Regenerative Medicine for Tendon and Ligament Disorders

The Advanced Musculoskeletal Ultrasound Skills Course
April 28-29, 2017

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Goals of the Presentation

- Regenerative Injection treatment of tendinopathy and ligament disorders
  - Prolotherapy
  - PRP
  - Needle tenotomy
  - Stem cells?

NO DISCLOSURES

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Clinics Review Articles

PHYSICAL MEDICINE AND REHABILITATION CLINICS OF NORTH AMERICA

Regenerative Medicine

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Outpatient Ultrasound-Guided Musculoskeletal Techniques

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PM&R
The Journal of Injury, Function and Rehabilitation

Supplement to

PHYSIOTHERAPIC APPLICATIONS OF STEM CELL THERAPIES IN REGENERATIVE TREATMENTS OF MUSCULOSKELETAL CONDITIONS

April 2015
Volume 7, Issue 4, Supplement, SI-S82
Physical Applications of Stem Cell Therapies in Regenerative Treatments of Musculoskeletal Conditions
Edited by Daniel A. Malanga
Goals of the Presentation

- Basic overview of the evolution of the current available techniques
- General principles in selecting amongst these treatments
- Patient Selection for regenerative treatments
- Where is the field headed?

What is regenerative sports medicine?

- Regenerative biomedicine is emerging at the forefront of medicine
- As it relates to musculoskeletal and sports medicine, this includes:
  - Prolotherapy and sclerosing agents
  - Extracorporeal shock wave therapy
  - Platelet rich plasma
  - Nitric oxide
  - Matrix metalloproteinase
  - Mesenchymal stem cells

The New York Times

The Athlete’s Pain
As Sports Medicine Surges, Hope and Hype Outpace Proven Treatments
Published: September 5, 2011

IOC consensus paper on the use of platelet rich plasma in sports medicine

• “….proceed with caution in the use of PRP in athletic sporting injuries. We believe more work on the basic science needs to be undertaken….”

• WADA:
  - Intramuscular injections prohibited until 2011, when approved
  - All other routes of administration, such as intra-articular, intra-or peritendinous are permitted and require a declaration of use.
  - Isolated growth factors are prohibited: IGF-1, VEGF, PDGF

Definition of Prolotherapy

- Prolotherapy = “Proliferative therapy”
  - “Method of injection treatment using irritant solutions designed to stimulate healing and pain relief.
  - Targets: Joint space, ligament, tendon insertion

PROLOURATION in the News

Scar Away Your Pain? Some Docs Back Prolotherapy

“...wouldn’t be skiing now if it wasn’t for prolotherapy.”
- Bode Miller
February 2006 ESPN interview

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  - Matrix metalloproteinase
  - Mesenchymal stem cells
Proposed Mechanisms of Prolotherapy

- Non inflammatory
  - 10% dextrose
    - Repair of tissue damage
    - Stimulation of growth factors
    - platelet derived growth factor
    - epidermal growth factor
    - fibroblast and connective tissue growth factors
- Neurolytic effects
  - Lysis or damage to c-fibers via hypertonic dextrose
- Inflammatory prolotherapy
  - 12.5-25% dextrose, phenol, sodium morrhuate
  - Causes inflammatory activation to produce growth factors

Solutions Used in Prolotherapy and their proposed mechanisms of action

<table>
<thead>
<tr>
<th>Injected Solution</th>
<th>Mechanism of Action</th>
</tr>
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<tbody>
<tr>
<td>Hyperosmolar dextrose</td>
<td>Creates hypertonic atmosphere, which leads to cell rupture</td>
</tr>
<tr>
<td></td>
<td>Upregulates expression of platelet derived growth factors</td>
</tr>
<tr>
<td>Morrhuate Sodium</td>
<td>Attracts inflammatory mediators Vascular sclerosant</td>
</tr>
<tr>
<td>Phenol – glycerine – glucose</td>
<td>Cellular irritant * no longer used</td>
</tr>
</tbody>
</table>

Dextrose Levels > 10% Stimulate the Inflammatory Cascade

- Osmotic effect – cell shrink – stress – leakage of lipids – temporary inflammation

Growth factors the Dextrose Elevates (non inflammatory effect)

- Ligament/tendon healing:
  - PDGF, TGFb, EGF, bFGF, CTGF
- Cartilage Healing
  - PDGF, TGFb, IGF,

The Needle Itself Stimulates Repair

- Cell membrane disruption
- Small blood vessel disruption
- Bleeding with platelet and blood effects
- Challenge to do injection control studies.

