Interventional Options for the management of cancer related pain:

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Purpose

- Importance of pain control
- Interventional/surgical options
  - Vertebro-augmentation
  - IT pump/catheter placement
- Patient selection
- Side effects/adverse events

Pain Control

- **Despite efforts, moderate to severe pain prevalence is high in the range of 60 to 80% in advanced cancer patients**
- **When present, cancer pain is moderate in severity and interferes with activity and enjoyment of life to a great extent**

Pain Control

- **Cancer pain can be relieved in 80% to 90% of patients using an opioid-based analgesic regimen and the WHO analgesic ladder as guidelines.**
- **In patients who do not get pain relief with systemic analgesic therapy, interventional pain procedures should be considered as part of multimodal approach to cancer pain management.**

Pain Control

- Frequent hospitalizations:
  - Increased morbidity/mortality
  - Decreased QoL
  - Increased Cost
- Common reason for hospitalizations in advanced stage cancer patients is uncontrolled pain

Vertebro-augmentation

- Osteoporosis (widely used)
- Compression Fractures (metastatic dz)
- Failed Conservative management
- Vertebroplasty/kyphoplasty
- Timing, Indications, Contraindications
- Risks/Side Effects

Clinical Consequences of Vertebral Compression Fractures (VCFs)

- Of clinically-detected fractures, 84% are associated with pain
- The greater the deformity of the fracture, the greater the pain and disability:
  - Reduced exercise tolerance
  - Early satiety and weight loss
  - Functional decline, reduced ability to perform ADLs
  - Depression, loss of self-esteem, sleep disorders
  - Kyphotic deformity resulting in gastrointestinal and pulmonary dysfunction
  - Increased hospitalization and mortality

Risk factors for VCFs

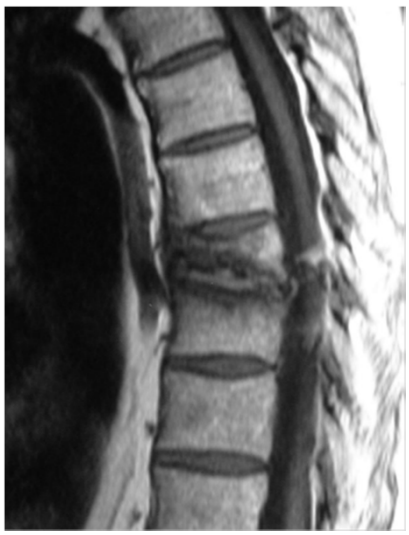
- National Osteoporosis Foundation predicts 1 in 3 women over age 50 will suffer a VCF as a result of osteoporosis
- Lifetime risk of symptomatic vertebral fracture for women is 16%; for men, 5%
- Secondary osteoporosis resulting from use of therapeutic drugs (often part of cancer patients' regimen):
  - Steroids
  - Anticonvulsants (neuropathic pain)
  - Chemotherapy
  - Heparin (DVT)

Effect of PMMA (used in vertebro-augmentation) on VCFs

- Main benefit of vertebroplasty: immediate pain relief
- While the precise mechanism of pain relief has not been proven it is believed to be achieved by:
  - Immobilization of the fracture
  - Relieving stress on the remaining bone by providing increased tensile strength and stiffness
  - Destruction of nerve endings by causing necrosis through:
    - Heat – exothermic reaction of monomer and polymer in the cement
    - Direct toxic effect

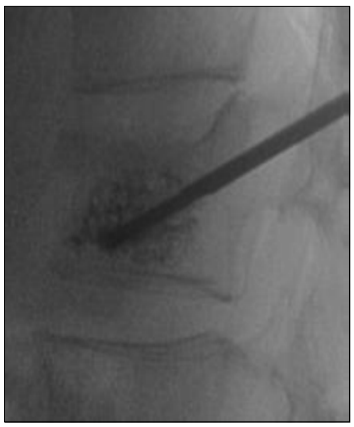
VCF Morphology

- Fracture Classifications
  - Superior endplate
  - Inferior endplate
  - Biconcave
  - Crushed
  - Vertebra Plana
- Posterior Wall Involvement
  - Burst
  - Intact but bulging posterior wall



Options

- Medical treatment
  - Pain control, Bracing, Bed rest
- Surgery often contraindicated
  - Too soft to hold instrumentation
- Inactivity may cause (1-4):
  - PE/Pneumonia/Bone & Muscle loss
- PMMA injection
  - Stabilizes fx
  - ↓ pain & ↑ ambulation
  - Decrease debilitation



