Low Back Pain: Novel Solutions

Douglas Keehn, DO
Advanced Pain Management
Madison, WI
Objectives

• Have awareness of the medical, social and economic impact of spinal pain

• Understand the role of interventional diagnostic approaches to evaluating spinal pain

• Be aware of interventional treatments available for the treatment of spinal pain
Epidemiology

- Pain is the second most common complaint of people seeking medical advice

- < 3 hours training of primary care physicians

- 60-90% U.S. adults will have back pain in their lifetime, 50% annual incidence

- 30% with back pain develop chronic pain

Epidemiology

• “The annual cost of chronic pain in the U.S. is estimated to be $560-635 billion including healthcare expenses and lost productivity”

• Most frequently filed workers’ compensation claim

• Most common reason for disability in patients <45 years

# Estimated Epidemiology of Spinal Pain

<table>
<thead>
<tr>
<th>Condition</th>
<th>Low Back</th>
<th>Neck</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDD/DDD</td>
<td>20-50%</td>
<td>20-30%</td>
</tr>
<tr>
<td>Facet joint mediated pain</td>
<td>15-45%</td>
<td>50-60%</td>
</tr>
<tr>
<td>Disc herniation</td>
<td>3-46%</td>
<td>3-50%</td>
</tr>
<tr>
<td>Spinal stenosis</td>
<td>2-12%</td>
<td>2-15%</td>
</tr>
<tr>
<td>Myofascial</td>
<td>10-20%</td>
<td>10-20%</td>
</tr>
<tr>
<td>Other causes</td>
<td>2-10%</td>
<td>2-10%</td>
</tr>
</tbody>
</table>
Spinal Pain

• Radicular
  – Inflammation of nerve root

• Axial
  – Myofascial
  – Facetogenic
  – Discogenic
Radicular Pain vs. Radiculopathy

• Radicular pain in distribution of nerve secondary to inflammation

• Radiculopathy is a specific neurologic deficit
  – May be painless
• Macnab I, *Pain*, 1971: Balloons in neural foramina of normal nerves and those with associated disc herniations
  – Normal levels produced painless neuro deficits
  – Affected levels produced pain
Radicular Pain Basics and Basic Science

- Chemical irritation from cytokine exposure to nerves: decreased NCV, damage to myelin, edema, coagulation

- Inflammatory mediators increase dorsal root ganglion sensitivity and ectopic firing

- Nucleus pulposus when placed on to the DRG causes excitation and mechanical hypersensitivity

- Only inflamed NR is painful if pressed or stretched

Corticosteroid Effects

• Suppression spontaneous ectopic firing
• Antinociceptive in themselves
  – Blocks C-fiber transmission
  – Transmission normalized upon removal of the corticosteroids


Epidural Steroid Injections: Indications

• Used in conjunction with conservative management
  – PT and/or manipulative medicine
  – NSAIDs
  – Muscle relaxants
  – Antiepileptics
  – Opioids?
Epidural Steroid Injections: Indications

- Radicular Pain
  - Disc herniation
  - Herpes zoster

- Spinal Stenosis

- Discogenic Pain
Epidural Steroid Injection

- Three routes:
  - Caudal
  - Interlaminar
  - Transforaminal
Interlaminar ESI

- Cervical
- Thoracic
- Lumbar
Interlaminar ESI

L3

L4

S1
Transforaminal ESI
Transforaminal Lumbar ESI
Complications and Adverse Effects

• Headaches
• Infection
• Bleeding
  – Coumadin Ticlid, Plavix, Asprin, Lovenox, etc.
• Paraplegia
• Nerve root injury
• Miscellaneous
  – Increased blood sugar
  – Hypertension
  – Pedal edema, CHF
Lumbar Stenosis: Types of Physical Therapy

• Multicenter RCT
  – Manual physical therapy, body weight supported treadmill walking and exercises (N=29)
  – Lumbar flexion exercises and treadmill walking (N=29)
  – Outcome measures
    • ODI
    • Global rating of change
    • At 0, 6 weeks, 12 months

Whitman, SPINE 2006
Bracing:

- The use of a lumbosacral corset/brace can increase walking distance and decrease pain in patients with LSS.
- There is no evidence that results are sustained once the brace is removed.

