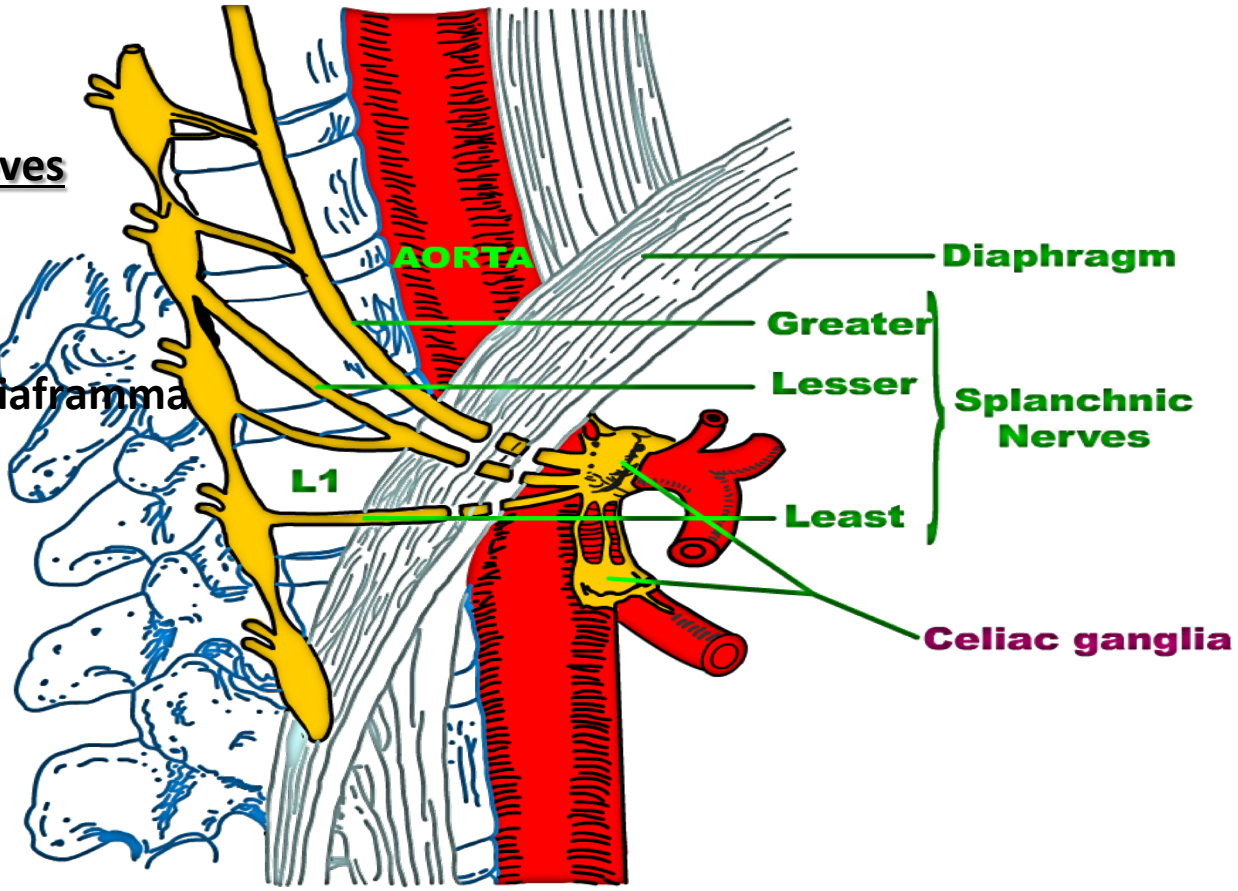
Celiac plexus and splanchnic nerves

Splanchnic Nereves

