Illinois Osteopathic Medical Society

Regenerative Medicine: Prolotherapy for the Treatment of Chronic Pain

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MACNEAL FAMILY MEDICINE
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Disclosures

Brian Ralston, MD has no relevant financial relationships with commercial interests to disclose

Objectives

- Describe the background and mechanisms of dextrose prolotherapy
- Review evidence supporting the safety and efficacy of dextrose prolotherapy
- Describe an example of prolotherapy in the treatment of low back pain
- Discuss translational research: implementing prolotherapy in clinical practice

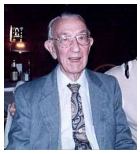
What is Prolotherapy?

- Injection of substances into tissue to stimulate body's healing response, reduce pain and increase function

Prolotherapy History

HHP
HACKETT HEMWALL PATTERSON FOUNDATION

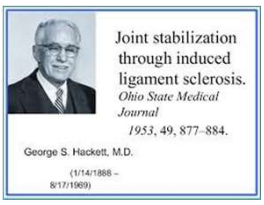
George S. Hackett, M.D.

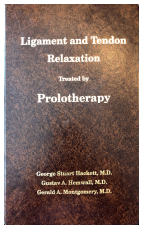


Gustav Hemwall, M.D.

Jeff Patterson, D.O.

George S. Hackett, MD





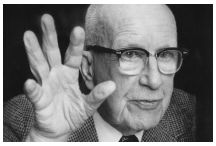
Gus Hemwall, MD - 1995

Jeff Patterson, DO

"Safe, simple, elegant, effective"

"Tensegrity" - Buckminster Fuller

- A structural principle of isolated components in compression inside a net of continuous tension
- Compressed members (such as bars or struts) do not touch each other
- Tensioned members (cables or tendons) delineate the system spatially.



"Biotensegrity"

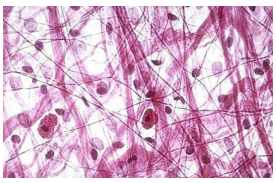
- Muscles, tendons and fascia provide continuous pull
- Bones float

Fascia

- *Do we have 600 muscles?*
- *Or one muscle and 600 fascial pockets?*

Connective Tissue Targets

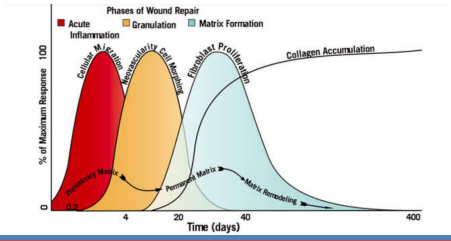
- Ligaments
- Tendons
- Cartilage
- Capsules
- Intra-articular



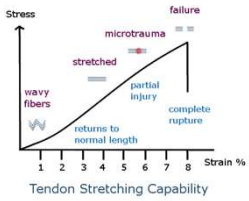
Connective Tissue Healing

- Phases
  1. Inflammation
  2. Granulation
  3. Remodeling
- Inflammation necessary for healing

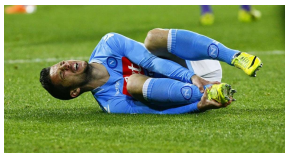
Healing Cascade



Acute Injury



Tendon Stretching Capability

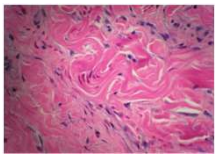


Chronic Injury

- Gradual
- Tissue microtrauma, initially asymptomatic
- Progressive tissue damage without adequate healing
- Weakness causes pain, alteration in motion and function

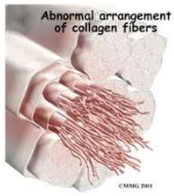
Tendinosis vs. “itis”

- No inflammatory cells
- Fragile, thin tendon fibrils
- Disorganized capillary proliferation (neovascularization)



Connective Tissue Insufficiency

- Decreased tensile strength, increased laxity
- Increased firing of mechanoreceptors
- Pain



Risks for Inadequate Healing

- Age, poor nutrition, smoking
- Chronic illness
- Decreased blood supply
- Overuse
- Steroids, NSAIDS

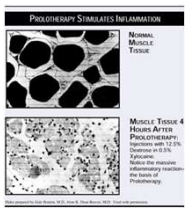
Enthesis

- Site of insertion of connective tissue into bone
- Superficial fibers attach to periosteum
- Deep fibers penetrate bone

"The weakness is in the weld."
- George S. Hackett, MD

Prolotherapy Treatment

- Solution: hyperosmolar dextrose (12-25%)
- Osmotic gradient initiates local aseptic inflammatory response
- Focus on entheses and joints to increase ligament and tendon strength, reduce pain