Insufficient evidence to address the role of:

- Traction, electrical stimulation or TENS
- NSAIDs, narcotics
- Muscle relaxants
- Analgesics
- Oral Prednisone

NASS Clinical Guidelines for diagnosis and treatment of degenerative lumbar spinal stenosis, 2007
Lumbar Stenosis: Adding gabapentin

- N=55, randomized 2 groups
  - PT, Brace, NSAIDs vs. PT, Brace, NSAIDs and Gabapentin

- Gabapentin 900 mg/day — increased to 2,400 mg/day

- Follow-up 15 days, monthly up to 4 months

- Gabapentin group showed better increase in walking distance, as well as better pain scores
  - Mean VAS change after 4 months
    - Treatment group (7.0/2.9)
    - Control group (6.7/4.7)

Yaksi, SPINE 2007 32(9)
Epidural Steroids and Spinal Stenosis

- Improvement in VAS pain scores correlated well with severity of symptoms and radiographic severity, as well as number of levels affected, except in patients classified as severe with >3 lumbar levels affected

- Grade of nerve root compromise on MRI correlated with ESI outcomes but not duration or S&S


Herniated Nucleus Pulposus

• With (1.8) transforaminal steroid injection, 75% of patients (N=69) had good outcomes at 80 weeks

• Transforaminal > Interlaminar > Caudal

• Cost effective

ESI Efficacy

• Manchikanti et. al.: Double-blind, randomized placebo controlled studies evaluating ESI for treatment
  – Chronic discogenic pain
  – Chronic radiculitis
  – Lumbar post laminectomy syndrome
  – Spinal stenosis

Manchikanti et. al.:

- Demonstrated efficacy in all 4 groups with functional improvement noted in:
  - Disc herniation and radiculitis group (79-91%)
  - Post laminectomy syndrome (55%)
  - Spinal stenosis (70%)
Can ESIs Prevent Surgery?

- 91 patients with HNP referred to spine surgeons
- 56% avoided surgery because of relief from 1 or more TF ESI


Can ESIs Save Money?

• The cost utility of epidural injections is superior to numerous other modalities of treatments including “usual care,” spinal cord stimulation and surgical interventions.


## ESTIMATED EPIDEMIOLOGY OF SPINAL PAIN

<table>
<thead>
<tr>
<th>Condition</th>
<th>Low Back (%)</th>
<th>Neck (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDD/DDD</td>
<td>20-50%</td>
<td>20-30%</td>
</tr>
<tr>
<td>Facet joint mediated pain</td>
<td>15-45%</td>
<td>50-60%</td>
</tr>
<tr>
<td>Disc herniation</td>
<td>3-46%</td>
<td>3-50%</td>
</tr>
<tr>
<td>Spinal stenosis</td>
<td>2-12%</td>
<td>2-15%</td>
</tr>
<tr>
<td>Myofascial</td>
<td>10-20%</td>
<td>10-20%</td>
</tr>
<tr>
<td>Other causes</td>
<td>2-10%</td>
<td>2-10%</td>
</tr>
</tbody>
</table>
What role does imaging play in the diagnosis of chronic axial low back pain?
Imaging in Chronic Axial Low Back Pain

• MRI correlates poorly with source of pain
  – Boden SD et. al., JBJS,72: 403-8, 1990

• CT correlates poorly with source of pain
  – Weisel et. al., The incidence of positive CAT scans in an asymptomatic group of patients. Spine, (9), 549-551, 1984
  – Rothman RH. The study of computer assisted tomography, Spine 9;548,1984

• X-ray correlates poorly with source of pain
Spinal Facet Joint

Facet Joints in Motion

Vertebral Body

Disc

Flexion (Bending Forward)  Extension (Bending Backward)

Facet Joint
Cervical Pain: Facets

- Stimulation of zygapophyseal joints causes pain in normal volunteers

- In patients with neck pain produces relief with anesthetizing joints


Figure 1. Maps showing the typical distribution of pain referred from each of the cervical zygapophysial joints when stimulated in normal volunteers (modified from Dwyer et al20).
Facet Referred Pain

- Gluteal
- Trochanteric
- Proximal thigh
- Groin
- Lumbar
- Considerable overlap

Neither clinical examination nor imaging is reliable for diagnosis.

