PAIN PUMPS

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- We manage over 600 pumps, Medtronic and Flowonix
- Implanting ~ 50 pumps or more a year

Negative Connotations of Pain Pumps

- They don’t work and aren’t helpful

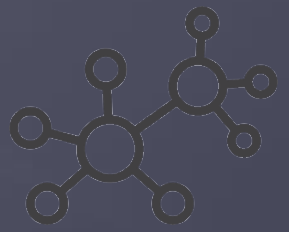
Factors affecting Drug Distribution

- Anatomical abnormalities
- Lumbosacral CSF volume
- CSF density
- CSF pulsation

Patient Specific

- Reaction kinetics
- Infusate lipophilicity

Drug Parameters



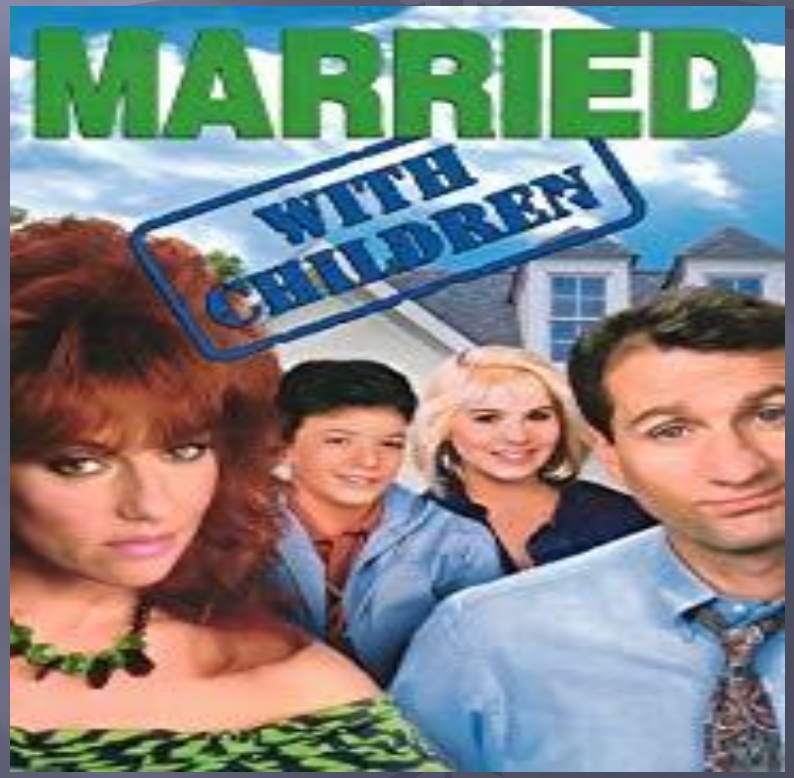
- Infusion flow rate
- Volume
- Velocity
- ITC position

Infusion Choices

Micro Bolus
Peristaltic

Negative Connotations of Pain Pumps

- Married to the pain patient for life !



Negative Connotations of Pain Pumps

- Difficulties and risk of filling a pump

- There are companies AIS HealthCare and Pentec Health that will fill the patient's pump at their home, they will bill the insurance company for pump medication (reportedly this can be done for Ziconitide trial and after maintenance) and patient's don't need to come in for visits
- Can manage titration and will even do initial fill under MD direction

Negative Connotations of Pain Pumps

- Cost reimbursement

Cost Reimbursement of Pumps

Description	Medicare Provider	Medicare ASC Facility
Pump; revision only **	N/A	N/A
Implantation or replacement of device for intrathecal or epidural drug infusion; programmable pump	$379.63	$13,235.18
Implantation, revision or repositioning tunneled intrathecal or epidural catheter, long-term	$396.39	$2,425.31
medication administration via an external pump or implantable reservoir/infusion pump; wo laminectomy		
Removal of subcutaneous reservoir or pump, previously implanted for intrathecal or epidural infusion	$292.09	$1,877.90
Electronic analysis of pump; with reprogramming	$54.21	$29.24
Electronic analysis of pump; with reprogramming and refill	$114.05	$91.60
Electronic analysis of pump; w/reprogramming/refill MD or OQHP	$118.90	$87.72

** carrier will base reimbursement based on medical records submitted

Disclosure

- No financial disclosures to disclose

So…

Objectives

- Discuss patient selection
- Discuss IT trialing dosage
- Discuss pump placement
- Discuss IT opioid maintenance and micro dosing

Criteria for Patient Selection

- For Active Cancer related pain, Opioids and Ziconitide (level of evidence I highly recommended)
- For non-cancer pain, Opioids by themselves III-2 (clinical based experiences), Opioids in combination II-3 (multiple series compared over time, surprising results in non-controlled experiences) and Ziconitide I

Criteria for Patient Selection

- Intractable pain
- Not able to tolerate oral medications from side effects or other reasons
- Needing to wean down on systemic opioids
- Failed other treatment modalities (procedures and SCS)

CONTRAINDICATIONS: presence of infection, inadequate body to accept the pump or spinal anomalies

It's always the ones you least expect

Criteria for Patient Selection

Criteria	N	Very important (%)	Somewhat important (%)	Not important (%)
Realistic expectations by patient	203	92	8	0
Failed medical therapy	201	80	18	2
Medical therapy was beneficial, but side effects were dose-limiting	201	78	21	0.5
Absence of major psychopathology	203	75	23	2
Clear etiology	201	66	32	2
Failure of minor interventional techniques	201	62	33	5
Presence of family or social support	202	46.5	50.5	3
Patient's willingness to participate in a pain rehabilitation program	199	42	45	13
Inefficacy of physical therapy	200	39	41.5	19.5
Absence of significant comorbid illness	200	17	59.5	23.5
Failed spinal cord stimulation	200	14	39	47

Respondents also indicated whether or not certain characteristics would discourage implant as summarized in the table below. However, most respondents (73%) would consider IT therapy if patients improved following psychiatric treatment.

