

Combining prolotherapy and perineural injection treatment (PIT[®]): Scientific literature and practical applications

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Outline of Today's Talk

- **Prolo and PIT overlap: Basic science**
- Clinical literature update: PIT
- Prolo + PIT: Rationale/observations.
- Prolo + PIT: General method.

Prolotherapy versus PIT or Prolotherapy and PIT?

- **Dextrose Prolotherapy:** Injection of a hypertonic or inflammatory concentration of dextrose with a **primary intended mechanism soft tissue repair**, with secondary restoration of function and pain reduction.
- **PIT:** Injection of D5W with a **primary goal of neuropathic pain treatment**, either subcutaneously or by hydrodissection, with secondary restoration of function and potential regeneration.

Do prolo and PIT overlap: Yes

Why? Dextrose non-inflammatory effects

- **Chondrogenesis effect. (Topol et al;12.5%;dilution)**
- Proliferative effect. (Yoshii et al;10%; no wbc's)
- Analgesic effect. (Smigel et al; 5%; ascends to L1)

The depiction here is not available to publish on a web site. This depiction shows an increase in the size of uptake of methylene blue on the surface of a knee with bone on bone severe knee OA after treatment with dextrose. The new area of uptake was biopsies with findings of a combination of I and II cartilage. For the original photographs, please email Dr. Reeves for the PDF for educational purposes.

Topol GA, Podesta LA, Reeves KD, et al. The chondrogenic effect of intra-articular hypertonic-dextrose (prolotherapy) in severe knee osteoarthritis. *PMR*. 2016;8(11):1072-1082.

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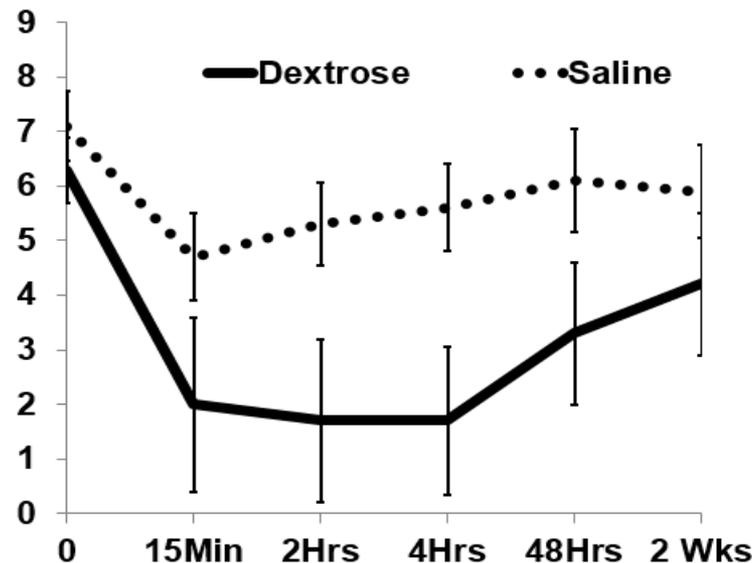
The depiction here is not available to publish on a web site. This depiction shows normal tissue but twice the thickness as the controlled site. For the original photographs, please email Dr. Reeves for the PDF for educational purposes.

Yoshii Y, Zhao C, Schmelzer JD, et al. Effects of multiple injections of hypertonic dextrose in the rabbit carpal tunnel: a potential model of carpal tunnel syndrome development. *Hand (N Y)*. 2014;9(1):52-57.