Medial Branch Block

A

B

C
Treatment - Facet Mediated Pain

• Conservative management
  – Lifestyle changes
  – Physical therapy
  – Manual medicine
  – Pharmacotherapy
    • NSAIDs
    • Muscle relaxants

• Interventional management
  – Facet injections
  – Medial branch blockade and RF denervation
Lumbar Facet Radiofrequency
Radiofrequency Ablation

• 60% of patients >90% relief, 87% had >60% relief at 12 months. (Dual comparative anesthetic blocks)

• 253 days before 50% pre-RF symptoms returned
Radiofrequency Ablation

“The evidence for conventional radiofrequency neurotomy in managing chronic low back pain of facet joint origin in the lumbar spine is good for short- and long-term relief.”

## ESTIMATED EPIDEMIOLOGY OF SPINAL PAIN

<table>
<thead>
<tr>
<th>Condition</th>
<th>Low Back</th>
<th>Neck</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDD/DDD</td>
<td>20-50%</td>
<td>20-30%</td>
</tr>
<tr>
<td>Facet joint mediated pain</td>
<td>15-45%</td>
<td>50-60%</td>
</tr>
<tr>
<td>Disc herniation</td>
<td>3-46%</td>
<td>3-50%</td>
</tr>
<tr>
<td>Spinal stenosis</td>
<td>2-12%</td>
<td>2-15%</td>
</tr>
<tr>
<td>Myofascial</td>
<td>10-20%</td>
<td>10-20%</td>
</tr>
<tr>
<td>Other causes</td>
<td>2-10%</td>
<td>2-10%</td>
</tr>
</tbody>
</table>
Discogenic Pain

• Discogenic pain does not refer to nerve root pain caused by disc herniation

• Discogenic pain refers to the pain arising from the disc itself
Discogenic Pain

- The outer third of the annulus is richly innervated
- This innervation constitutes the anatomic substrate for discogenic pain
Discogenic Pain: Clinical Features (IASP: 1994)

• Lumbar spinal pain, with or without referred pain in the lower limb girdle or lower limb; aggravated by movements that stress the symptomatic disc
Discogenic Pain - Imaging

- Decreased disc height
- Endplate changes
- Decreased T2 signal
- High intensity zone
- May be asymptomatic
Discogenic Pain - Treatment

• Some evidence for ESI
• Conservative management predominates
  – Lifestyle changes
  – Manual medicine
  – Medication management
• Evidence for surgical intervention limited
• Spinal cord stimulation?
Neurostimulation

- Neurostimulation is a pain treatment that delivers low voltage electrical stimulation to the spinal cord to inhibit or block the sensation of pain.

- Trial screening to evaluate patient response to neurostimulation is performed prior to committing to a full implant.
Neurostimulation Theory

• Gate control theory
  – Melzack and Wall (1965)

• Aβ-fibers
  – Myelinated (fast)
  – Light touch
  – Vibratory sense

• C-fibers
  – Unmyelinated (slow)
  – Pain
Overview of Trial Procedure

- A percutaneous lead is positioned in the epidural space on the dorsal aspect of the spinal cord at the appropriate nerve root level(s)

- Electrical current from the lead generates paresthesia that can be adjusted in intensity and location to achieve the best pain coverage

- Leads are attached to an external pulse generator (screener), which supplies the current

- Patients can use the screener to adjust stimulation to meet pain management needs
Indications for Neurostimulation

Most Common Indications for Neurostimulation

- Post-laminectomy associated chronic pain
- Refractory neuropathic back and leg pain
- Complex Regional Pain Syndrome Types I and II

Neurostimulation is perhaps best utilized for the treatment of neuropathic pain of peripheral origin vs. nociceptive origin.\(^1,2\)

Patient Selection

• Objective evidence of pathology
  – Use appropriate diagnostic studies to establish pain etiology, to rule out other causes such as a tumor

• Inadequate pain relief and/or intolerable side effects after treatment with more conservative therapies

• Psychological evaluation
  – Is the patient physically and mentally able to handle the procedure and associated maintenance and/or follow-up?