Criteria	Characteristic would discourage implant (% agreed)
Current alcohol or substance abuse	96%
Repeated history of opioid contract violation	92%
Significant secondary gain	89%
Significant history of noncompliance with medication	87%
Satisfaction with current level of function	74%
Somatization disorder	69%
Antisocial personality	63%
Borderline personality	53%
Major depression	42%

IT Trialing -Fentanyl Trial (for opioids)

- I trial doing a CSE combined spinal epidural technique under fluro via 3.5 inch 18 or 20 gauge touhy (for easy and insurance of being in epidural space and ease for guiding the spinal needle). After I get loss of resistance, I place a 5 inch pencil tip 25 gauge spinal needle and feel pop of the dura membrane, verify placement with free flow of CSF and fluro / myelogram
- Use PF Fentanyl 20-25 mcg with PS NS total volume 1 ml as no worry of delayed respiratory depression, done in outpatient center, patient kept there varying from 2-4 hours
- Pain log kept of VAS before and after procedure

IT Ziconitide Trial

- 1-3 mcg IT push
- Observe patient for 1-4 hrs
- Start at 1-3 mcg per day, slow titration, max 19.2 mcg per day
- Side effects: cognitive or neuropsychiatric results
- Abrupt discontinuation does not cause withdraw

IT Baclofen Trial

- GABA-B
- To help treat spasticity with CP, MS, SCI and others
- IT bolus 40-50 mcg at site of lesion with ITC
- side effects: urinary retention, constipation, fatigue, flaccid
- Abrupt w/d: CNS activation, autonomic dysfunction, extreme muscle rigidity resembling neurolytic syndrome and malignant hyperthermia and potential death

IT Morphine Trial

Publication	Method or Guideline
Grider, et al. (2011)[15] Grider, et al. (2016)[5]	Continuous infusion trialing with initial dose of 25 µg/day then titrated every 12 hours until pain relief or therapy-limiting side effects: Day 1, 6 a.m.: 25 µg/day Day 1, 6 p.m.: 50 µg/day Day 2, 6 a.m.: 100 µg/day Day 2, 6 p.m.: 200 µg/day Day 3, 6 a.m.: 400 µg/day
Hamza, et al. (2012)[6]	IT morphine bolus doses every 24 hours: 250 µg morphine, 500 µg morphine, or 0.5 mL normal saline (patient blinded to order)
Wilkes, et al. (2018)[14]	Various trial doses (bolus injection) were attempted, ranging from 12.5 µg to 125 µg. The most common dose used was 50 µg. A 12.5 µg dose was selected if patients were completely intolerant of systemic opioid side effects.
PACC guidelines (2017)[24]	The PACC guidelines do not include a different trialing recommendation when low-dose intrathecal morphine monotherapy is planned. ▪ Trial with the lowest reasonable starting dose possible. Titration should be slow and based on response to pain relief, improved function, and side effects. ▪ For either a continuous trial or bolus dose trial, recommended starting dose for morphine is between 100 and 500 µg.

PACC: Polyanalgesic Consensus Conference

ITC Placement

Currently, there are no published clinical studies that have demonstrated optimal catheter tip placement for IT drug delivery for chronic pain. However, there are a number of published best practice and consensus guidelines that offer recommendations regarding catheter tip placement. In addition, the low-dose intrathecal morphine studies by Hamza and Grider specified catheter tip placement but did not discuss rationale for catheter tip placement.

Publication	Approach or Guideline
Grider, et al. (2011)[15] **Grider, et al. (2016)[5]**	T10-T11 in dorsal aspect of spinal canal
Hamza, et al. (2012)[6]	T11–T12
PACC guidance for improving safety/mitigating risks[25]	"... posterior catheter location with the catheter tip at the dermatome level congruent with pain if anatomically indicated."
PACC best practices and guidelines (2017)[20]	Consensus point: "Limited data exist as to appropriate and best catheter tip placement. The catheter should ideally be centered in the spinal dermatome associated with the pain generator. The consensus recommendation is that the doctor use clinical judgment based on the clinical setting."
Saulino, et al. (2014) [26]	The authors stated "available evidence supports the concept that the catheter tip must be placed within a few centimeters of the nerves associated with the pain source." However, the authors also noted that the IT morphine prescribing information "recommends administration in the lumbar region to reduce concerns about adverse effects."

PACC: Polyanalgesic Consensus Conference

IT Placement with Flowonix

- For neck and arm pain placing ITC at T2-T6
- For low back and legs placing ITC at L1
- PACC consensus of placing ITC at dermatomal pain generator