Treatment Paradigm for Prolotherapy

- Technique: important concepts = “ABC’s”:
  - Anatomy: entheses, vasculature, nerves
  - Bony endpoint: always touch bone with needle tip before injecting
  - Compression of superficial tissues while injecting to maximize accuracy
Scientific evidence for treatment of tendinopathy

- Clinical series
- Double blind controlled studies

Best practice recommendations for dextrose prolotherapy: 2017

- TMJ with painful laxity
  - No specific recommendation
- Achilles tendonopathy*
  - The combination of DPT and ELE may be utilized as potentially superior to either treatment alone
- Lateral Epicondylitis*
  - DPT may improve pain and function in those who failed other treatments
- Plantar fasciosis
  - DPT may improve functional status
- Rotator cuff tendonopathy*
  - DPT in combination with PT if no sustained response to PT

Adapted with permission from Dr. Dean Reeves

TREATMENT: PROLOTHERAPY

  - Pilot study
  - RCT: prolotherapy (dextrose-sodium morrhuate) (n=10) vs saline (n=10) with refractory lateral epicondylitis
  - Clinical and MRI confirmed diagnosis.
  - Injections at 0, 4 and 8 week intervals
  - Statistically significant improvement of prolotherapy group over control group in pain and function out to 1 year post-injection.

**DASH stands for “Disabilities of the Arm, Shoulder and Hand.”

Prolotherapy and Tendinopathies

- Studies in chronic tendinopathies
  - Lateral epicondylitis
    - Scarpone, et al
    - Carayonopoulos, et al
  - Achilles tendonopathy
    - Yelland et al
    - Maxwell et al
    - Ryan et al
  - Plantar fasciopathy
    - Ryan et al
    - Panula tendinopathy
    - Ryan et al
    - Hip adductor tendinopathy
    - Topol and Reeves
    - Osgood Schlatter's
    - Topol, Podesta, Reeves, et al.
  - Rotator cuff tendonopathy
    - Bertrand, Reeves, et Al.

Prolotherapy vs. corticosteroid therapy for treatment of lateral epicondylitis.

- Patients with chronic lateral epicondylitis (>3mos) recruited to a non-inferiority trial.
- Double blinded study comparing
  - DPT/sodium morrhuate
  - Vs. depomedrol (40mg) plus procaine
- Primary outcome measures
  - VAS
  - QVAS
  - **DASH**
- Secondary outcome measures
  - Grip strength
- 3 office visits and 1 phone f/u at 6mos.

**DASH stands for “Disabilities of the Arm, Shoulder and Hand.”

Results:
- 24 patients recruited
- 17 completed study
- Paired T-test analysis between the two treatment groups
  - Inconclusive due to small sample size.
- Unpaired t-test analyses within each treatment group demonstrated a change

Conclusion:
- A benefit for prolotherapy in the treatment of lateral epicondylitis appears to exist. Similar randomized controlled trials using larger sample sizes is warranted

Figure 2. Surface anatomy of injection sites. (A) Common extensor tendon. (B) Lateral collateral ligament. (C) Acromio-clavicular ligament.
Interventions: participants randomized

- Prolotherapy

Participants: 43 patients with painful mid-portion achilles tendinosis with pain at least 6 weeks

Interventions: participants randomized
- 32 week program of eccentric loading
- Prolotherapy: hypertonic glucose and lidocaine
- Combined

Outcome measures
- VISA-A,
- Pain
- Stiffness and limitation of activity scores
- Treatment costs

Results

- Decreased neovascularity by 55% in painful achilles tendinosis and prolotherapy give more rapid improvement in symptoms than ELEs alone, but long-term VISA-A scores are similar

Conclusions

- Subjects and methods
  - 36 consecutive patients
  - Symptoms > 3mos
  - Sonographically guided intratendinous injections of 25% dextrose every 6 weeks until symptoms resolved or no improvement shown
    - VAS 1 (rest pain), VAS 2 (ADL pain), VAS 3 (sports)
    - Sonographic parameters
      - Tendon thickness
      - Echogenicity
      - Neovascularity

Favorable outcome after sonographically guided intratendinous injection of hyperosmolar dextrose for chronic insertional and midportion achilles tendinosis

- Objective
  - Short term and 2 year follow up for us guided prolotherapy injections

- Subjects and methods
  - 108 tendons: 86 midportion; 22 insertional
  - Pain > 6 mos
  - 25% dextrose intratendinous