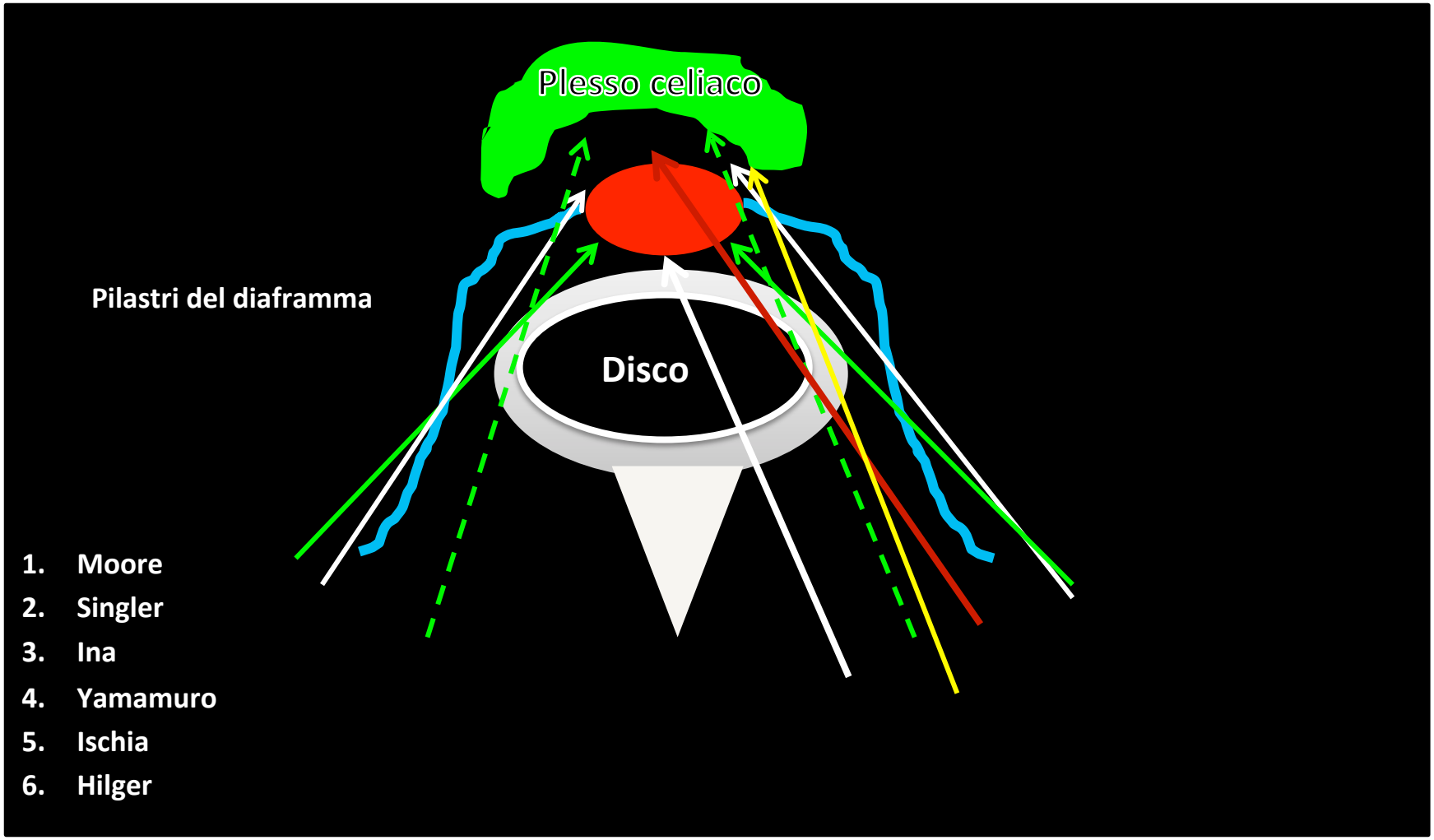
Limitato:
inferiormente
dai pilastri del diaframma