• Absence of drug-seeking behavior

• Patients with predominant nociceptive pain may not respond to treatment with neurostimulation

• Potentially adverse psychosocial factors should also be considered prior to treatment with neurostimulation:
  – Noncompliance to treatment
  – Severe depression
  – Untreated drug dependency
Advantages of Implanted Neurostimulators for Pain

• Effective method of pain control\(^1\)
• Screening trial allows patient response to be tested before a full implant
• Systems reprogrammable without surgery
• Patient control within physician set limits
• Nondestructive procedure compared with surgical alternatives
• Reduction of pain medications\(^2\)

Failed Back Surgery Syndrome: Percentage of patients receiving satisfactory pain relief up to 1 year and 22 years (n=220)\textsuperscript{1}

Neurostimulation: Pain Relief

CRPS I/II: Percentage of internalized patients receiving satisfactory pain relief up to 1 year and 22 years (n=22)¹

<table>
<thead>
<tr>
<th></th>
<th>Up to Year 1</th>
<th>Up to Year 22</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRPS I/II</td>
<td>87.5%</td>
<td>72.0%</td>
</tr>
</tbody>
</table>

Peripheral Neuropathy: Percentage of internalized patients receiving satisfactory pain relief up to 1 year and 22 years (n=17)¹

<table>
<thead>
<tr>
<th></th>
<th>Up to Year 1</th>
<th>Up to Year 22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral Neuropathy</td>
<td>82.4%</td>
<td>71.0%</td>
</tr>
</tbody>
</table>

¹ Kumar K et al. Neurosurgery. 2006;58:481-496.
Neurostimulation: Pain Relief

62% of patients with FBSS achieve at least 50% sustained, long-term pain relief with neurostimulation.¹

88% of patients with unspecified FBSS were satisfied with neurostimulation treatment¹

70% of patients with predominantly axial low back pain were satisfied with neurostimulation treatment²

Patient Satisfaction with Neurostimulation for Predominant Complaints of Chronic Intractable Low Back Pain (% of Patients)¹

75.8%  
Have Neurostimulation Again

78.1%  
Recommend Neurostimulation

A majority of patients would have neurostimulation again and/or recommend the treatment

Neurostimulation for FBSS resulted in a cost savings after 2.5 years compared with conventional medical management.

A retrospective study showed an inverse relationship between the onset of the chronic pain syndrome and SCS therapy success.¹

PROCESS Study design

• International RCT on the effectiveness and cost-effectiveness of SCS vs. CMM in patients with FBSS

• 100 patients with chronic neuropathic pain predominantly in the leg(s) following at least one spinal surgery, randomized 1:1

• 12 centers in Europe, Australia

• Pragmatic trial:
  – Intent-to-treat (ITT) analysis until 6 months with crossover allowed after 6 months
  – Long-term follow-up to 24 months

• Treatment definition
  – CMM: any therapy advised by a physician, except reoperation and intrathecal drug delivery (IDD)
  – SCS (+CMM): implantable stimulation system (Synergy® system)
PROCESS Study design: Sample Size and Objectives

• Assumptions for sample size based on previous trial:\(^1\)
  – 42.5% of SCS patients reach ≥50% leg pain relief at 6 months
  – 14.5% of CMM patients reach ≥50% leg pain relief at 6 months
  – 20% attrition

• Primary outcome:
  – Proportion of patients with ≥50% leg pain relief at 6 months
    (≥50% reduction in leg VAS)

• Secondary outcomes evaluated at 1, 3, 6, 9, 12, 18 and 24 months:
  – Pain relief (leg and back VAS)
  – Quality of life (SF-36® and EQ-5D)
  – Function (Oswestry Disability Index)
  – Patient satisfaction
  – Drug/nondrug therapy use
  – Time away from work
  – Adverse events

---

Primary Outcome at 6 Months

≥50% leg pain relief
Significantly more SCS patients (48% vs 9%) achieved the primary outcome (P<0.001)

![Graph showing percent of patients achieving ≥50% leg pain relief over 1, 3, and 6 months. CMM vs SCS.](chart)

- 1 month: CMM 2%, SCS 47%
- 3 months: CMM 9%, SCS 56%
- 6 months: CMM 9%, SCS 48%

N = 47, 51, 44, 50

*a* Significant difference (P<0.001) between groups at 6 months
Secondary Outcome at 6 Months

VAS leg pain
Significantly greater reduction in leg pain with SCS (P < 0.0001)

- **a** Significant difference (P < 0.0001) between groups at 6 months
- **b** Significant difference (P < 0.0001) in SCS group between 6 months and baseline
- **c** Significant difference (P = 0.03) in CMM group between 6 months and baseline
Secondary Outcome at 6 Months