- Results
  - Mean of 5 injections 6 weeks apart
  - Significant improvement in pain scores for both groups
  - Reductions in the size and severity of hypoechoic regions, intratendinous tears and neovascularity

Maxwell, Ryan et al. 2007

- Results
  - Statistically significant reductions in pain scores at 6 weeks
  - Decreased neovascularity by 55%
  - No significant change in hypoechoic areas
  - Excluded patients without improvement in their data analysis. No control group.
  - Referred one patient for surgery

Maxwell, Ryan et al. AJR 2007

- Eccentric loading exercises
  - Twice daily in 3 sets of 15 repetitions with the knee straight
  - Twice daily in 3 sets of 15 repetitions with the knee bent
  - Not to exceed pain intensity of 4/10
  - As pain eases, weights added to backpack

- Prolotherapy injections
  - Tender points in the subcutaneous tissues adjacent to the affected tendon with 20% glucose solution for 4-12 treatments, using the technique described by lyftogt
  - At each point: 5-1.0 cc of solution used.
  - Treated until pain free

Efficacy of Dextrose Prolotherapy in Elite Male Kicking-Sport Athletes with Chronic Groin Pain

- **Participants**
  - 22 rugby and 2 soccer players with chronic groin pain that prevented full sport participation and who were non-responsive both to therapy and to graded re-introduction into sports activity
- **Intervention**
  - Monthly injection of 12.5% dextrose and 0.5% lidocaine
  - Injected sites
    - Adductor origins
    - Suprapubic abdominal insertions
    - Symphysis pubis
  - **Injections were given until complete resolution of pain or lack of improvement for 2 consecutive treatments. Average of 2.8 treatments

Prolotherapy in Athletes with Chronic Groin Pain (cont.)

- **Results**
  - 20 of 24 patients had no pain and 22 of 24 were unrestricted with sports at final data collection an average of 17.2 mos after treatment
- **Conclusion**
  - Dextrose prolotherapy showed marked efficacy for chronic groin pain in this group of elite rugby and soccer athletes

Efficacy of Dextrose Prolotherapy in Elite Male Kicking-Sport Athletes with Chronic Groin Pain

- **Objective**
  - Multi-sport and long term data on prolotherapy on career-threatened athletes
- **Design**
  - Monthly injections of 12.5% dextrose abdominal and adductor attachments

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*Ryan M et al. AJR 2010;194:1047-1053 ©2010 by American Roentgen Ray Society*
Efficacy of Dextrose Prolotherapy in Elite Male Kicking-Sport Athletes with Chronic Groin pain

- Results
  - 75 athletes enrolled
  - 72 completed treatment
  - Average # treatments: 3
  - 66 returned to unrestricted sport
  - Return to sport occurred in average of 3 mos.
  - VAS sport and Nirschl measured at 0 and avg 24 mos after treatment
    - Avg VAS: 82% improved
    - Avg Nirschl: 78% improved


Sonographically guided intratendinous injections of hyperosmolar dextrose/lidocaine: a pilot study for the treatment of chronic plantar fasciitis

- Case series
- 20 patients
  - Average age: 51
- Interventions
  - 27g needle
  - 25% dextrose under US guidance
  - 6 week intervals for 3 visits

Wong SM, Ann Rheum Dis 2001;60:639

Ultrasound guided injections of hyperosmolar dextrose for overuse patellar tendinopathy: a pilot study

- Methods
  - 47 consecutive referrals
  - Patients failed conservative treatment
  - US Guided 25% dextrose with lido into the area of tendinopathy until they were satisfied with treatment
  - Primary outcome measure: 3 part VAS
  - Secondary outcome measure: US appearance of tendon


Hyperosmolar Dextrose injection for recalcitrant osgood-schlatter disease

- Objective
  - dextrose vs lidocaine vs supervised usual care in adolescent athletes with Osgood-Schlatter
- Patients and methods
  - Randomly assigned to either therapist-supervised usual care or double blind injection of 1% lidocaine with/without 12.5% dextrose
  - Monthly injections x 3 mos.
  - Measured: unaltered sport (Nirschl pain score <4) and asymptomatic sport (Nirschl pain score = 0) at 1 year
- Results/Conclusions
  - Significant symptom reduction efficacy of injection therapy over usual care. A significant component of the effect seems to be associated with the dextrose component.

Anteroposterior photograph of knee showing injection points starting over the most distal area of pain on the tibial tuberosity and moving proximally in 1-cm increments to the most proximal painful point with pressure.