Pain Pump Placement

- Abdomen
- Back flank

Pain Pump Pocket

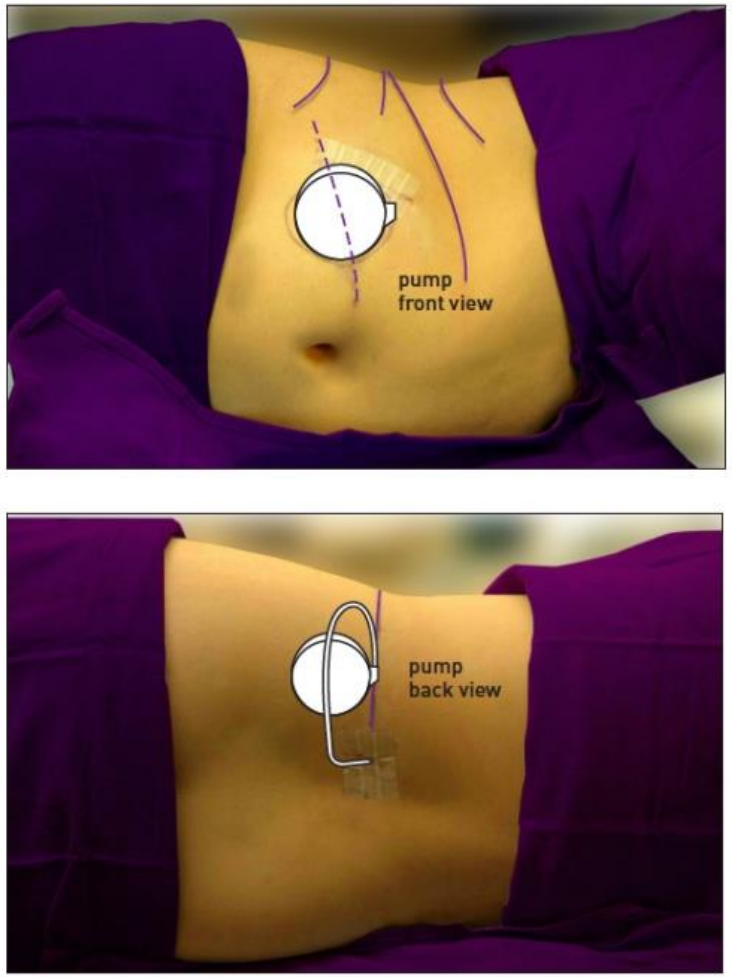
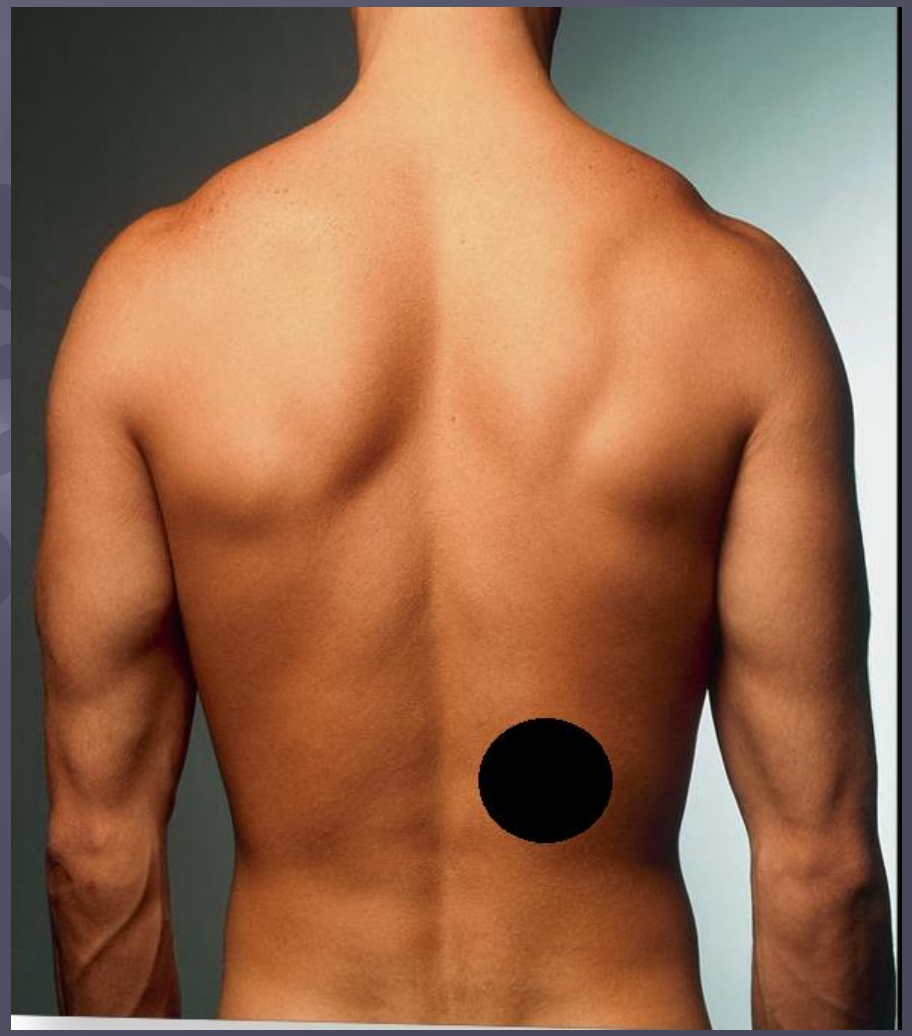


Figure 1: Placement of intrathecal drug delivery system in a patient.



Pump Placement

- I’m placing 90% of my pumps in the back paravertebral
- Less risk of seroma, less risk of pump moving and flipping as it’s firmly anchored to fascia, easier access and also placement as now patient is just prone and using AP fluro imaging (not lateral)
- Adds to lumbar curvature

Schultz Survey of 303 patients

- 76% of our pump patients with upper buttock pumps like the pump in this location whereas 8% of buttock pump patients would rather have the pump in an abdominal site. Regardless of whether the pump is implanted in the upper buttock or abdomen, most patients are happy with the location of the pump and only 8% would prefer a different location.