VAS back pain
Significantly greater reduction in back pain with SCS (P = 0.008)

\[ a \] Significant difference (P=0.008) between groups at 6 months

\[ b \] Significant difference (P=0.007) in SCS group between 6 months and baseline
Secondary Outcome at 6 Months

- Medication intake
- Significantly fewer patients on anticonvulsants in SCS group (P = 0.02)
- Trend regarding antidepressants (P = 0.06)
- No difference in opioids and NSAIDs

---

**Baseline**

<table>
<thead>
<tr>
<th>Medication</th>
<th>CMM</th>
<th>SCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidepressants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**6 months**

<table>
<thead>
<tr>
<th>Medication</th>
<th>CMM</th>
<th>SCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidepressants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Significant difference P=0.02 between groups at 6 months
Mechanism of Action High Frequency Stimulation

- Anatomically placed leads
- 10K Hz
- SCS releases GABA
- High frequency allows natural firing rate of neurons, higher efficiency
High Frequency vs. Traditional SCS Responder Rates

**Back Pain**

<table>
<thead>
<tr>
<th>Month</th>
<th>Test (HF10 therapy)</th>
<th>Control (Traditional SCS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>84.3%</td>
<td>43.8%</td>
</tr>
<tr>
<td>6</td>
<td>76.4%</td>
<td>51.9%</td>
</tr>
<tr>
<td>12</td>
<td>78.7%</td>
<td>51.3%</td>
</tr>
</tbody>
</table>

**Leg Pain**

<table>
<thead>
<tr>
<th>Month</th>
<th>Test (HF10 therapy)</th>
<th>Control (Traditional SCS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>83.1%</td>
<td>55.0%</td>
</tr>
<tr>
<td>6</td>
<td>80.9%</td>
<td>54.4%</td>
</tr>
<tr>
<td>12</td>
<td>78.7%</td>
<td>51.3%</td>
</tr>
</tbody>
</table>

Analysis of permanent implant population:

Superiority p-value <0.001
Pain Score was Primary Endpoint

- Average **back pain of ≥5/10**
- Average **leg pain of ≥5/10**
- **Severely disabled or crippled** as defined by an Oswestry Disability Index score of 41-80 out of 100

- **Primary endpoint involves ≥50% back pain reduction at 3 months**

Analysis of permanent implant population
At 12 months, mean back pain VAS decreased 66% with HF10 therapy compared to a decrease of 45% for traditional SCS therapy.

Superiority p-value <0.001

Analysis of permanent implant population
At **12 months**, **63%** of HF10 therapy subjects had minimal or moderate disability compared with **46%** of traditional SCS subjects

**ODI = OSWESTRY DISABILITY INDEX**

**SUPERIORITY DEMONSTRATED (P=0.03)**

Analysis of permanent implant population
HF SCS: Decreased Opioid Use from 84 mg to 27 mg

% of Patients Using Opioids

Baseline: 86% (N=72)
12 Month: 54%* (N=68)
24 Month: 57%* (N=65)

34% reduction in # patients

Mean mg Morphine per Patient

Baseline: 84 (N=72)
12 Month: 29* (N=68)
24 Month: 27* (N=65)

68% reduction in dose

p-value < 0.001
Neural Targeting SCS

• Multiple Independent Current Control (MICC)
  – One current source for each contact vs. one current or voltage source for all contacts
  – Fractionalization for fine movement of the Central Point of Stimulation (CPS)
Neural Targeting SCS Model

Resistivity values and density of nodes of the FEM domains

<table>
<thead>
<tr>
<th>Material</th>
<th>Resistivity (Ω mm)</th>
<th>Density (nodes/mm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White matter (longitudinal)</td>
<td>1666</td>
<td>150</td>
</tr>
<tr>
<td>White matter (transverse)</td>
<td>12,048</td>
<td></td>
</tr>
<tr>
<td>Gray matter</td>
<td>4347</td>
<td>101</td>
</tr>
<tr>
<td>CSF</td>
<td>588</td>
<td>80</td>
</tr>
<tr>
<td>Epidural space</td>
<td>25,000</td>
<td>39</td>
</tr>
<tr>
<td>Dura</td>
<td>1666</td>
<td>113</td>
</tr>
<tr>
<td>Vertebral bone</td>
<td>50,000</td>
<td>0.6</td>
</tr>
<tr>
<td>Electrode contact</td>
<td>0.0002</td>
<td>16,588</td>
</tr>
<tr>
<td>Electrode insulator</td>
<td>$10^9$</td>
<td></td>
</tr>
<tr>
<td>Surrounding layer 1</td>
<td>250,000</td>
<td>0.5</td>
</tr>
<tr>
<td>Surrounding layer 2</td>
<td>0.0002</td>
<td></td>
</tr>
</tbody>
</table>