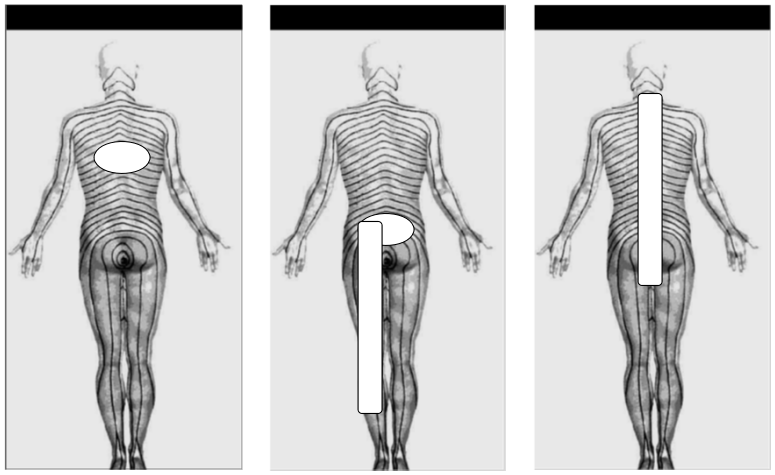
Indications for Vertebroplasty

- Painful osteoporotic fractures less than one year old
- Pain refractory to traditional medical therapy
  - No long-term relief with analgesics (and/or side effects to dosage includes excessive drowsiness, confusion or constipation)
  - Pain negatively impacting mobility and ADLs
  - Worsens with weight bearing
  - Relieved with rest or when recumbent
- Painful fracture related to benign or malignant tumor (metastatic disease, hemangiomas)
- Patient with multiple compression fractures for whom further collapse would result in compromised pulmonary or GI function

Contraindications

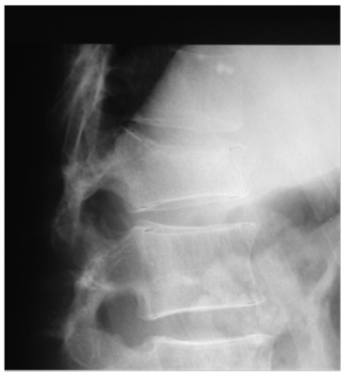
- **Absolute-**
  - **Coagulopathy, infection, refusal**
  - **Unstable Fx involving posterior element**
  - **Lack of definable level of vertebral collapse**
- **Relative-**
  - **Inability of the patient to lie prone**
  - **Lack of surgical backup (NS or Spine)**
  - **Lack of proper facilities and monitoring equipment (ASA)**
  - **Presence of neurological compromise**
  - **Compression greater than 50% of the original vertebral body height**
  - **Mild retro-pulsion without impending neurological consequences**

Pain distribution in VCF

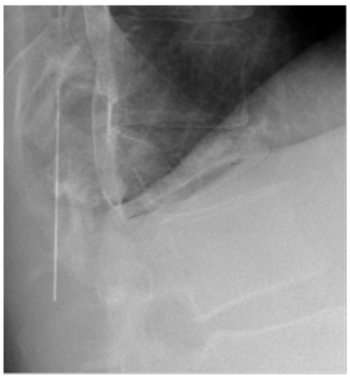


Fracture Age and Timing of Treatment

- ***Osteoporotic VCF progressively collapse over 6-18months***



Nov 28, 2004



Feb 23, 2005

Fracture Age and Timing of Treatment

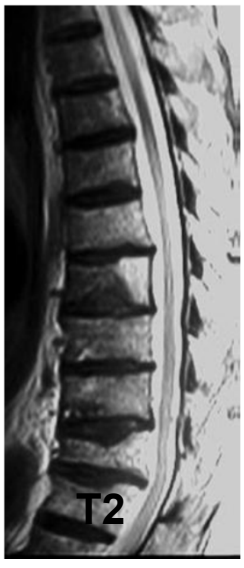
- **Acute Stage of fracture**
  - **3 months or less**
  - **Prevention of functional decline**
  - **Decrease adverse side effects of medical management**
- **Sub-acute/chronic**
  - **1 year or less:**
    - **NEJM study noted no difference between conservative management vs vertebroplasty**

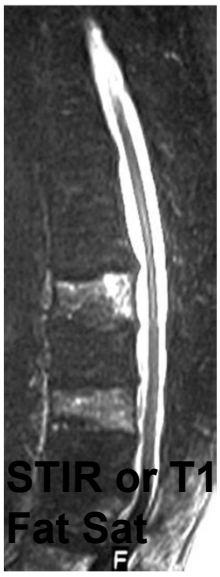
Pre-Procedure Imaging

- X-rays
  - Compare w/ prior studies (is it really acute?
  - Evaluate height loss (>50%)
  - Look for retropulsed fragment
  - Degree of canal invasion
- Bone Scan
  - Note metastatic disease
  - Infection

Pre-Procedure Imaging

- MRI
  - T1, T2, STIR sequences (w/n 3 months)
  - Assess for marrow edema
  - Exclude critical stenosis
  - Assess cortical integrity (obviously CT scan better for bone details)





Height Restoration - Kyphoplasty

- McKiernan, et al (Spine 2003)
  - "magnitude of height restoration very variable with conventional kyphoplasty, nearly 4-fold depending on fx severity & reporting method.
- More appropriate in T-spine

Height Restoration

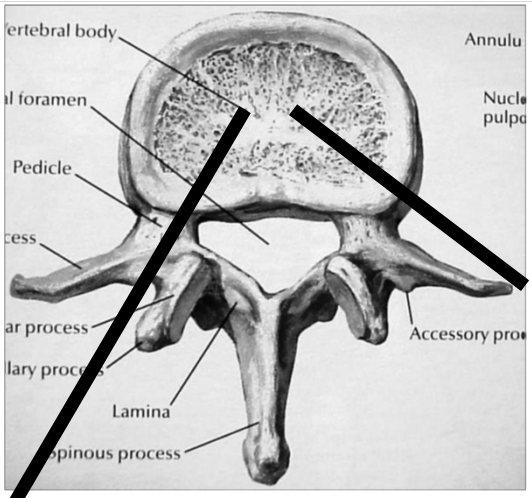
Kyphoplasty

- Lieberman (Spine, 2001)
  - 35% mean ↑ in height (2.9 mm)
- Rhyne (J Ortho Trauma 2004)
  - Ant restoration - 4.6 mm
- Gaitanis (Eur Spine J 2005)
  - Restoration of 4.3 mm
- Feltes (Neurosurg Focus 2005)
  - No height restoration