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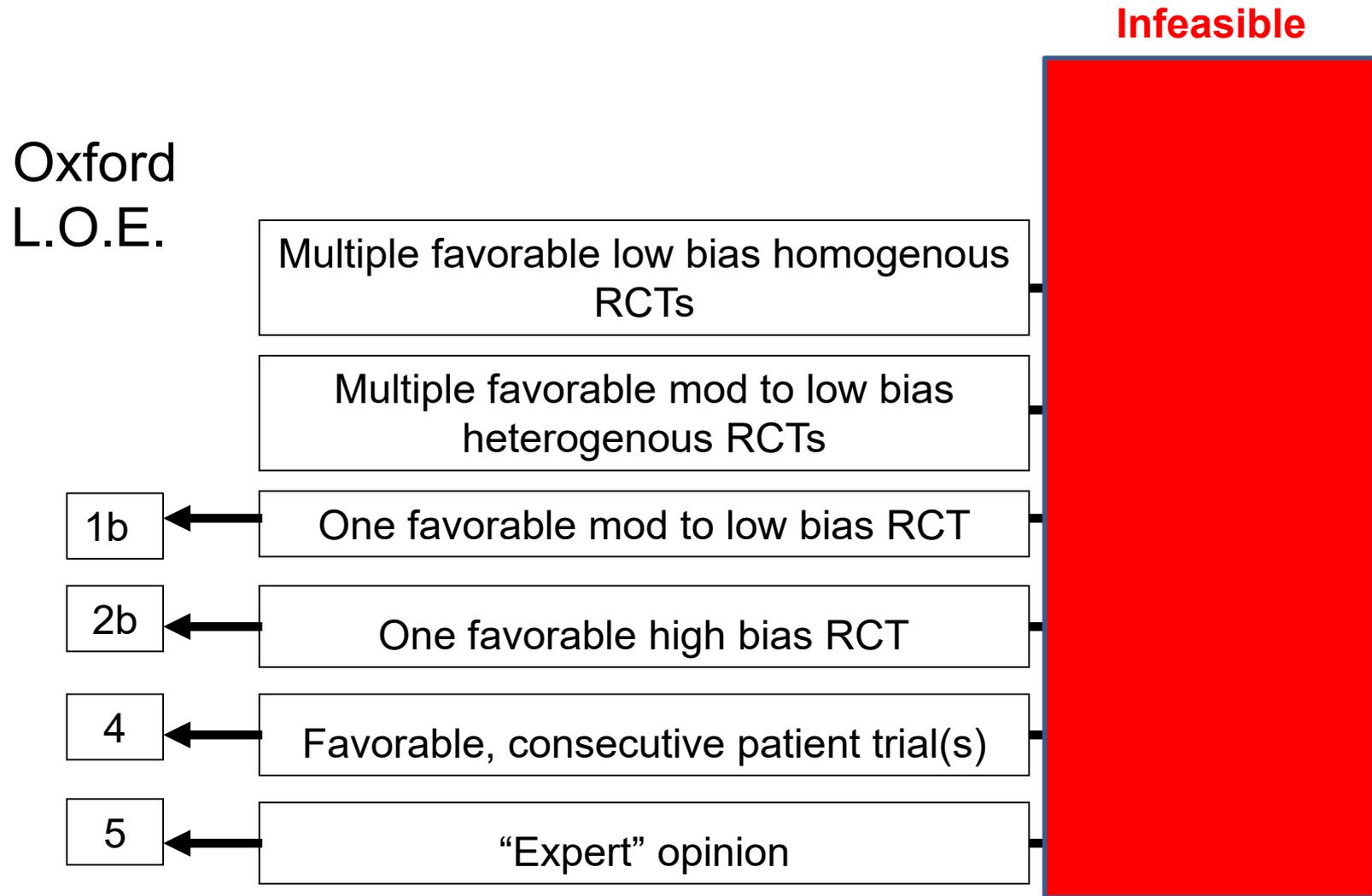


Maniquis-Smigel L, Reeves RD, Rosen JH, Coleman C, Lyftogt J, Cheng AL, Rabago D. Short Term Analgesic Effects of 5% Dextrose Epidural Injections for Chronic Low Back Pain: A Randomized Controlled Trial. *Anesth Pain Med* 2016;7(1):e42550. doi: 10.5812/aapm.42550 PMID: 28920043

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SORT evaluation not feasible: Too few studies. Evaluation is of individual studies.



Achilles Tendon: PIT vs Eccentric Lengthening Exercises (ELE) or Both

- Prolo or PIT? Both. 20% dextrose. Peritendinous. Terminal nerves.
- Handicaps: Incomplete prolo, incomplete PIT & underpowered, with strong active treatment control.
- Nevertheless: PIT and ELE and PIT+ELE all resulted in significant improvements in VISA-A and ELE + PIT outperformed ELE alone in amount of VISA-A improvement at 6 weeks and 1 year.
- Given frequent PIT approach, PIT was somewhat more costly.
- Overall: Given the strong literature support for ELE, an equal or superior result of PIT in a high quality RCT is level B evidence of PIT efficacy.

Yelland MJ, Sweeting KR, Lyftogt JA, Ng SK, Scuffham PA, Evans KA. Prolotherapy injections and eccentric loading exercises for painful Achilles tendinosis: a randomised trial. Br J Sports Med. 2009;45(5):421-428.

