Emerging Pain technologies to decrease opiate use and improve surgical outcomes

Nileshkumar Patel MD, MBA
Advanced Pain Management
825 Nonmedical users
130 Misuse or abuse
32 Emergency room visits
10 Hospital admissions
1 Death

What is not readily apparent...?
US opioid Rx (2014): 300MM\textsuperscript{1,2}

Unique US opioid patients: 32MM\textsuperscript{3}

Opioid patients at high risk for overdose: 16MM+\textsuperscript{1,4}

ER visits: 500k\textsuperscript{5}

Fatalities: 19k\textsuperscript{6}

- $9 Bn opioids alone (2012)
- $55.7 Bn for abuse, misuse and dependence (2011, 2015)
- $53.4 Bn for nonmedical use of prescription opiates (2010)


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Unique US opioid patients: 32MM$^3$

Opioid patients at high risk for overdose: 16MM$^{1,4}$

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Fatalities: 19k$^6$

$\text{\textbf{\$20.4 Bn in 2009}}$

$\text{\textbf{\$2.2 billion direct costs: inpatient, ED, MDs, ambulance. \$18.2 billion indirect costs: lost productivity from absenteeism and mortality}}$

$\text{\textbf{\$37,274 cost per opioid overdose event}}$

Inocencio TJ et al. Pain Medicine 2013

Excess health care costs per patient (based on claims data analysis of privately insured and Medicaid) in just 10 states: $\text{\textbf{\$55 billion}}$


1. SDI/Vector data – FDA presentation, July 2010
3. Wolters Kluwer, 10/12
4. Leider et al, AJMC vol 17, No.1
5. GAO Report: Rx Pain Reliever Abuse
6. CDC December 18, 2015.
$72.5 billion in health care costs\(^1\)

Opioid abusers generate, on average, annual direct health care costs 8.7 times higher than nonabusers\(^2\)

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National Overdose Deaths
Number of Deaths from Prescription Drugs

- **47,055** US deaths from ALL drug overdoses in 2014
- Deaths related to prescription opiate increased by 16% to **18,893**
- Prescription opiate deaths up **3.4-fold between 2001 and 2014**

Source: National Center for Health Statistics, CDC Wonder
Deaths from Heroin (2001-2014: 6-fold increase)

Many of these individuals started off with prescription opioids!
Mostly men, but recent surge in women's death due to heroin.

Source: National Center for Health Statistics, CDC Wonder
Joint Commission (JCAHO) Accredited

Source: National Center for Health Statistics, CDC Wonder
Justice Department Recovers $2 Billion for Fraud Against the Government in Fy 2007; More Than $20 Billion Since 1986

Source: National Center for Health Statistics, CDC Wonder
Source: National Center for Health Statistics, CDC Wonder
LBP: Sitting Intolerance

- 52 yr old female, increased back pain upon sitting; straining in the bathroom
- Prior diagnostic workup - negative for SI joint and facet joint pain.
- Unresponsive to physical therapy and medications.
- Diagnostic evaluation:
- Neurosurgeon referred her for discogram
  - Is this appropriate?
  - Therapeutic options
  - If positive and she has surgery, what is the cost and what is the success
  - If she “fails surgery” then what?
Here is how he progressed.....

55 year Old

- Urgent Care
- oxycodone
- valium
- PCP
- Foot & Ankle

- PT
- Foot & Ankle
- PM & R

- Surgery Declined or performed
  Patient still in pain
- Surgery Performed & Pain Resolved
Weight restrictions, posture training ergonomics are important but in of themselves, may not suffice
Spinal Stenosis and LBP

- 74 yo moderately obese male
- Ambulation induced bilateral back pain
- No buttock or leg pain
- No paresthesia
- Unable to ambulate more than 50 yards without having to sit
- Unable to stand for more than 15 minutes
- No previous history of surgery
Spinal Stenosis and LBP
Lumbar Stenosis: Types of PT matters..