Neural Targeting Clinical Data

• Retrospective, *consecutive* patients
  – 213 consecutive patients
  – Across 13 sites
  – Long-term follow-up to 2 years
Neural Targeting Long-Term Results

- LUMINA Clinical Data
  - Real world, multicenter, 213 patients, 24 month follow-up
Neural Targeting Long-Term Results

• LUMINA Clinical Data
  – Real world, multicenter, 24 month follow-up

Low Back Pain Only

![Graph showing pain reduction and statistical significance over time.

- Baseline (N=89)
- 3 Mos (N=76)
- 6 Mos (N=74)
- 12 Mos (N=73)
- 24 Mos (N=70)

- Baseline (N=49)
- 3 Mos (N=43)
- 6 Mos (N=42)
- 12 Mos (N=41)
- 24 Mos (N=38)

Δ = 4.12 (p < 0.0001)
Δ = 5.62 (p < 0.0001)
Neural Targeting Long-Term Results

- LUMINA clinical data, 24 month follow-up
Neural Targeting Therapeutic Options

• Real-World Utilization of Multiple Waveforms

![Pie chart showing the distribution of waveforms used in clinical outcomes.](chart.png)

- Single Waveform: 28%
- Multiple Waveforms: 72%

N=800

RELIEF - Real-World Clinical Outcomes of Spinal Cord Stimulation: A Prospective Global Registry Study, Berg et al., NANS 2015
Incredible progress in neuromodulation for the pain patient in 2016

“More than half of all patients with chronic painful conditions experience sustained and significant levels of pain reduction following SCS treatment. Although only limited evidence exists for burst stimulation, there is now Level I evidence for both dorsal root ganglion SCS and high-frequency SCS that demonstrates compelling results compared with traditional therapies. The body of evidence built on traditional SCS research may be redundant, with newer iterations of SCS therapies such as dorsal root ganglion SCS, high-frequency SCS, and burst SCS. A number of variables have been identified that can affect SCS efficacy: implanter experience, appropriate patient selection, etiologies of patient pain, existence of comorbidities, including psychiatric illness, smoking status, and delay to SCS implant following pain onset. Overall, scientific literature demonstrates SCS to be a safe, effective, and drug-free treatment option for many chronic pain etiologies.

Acute to Chronic Pain Cycle

Pathophysiology of Maintenance
- Radiculopathy
- Neuroma traction
- Myofascial sensitization
- Brain pathology (loss, reorganization)

Secondary Pathology
- Muscle atrophy, weakness
- Bone loss
- Depression
- Cortical atrophy

Psychopathology of maintenance
- Encoded anxiety dysregulation
- PTSD
- Emotional allostodynia
- Mood disorder

Acute injury and pain

Central sensitization
- Lower threshold

Peripheral Sensitization
- Glial activation
- Pro-inflammatory cytokines
- Blood-nerve barrier disruption

Neurogenic Inflammation
- Less active, kinesiophobia
- Decreased motivation
- Increased isolation
- Role loss

Disability
Here is why EARLY referrals are critical
Delayed interventions = Poor outcomes

- **Facet RF**: Cohen et. al., CJP 2007
- **Epidural steroids**: Kwon et. al., Skel Radiol 2007, Benzon Pain 1984
- **Pharmacotherapy for CRPS**: Perez et. al., Pain 2003
- **IA injections for knee OA**: Tanaka et. al., Rheum Int 2002
- **Physical therapy for DJD**: Jansen et. al., Eur J Phys Rehabil Med 2010
- **Vertebroplasty**: Ryu and Park J Korean Neurosurg Soc 2009

**Take-Home Message: Intervene Early**
Modern Pain Management:
A More Flexible Approach - Customized

- Different time frames
- Multiple therapies at one time
- Different starting points