**Injection Sites**
- Anterior View
  - 3 cm
  - 2 cm
  - 1.5 cm
- Posterior Injection
  - 1 cm
  - 3 cm

**Summary: Where does prolotherapy fit in the treatment of tendinopathy?**

<table>
<thead>
<tr>
<th>Injectable</th>
<th>Pros</th>
<th>Cons</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid</td>
<td>Short term relief</td>
<td>Avoid intra-tendinous</td>
<td>Avoid weight bearing tendons</td>
</tr>
<tr>
<td>Prolotherapy</td>
<td>Less expensive</td>
<td>Treat region, not point</td>
<td>Evidence suggests applicable to tendon / enthesis</td>
</tr>
<tr>
<td>PRP</td>
<td>More research needed</td>
<td>Needling effect may be primary</td>
<td></td>
</tr>
<tr>
<td>Platelet Rich Plasma</td>
<td>More data for intra and peri-tendinous application</td>
<td>Small volume</td>
<td>Expensive</td>
</tr>
</tbody>
</table>

**Prolotherapy and Recalcitrant Tendinopathy: Clinical Recommendations 2017**

- “The current, most promising indication for the use of prolotherapy appears to be the treatment of tendinopathies” (Distel and Best 2011)
- Relatively safe. Few adverse effects
- Growing evidence to support use in refractory tendinopathies
  - Lateral epicondylopathy
  - Achilles tendinopathy
- Treatment paradigm to consider
  - Peritendinous / intratendinous with US guidance
  - Enthesis
  - Treat region, not point.
- Further research needed
The optimal techniques for application need to be determined:

- Frequency-weekly vs. 3-6 weeks
- Concentration of solutions-10-15-25%
- Optimal solutions – dextrose only vs. with phenol, sodium morhuate, pumice, platelet rich plasma
- Placement and volume of injections.

**PRP and Tendon**

PRP in the Sports News

Just prior to the kickoff of superbowl XLIII, on field reporters from NBC credited Hines Ward’s rapid recovery with a knee sprain (MCL) to Platelet Rich Plasma therapy.

Takashi Saito, a star pitcher for the LA Dodgers suffered a tear of his ulnar collateral ligament.

IOC consensus paper on the use of platelet rich plasma in sports medicine

- WADA:
  - Intramuscular injections prohibited until 2011, then approved
  - All other routes of administration, such as intra-articular, intra-or peritendinous are permitted and require a declaration of use.
  - Isolated growth factors are prohibited: IGF-1, VEGF, PDGF

**Platelets: Not just for clotting**

- Platelets are the first cells to arrive at the site of injury
- Responsible for initiation of healing cascade
- α-granules and dense granules

Why the Controversy?

- Need to define what is in the PRP
  - Platelet concentration
  - Leukocytes count/presence
  - RBC = RBC -
- Need to define the procedure
  - US guidance
  - Needle type
  - How many times?
  - Activator used
- Rehabilitation methods
  - Need to be validated
  - Immobilization
  - Timing of exercises
  - May need to separate out different body parts
- Do allow tendons behave differently than Achilles tendon?
Aim: IRB approved prospective pilot study to evaluate the efficacy of using PRP as a potential treatment for chronic severe epicondylar tendinosis.

Methods: 140 patients were evaluated for this study. 20 patients (15%) met strict inclusion criteria. 55 ml of whole blood was processed to produce 5 ml of PRP with a mean increase of 5.4x above baseline. 2-3 ml of either PRP or bupivacaine (control) were injected using a 22-g needle into the common extensor tendon. 80 patients were randomized to receive PRP and 60 patients were randomized to receive control.

Results: Outcome Data

<table>
<thead>
<tr>
<th>Time</th>
<th>Visual Analog Pain Scores</th>
<th>p value</th>
<th>Mean Mayo Elbow Scores</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>80.3</td>
<td>0.259</td>
<td>50.3</td>
<td>0.838</td>
</tr>
<tr>
<td>1 month</td>
<td>43.4</td>
<td>0.028</td>
<td>71.3</td>
<td>0.061</td>
</tr>
<tr>
<td>2 month</td>
<td>32.0</td>
<td>0.001</td>
<td>76.3</td>
<td>0.008</td>
</tr>
<tr>
<td>3 month</td>
<td>15.1</td>
<td>-</td>
<td>84.3</td>
<td>-</td>
</tr>
<tr>
<td>12 month</td>
<td>3.7</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