PIT Related Clinical Studies

Indication	Saph/Sural Dextrose PIT	Yelland 2008	Median Neve Dextrose HD	Wu 2017	Median Nerved PRP HD	Wu 2017	Caudal Epidural D5W HD	Smigel 2018	Regional HD	Lam 2017 - Dextrose
Achilles tendinosis		B								
Carpal Tunnel Syndrome				B		B				
LBP ± Buttock/Leg								C		
Regional Neuropathic Pain: All comers –Pilot Retrospective Data										P

Carpal Tunnel D5W HD 2017 Wu

- Single session perineural hydrodissection of D5W with ultrasound guidance versus same volume normal saline resulted in significant reduction in pain and disability, improvement on electrophysiological response measures, and decreased cross-sectional area of the median nerve compared to control. (Versus same volume normal saline)
- Findings reinforced by editorial from neurology department of Mayo Clinic.

Wu YT, Ho TY, Chou YC, et al. Six-month efficacy of perineural dextrose for carpal tunnel syndrome: A prospective, randomized, double-blind, controlled trial. *Mayo Clin Proc.* 2017;92(8):1179-1189.

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Carpal Tunnel PRP HD 2017 Wu

- The PRP group exhibited a significant reduction in the VAS score, BCTQ* score, and CSA** of the median nerve compared to the those of control group 6 months post-treatment. ($p < 0.05$). Control group was a splint.

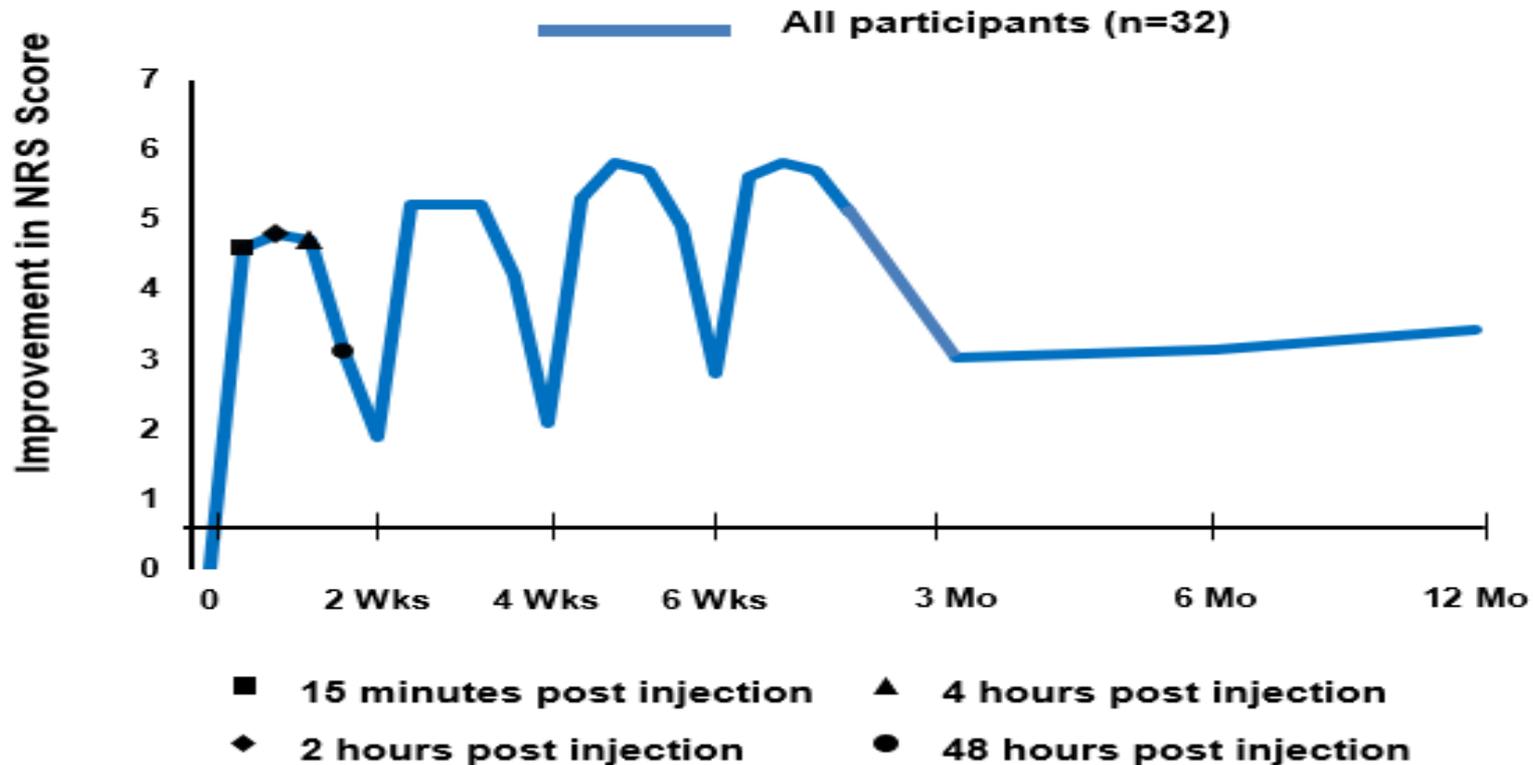
Wu YT, Ho TY, Chou YC, et al. Six-month efficacy of platelet-rich plasma for carpal tunnel syndrome: A prospective randomized, single-blind controlled trial. *Sci Rep*. 2017;7(1):94.