Whitman, SPINE 2006

• 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, 6wks, 12 mos.
Lumbar Stenosis: TENS, Brace, Meds

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

Yaksi, SPINE 2007 32(9)

- N=55, Randomized 2 groups
  - PT, Brace, NSAIDS versus PT, Brace, NSAID & GABAPENTIN

- GABAPENTIN 900mg/day—increased to 2400mg/day
- F-up 15 days, monthly up to 4 months

- GABAPENTIN group showed better increase in walking distance as well as represent better pain scores
  - Mean VAS change after 4 months
    - Treatment group (7.0 / 2.9)
    - Control group (6.7 / 4.7)
Spinal Stenosis and LBP

• Failed 2 TFESIs at L3/4 and 4/5 levels

• Failed one caudal ESI

• Failed L3,4,5,S1 MBBs

• Had one positive bilateral SIJ lasting for about 2 weeks, but failed LBBs

• Seen by surgery. Not a surgical candidate

• “I like you, but I am tired of seeing you. 50th anniversary plans to go to Ireland are not going to happen”
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Failed Back

- **45** yo electrical engineer
- Presenting with axial back pain
  - VAS **5/10** with daily variations
- History of previous fusion for lumbar radiculitis (5 years prior)
- 150 mg of **tramadol** and daily low doses **hydrocodone**
- Pain localizes to the upper low back (above and at the scar)
- No radiation, bilateral, worsened by sitting, worse in the mornings, worsened by physical activity (lifting his small children)
- Work-up after MRI included negative MBBs, 2 unsuccessful TFESIs, 1 unsuccessful caudal ESI
“Failed back”
### Traditional SCS: Reserved for extremity Pain
Published Prospective SCS Studies with > 6 mo follow-up

<table>
<thead>
<tr>
<th>Study</th>
<th>System</th>
<th>Patients</th>
<th>Trial Success</th>
<th>VAS</th>
<th>Response</th>
<th>Base</th>
<th>6m</th>
<th>12m</th>
<th>24m</th>
<th>Base</th>
<th>6m</th>
<th>12m</th>
<th>24m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schultz 2012</td>
<td>Medtronic Restore Sensor</td>
<td>Predom Leg Pain</td>
<td>NA</td>
<td>—</td>
<td>5.9</td>
<td>4.3</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>North 2005</td>
<td>Medtronic Itrel</td>
<td>Predom Leg Pain</td>
<td>17/24 71%</td>
<td>—</td>
<td>7.6</td>
<td>4</td>
<td>4.4</td>
<td>4.4</td>
<td>4.4</td>
<td>5.5</td>
<td>4.1</td>
<td>4.5</td>
<td>4.8</td>
</tr>
<tr>
<td>Kumar 2008</td>
<td>Medtronic Synergy</td>
<td>Predom Leg Pain</td>
<td>43/52 83%</td>
<td>—</td>
<td>4</td>
<td>4.4</td>
<td>4.4</td>
<td>4.4</td>
<td>4.4</td>
<td>5.5</td>
<td>4.1</td>
<td>4.5</td>
<td>4.8</td>
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**NR:** Not reported
Superior Responder Rates with HF10
Results better and more enduring

• Average back pain of $\geq 5/10$
• Average leg pain $\geq 5/10$
• Severely disabled or crippled as defined by an Oswestry Disability Index score of 41 – 80 out of 100
• Primary endpoint involves $\geq 50\%$ back pain reduction at 3mo

HF SCS: Results better and enduring

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

Kapural et al Anesthesiology 2015
Human resolve is such that we will innovate alternative therapies..

**US Multicenter, prospective, randomized, controlled trial (n=171) to 24 months**

**EU: Multicenter, prospective trial (n=72) to 24 months**
FDA Sanctioned Trial: Decreased Opioid Use (84mg to 27mg).....well below the CDC guideline...covered by commercial but not State...

Kapural et al. (Senza trial) Anesthesiology 2015
“Failed Back” Pain and Opioids
Failed Back

• HF10 Therapy: Trial Phase
  – Typical T8 and T9 placement

• HF10 Therapy Trial Results
  – 100% improvement in back pain during the trial
  – 90% improvement in pain after implantation
  – off of all daily medications for 5 months
  – recently seen in follow up
Primary afferent nociceptors convey noxious information to projection neurons within the dorsal horn.

A subset of these projection neurons transmits information to the somatosensory cortex via the thalamus, providing information about the location and intensity of the painful stimulus. Other projection neurons engage the cingulate and insular cortices via connections in the brainstem (parabrachial nucleus) and amygdala, contributing to the affective component of the pain experience. This ascending information also accesses neurons of the rostral ventral medulla and midbrain periaqueductal gray to engage descending feedback systems that regulate the output from the spinal cord.
Origins of Burst Stimulation

• Burst is a naturally occurring signaling modality in human physiology. For example, the “lateral pain system” fires in a tonic manner, but the “medial pain system” fires in burst\(^1\).

• First applied to SCS by Dirk De Ridder MD, PhD, Antwerpen Belgium.

• Published Experience:
Pain stimuli are processed in parallel by two pathways:

- **Lateral discriminatory pathway.**
  - WDR neurons firing in tonic -> PH (lam. 1, 4-6) -> Thalamus (VPL, VPM) -> 1 & 2 SSC.
  - Fires tonically\(^2\).