Vertebroplasty

- Teng (AJNR 2003)
  - 27% mean ↑
- Hiwatashi (AJNR 2003)
  - ↑ of 2.7 mm
- McKiernan (Spine 2003)
  - Height restoration in 23 of 65 pts
- Mean restoration 3.0 mm
- Dublin (AJNR 2004)
  - 49% mean ↑

Different Approaches



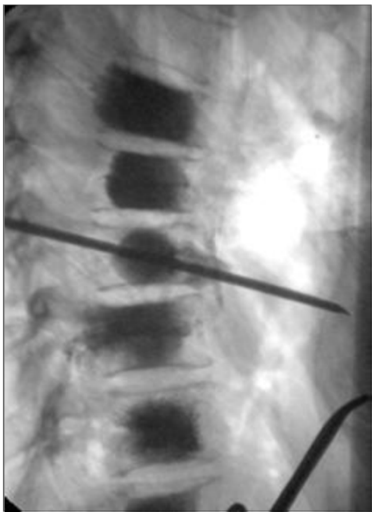
Parapedicular

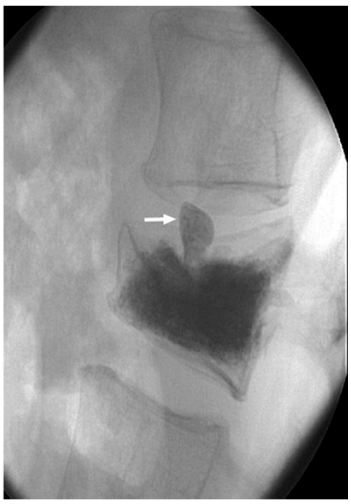
Transpedicular

Risks and Adverse Effects

- Infection, nerve injury, paralysis, PE, stroke, death
- Adjacent compression fractures:
  - Most Common:
    - Up to 52%
  - Factors found to contribute:
    - Lower bone mineral density
    - Greater restoration rate of vertebral height
    - Pre-existing fracture
    - Intradiscal cement leakage

Risks and Adverse Effects

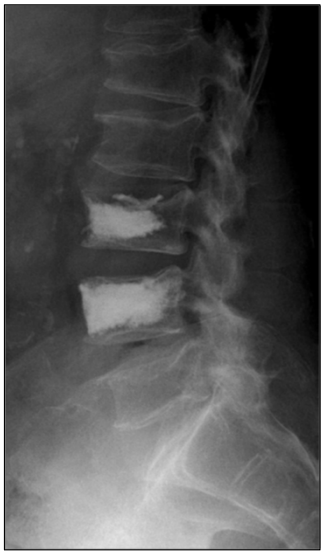
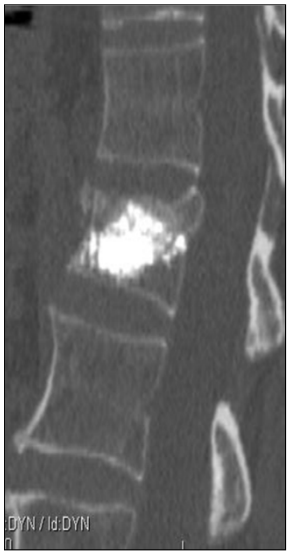


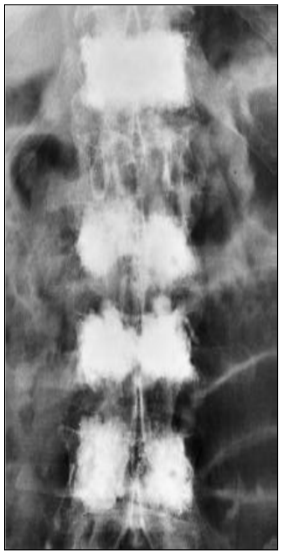


Possible utilization of vertebro-augmentation

- Acute pain due to compression fracture
  - Less than 12 weeks
    - Fractures heal significantly within 6-8 weeks
- Severe Immobilizing pain
  - Inpatient setting
  - Elderly:
    - Prone to deconditioning syndrome
  - Patients with intractable cancer pain
- Possibility of bone bx if needed

Pictures

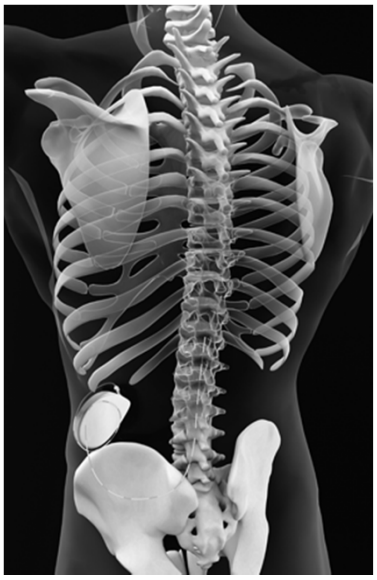


Intrathecal Pain Pump Therapy

- Understanding of the modality
- Patient selection
- Adverse events/safety record
- Current available medications
- Indications/Contraindications

