

Nonsurgical options for Osteoarthritis and Tendinopathy

J. Keith Spain, MD, CAQSM

The Orthopaedic Group, PC

July 15, 2017



KSpain@theorthogrou

Disclosures

Financial disclosure: Consultant for Tenex Health

Off label use disclosure: Most biological and pharmacological treatments mentioned in this presentation are off label and/or not FDA-approved for the treatment of given condition...

Objectives

- Define our “problem” of tendinopathy & osteoarthritis
- Understand definitions & incidence of chronic tendinopathy & arthritis
- Discuss non-surgical treatment options for tendinopathy & osteoarthritis
- Discuss the current evidence for historical and current treatment options
- Discuss a potential treatment approach for tendinopathy & arthritis based on currently available treatment options & guidelines
- Discuss new nonsurgical treatment options for both tendinopathy & osteoarthritis

Tendinopathy Outline

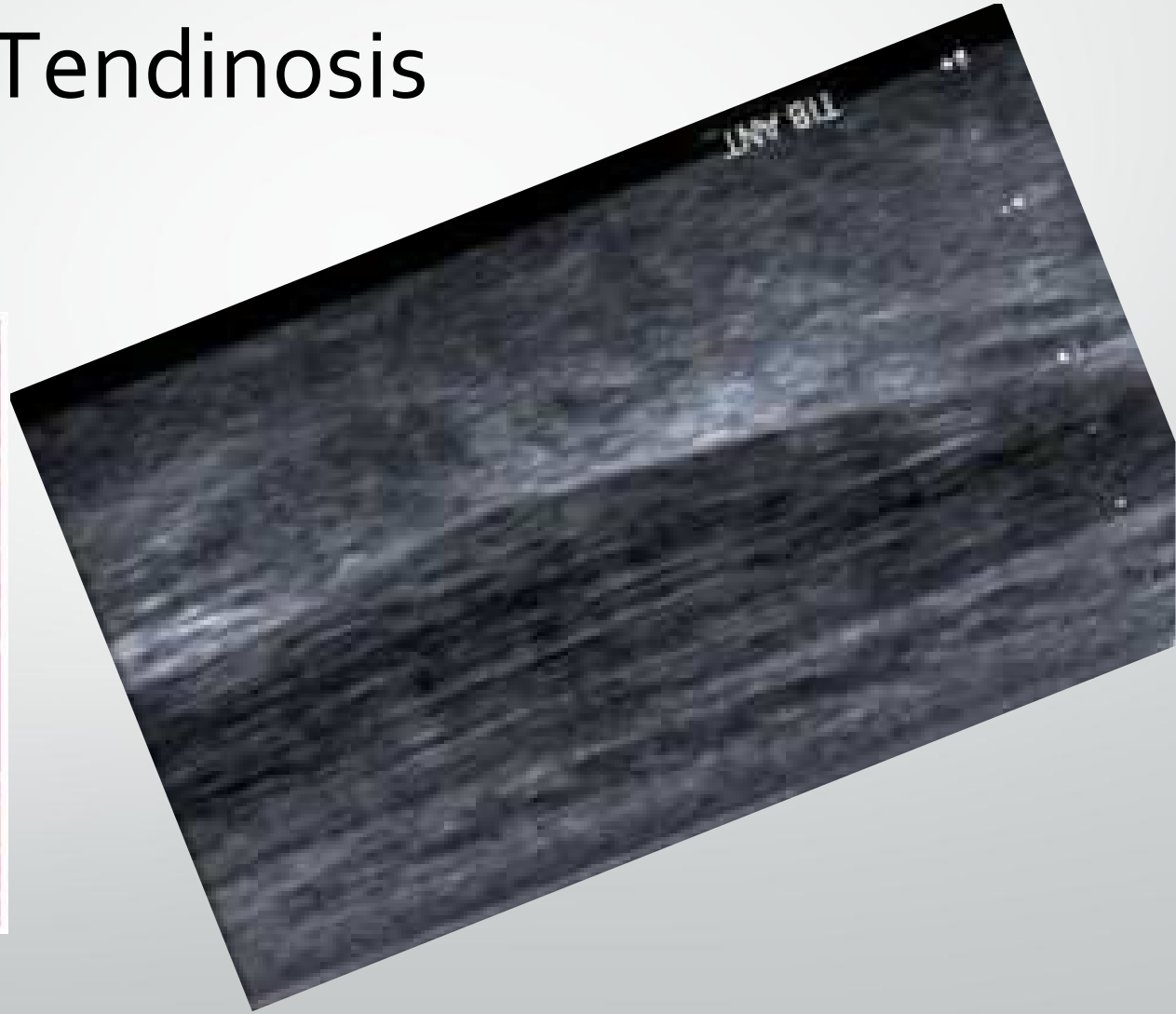
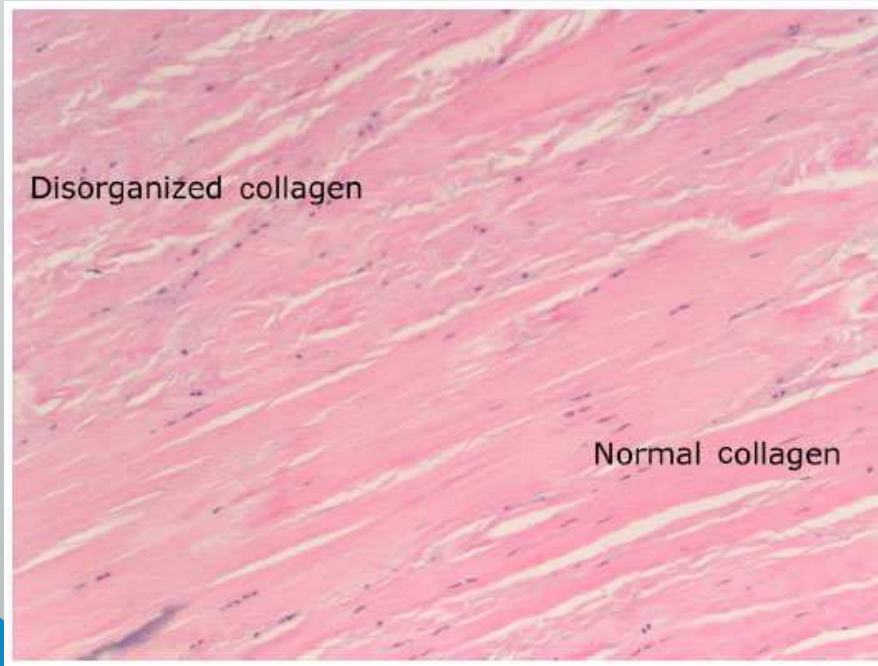
- Definition of tendinitis/tendinosis/tendinopathy
- Anatomy
- Epidemiology of elbow tendinopathy
- Historical treatments
 - Rest
 - Corticosteroids
 - Physical therapy
 - Counterforce bands
 - Surgery
- New Treatment options
 - Topicals
 - NSAIDs
 - Nitroglycerine
 - Injections
 - Prolotherapy
 - Platelet Rich Plasma
 - Autologous whole blood
 - Amniotic membrane
 - Mesenchymal stem cell
 - Ultrasound guided procedures
 - Tendon scraping
 - High volume image guided injections
 - Tenex