- *BCTQ: Boston carpal tunnel questionnaire
- ** CSA: Cross sectional

PIT Related Clinical Studies

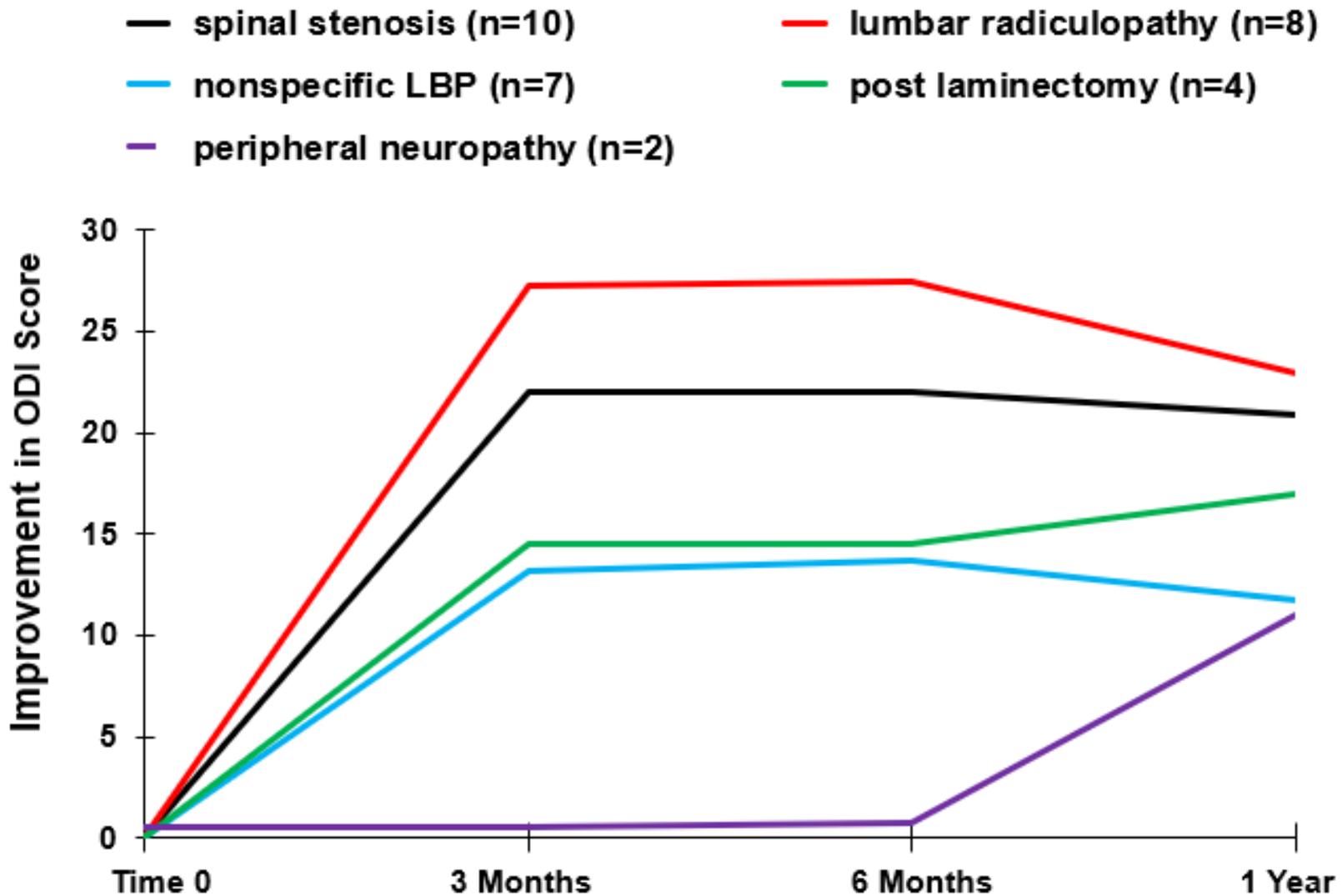
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Evidence of repeated injection effect of caudal D5W in all comers with back pain (Emphasis spinal stenosis) Note these are **CHANGE** scores