Patient Selection

- A treatment for individuals with severe pain due to:
  - Metastatic Dz
  - Failed back surgery
  - Post Chemo neuropathy
  - Failed or intolerant to oral therapy
  - Pain not controlled by multiple modalities
  - Progressively worsening pain
  - Chronic pain
- Can be used with or in place of orally administered medications
- Nondestructive, adjustable, and reversible therapy (by pump explantation)



How IT Therapy Works

- Uses an implantable, programmable SynchroMed® II pump to deliver precise amounts of medication intrathecally, directly to the site of action at the spinal cord via the cerebrospinal fluid (Targeted Drug Delivery Therapy)
- Because IT Therapy delivers medication directly to the spinal cord, a fraction of the oral medication dose may be needed (300:1 oral:IT morphine)

The SynchroMed II Infusion System

- Consists of two fully implantable components
  - SynchroMed II pump
  - Intraspinal Catheter
- Uses a clinician programmer to deliver precise and customized therapy to patients
- Can deliver medication at either a constant rate or a variable rate
- Available patient controlled system for bolus infusions

Device Reliability

- SynchroMed II 20 mL pumps are 98.3% reliable* (event-free) at 48 months and 51 months[1]
- SynchroMed II 40 mL pumps are 99.2% reliable* (event-free) at 48 months and 51 months[1]
- Battery life averages 5-7 years
- Replaced surgically

Reliability is the probability a pump remains event-free through the time interval. Events are defined as any change that prevented delivery of the therapy to the intended location, required surgical intervention to correct, and were related to a problem with the pump.

1. Medtronic Product Performance Report. http://professional.medtronic.com/performance09/downloads/NeuroPain_PPRinfusion_FY10_200903263aEN.pdf. Accessed June 22, 2010.

Device Reliability

- **Most common cause of pump failure:**

Intrathecal Drug Delivery System Product Performance Events

Event	Number of Product Performance Events	Number of Patients with Events	Percent of Patients with Event (n=5,362)
Catheter kink/occlusion	189	170	3.17%
Catheter dislodgment from intrathecal space	167	152	2.83%
Catheter break/cut	118	107	2.00%
Motor stall	52	52	0.97%
Medical device complication	31	31	0.58%

Medications

- **Opioids:**
  - **Morphine**
  - **Hydromorphone**
  - **Fentanyl**
  - **Sufentanil**
- **Local Anesthetic:**
  - **Bupivicaine**
- **Clonidine (α_2 adrenergic agonist)**
- **Ziconotide: N-Type V-gated Ca Blocker**
- **Baclofen (for spasticity)**

Medications

2012 Polyanalgesic Consensus Guidelines for Management of *Nociceptive* Pain by Intraspinal Drug Delivery Line Recommended Regimen

- **Line 1: Morphine or Hydromorphone or ziconotide or Fentanyl**
- **Line 2: Morphine + bupivacaine or ziconotide + opioid or hydromorphone + bupivacaine or fentanyl + bupivacaine**
- **Line 3: Opioid (morphine, hydromorphone, or fentanyl) + clonidine or sufentanil**
- **Line 4:Opioid + clonidine + bupivacaine or bupivacaine + clonidine**
- **Line 5: Sufentanil + bupivacaine + clonidine**

Deer TR, et al. ***Neuromodulation. 2012;15(5):436-464. PMID: 22748024.***

Medications

2012 Polyanalgesic Consensus Guidelines for Management of *Neuropathic* Pain by Intraspinal Drug Delivery Line Recommended Regimen

- **Line 1: Morphine or Morphine+Bupivicaine or Ziconotide**
- **Line 2: Hydromorphone or hydromorphone + bupivacaine or hydromorphone + Clonidine or Morphine + clonidine**
- **Line 3: Clonidine or ziconotide + opioid or fentanyl or fentanyl + bupivacaine or fentanyl + clonidine**
- **Line 4: Opioid + clonidine + bupivacaine or bupivacaine + clonidine**
- **Line 5: Baclofen**

Deer TR, et al. ***Neuromodulation. 2012;15(5):436-464. PMID: 22748024.***

Adverse Events

- Possible adverse events may include:
  - Respiratory/CV depression
  - Somnolence
  - Nausea
  - Vomiting
  - Headaches
  - Convulsion
  - Dizziness
  - Paresthesia

Adverse Events

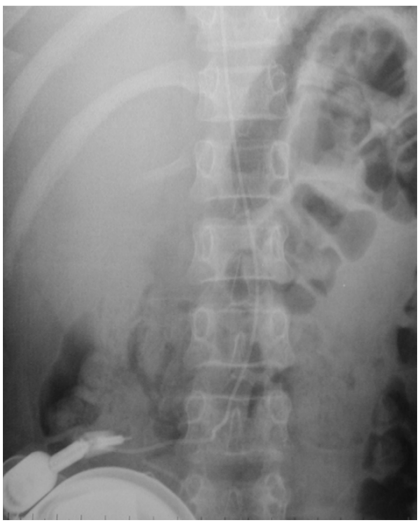
- Overdoses have been identified and in extreme cases may be life threatening
- No deaths been reported for overdosing in Ziconotide
- Possible device complications may include:
  - Catheter or pump moving within the body or eroding through the skin
  - Catheter leak, tear, kind, or dislodgement, resulting in under dose or no medication infusion
  - Pump failure may cause overdose or under dose of intrathecal medication