lateralmente
dalla pleura

anteriormente
dai vasi

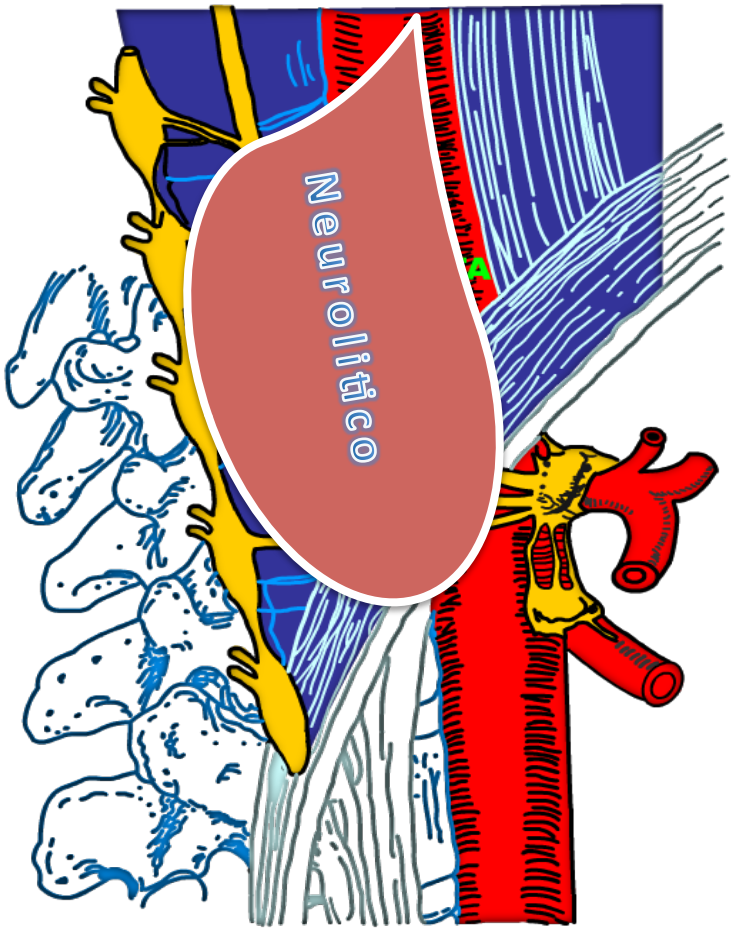


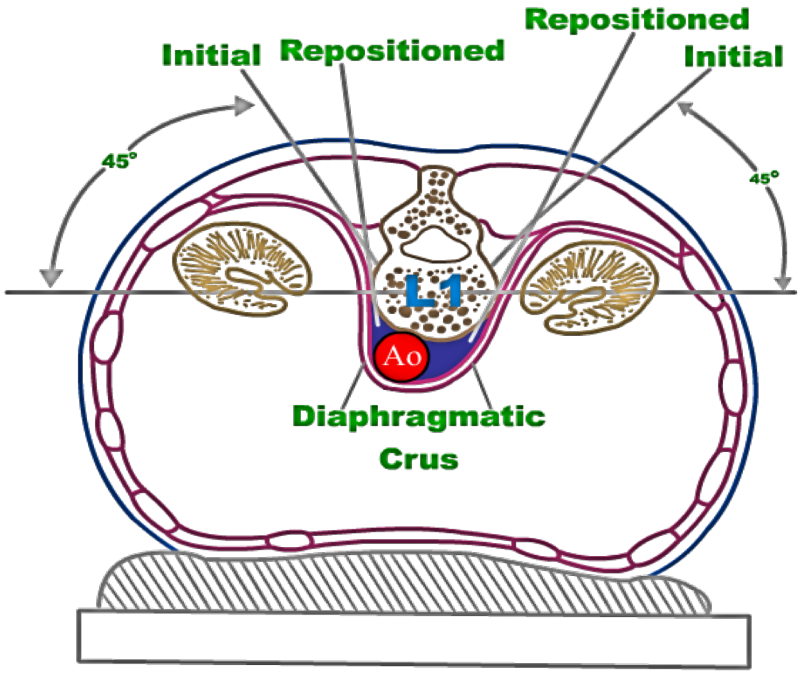
Celiac plexus block: classification