Trialing and Maintenance Dosing Using a Low-Dose Intrathecal Opioid Method for Chronic Nonmalignant Pain: A Prospective 36-Month Study Grider, et al. (2016)

Study Design: Prospective, single center study with follow-up visits at 6, 12, 24, and 36 months

Patient Population: 58 patients » 23 men (mean [SD] age, 58.1 [11.6] years) » 35 women (mean age, 63.6 years)

Treatment Indications » Degenerative Disc Disease (DDD, n = 23) » Failed Back Surgery Syndrome (FBSS, n = 20) » Spinal Stenosis (n = 11) » Complex Regional Pain Syndrome (CRPS, n = 1) » Scoliosis (n = 1)

Outcomes Measured By: Visual Analog Scale, Global Pain Scale, and Multidimensional Pain Index

Mean Intrathecal Morphine Dose » Inpatient catheter trial: 221 µg/day » 36 months: 325.4 µg/day

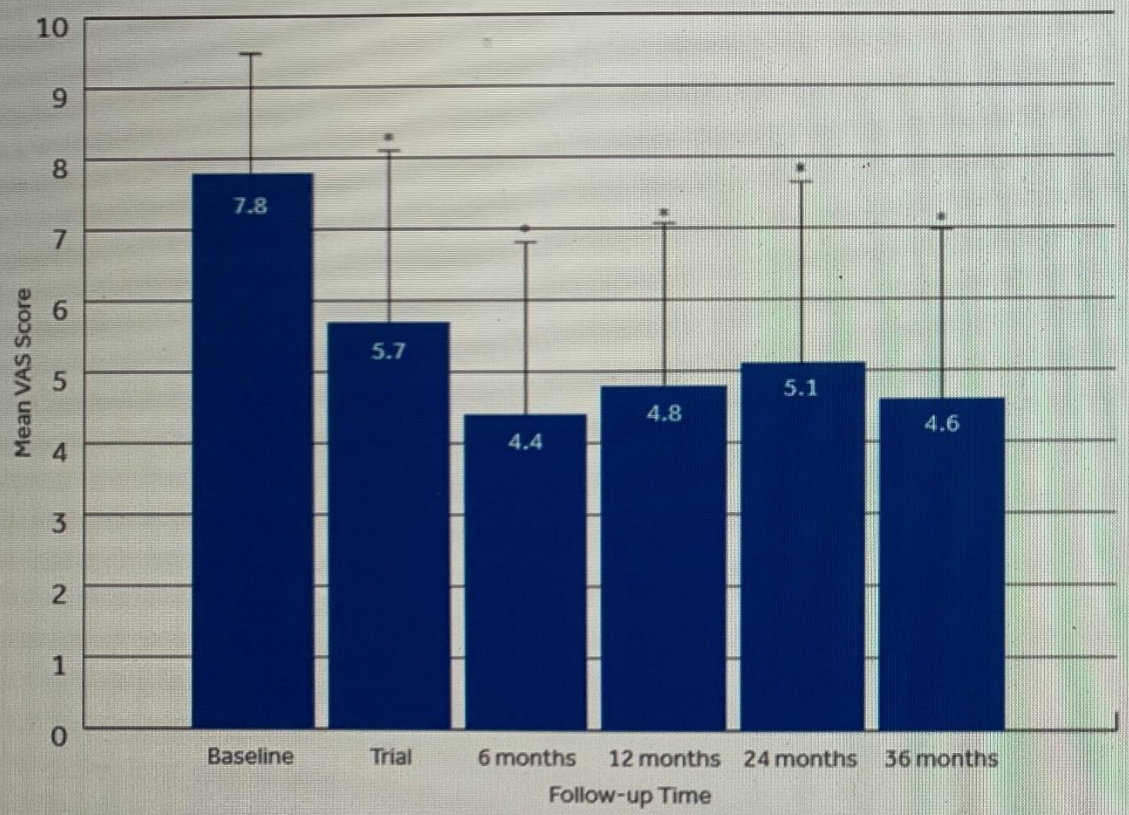
Mean Systemic Opioid Dose Prior to Taper: 64 mg/day

Systemic Opioid Dose Postimplant: One patient received 20 mg/day postimplant after experiencing an acute compression fracture. One additional patient preferred oral opioids to TDD and withdrew from the study.