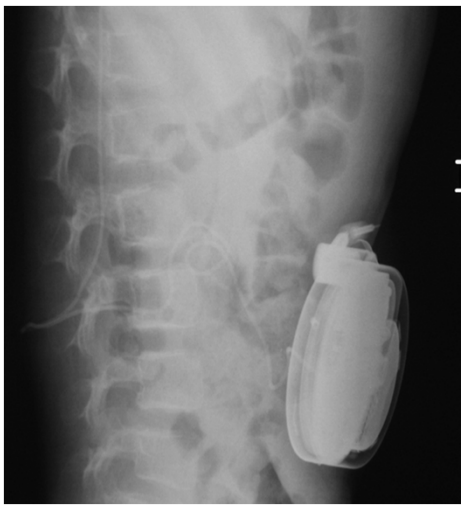
Contraindications

IT Drug Therapy and implantation of the SynchroMed programmable pump are contraindicated:

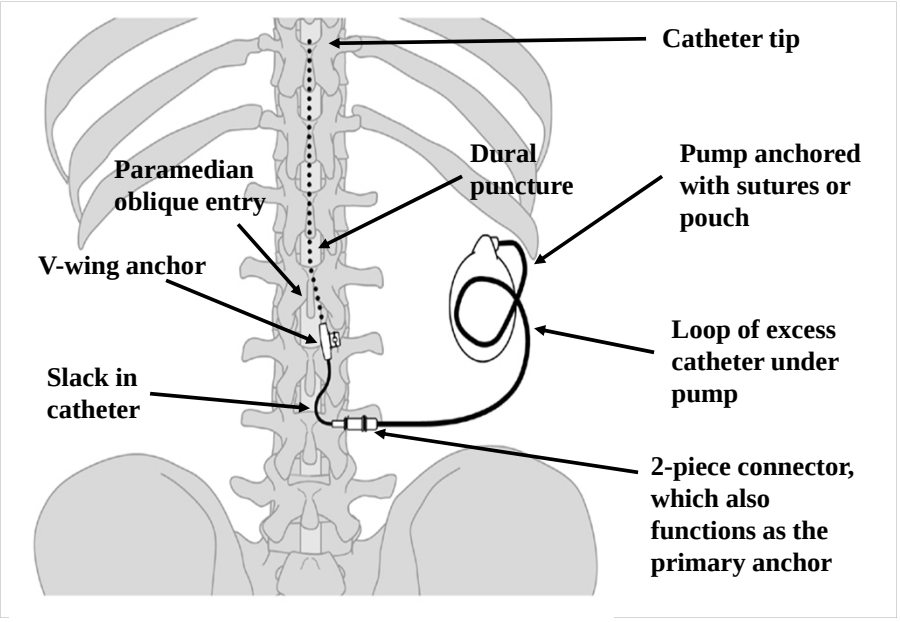
- **In the presence of infection or spinal anomalies**
- **When the pump cannot be implanted 2.5 cm or less from the surface of the skin**
- **In patients whose body size is not sufficient to accept the pump bulk and weigh**
- **In patients with hypersensitivity to infused medication**
- **Infusion of medication pH<3**
- **Safety and effectiveness in pediatric patients below the age of 4 have not been established.**

ITB Pump and Catheter





ITB Pump and Catheter



Summary

- Pain is common in cancer patients and can be difficult to manage in severe cases
- Interventional techniques can be an option to help with the management of pain for these patients
- Vertebro-augmentation may be an option for acute vertebral fractures in these patients
- Ultimately if other modalities fail or if the pain is anticipate to worsen, IT pump therapy is a very good option

References/acknowledgements:

- Neurotherm vertebroplasty workshop
- A Randomized Trial of Vertebroplasty for Osteoporotic Spinal Fractures Kallme et al, NEJM 2009
- Risk Factors of New Compression Fractures in Adjacent Vertebrae after Percutaneous Vertebroplasty, Kim et al, ASJ 2011
- Percutaneous vertebroplasty: indications, contraindications, and technique, PEH et al, BJS 2003
- Prialt Medtronic education lecture
- Deer TR, et al. *Neuromodulation. 2012;15(5):436-464. PMID: 22748024.*
- Pain Medicine News April 2014;34-39

Radiofrequency Ablation
Hip
Knee
Sacroiliac joint

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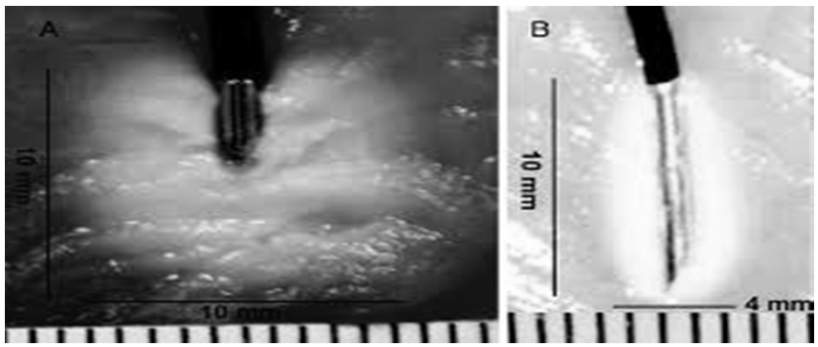
Radiofrequency Ablation (RF)

- Lesions peripheral nerves
  - Conventional: >45 degrees Celsius
  - Pulsed: less than 42 degrees
- Uses high frequency alternating current to heat tissue
- RF typically provides pain relief for over 6 months

Lesion Size and Probe

- Conventional RF needle:
- Water-cooled RF needle:



Why Consider RF?