Prolotherapy Mechanisms

- Inflammation stimulates fibroblast formation to repair connective tissue
- Decreases neovascularization
- Decreases pain (ligaments rich in nerves)
- Reconstruct "tensegrity"

Connective Tissue Growth

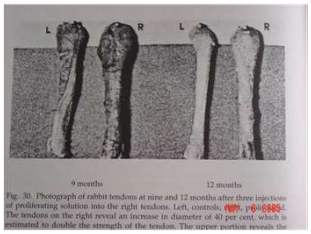


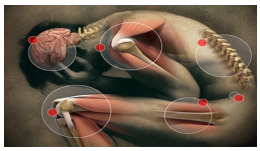
Fig. 30. Photograph of rabbit tendons at nine and 12 months after three injections of proliferating solution into the right tendons. Left, controls; right, p<0.0005. The tendons on the right reveal an increase in diameter of 40 per cent, which is estimated to double the strength of the tendon. The upper portion reveals the

Role of Prolotherapy in MSK Medicine

- Repair soft tissue/joint injuries or laxity
  - Acute or chronic
  - Any accessible ligament, tendon, joint
- Shorten rehabilitation time
- Prevent surgery

Indications - Examples

- Cervical, thoracic, lumbar pain
- Rotator cuff injuries, instability
- Tennis elbow (epicondylosis)
- Carpal tunnel, wrist pain
- Hip and knee arthritis and pain
- Achilles tendinosis
- Plantar fasciosis

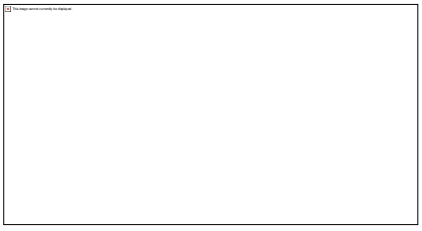


Supplies

Clinical Evaluation

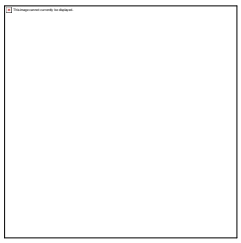
"The best diagnostic tools are at the tips of our fingers."
- Jeff Patterson, DO

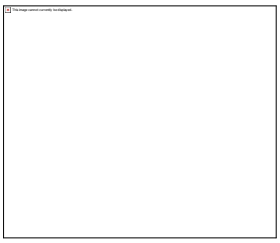
Position



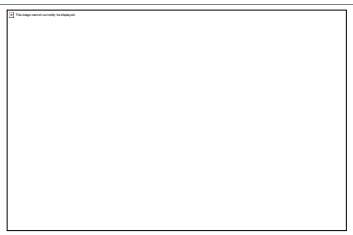
Palpation

Marking - Lumbar

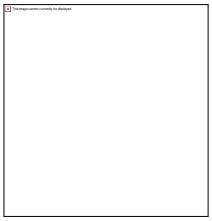


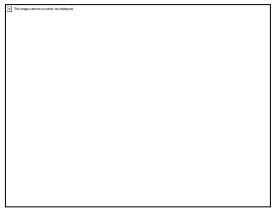


Marking - Sacral

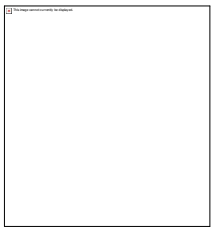


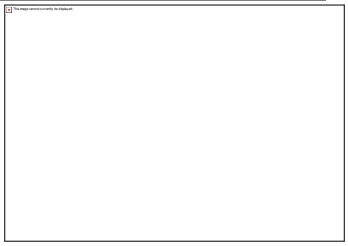
Injections





Technique – Skin Slide





Treatment Course

- Average trial: 3 treatments, 2-6 weeks apart
- Medications
  - No NSAIDS or corticosteroids
  - Use acetaminophen, other non-NSAIDS prn
- Post-injection
  - Soreness 2-4 days
  - Gradual rehabilitation

Safety

- Standard precautions
  - Hand hygiene, PPE
- Needle safety
  - No recapping, sharps disposal
- Skin prep
  - Extra-articular: 70% isopropyl alcohol
  - Intra-articular: chlorhexidine-alcohol
- Post-exposure plan
  - Test source and exposed persons
  - HIV, HCV, HBV
  - Consider HIV PEP – 3-drug regimen started in 1-2 hours