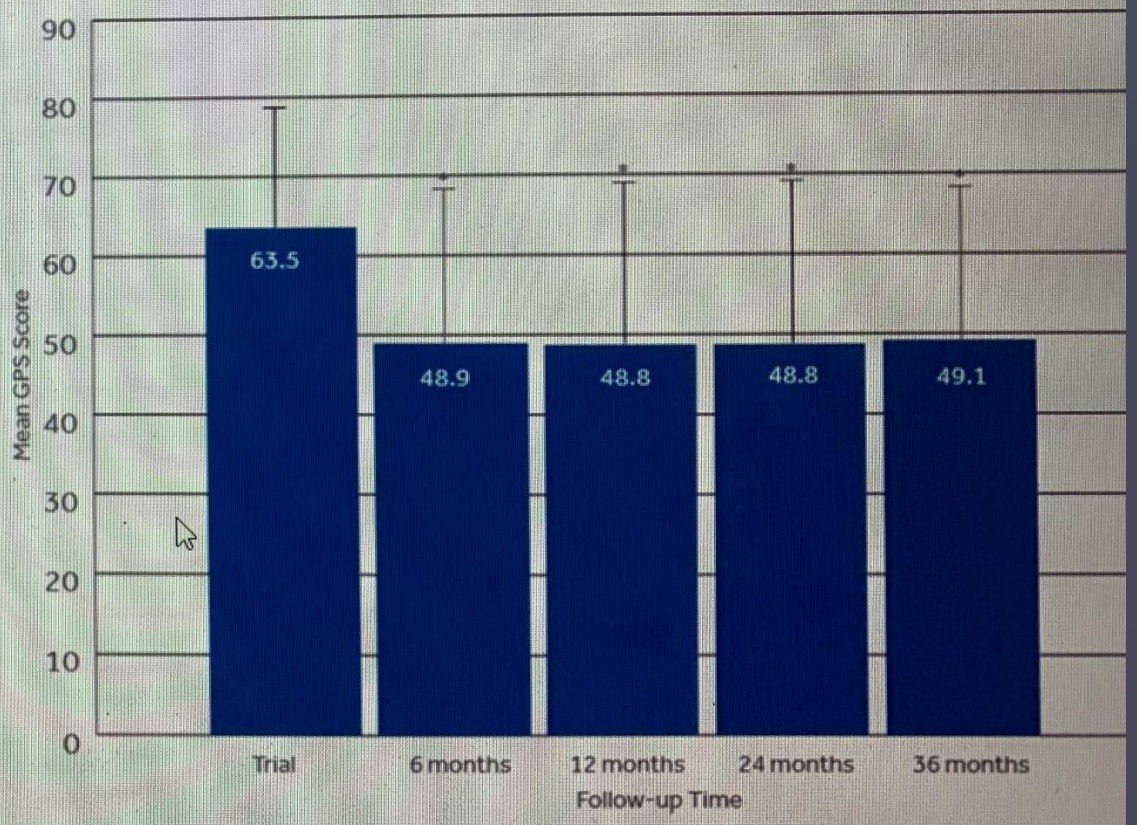
Complications: pruritis (n = 3), peripheral edema (n = 3), catheter breakage (n = 3), urinary retention (n = 2), compression fracture (n = 2), withdrawal from IT drug delivery (n = 2), seroma (n = 2), wound infection (n = 1), and catheter movement from the IT space due to pump flipping (n = 1)

Trialing and Maintenance Dosing Using a Low-Dose Intrathecal Opioid Method for Chronic Nonmalignant Pain: A Prospective 36-Month Study

Grider, et al. (2016)[5]



Visual Analog Scale (VAS),* $p < 0.001$ compared to baseline



Global Pain Scale (GPS),* $p < 0.05$ compared to trial

Prospective Study of 3-Year Follow-Up of Low-Dose Intrathecal Opioids in the Management of Chronic Nonmalignant Pain Hamza, et al. (2012)

Study Design: Prospective single center study with follow-up visits at 6, 12, 18, 24, and 36 months § Patient Population: 58 patients » 23 men » 35 women » Mean (SD) age: 59.2 (13.5) years

Treatment Indications » FBSS (n = 35) » Low back pain (n = 16) » CRPS (n = 3) » Abdominal pain (n = 2) » Pelvic pain (n = 2)

Outcomes Measured By: Brief Pain Inventory (average pain; worst pain; physical function, behavior and enjoyment); patient impression of change for pain and function

Mean Intrathecal Morphine Dose » Trial: .25 mg, .5 mg, and 0.5 mL normal saline in random order » Starting dose: based on effective trial dose » 6 months: 1.4 mg/day » 18 months: 1.43 mg/day » 24 months: 1.57 mg/day » 36 months: 1.58 mg/day

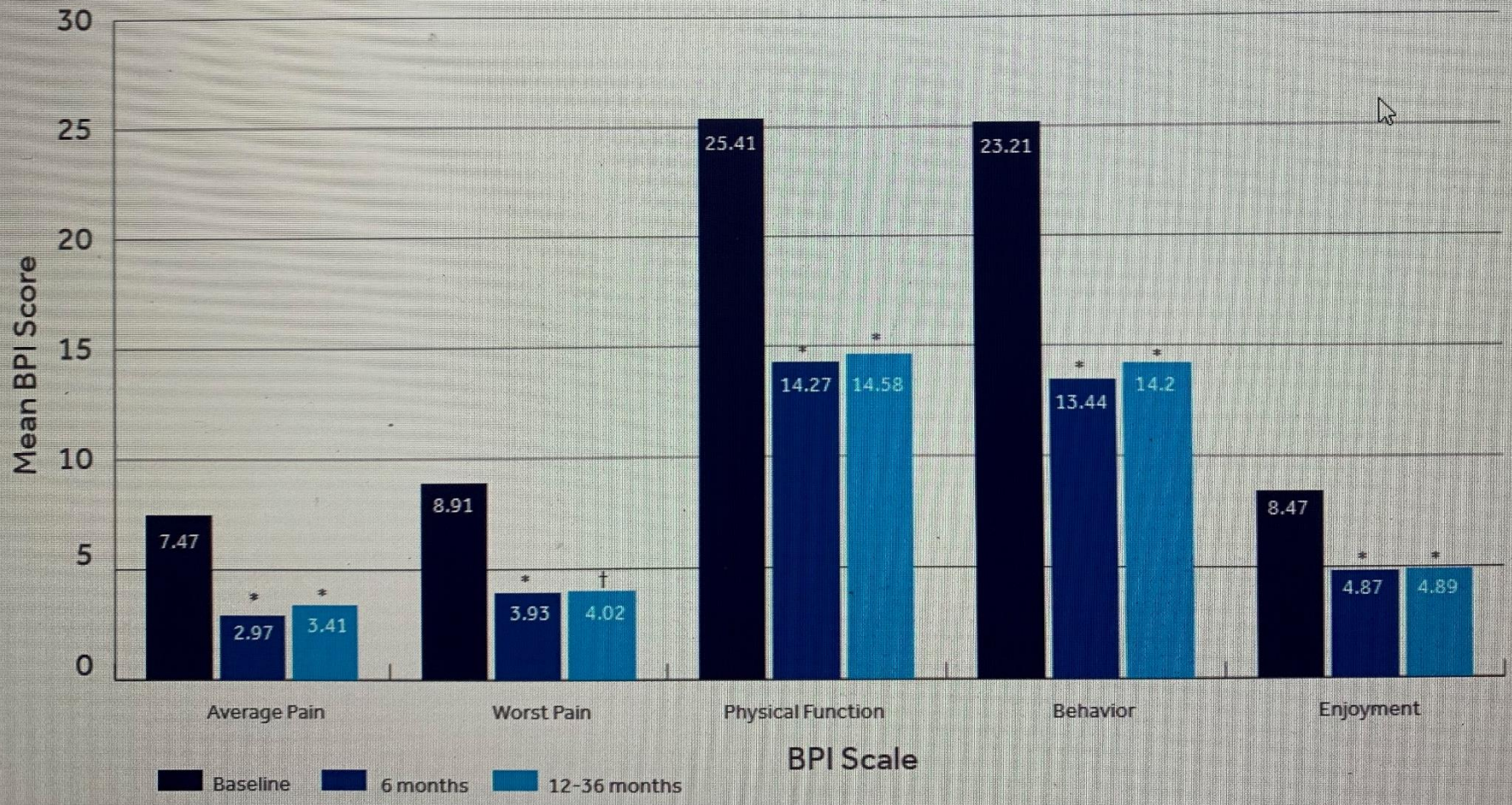
Mean Systemic Opioid Dose Prior to Taper: 126.71 (SE, 12.92) mg/day