- Minimally invasive
- Recovery time is minimal
  - 2-5 days
- Excellent choice for patients who
  - Are not good surgical candidates
  - Don’t want surgery
  - Pain despite surgery

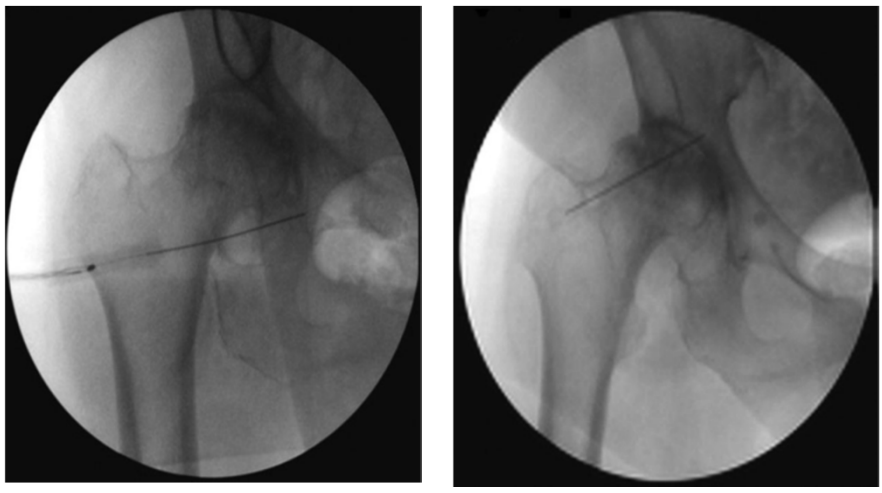
How much relief?

- “You get to try it before you buy it”
- Diagnostic blocks are done with local anesthetic before radiofrequency ablation
- Typically at least one block is done first
- RF procedure considered if patient gets at least 50% pain relief

RF for Hip

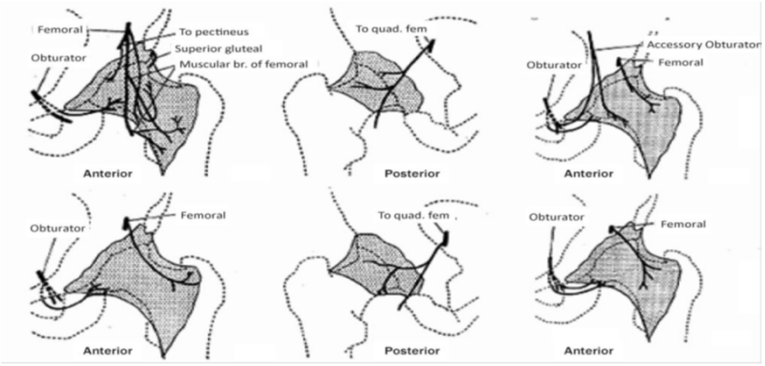
- Who is a good candidate
  - Patients with prior hip replacement
  - Also an option for cancer pain
  - Not surgical candidates
- The target nerves are the sensory branches of the femoral and obturator nerves
- Sensory testing is performed prior to ablation

RF Hip



Sensory innervation of the hip

Femoral and obturator primarily innervate the anterior lateral and medial capsule



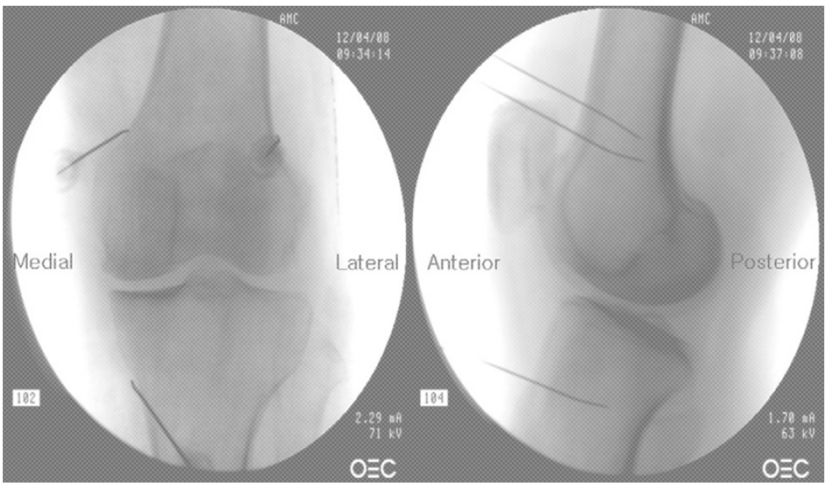
Evidence Based Medicine

- **Most of the evidence is based on case reports**
- **No large, multicenter placebo controlled studies have been done for the hip**
- **Many confounding factors which is why diagnostic block is vital to decide if this procedure is appropriate for patients**