Maniquis-Smigel L, Reeves KD, Rosen HJ, Lyftogt J, Graham-Coleman C, Cheng AL, Rabago D. Analgesic effect and potential cumulative benefit from caudal epidural D5W in consecutive participants with chronic low back and buttock/leg pain. *Jnl Atl Compl Med*. In press.

Functional changes (ODI improvement) over time by diagnosis



PIT Related Clinical Studies

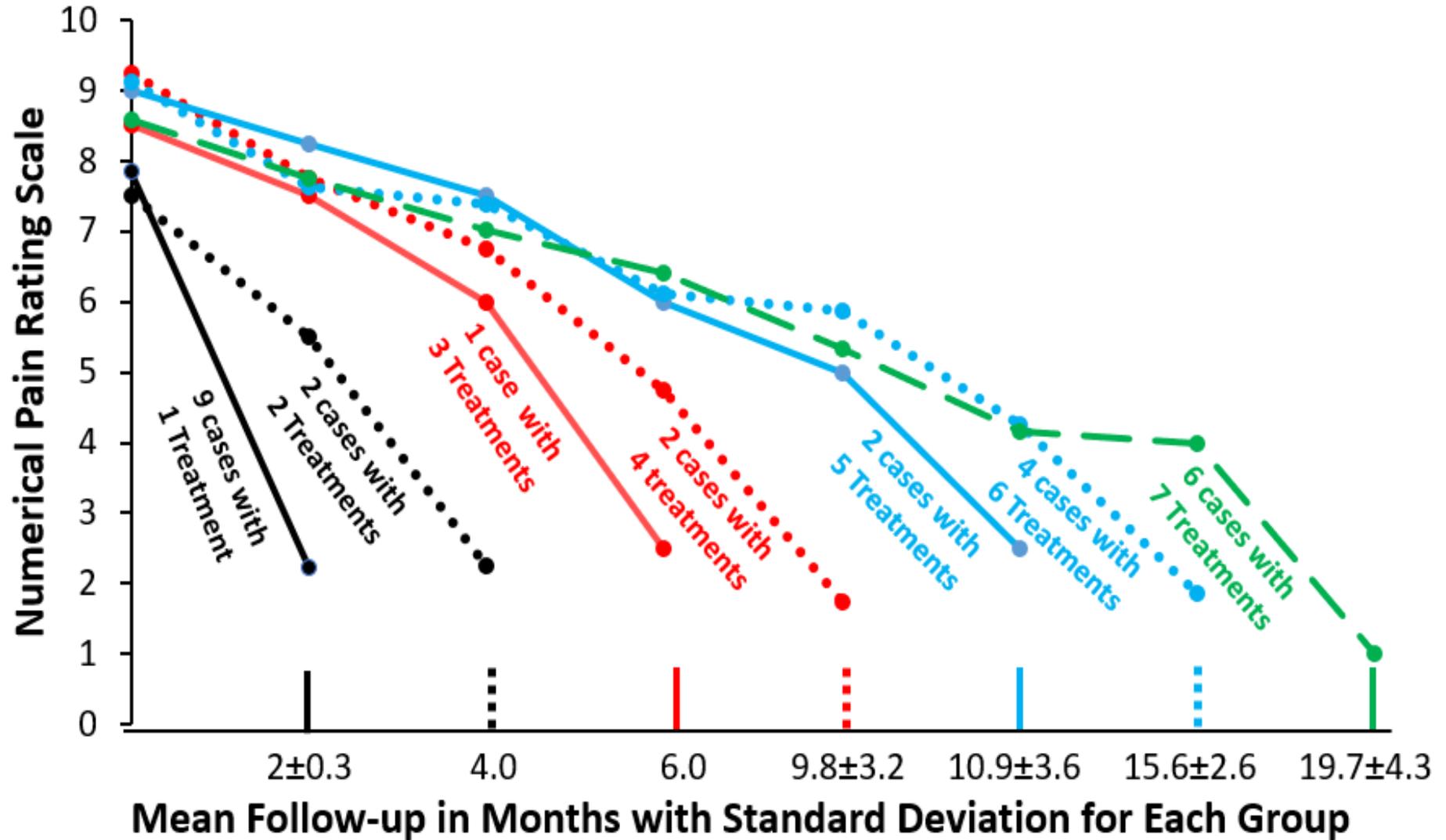
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Lam: 2017 Regional D5W Hydrodissection. (Retrospective) Diagnoses/Areas Treated