Tendinopathy

Tendinitis? Tendinosis?

- Tendinitis
 - INFLAMMATION of the tendon
 - Results from micro-tears that happen when the musculotendinous unit is acutely overloaded with a tensile force that is too heavy and/or too sudden.
 - Very common diagnosis, but research suggests often times “tendinitis” is usually tendinosis
- Tendinosis
 - A degeneration of the tendon’s collagen in response to chronic overuse
 - When overuse is continued without giving the tendon time to heal and rest (such as with repetitive strain injuries) tendinosis may result
 - Results in thickened, weakened, disorganized tendon fibers

Tendinosis



Epidemiology

Lateral Epicondylitis “Tennis Elbow”

- Annual prevalence: 1-2 % of the general population
- 40-50% of recreational tennis players will suffer w/ tennis elbow at some point
- High rates in occupational positions: politicians, municipal utility employees, nursery school cooks.
- Study at a meat processing factory
 - 11.3 % sausage makers; 7% in meat packers; 6.4 % meat cutters



Epidemiology

Medial Epicondylitis “Golfers Elbow”

- Lower incidence compared to lateral epicondylitis
- Repetitive wrist flexion activities
- “At Risk Patients” similar to those for lateral epicondylitis
 - 30-50 years old
 - Laborers
 - Smokers
 - Obesity



Historical Treatments

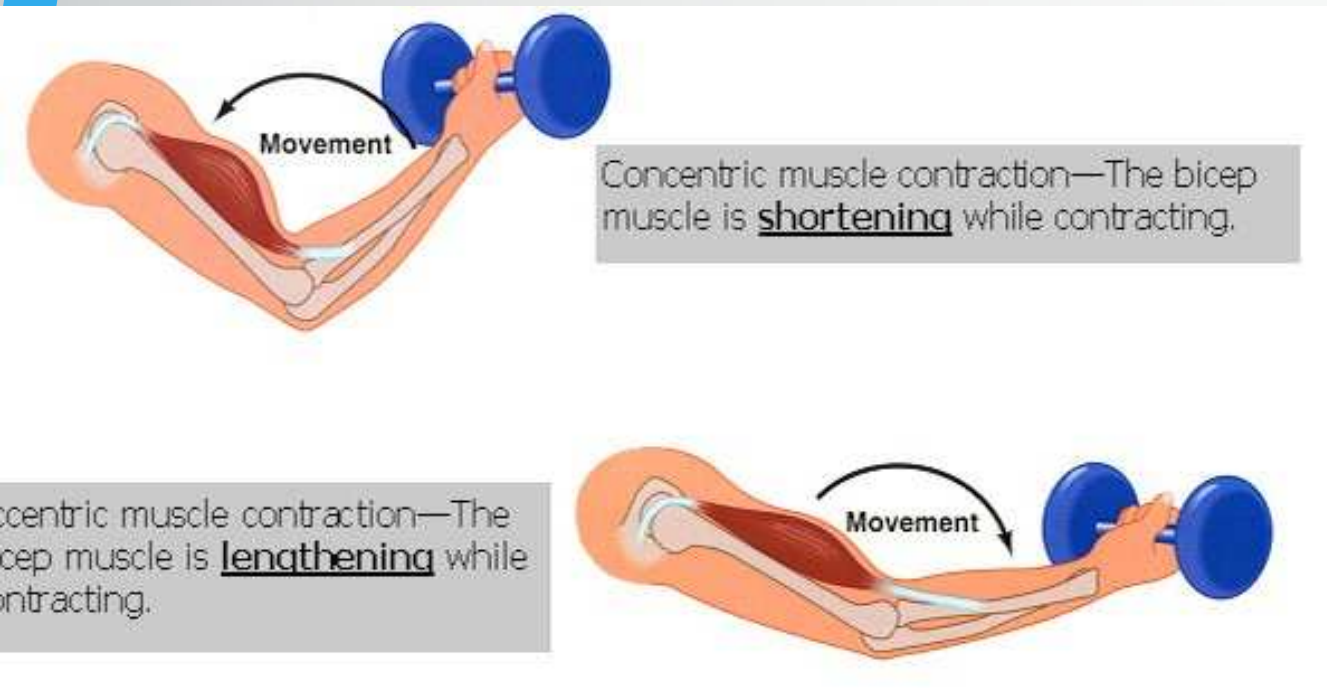
- Rest
- Corticosteroid injections
- Physical Therapy
- Counterforce Bands
- Surgery

Physical Therapy

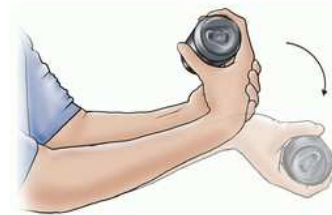
- Cross friction massage
- Electrical and thermal modalities
- Bracing
- Therapeutic exercise
 - Eccentric Exercise

Eccentric Strengthening

- Strength training, particularly eccentric-emphasis, has the best evidence supporting its use for tendinopathy of any treatment available
- Alfredson 1998, Gardin 2010, Kongsgaard 2009, Murtaugh 2013, Yu 2011



Lateral Epicondylitis (Tennis Elbow) Rehabilitation Exercises



Eccentric wrist flexion



Eccentric wrist extension



Wrist radial deviation

Counterforce Bands

Numerous studies comparing bracing to placebo

- Increased strength and decreased pain in short and long term with bracing
- Many studies inconclusive
- Few show harm