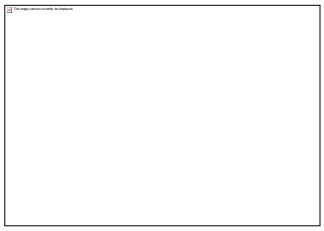
Risks

- Generally safe
- Infection rare @ 1:50,000 (dextrose is bacteriostatic)
- Needle induced trauma
- Allergic reactions

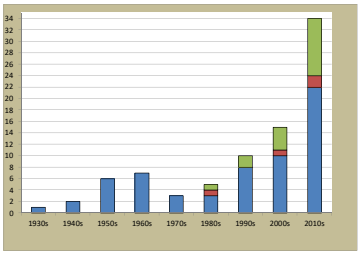
Contraindications

- Acute infection or inflammatory disease
- Acute non-reduced subluxations, dislocations, fractures
- Allergies to solution(s)
- Prosthetic joints
- Relative Contraindications
  - NSAIDS within 48 hours
  - Local injection or systemic corticosteroids within 2 weeks
  - Anticoagulation w/high INR
  - Cancer

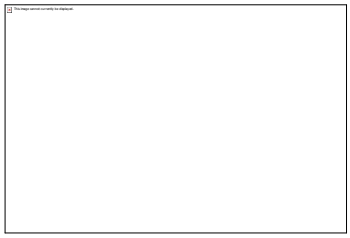
Research



Prolotherapy Research Publications by Decade



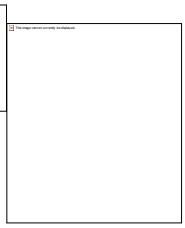
Strength of Evidence



Research

- Rábago et al, CJSM, 2005
  - Systematic review
  - >3609 patients, 12-88 years old
  - Pain from months to decades, refractory to multiple prior interventions
  - Multitude of diagnoses, e.g., cervical pain, LBP, elbow, shoulder
- Conclusions
  - General clinical success in all studies ranging from 51-82%
  - Minimal adverse events from injections
  - Mixed quality, potential for bias but overall positive outcomes

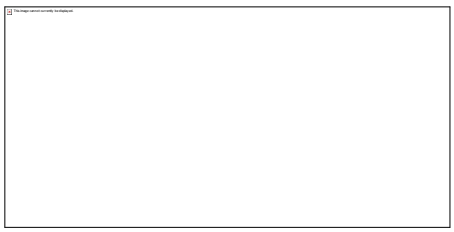
Prolotherapy for Knee Osteoarthritis



Design and Outcome Measure

- Double-blind RCT
- 3 Groups – statistically similar demographics
  1. Injection: Prolotherapy
  2. Injection: Saline control
  3. At-home exercise
- Western Ontario and McMaster University Osteoarthritis Index (WOMAC)
  - Pain, stiffness, function

Results: Rábago et al



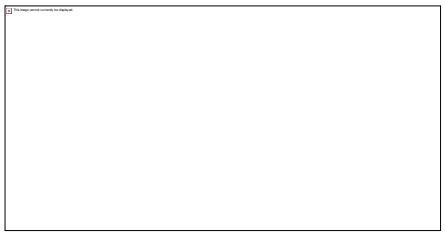
Results: Rábago et al

- 15.3 point average improvement from baseline in prolo group
- Safe, well tolerated, high satisfaction
- **"Prolotherapy resulted in clinically meaningful sustained improvement of pain, function, and stiffness scores for knee osteoarthritis compared with blinded saline injections and at-home exercises."**
- **Dextrose is doing part of the work**

Prolotherapy for Low Back Pain

- Yelland M, et al. Prolotherapy injections, saline injections, and exercises for chronic low back pain: a randomized trial. Spine. 2004;29(1):9-16
- 110 subjects over 14 years
- Dextrose vs. saline w and w/o exercise PT
- Outcomes: pain, disability, 50% pain reduction

Results: Yelland et al



Conclusions: Yelland et al.

- Saline control and dextrose injection subjects both improved
- Safe, satisfactory to patients
- Illustrates methodological challenge of saline or other injection controls: they are active therapy!
- Clinical trial evidence for the efficacy of prolotherapy for low back pain is substantial but is less strong than for knee osteoarthritis.

MacNeal Family Medicine QA

- Prolotherapy in a Family Medicine Clinic: A Quality Assessment Study
  - Brian Ralston, MD
  - Joe Crisman, MD
  - David Rábago, MD
- Assess the feasibility of including prolotherapy in a primary care practice
- Evaluate whether prolotherapy will reduce pain and improve function
- Evaluate whether prolotherapy is acceptable and satisfying to patients

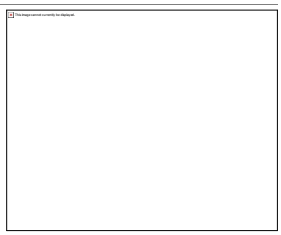
Purpose of QI Project – Why do this?