N	Diagnosis	Pain Area	PV	SG	SCBP	ISBP	CR
3	Cervical root compression	Neck and arm			2	3	3
2	Cervical root compression	Neck					2
1	Post herpetic neuralgia	Neck					1
3	Post herpetic neuralgia	Chest	3				
3	Acute herpes zoster	Neck					1
3	Acute herpes zoster	Chest	2				
2	Thoracic outlet syndrome	Arm			2		
1	Thoracic outlet syndrome	Arm		1	1		
1	Thoracic outlet syndrome	Arm			1		
1	Thoracic outlet syndrome	Neck and arm)			1		1
1	Neuropathic pain	Head and neck		1			
1	Neuropathic pain	Head and neck		1			
1	Cervicogenic headache	Head and neck		1			
1	Brachial plexus stretch injury	Arm and hand		1	1		
1	Chronic regional pain syndrome	Arm and hand		1	1		
1	Neuropathic pain thorax	Thorax	1				
1	Neuropathic pain thorax	Thorax	1				
1	Neuropathic pain arm	Neck, arm and hand			1	1	1
1	Cervical sprain	Neck and arm		1	1		

Lam SKH, Reeves KD, Chang AL. Transition from deep regional blocks toward deep nerve hydrodissection in the upper body and torso. Method description and results from a retrospective chart review of the analgesic effect of 5% dextrose water as the primary hydrodissection injectate. *Biomed Res Int* 2017;7920438

Lam: 2017 Regional D5W Hydrodissection. (Retrospective) Diagnoses/Areas Treated Response by number of treatments received.



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Neurogenic inflammation + Multidirectional protein transport + Modified Hilton's Law : Key combination

- **Neurogenic inflammation:** 40% of our sensory nerves, when dysfunctional, produce proteins that cause pain; i.e., substance P, and promote degeneration; i.e., CGRP, in soft tissues and within joints.
- **Multidirectional protein transport:** All nerves have bidirectional protein transport systems and can transport degenerative proteins throughout all structures in their “tree.”
- **Modified Hilton's Law:** The nerve supplying the skin over joints, ligaments and tendons also supplies those joints, ligaments and tendons.
- **Conclusion:** A dysfunctional nerve is capable of creating pain and degenerative signaling in all structures from skin surface to bone.

Unpublished Observations

- PIT of associated nerves enhances efficiency and success with prolotherapy. (Reduced pain magnification, reduced degenerative signaling, other mechanism)
- Prolotherapy enhances efficiency of PIT. (Cascade stim, multiple dorsal rami, end branch effects?)
- Treating multiple areas in the nerve tree simultaneously reduces number of treatments needed.
- Idiopathic neuropathy is highly likely to be neurogenic and at least partly reversible.

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Combining prolo and perineural injection: Key points

- Treating superficial penetrators at muscle soft tissue interface with ultrasound guidance.
- Ultrasound to avoid tapping bone, for nerve sparing effect
- Tumescence anesthesia for artfulness and to treat penetrators at several levels in the nerve tree
- Treatment of multiple points of compression
- Regional treatment and bilateral treatment.

General method example: Patient Jane Doe, day before arrival at this conference.

- Patient DM, age 70, lumbar back pain since 2004, within 3 inches of midline. pain with standing or walking within 10 minutes, and increasing with time up. No pain with extension.
- Surgical history: L3-4 discectomy on L with elimination of L anterior thigh pain and no change in back pain, Sept 2016.
- Working with trainer on core strengthening.
- Radiography: Latest lumbar CT/MRI scans (Dec 2016; post surgical) with no significant stenosis, substantial facet arthropathy and DDD L-3 through S1.
- Exam: No imitation with extension. No leg pain with standing. No imitation with loading in flexion. No pain with sitting.

General method axial, hip and shoulder girdles: Patient J.D

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47 year old, seen April 18, 2018, for _____ primary issues:

Issue One: Slowly recurring widespread axial, shoulder, buttock and hip pain despite anti-inflammatory diet, other functional medicine approaches and trainer-supervised yoga.