Corticosteroid Injections ⁽¹⁾

- In 3 trials that compared corticosteroid injections with no intervention
 - Corticosteroid injections **were effective in the short term** in pain reduction [standard mean difference (SMD), 1.44; 95% confidence interval (CI), 1.17-1.71], in improving function (SMD, 1.50; 95% CI, 1.22-1.77), and in overall improvement [relative risk (RR), 3.47; 95% CI, 2.11-5.69].
 - In the intermediate and long term, **corticosteroid injections were less effective than no intervention.**
- In comparison with placebo injection (4 studies),
 - **“there was limited evidence for the effectiveness of corticosteroid injection in relieving pain”.**
- In comparison with physiotherapy (4 studies)
 - Corticosteroid injection was **more effective in the short term** for improving function (SMD, 1.29; 95% CI, 1.03-1.55) and in overall improvement (RR, 2.37; 95% CI, 1.75-3.21), and there was strong evidence among heterogeneous studies for reducing pain.
 - **Intermediate and long-term results were worse in pain and function for the corticosteroid injection intervention.**
- Corticosteroid injections were more effective than orthotic devices for the wrist or elbow for overall improvement in the short term **but not in the long term** (2 studies).

“Cortisone shot” take home point

- Short term relief: likely
- Long term harm: likely
- Likely better off without it!
- Fortunately we have better options



Surgery

- Open vs arthroscopic debridement of the ECRB
- Studies promising
 - Baker did study reporting 95% success for arthroscopic Baker's procedure
- Open procedure for Epicondylitis
 - Nirschl procedure
- Variable downtime from 1.5 – 6 months with variable immobilization period

NEW TREATMENT OPTIONS

- Tonicals

- NSAIDs
- Glyceryl Trinitrate (Topical Nitroglycerin)

- Injections

- Prolotherapy
- Platelet Rich Plasma
- Autologous Whole Blood
- Amniotic Membrane Injections
- Mesenchymal Stem Cell

- Ultrasound Guided Procedures

- Tendon Scanning
- High Volume Image Guided Injection
- Percutaneous Needle Tenotomy
- Percutaneous Ultrasound Tenotomy (PENT)

NSAIDs

- A Cochrane review in 2013 looked at 17 comparisons of 759 participants and noted that “There remains **limited evidence** from which to draw firm conclusions about the benefits or harms of topical or oral NSAIDs in treating lateral elbow pain. Although data from five placebo-controlled **trials suggest that topical NSAIDs may be beneficial in improving pain** (for up to 4 weeks), non-normal distribution of data and other methodological issues **precluded firm conclusions**



Glyceryl Trinitrate

- Mechanism
 - Affects local Nitrous Oxide levels
 - Stimulates collagen synthesis in fibroblasts
 - Has proven to improve fracture healing in animal models



Topical Nitroglycerin

Does it work? ⁽⁴⁾

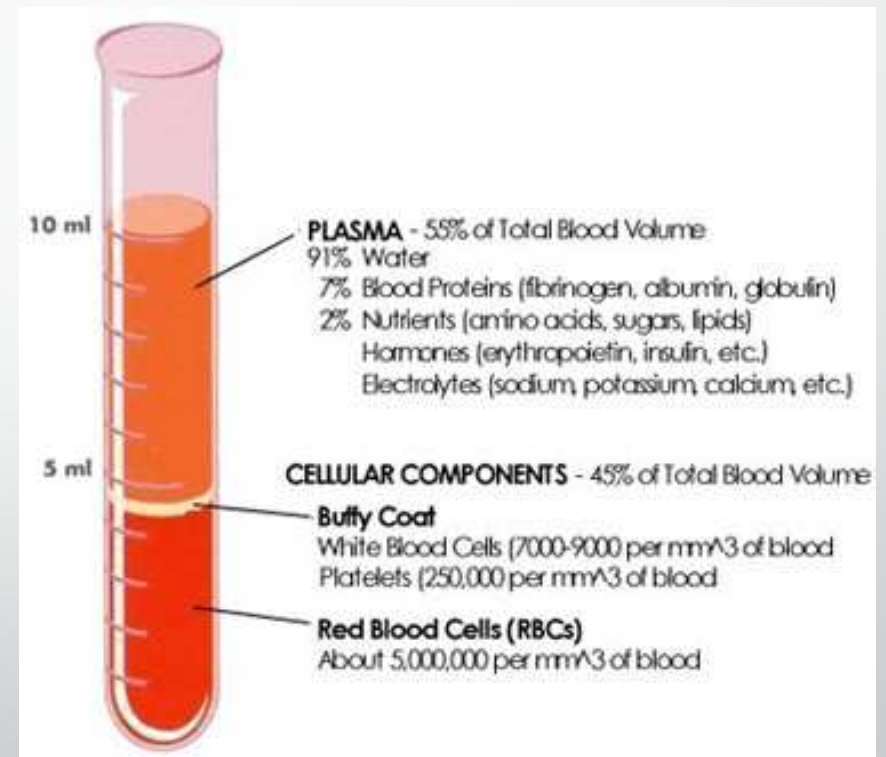
- STUDY: Eighty-six patients with extensor tendinosis
- Randomized into two equal groups; both were instructed to perform a standard tendon rehabilitation program.
 - One group received an active glyceryl trinitrate transdermal patch
 - The other group received a placebo patch.