- Important to measure what we do
  - e.g., HTN management – how many patients reach BP goal?
- Stakeholders need to know whether prolotherapy works
  - Patients
  - Colleagues
  - Payers
- Demonstrates how to bridge research and applied knowledge
- Implementation of a good idea: Translation to care

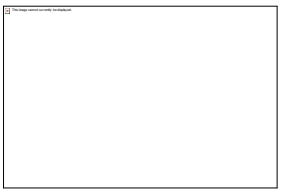
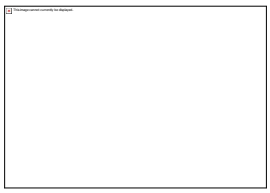
Translational Medical Research

MacNeal Hospital

- 374 licensed beds
- ~13,000 annual discharges
- ~48,000 annual ED visits



MacNeal Family Medicine Residency

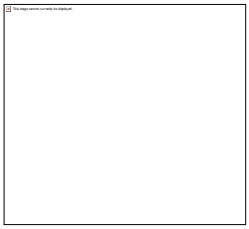



Privileges

- Created qualifications to practice prolotherapy
  - Completion of training course
  - Five supervised procedures by a provider with privileges
  - Case log of 20 cases per 2-year period to maintain
- Reviewed and approved at MacNeal Hospital
  - Credentials Committee
  - Medical Executive Committee (MEC)
  - Added as special privilege to Ambulatory Family Medicine "Privilege Card"

Operational Considerations

- Scheduling
- Coding and Billing
- Supplies
- Documentation

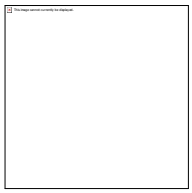


Scheduling

- "Prolotherapy Clinic" ½ day per week
- Reserved appointments for prolotherapy
- Unfilled appointments open to other patients

Coding and Billing

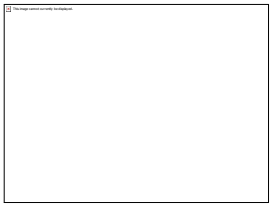
- 1st appointment for evaluation (E&M coding)
- Treatment appointments: self-pay, collected before visit
- Treatment categories
  - Small: hand/wrist, elbow, ankle/foot
  - Large: spine, shoulder hip/pelvis, knee

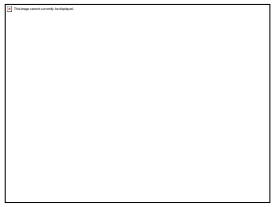


Coding and Billing

- RVU (Relative Value Units)
  - Prolotherapy "small" = 1.7
  - Prolotherapy "large" = 2.9
  - Comparisons:
    - 99214 visit (est. patient, moderate) = 1.5 RVU
    - 20610 (injection, large joint) = 0.79 RVU

Supplies





Methods

- Record average + highest pain score before treatment (0-10)
- Consent (procedure and QI project)
- Treatment protocol
  - IART procedural guide, clinical judgment
  - Record solution volumes and locations injected
- Total # of treatments per condition variable

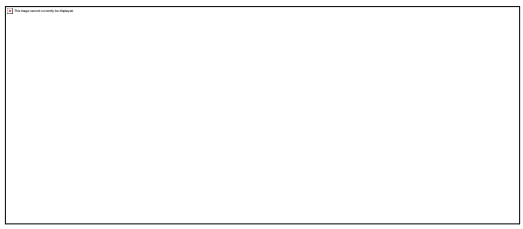
Results: Acceptance of Therapy

- Number of patients offered: 51
- Number of patients treated: 29
- **Acceptance: 56%**
  - Limitation: unclear denominator (underreporting of patients offered Tx)

Treatment Statistics

- Number of patients treated: 29
- Average patient age: 56 (range 38 – 86)
- Sex ratio
  - 45% Male
  - 55% Female
- Total number of treatments: 90
- Average number of treatments per patient: 3.1 (range 1-10)

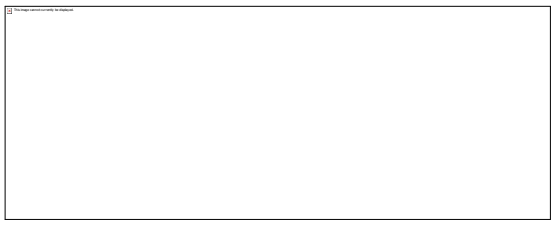
Body Areas Treated



Interim Results: Outcomes Assessment

- 18 patients completed survey
- Data
  - **Pain** Score (0-10)
  - **Improvement** Score
  - **Satisfaction** Score
  - **Willingness to Recommend** Score