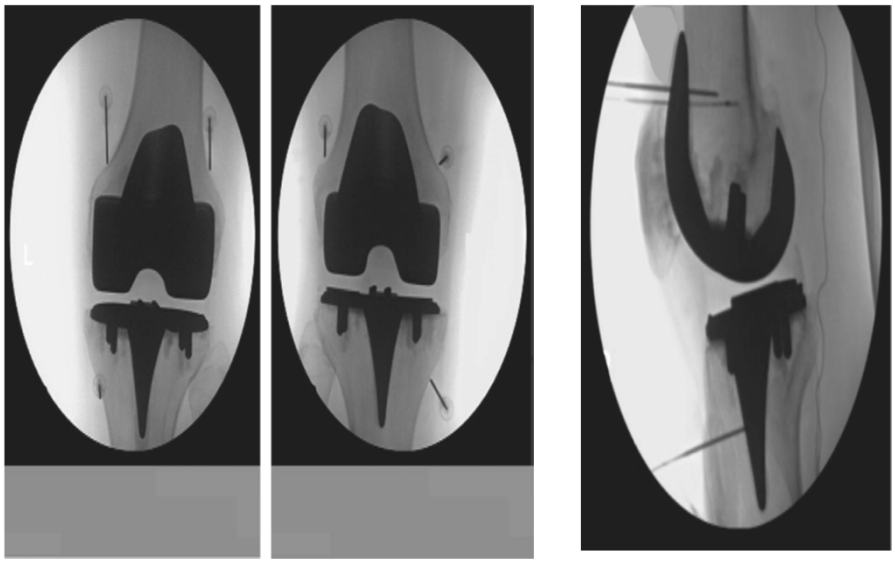
RF Knee

- Can be done with both conventional and water cooled RF needles
- Target are the genicular nerves
  - Superior lateral and medial
  - Inferior medial
- Diagnostic block done prior to ablation
- Sensory stimulation done to isolate nerve
- Great option for patients who are non-surgical candidates

RF Knee Conventional



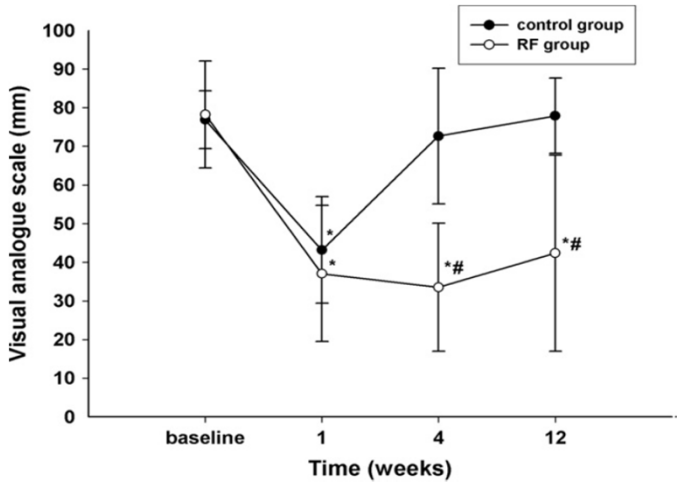
RF Knee- water cooled



EBM Knee

- Many case reports to support procedure
- One recent placebo controlled double blinded study to support RF knee
  - 19 patients in each treatment arm
    - Control (lidocaine) vs RF
- Study found the VAS, oxford knee score, and global perceived effect all improved 4 and 12 weeks in the RF group

RF Knee- EBM



Clinical Experience

- **RF for orthopedic injuries allow patients to perform physical therapy, overcome painful exacerbations, and sometimes are done prior to their surgery**
- **Goals and expectations must be clearly explained to patient**
- **Functional improvement, weight loss, decrease in pain medications are common goals**

Sacroiliac Joint Dysfunction

- Common cause of 5-30% of low back pain
- Low back, buttock, groin, and/or posterior leg pain
- More common if:
  - Lumbar fusion
  - Spondyloarthropathies (ie ankylosing spondylitis)
  - Gait abnormality
  - Leg length discrepancy

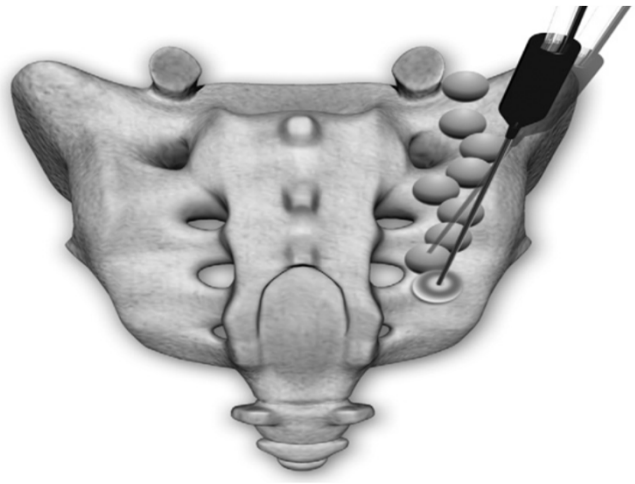
Sacroiliac joint dysfunction

- Conservative management
  - Physical therapy (aquatic and land based)
  - Manipulation, osteopathic or chiropractic
  - Oral medications
  - Sacroiliac joint belts
  - Massage therapy
  - CAM (acupuncture, etc)