Mean Systemic Opioid Use at Three Months Postimplant: 3.80 (SE, 0.90) mg/day ($p < 0.001$ compared to baseline) §

Complications: Wound infection (n = 3), pruritus (n = 3), peripheral edema (n = 2), and seroma (n = 2). Two of the patients with infection required explant, but were subsequently reimplanted.

Prospective Study of 3-Year Follow-Up of Low-Dose Intrathecal Opioids in the Management of Chronic Nonmalignant Pain

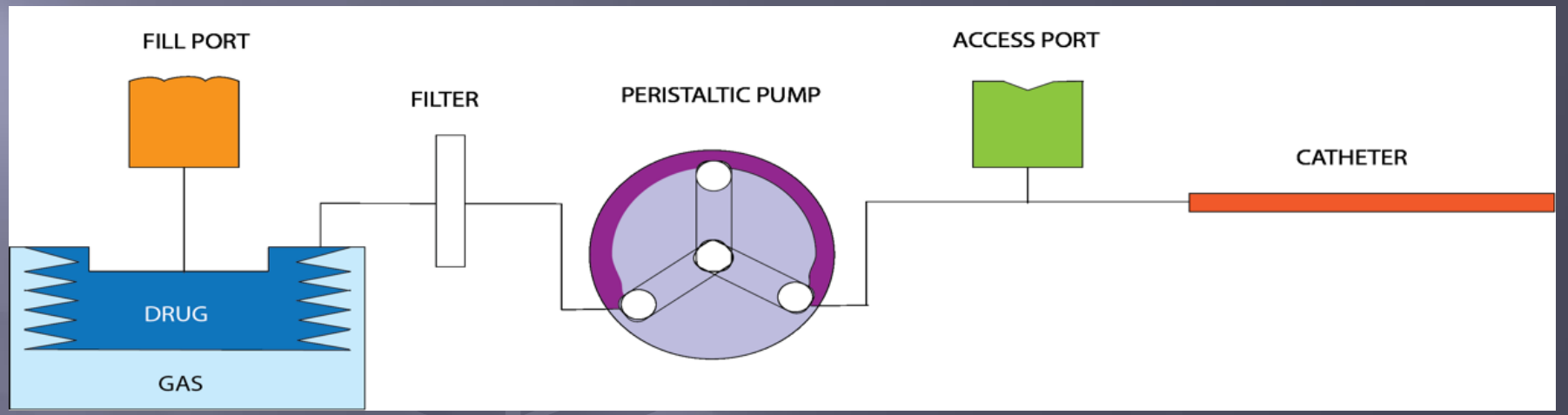
Hamza, et al. (2012)[6]