- RESULTS: Patients in the glyceryl trinitrate group had:
 - Significantly reduced elbow pain with activity at 2 weeks
 - Reduced epicondylar tenderness at 6 and 12 weeks,
 - Increase in wrist extensor mean peak force and total work at 24 weeks.
 - At 6 months, 81% of treated patients were asymptomatic during activities of daily living, compared with 60% of patients who had tendon rehabilitation alone.

Platelet Rich Plasma

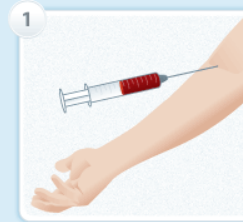
- PRP is an autologous **concentration of platelets** made from whole blood
- Platelet concentration variable
- White blood cell content variable



How does PRP Work

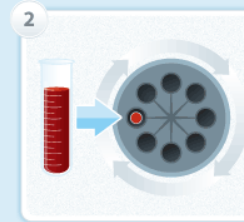
- Platelets deliver growth factors
- Increase fibroblast DNA synthesis
- Increase collagen production
- Provide matrix for migration of tissue forming cells
- Chemotactic factors
- Stimulate and regulate 3 phases of tissue healing
 - Inflammation → repair → remodeling
- Decrease blood flow
- Decrease infection

PROCESS OF PRP THERAPY



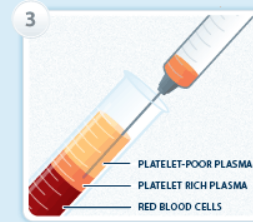
1 Collect blood

30-60ml of blood is drawn from the patient's arm.



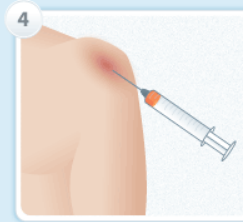
2 Separate the platelets

The blood is then placed in a centrifuge. The centrifuge spins and separates the platelets from the rest of the blood components.



3 Extract platelet-rich plasma

Extract 3-6ml of platelet-rich plasma.



4 Inject injured area with PRP

Using the concentrated platelets, we increase the growth factors up to eight times, which promotes temporary relief and stops inflammation.

DOES PRP WORK?

- Mishra and Pavelko evaluated 140 patients with elbow epicondylar pain ⁽⁵⁾
- Administered either a single percutaneous injection of platelet-rich plasma or bupivacaine (control group)
- 8 weeks after therapy
 - 60% pain improvement in the group who received the platelet-rich
 - 16% pain improvement in the control group.
- Raeisadat et al performed a randomized clinical trial involving 40 patients who had symptoms consistent with lateral epicondylitis for greater than 3 months. ⁽⁶⁾
- Comparing PRP with autologous blood.
- Both groups were given a counterforce brace and a home exercise program.
- At 4 weeks, Mayo and visual analogue scale (VAS) scores significantly improved in both the PRP and the autologous blood groups.
- However, only the PRP group demonstrated significant improvement at 8 weeks with respect to the VAS and Mayo scores

More PRP Studies...