Sacroiliac joint dysfunction

- Diagnosis is made clinically and confirmed with sacroiliac joint injection
- Ablation is considered if injection only provides short term relief
- Two common methods to ablate the sacroiliac joint (L5-S3 medial branch nerves)
  - Water cooled (Synergy)
  - Multi-lesion probe (Simplicity)

Water cooled Sacroiliac joint ablation



Evidenced Based Medicine

- 2 recent studies using water cooled method
  - Steltzer: retrospective case series of 126 patients

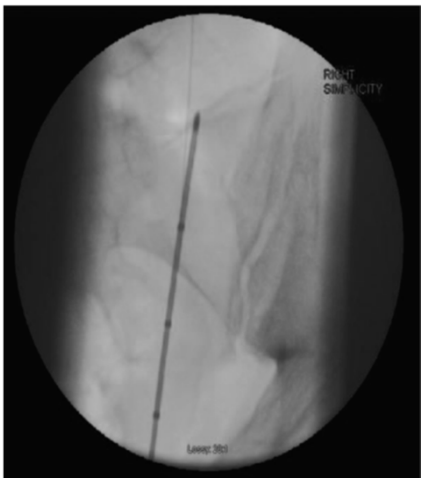
Evidenced Based Medicine

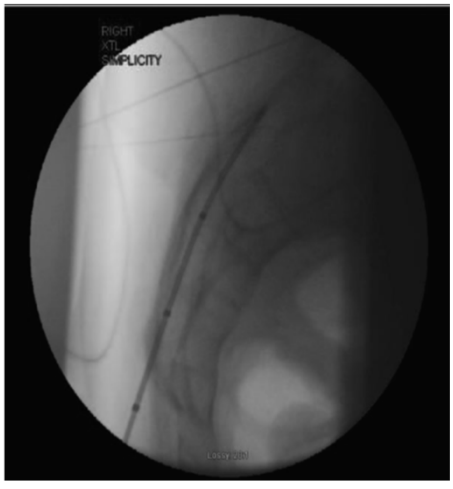
- Patel: prospective, placebo (sham intervention) , single site study of 52 patients
- Outcomes were measured at 12 months
- Mean decrease in NRS (numeric rating scale) was 2.7
- Function improved based on SF-36 of 15.8
- Oswestry disability scale decrease of 13.9

Simplicity Probe

- **'Strip lesion' along the entire sacroiliac joint created**
- **Less timing consuming, similar recovery time**

Sacroiliac joint RF





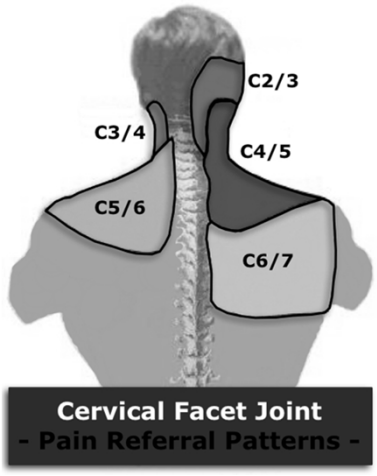
Evidenced Based Medicine

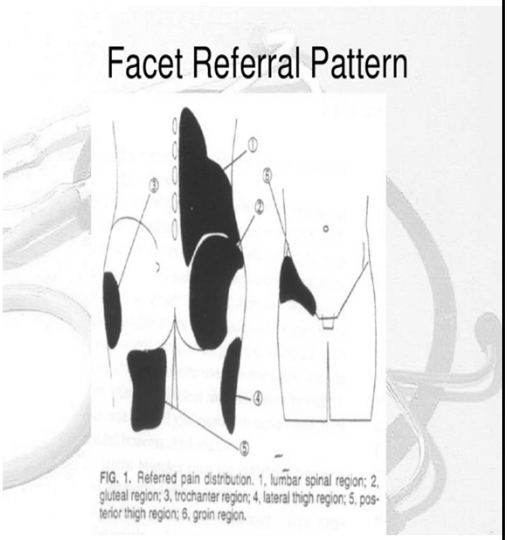
- Schmidt: Retrospective study of 77 patients from two academic centers (Virginia Mason, and Univ of Virginia)
- 16 out of 77 failed to respond
- 55% had greater than 50% pain relief at 6 months
- Inclusion criteria was not as selective as the water cooled study- steroid was used in diagnostic injection

Lumbar/Cervical facet pain

- Most common and most studied use of RF for chronic pain
- Addresses primarily axial pain arising from cervical, thoracic, and lumbar facet joints
- Very common cause of pain after surgery
  - Failed back syndrome, junctional disease
  - After lumbar laminectomy

Pain Referral Patterns





Contraindications to RF

- Patient does not want procedure
- Platelets less than 75
- Unable to stop blood thinner
  - Bleeding disorder
- Active infection

Complications

- Serious complications are uncommon
  - Infection
  - Hematoma
  - Nerve injury (motor testing done prior to RF)
- Post-procedural pain, 2-5 days
- Post-op neuritis
  - 'sunburn', hypersensitivity of skin

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