PRP patients: 64% improvement in pain, 84% disability

PRP vs Corticosteroid in Lateral Epicondylitis: Netherlands Study. AJSM Feb 2010

• Purpose: determine effectiveness of PRP vs corticosteroid injection in patients with chronic LE
• Design: randomized controlled trial
• 100 patient
  • 51 PRP
  • 49 steroid
• Technique: peppering technique plus site of maximal tenderness
• Outcomes: VAS and DASH
• Successful treatment: >25% improvement in VAS or DASH without reinervention after 1 year

Chronic Elbow Tendinosis

Key Points:
- PRP treated patients demonstrated significant improvement with a single injection that was sustained over time.
- There were no reported complications (specifically, no infections, neurovascular changes, or worsening of patient’s epicondylar pain).
- Treatment of patients with chronic elbow tendinosis with buffered PRP significantly reduced pain.
- PRP may be considered before surgical intervention.

PRP vs Corticosteroid in Lateral Epicondylitis: Netherlands Study. AJSM Feb 2010

• Results:
  - VAS scores: 49% improved in steroid group
  - VAS scores: 73% in the PRP group improved
  - DASH: 51% in steroid group improved
  - DASH: 73% in the PRP group
  - PRP group kept getting better over the next year.
    • PRP patients: 64% improvement in pain, 84% disability
    • Steroid group: 24% improvement in pain, 17% disability
Comparison of Surgically Repaired Achilles Tendon using Platelet-Rich Fibrin Matrices

- 12 male athletes with spontaneous complete rupture of Achilles tendon.
  - 6 received platelet-rich fibrin matrices
  - Regained ROM earlier (P=.025)
  - Less time to take up gentle running (P=.042)
  - Resumed training activities earlier (P=.004)
  - Less increase in cross-sectional area (P=.009)


- Blinded, prospective, randomized trial of PRP vs placebo in patients undergoing surgery to repair a torn rotator cuff.
- There was no difference in pain relief or in function between the 2, said Stephen C. Weber, MD.
- All patients had arthroscopic rotator cuff repair under general anesthesia, and those randomized to PRP received it at the conclusion of the repair.
- However, VAS scores and postoperative narcotic use did not differ between the 2 groups and, at 3 months postop, both groups showed residual defects on magnetic resonance imaging (MRI).

Medscape orthopedics 2010

Platelet-Rich Plasma Injection for Chronic Achilles Tendinopathy
A Randomized Controlled Trial

Robert L. de Veer, MD
Mark W. Ha, MD
Mark A. Joyce, MD, PhD
Miriam W. Wamboldt, MD, PhD
Peter L. Whipple, MD
Brian D. Ross, MD
Robert J. Ruch, MD, PhD

Objective: To examine whether a PRP injection would improve outcomes in chronic Achilles tendinopathy.

Methods: Prospective, randomized, single-blinded, parallel-group study conducted at a single center. The study included 28 patients with chronic Achilles tendinopathy with a mean duration of symptoms of 2.2 ± 2.1 years. All patients were randomized to either saline or PRP injection.

Results: There was no difference in terms of the pain and function scores in the two groups.

Conclusion: PRP injection did not result in better outcomes in chronic Achilles tendinopathy compared to saline injection.

PRP and tendon

Platelet-rich plasma: New clinical application A pilot study for treatment of jumper's knee
Elizaveta Kon, Giuseppe Filardo et al. Injury 2009

- 20 male athletes with a mean history of 20.7 months of pain received treatment,
  - Baseline injection then 2 additional injections at 35 day intervals
  - PRP activated with Calcium chloride
  - Outcomes were prospectively evaluated at 6 months follow-up.
  - No severe adverse events were observed,
  - Statistically significant improvements in all scores were recorded.

Monto et al. PRP in chronic achilles tendinopathy

- AAOS annual meeting March 19, 2010
- 30 patients with chronic refractory achilles tendinopathy > 8mos.
- 1 MSK US guided 4cc injection into abnormal area
- 48 hrs in CAM walker, then activity as tolerated
- AOFAS hindfoot scores improved
  - 34 pre
  - 84 post
  - 92 at 6 mos follow up
Significant improvement was observed in the clinical and imaging results.

- The AOFAS scale improved from a baseline median of 55 points to 96 points at 18 months (p=0.000655), while the VISA-A scale improved from a baseline of 24 to 96 (p=0.000655) in the final evaluations.
- During the final evaluation, one subject experienced minor pain following prolonged daily activity, while another subject complained of pain following overloading activity.
- **CONCLUSION:** Local, accurate PRP administration improved symptoms of non-insertional Achilles tendinopathy.