- She was last seen 8 months ago for DPT (dextrose prolotherapy) of whole back, hip and shoulder girdle treatment, with primarily dextrose prolotherapy (DPT), supplemented by acellular PRP in 1/4 ml aliquots at all posterior rami levels and in SI and IL ligaments.
- Walking improved to 1 mile, yoga handled much better, rare narcotic intake, more homemaking feasible.
- Current goal helping care for a 1st grandchild coming soon and stop narcotics to avoid OIH (opiate induced hyperalgesia).

47 year old, seen April 18, 2018, for _____ primary issues:

Interventions for Issue One. PRP in areas underlined

- **Chronic neck pain, with neurogenic contribution from the posterior supraclavicular nerve, deep cervical plexus, posterior cervical rami, dorsal scapular nerve, and connective tissue contribution from cervical multifidi, cervical facet ligaments, posterior superior trapezius, and levator scapulae.**
- **Chronic shoulder pain with neurogenic contribution from suprascapular nerve and connective tissue contribution from supraspinatus insertion, inferior glenohumeral ligament and origins of the infraspinatus, teres major and teres minor.**
- **Chronic upper back pain, with neurogenic contribution from thoracic posterior rami and connective tissue contribution from thoracic multifidi, facet ligaments, and costotransverse ligaments.**
- **Chronic low back, buttock and hip pain, with neurogenic contribution from lower thoracic and lumbar posterior rami, superior cluneal, iliohypogastric and ilioinguinal, superior, middle and inferior cluneal nerves, and connective tissue from SI and IL ligaments, lumbar multifidi, facet ligaments and intertransversarii, proximal gluteal origins, iliofemoral ligament, sacrospinous and sacrotuberous origin, sacrospinous insertion, gemellar origin, gemellar and obturator externus insertions at base of trochanter, and gluteal insertions on the greater trochanter.**

47 year old, seen April 18, 2018, for _____ primary issues:

Issue Two: Follow-up for PTSD and repeated head and chest trauma.

- V.S.'s spouse advised me at the August, 2017, visit of V.S.'s recurring PTSD symptoms. At that time V.S. related inability to leave her home due to fear of men. She provided more details of long history of prior domestic abuse (former spouse; now deceased) with multiple episodes of strangling, near drowning, and beatings about head and chest. Specifically repeated blows to R chest until unable to do self care and her then helped her take care of herself.
- A deep cervical plexus hydrodissection on the August, 2017, visit immediately reduced anxiety and hypervigilance >90%. Head pain was prominent as well and treated due to interactions between cervical plexus and nerves causing head and atypical facial pain. For unclear reason head pain required treatments twice in September, 2017. On the second visit in September, 2017, V.S. revealed that prior to August of 2017 she had been banging her head against a wall on multiple occasions because, "cutting did not hurt enough," to the point of semi consciousness, explaining the stubborn response to treatment of the trigeminal and occipital nerve territories. No head bangings or thoughts of self-harm except mild recurrence in March, 2018, when seen briefly for just the bilateral deep cervical plexus hydrodissection.

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Interventions for Issue Two

- **Chronic head pain, with neurogenic contribution from occipital nerves, trigeminal nerves and subauricular plexus and connective tissue contribution from semispinalis, splenius and rectus capitis.**
- **PTSD related to autonomic hypervigilance, with neurogenic contribution from deep cervical plexus, and connective tissue contribution from cervical multifidi, cervical facet ligaments, posterior superior trapezius, and levator scapulae.**
- **Chronic left chest wall pain with neurogenic contribution from lateral branches of the ventral rami.**

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Issue Three: Follow-up for neuropathic leg pain, multiple nerves with recurring symptoms.