CURRENT PUMP TECHNOLOGY

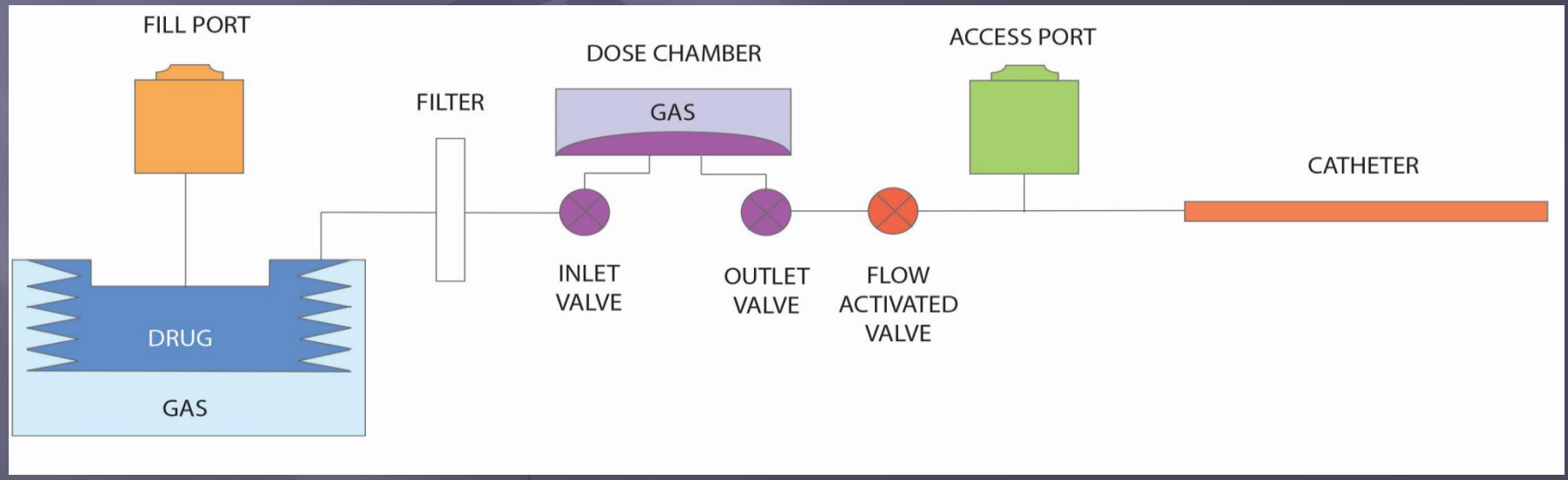
Peristaltic

Medtronic



Micro Bolus

Flowonix

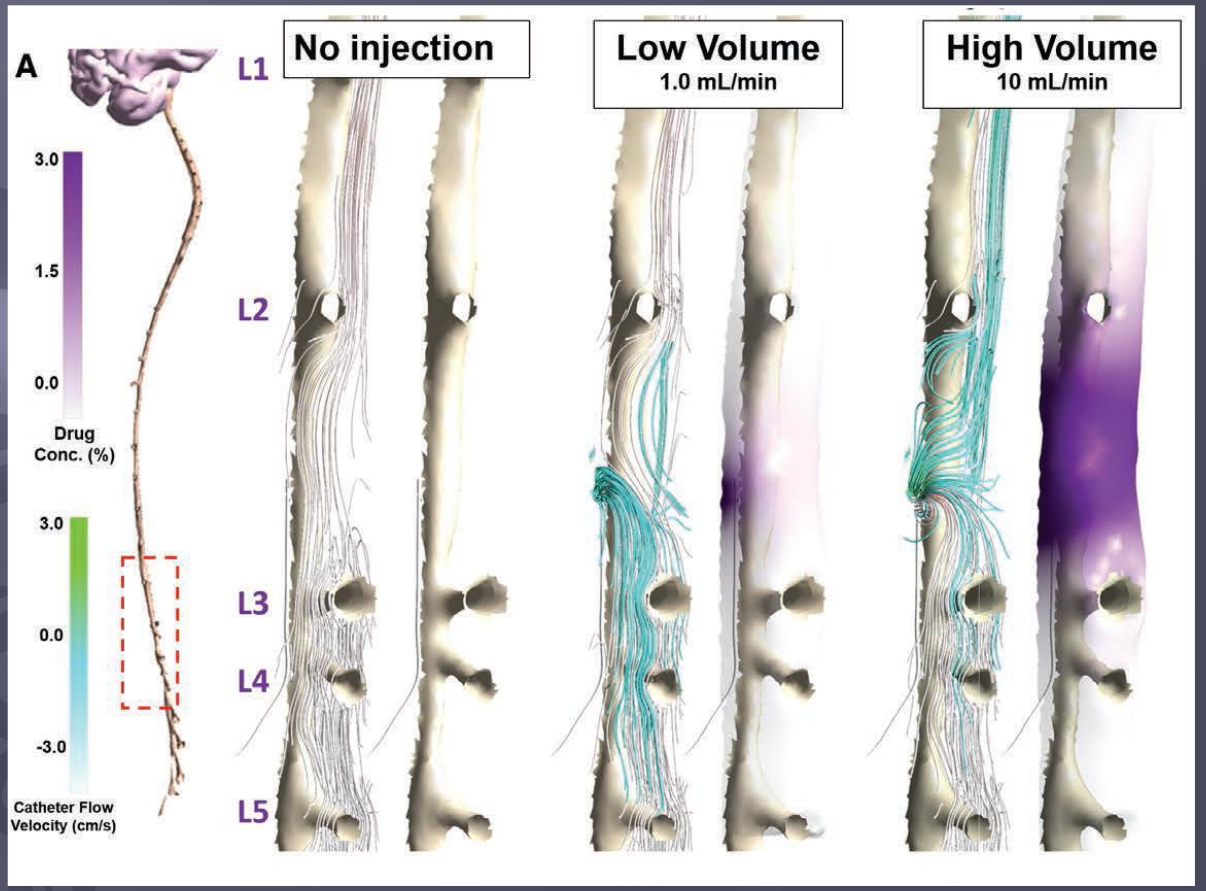


Pain Pumps

- Medtronic - MRI safe, still need to re-interrogate after MRI, less accurate
- Flowonix – recommend removing reservoir medication and then refilling after MRI (company has Reps that will do that for you at the MRI suite)

INFUSION METHOD IMPACTS DRUG SPREAD[7]

- Limited guidelines on pump infusion settings, drug choice & target reach exist
- Models simulated traditional continuous vs. micro-bolus injection
  1. **Injection Volume**
  2. **CSF Pulsations**
  3. **Drug Profiles**
- Flow rate of 0.0167 mL / min does <u>not</u> alter CSF flow dynamics
- Rates of 10 mL/min will disperse the drug throughout the CSF
- Currently no Pain Pumps infusing at 10 ml/min