**PRP fails to improve long term outcome after surgical rotator cuff repair**

- Randelli et al: *JSES, 2010.* PRP in arthroscopic rotator cuff repair: A prospective RCT study: 2 years follow up
  - Looked at double row repair in small to medium RTC tears
PRP for ligament injury

- ACL
  - No benefit to surgical reconstruction after 24 mos. May accelerate graft to bone incorporation, improve healing, reduce edema, inflammation
- MCL
  - One case report
- Ankle sprain
  - Double blind RCT comparing PRP to saline placebo: no significant difference at 30 days (Rowden et al. 2015)
  - Other study: added US guided PRP injection to rehab of ATFL in elite athletes: accelerated return to play by 3 weeks, improved joint stability and reduced pain (Laver et al. 2015)
- UCL
  - Case series demonstrated favorable outcome for tx of partial UCL tears of the elbow (Podesta et al. 2013)

Percutaneous tenotomy

- US guided PNT has been used as an independent strategy or in combination with orthobiologics
- PNT: passes a needle through a tendon with the goal of disrupting the chronic degenerative process.
- Minimal research on PNT alone.
- Complications are rare.

Automated percutaneous tenotomy

- MSK ultrasound guidance
- Local anesthetic
- Longitudinal vibration energy at a specific frequency debrides and aspirates the targeted damaged tendon tissue

High Volume Injection and Percutaneous Needle Scraping

- MSK ultrasound guidance
- Local anesthetic
- Longitudinal vibration energy at a specific frequency debrides and aspirates the targeted damaged tendon tissue

Emerging treatments for chronic tendinopathy

- Stem cell use
- Bioscaffolds

Stem cells for rotator cuff (fat and BMSC)
A summary of cell therapies in different cell origins

- Mesenchymal stem cells
- Fibroblasts
- Tendon progenitor stem cells

Muscle derived mesenchymal stem cells

- Limited evidence in tendon therapy

Dermal Fibroblasts

- In vitro and animal studies have shown that dermal fibroblasts have potential in tendon engineering and repair
- Connell et al: human study for chronic lateral epicondylosis
  - Clinical pilot
    - 12 patients with refractory lateral epicondylopathy
    - 4mm punch biopsy for skin sample
  - Fibroblasts expanded in number in the laboratory and collagen producing cells with features similar to tenocytes were identified
  - these cells were embedded into the patients own plasma and injected under ultrasound guidance.
  - Improved ultrasound appearance, decreased pain and improved function at 6 mos.


Dermal Fibroblasts

- 60 tendons from 46 patients with refractory patella tendinopathy
  - Randomized controlled trial
  - 4mm skin biopsy to grow tenocyte-like collagen producing cells
  - Randomized
    - Cells plus autologous plasma
    - Autologous plasma alone
  - Results: 6 mos. Follow up.
    - Ultrasound guided injec of autologous skin-derived tendon-like cells can be safely used in the short term to treat patella tendinopathy
    - Faster response and greater improvement in pain and function over plasma alone


Figure 8. A, ultrasound of the right patellar tendon in the longitudinal plane showing patellar tendon before (inset) and after treatment with plasma only. The large arrow shows echogenic scar tissue adjacent to the tendinous insertion adjacent to the patella. B, ultrasound of the left patellar tendon in the same patient treated with plasma and with cells shows almost complete replacement of the initial hypoechogenic abnormality (inset; small arrow) with normal appearing fibrillar tendon material (large arrow).

A summary of cell therapies in different cell origins

- Mesenchymal stem cells
- Fibroblasts
- Tendon progenitor stem cells

Bioscaffolds

- A number of studies demonstrate that seeded constructs have better histological and biomechanical properties than scaffold alone
- Studies
  - Synthetic biodegradable polymers
  - PLGA (poly-lactic-co-glycolide)
  - Acellularized tendon grafts
  - Collagen sponge

Tendon Stem / Progenitor cells

- Multipotent stem cells exist inherently in tendons and ligaments
- Rabbit and porcine research using bioscaffolds seeded with tenocyte or intrasynovial tendon cells suggests better tendon healing (1,2)
- In vitro studies demonstrate that platelet-rich plasma releasate promotes differentiation of tendon stem cells into active tenocytes (3)

Take home points

- Literature provides promising evidence with regard to the application and effectiveness of regenerative injection therapies in tendinopathy
- The ideal injectate, technique, scaffold and cell source for tissue engineering and tendon repair remains uncertain
- More research needed.
- Regulation must be considered

THANK YOU

Joanne Borg Stein, MD
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