Retrocrurale approach

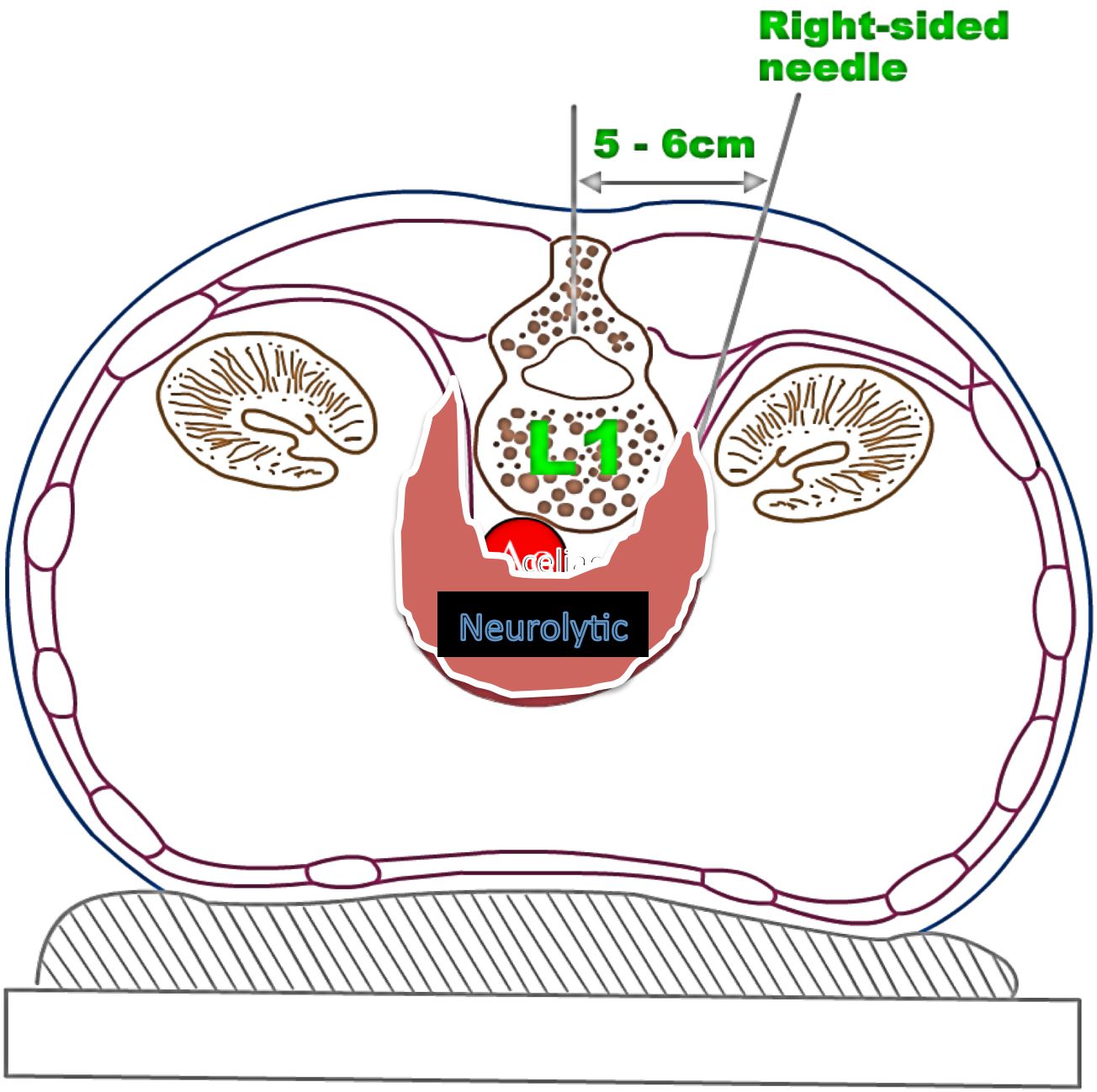
- Splanchnic block (T12-L1).
- Approach bilateral/central.
- Needle placement, behind the pillar diaphragmatic.