COMPARING PERISTALTIC & MICRO BOLUS DELIVERY

Daily Dose: 1 mg/day
Concentration: 10 mg/mL

12:00 1:00 2:00 3:00 4:00 5:00 6:00 7:00 8:00

SIMPLE CONTINUOUS INFUSION

Medication delivered in continuous flow at rate of 0.004 mL per hour (total flow rate of 0.10 mL/day)[4]

Total Daily Dose
1 mg/day
Total Volume Per Day
0.1 mL

CONSTANT FLOW

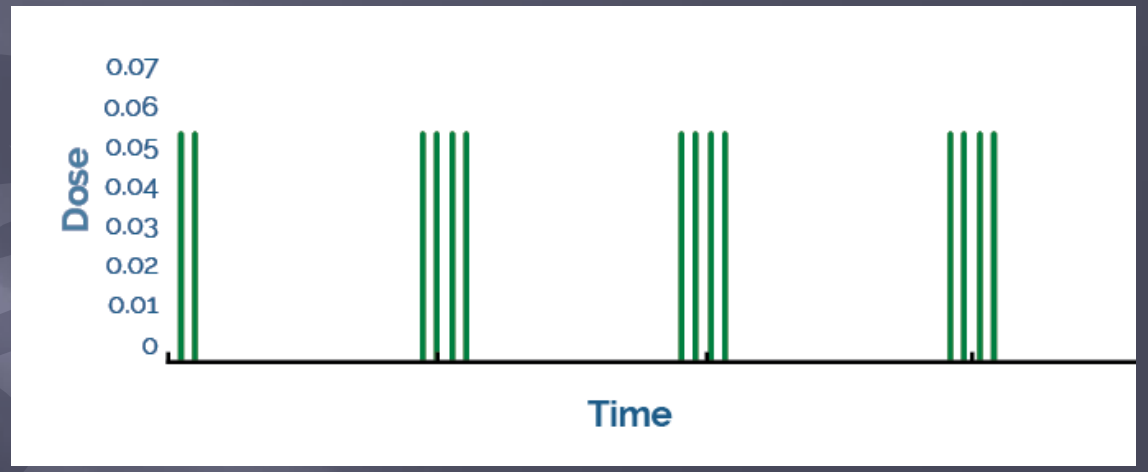
2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl

Medication delivered in 2 mcl boluses every 30 minutes with NO FLOW BETWEEN BOLUSES (~50 microboluses per day)[3]

Total Daily Dose
1 mg/day
Total Volume Per Day
0.1 mL

NOVEL PROGRAMMING– PERIODIC FLOW

- Flowonix pumps deliver medication at 6500 x faster velocity than Medtronic
- Delivers medication in a sequence of periodic infusions with zero flow between boluses
- Medication dose, the time over which the dose is delivered (duration), and the interval at which the dose is repeated (period) are programmed by clinician
- Flow between periodic boluses can also include a basal rate



COMPARING CONSTANT & PERIODIC FLOW

CONSTANT FLOW

2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl 2 mcl

Medication delivered in 2 mcl boluses every 30 minutes with NO FLOW BETWEEN BOLUSES (~50 microboluses per day)[3]

Total Daily Dose
1 mg/day
Total Volume Per Day
0.1 mL

PERIODIC FLOW

0.016 mL 0.016 mL 0.016 mL

Medication delivered in sets of 2 mcl boluses delivered over 1 minute every 4 hours with NO FLOW BETWEEN BOLUSES (6 sets of eight (8) microboluses; total of ~50 microboluses per day)[3]

Total Daily Dose
1 mg/day
Total Volume Per Day
0.1 mL

MICRO BOLUS TECHNOLOGY CLINICAL OUTCOMES

- **Low Granuloma and Serious Adverse Events (SAE)**
  - One granuloma (0.25%) reported to date in 402 patient prospective post-market study[9]
  - Significantly lower device-related serious adverse event rates in the Post Approval Study than what would be expected from comparable IT therapy studies of similar patient enrollment and size[9]
- **Reduced Dose Escalation, Medication Reduction and Sustained Pain Relief**
  - Data reflects 1/3 of the dose escalation seen with peristaltic pumps at 24 months post de novo implant[10]
  - Data reflects equal or better pain relief at 20-30% less dose following replacement of peristaltic pump with valve-gated pump[11]
  - Data shows periodic bolusing w/ no basal rate yields minimal dose escalation while yielding 20% reduction in VAS[12]


DAY 33
THEY STILL SUSPECT NOTHING

Daily Practice

- Failing other interventional modalities, needing to wean down on oral opioids (will be honest some have been on 90 MME or higher)
- Will set them up for a Opioid IT trial with Fentanyl 25 mcg
- In past started them on either Morphine / Dilaudid as more hydrophilic and better spread, consensus was better to start with just opioids (or one agent) as less side effects, but lately starting with Morphine / Dilaudid (1 mg per cc concentration) and Bupivivaine (1mg per cc) and starting at a 30-40 mcg bolus over 3 minutes every 4-3 hr (6 to 8 x day), no basal rate
- Finding more of my patients tend to be favoring q3h (8 x day) bolusing

Microdosing

- Would recommend weaning down on all opioids or off opioids for best results
- Then starting again micro dose bolusing with no basal

Daily Practice

- Have over 50 pain pump patients now that I've been micro bolus dosing with Flowonix pumps, mostly all under less than a mg a day of Morphine or Dilaudid (with or without Bupivacaine) and they can all say how helpful their pump is for them

- Would hope others would consider pain pumps for their patients and practice as helpful or if in Austin area can refer them to us

Finally some good news

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