- **Medial affective/attentional pathway.**
  - Nociceptive specific neurons firing in bursts -> PH (lam. 1) -> Thalamus (MDvc, VMpo)
    -> Anterior Cingulate, Anterior Insula, Amygdala.
  - Fires in bursts\(^2\).

Burst Stimulation can have an effect on the affective component of pain.

Burst Waveform Growing Body of Clinical Data*

Burst vs. Tonic Clinical Experience

- Consistent results across studies and sites
- Patient preference for Burst over Tonic
- Reduced paresthesia
- Improved activity levels
- Reduced attention to pain
- No increase in recharging frequency

* Deridder Presented at WVSIPP, PR, USA Territory 2014
Shoulder and Neck Pain

• A 36 year old right handed female complains of left sided cervical pain radiating to the shoulder with paresthesias in the 4\textsuperscript{th} and 5\textsuperscript{th} fingers. She was involved in a motor vehicle accident 8 months ago. She was restrained by a seatbelt at the time of the T-bone impact. She does not recall loss of consciousness nor striking the vehicle interior.
• She is unimproved by 4 months of ibuprofen, cylobenzaprine, chiropractic and physical therapy.
• Cervical MRI was reportedly normal.
• She is frustrated that she is still suffering.
• Her physical examination is remarkable for pain on range of motion and diffuse ipsilateral cervical tenderness. Motor, sensory and deep tendon reflexes are intact.
• What Do I do?
C5-C6 and C6-C7
Recent Cervical Radiofrequency Studies confirm that in real life this stuff works!


<table>
<thead>
<tr>
<th></th>
<th>Practice A</th>
<th>Practice B</th>
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<tbody>
<tr>
<td>Treated</td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td>Complete relief of pain (VAS = 0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restoration of all ADLs</td>
<td>74%</td>
<td>61%</td>
</tr>
<tr>
<td>No need for other health care</td>
<td></td>
<td></td>
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<tr>
<td>Return To work</td>
<td></td>
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</table>
Headache Patient

• 38 year old school teacher
• 3 years ago started with headaches
• Initially “migraines”
• 105 days of school in the previous year
• Failed prophylactic and abortive therapy
• Negative Work up at Mayo and Diamond
• Placed on Methadone
C2/3 Joint or Third Occipital Nerve Source


- 54%: Headache Main complaint
- 88% Complete relief of headaches lasting for 297 days
Chronic Abdominal Pain

• 45 yr old male, urology & gastroenterology workups are negative for source of pain.
• Methadone works but nothing else has helped
• Diagnostic evaluation:
  • Where is pain originating?
  • What can be done?
• Interventional choices?
• Chronic Pain Program?
Abdominal Pain

- Approximately 2 million patients in US with severe abdominal pain
- Pain-most prevalent symptom in any GI clinic
- Multitude of imaging studies and surgeries before referred to a chronic pain specialist
- Etiology of some abdominal pains remains elusive
- Impact on the patient’s socioeconomic status
- Strong affective responses
- Burden on our healthcare system

Visceral Afferent Flow From The Female Reproductive Tract

Don’t forget abdominal and pelvic pain is amenable to interventions
RSD in patients with post surgical pain: Lumbar Sympathetic Block

- **Indication:** Diagnosis and treatment of sympathetically mediated pain of lower extremities
- **Rationale:** Interrupt sympathetic input mediating pain in lower extremities

If the patient does not respond to Stellate and therapy, Spinal stimulation or even intrathecal Ziconatide, clonidine, bupivacaine
Case Highlight DRG...CRPS of the Foot

- 60 year-old male
- CRPS type-1 after minor fracture
- Pain in left leg (67 mm VAS) and foot (91 mm VAS) showing signs of severe erysipelas

Case Highlight DRG…CRPS of the Foot

Baseline

- 100% coverage of pain.
- VAS Scores of 0 mm at 6-month follow-up.