Neurolítico


Initial
Repositioned
Repositioned
Initial
45°
45°
L1
Ao
Diaphragmatic
Crus

Trancrurale approach

- Celiac plexsus block.
- Approach bilateral/central.
- Needle pleacement before diaphragmatic pillar.


Right-sided needle
5 - 6cm
L1
Neurolytic

Complication

- HYPOTENSION
- DIARRHEA
- PAIN AT THE INIECTION SITE
- NERVE ROOT LESION AND ORGANS
- VESSEL LESION
- INIEZIONE EPIDURALE O SUBARACNOIDEA
- IMPOTENCE
- PARAPLEGIA (TECNICA RETROCRURALE)

Davies ,DD, 1993. Incidence of maior complication of neurolitic coeliac plexus block. Soc Med. 86: 264-266

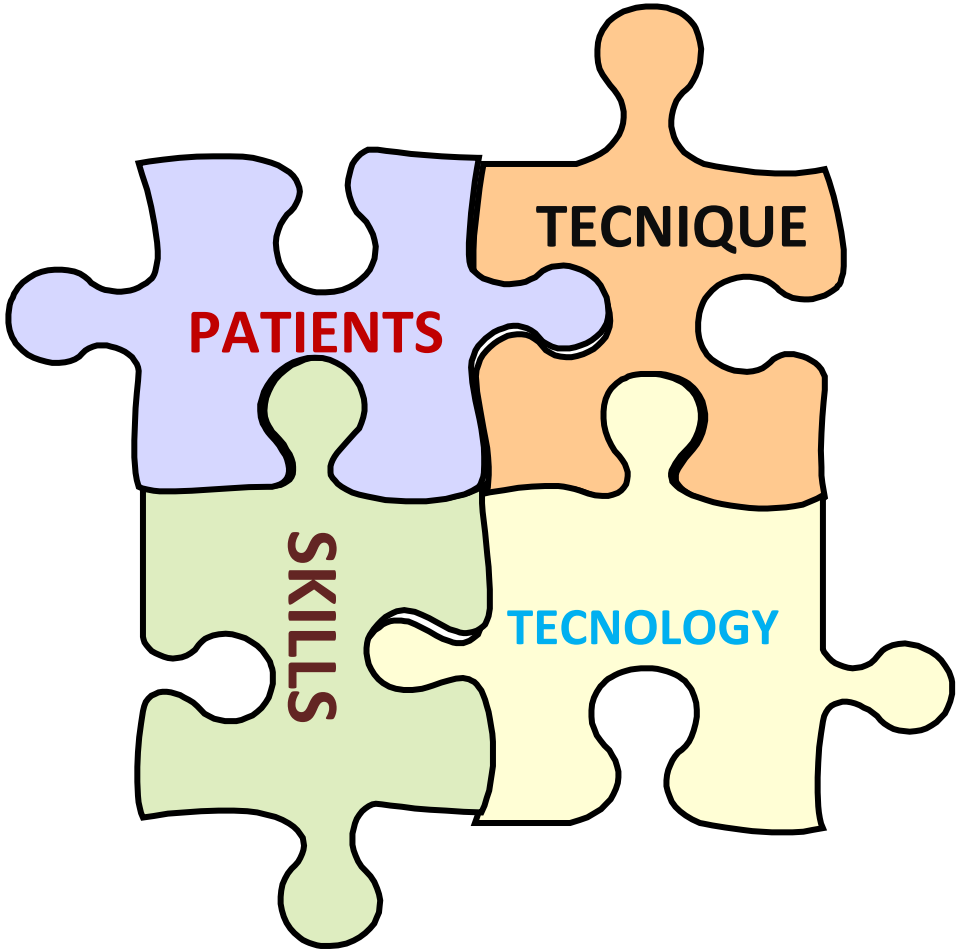
The Splanchnic block vs Celiac block: who prefer?

- There are not difference in terms of pain relief between the two blocs. The neuroliytic spreads in periaortic site also producing a block precrurali components.

Ischia et al. 1992

More et al. 1981

PAIN RELIEF IN CHRONIC CANCER PAIN



GRAZIE