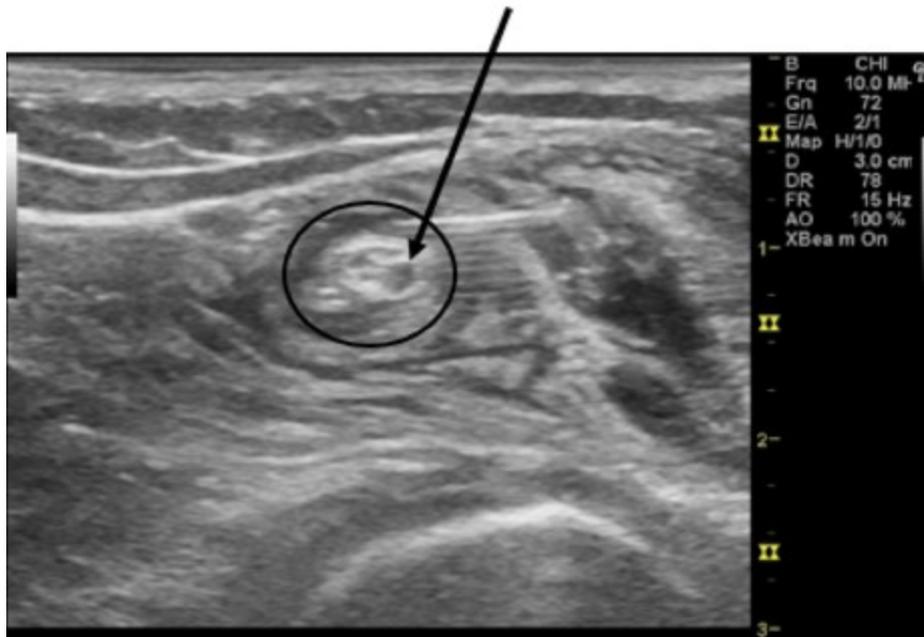
- Seen in 2012 for radiating pain and numbness from multiple directions into legs with feeling of walking on glass shards with inability to tolerate walking and marked reduction in rest at night with tingling and burning in top and bottom of feet.
- **2012 to 2015: Hydrodissected interdigital nerves and injected plantar fascial origin and short plantar ligament insertion** → Slow improvement in plantar pain.
- **Sept, 2015: Hydrodissected tibial nerve at tarsal tunnel and interosseous nerves** → Plantar pain resolved, but heel pain minimally changed.
- **Feb, 2016: Hydrodissected tibial nerve at knee and injected plantar fascial origin** → Heel pain resolved. Foot pain still limits longer walking.
- **Jan, 2017: Hydrodissected tibial and fibular nerves at knee** → Walking distance improved.
- **August, 2017: Hydrodissected tib/fib at knee, sciatic at its bifurcation with PRP added** → Walking distance further improved.
- **Today: Recurring radiation into legs, numb toes. Walking a mile.**

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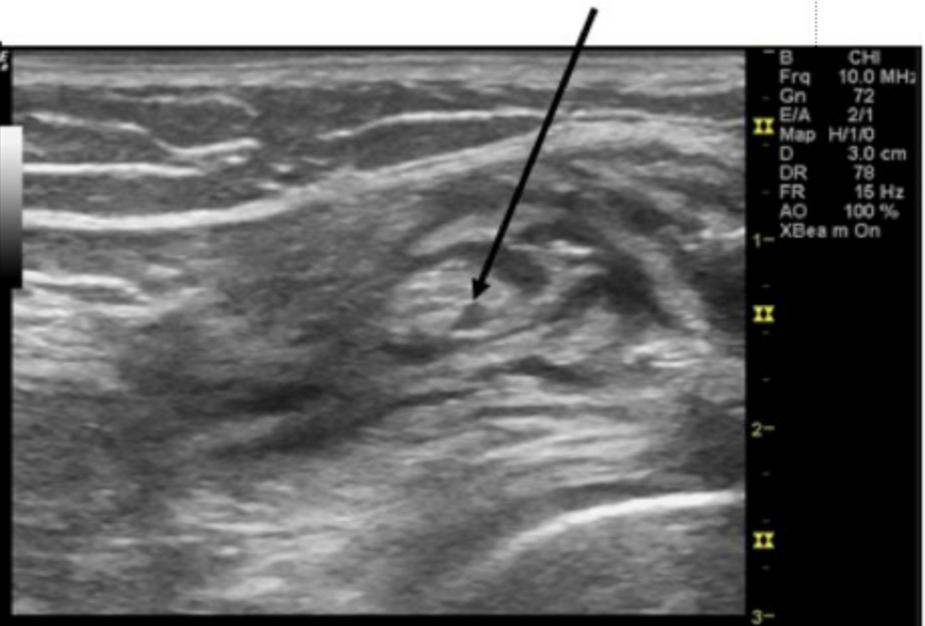
Interventions for Issue Three. PRP in areas underlined

- **Foot pain with neurogenic contribution from the sciatic nerve at its bifurcation, and tibial and fibular nerves at the knee.**

Swollen fascicle in L fibular nerve with needle reverberations seen



Swollen fascicle in R fibular nerve



Any Questions?