6 months

Paresthesia Map

The Dorsal Root Ganglion (DRG)

- Predictable location within the epidural space
- Lack of CSF allows for increased energy efficiency and lower energy consumption than conventional SCS

- In the epidural space
- Within the neural foramen
- Between the medial and lateral aspects of the pedicle
The Dorsal Root Ganglion (DRG)

- The DRG plays a pivotal role in the development and maintenance of chronic pain\(^1\)

- Hypersensitization of the primary sensory neurons provide a physiologic underpinning of hyperalgesia and allodynia\(^2\)

- Cross-dermatomal innervation patterns allows for both broad and specific coverage in painful anatomy

- Known target for chronic pain but other therapies have limited effectiveness or duration of action

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DRG Modulation Inhibits Pain Transmission

Stimulation induced after discharge of DRG neurons (Aβ) suppressed by **chemically** (left) or **electrically** (right) blocking DRG evoked bursting

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Song et al. *Pain*. 2012

Koopmeiners et al. *Neuromodulation*. 2013
The Dorsal Root Ganglion: Target for Neuromodulation

Dorsal Column Stimulation

DRG Stimulation: Stimulation at the PSN

Abdomen/Back
Hip/Waist/Back
Upper Leg and Low Back
Upper Leg and Low Back
Leg and Low Back
Foot/Lower Leg/Low Back
2014 – Long-term International Data$^1,2$

- Stable, anatomical specific pain relief over 12 months
- Targeting of difficult anatomical areas such as the foot
- Minimal postural effects - Stable stimulation during change of position$^2$
- Stimulation covered painful areas with minimal extraneous coverage$^1$
- Improvements in QOL, Function, and Psychological Disposition$^1$

RSD in patients with post surgical pain: Stellate Ganglion Blocks

If the patient does not respond to lumbar sympathetics and therapy, Spinal stimulation or even intrathecal Ziconatiinde, clonidine, bupivacain
Contemporary Approach to Chronic Pain: A More Flexible, Customized Approach

Knee and Hip pain: Work Injury
Off of Work for 15 Years on Oxycontin 160 mg daily referred by Case Worker


Figure 1: Articular branches of the obturator nerve and target region for radiofrequency denervation. Covering the right hip are tracings of the anteroposterior projections of the metal wires used to mark the location of the articular branches in cadavers. In each cadaver, articular branches were spread across band-like areas. The bold lines represent the upper boundary of each area, and the dotted lines represent the lower boundary. The stem of each band was located below the teardrop shape of the inferior end of the acetabulum. Over the left hip, the matrix of lesions required to coagulate the articular branches is illustrated. Its medial margin lies opposite and below the teardrop silhouette of the acetabulum. For reference, tracings of wires covering the obturator nerve have been depicted.

<table>
<thead>
<tr>
<th></th>
<th>VAS</th>
<th>Harris</th>
<th>WOMAC</th>
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<tbody>
<tr>
<td><strong>pre-procedure</strong></td>
<td>9.52</td>
<td>28.64</td>
<td>75.7</td>
</tr>
<tr>
<td><strong>6 month follow up</strong></td>
<td>6.35</td>
<td>43.88</td>
<td>63.7</td>
</tr>
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Patients with hip joint pain may suffer from groin, thigh, and trochanteric pain. **Groin pain and thigh pain** arise from the articular branches of obturator nerves. A trochanteric (lateral) pain arises mainly from the articular branches of femoral nerve.

Preemptive Patient factors

• 70% of non-smokers returned to work vs only 50% of smokers RTW after spinal fusion
• Rotator-cuff surgical patients revealed that only 35% of smokers healed well
• Smokers in general require more analgesia than those who do not smoke

Health Care has finite resources

To reduce the growth of HC costs:
1. Individuals must take greater responsibility
2. Providers must make more responsible treatment decisions
3. Insurers must encourage early use Preventive Medicine principles

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
- **Vertebroplasty**: Ryu & Park J Korean Neurosurg Soc 2009

**TAKE HOME MESSAGE:** INTERVENE EARLY
LATE REFERRALS
(STANDARD CYCLE)
Step 1
Initial Pain

Step 2
Diagnostic Interventions
Obesity,
Smoking

Step 3
Treat the Pain

Step 4
Refer EARLY to Complementary Providers as Needed

Early referrals
Late referrals... lessen chances for functional improvement

EARLY referrals... improve chances for functional restoration
Modern Pain Management: A More Flexible Approach….Customized

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

Take Home Messages

• Utilize multimodal approach because CBT, adjuvants, interventions, implantable can collectively decrease opioid burden

• Based on CDC’s analysis of data from 2010-2015… utilize lowest doses, PDMP, Naloxone, short acting opiates

• Interventional pain clinics do much more than injections
  • Early on: Interventions are an alternative to opioids
  • Later on: Interventions facilitate an opioid taper or decrease
Take Home Messages

• Chronic Pain is a Disease…personal, societal, economic consequences
• Early referrals
• Comprehensive approach
• Patient satisfaction is here to stay…and you can get high scores with out just opiates
• Be aggressive early on as established patterns are hard to reverse
• Once you reached a plateau please think of other treatments