Per Patient Interim Results: Pain (0–10)



Interim Results: Average Pain Scores

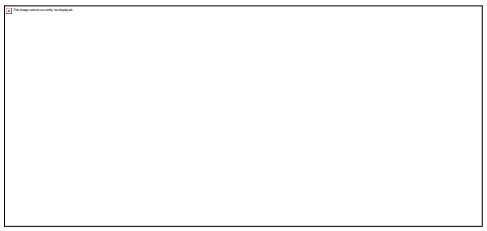
- Average pain (18 patients, 0-10 scale)
  - Before treatment: **5.27**
  - After treatment 6-12 months: **2.55**
- **Pain difference: 2.72**

- Minimum Clinically Important Difference (MCID)
  - Used to interpret the relevance of treatment effects
  - **For pain, 1.5-2 considered meaningful and beneficial**

Interim Results: Overall Improvement - 7-Point Scale

- +3: very much improved
- +2: much improved
- +1: minimally improved
- 0: no change
- -1: minimally worse
- -2: much worse
- -3: very much worse

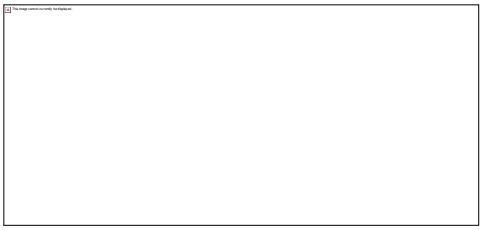
Interim Results: Improvement



Interim Results: Satisfaction – 5-Point Scale

- +2: very satisfied
- +1: satisfied
- 0: neutral
- -1: unsatisfied
- -2: very unsatisfied

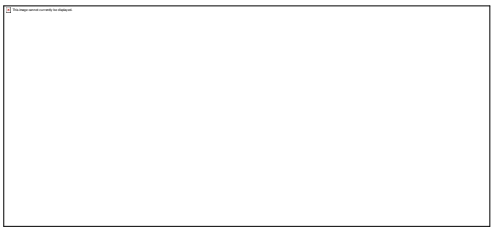
Interim Results: Satisfaction



Interim Results: Willingness to Recommend: 5-Pt Scale

- +2: definitely yes
- +1: probably yes
- 0: neutral
- -1: probably no
- -2: definitely no

Results: Willingness to Recommend

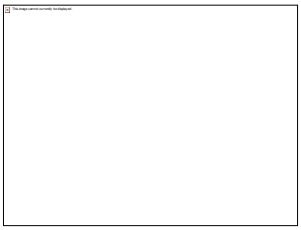


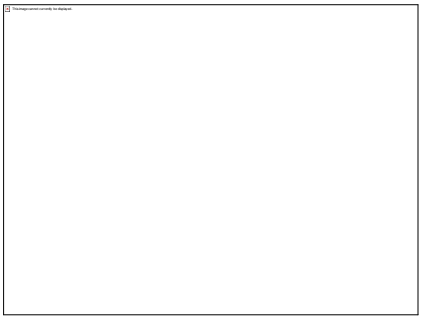
QI Study Conclusions

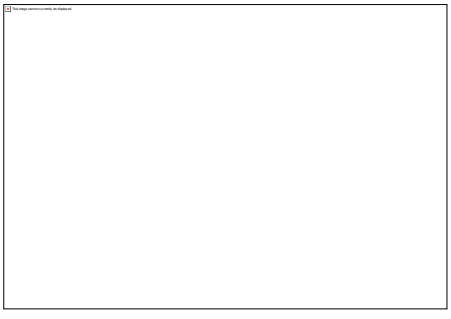
- Feasible to integrate prolotherapy into primary care practice
- Initial results from this QI project indicate
  - Acceptance of the therapy by the institution and patients
  - Clinical effectiveness based on pain reduction and overall improvement
  - High patient satisfaction, strong willingness to recommend
- Interim data suggests prolotherapy is acceptable and effective in primary care

HHPF Service-Learning Trips

HACKETT HEMWALL PATTERSON FOUNDATION







Summary

- Prolotherapy is a safe, effective treatment option for MSK injuries and chronic pain
- Cost-effective, non-opioid, non-surgical
- Increasing use and research in MSK

Thank you!