- Mishra et al compared tendon needling with PRP in patients with chronic tennis elbow compared with an active control group (230 patients). (7)
- No significant differences were found at 12 weeks in this study
- However, at 24 weeks, clinically meaningful improvements were found in patients treated with leukocyte-enriched PRP compared with an active control group.
- Krogh et al compared a single injection of platelet-rich plasma (PRP) vs placebo (saline) with or without glucocorticoid in reducing pain in adults with lateral epicondylitis (LE) after 3 months. (8)
- The authors conclude that either injection of PRP or glucocorticoid was superior to saline with regard to pain reduction in LE at the primary endpoint at 3 months.
- Glucocorticoid had a short-term pain-reducing effect at 1 month in contrast to the other therapies.

PRP Bottom Line

- We need more studies, but it looks like it helps
- Low Risk
- Variability in technique may play a factor in success



Autologous Whole Blood Injections

- Mechanism
 - Similar to PRP but with more RBC & WBC → free radicals, proteolytic enzymes, etc
 - Studies not as promising
 - But...

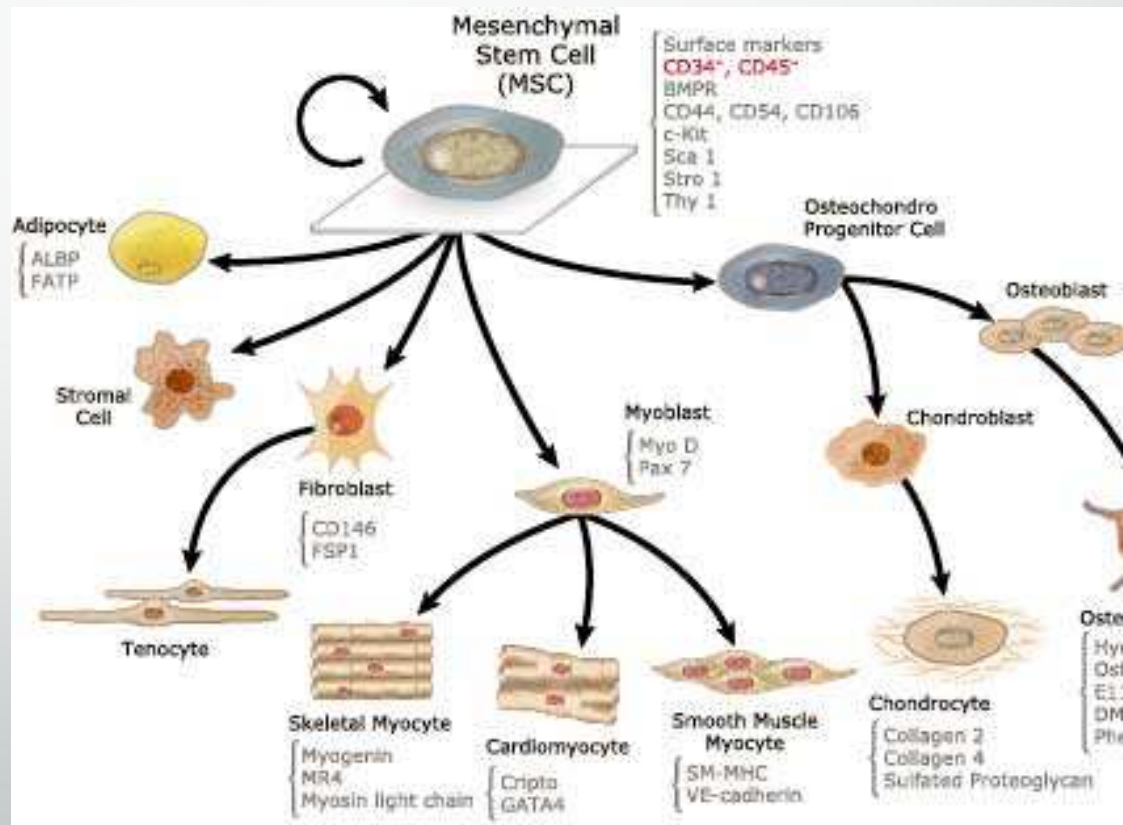


Platelet Rich Plasm VS Autologous Whole Blood ^(2,3)

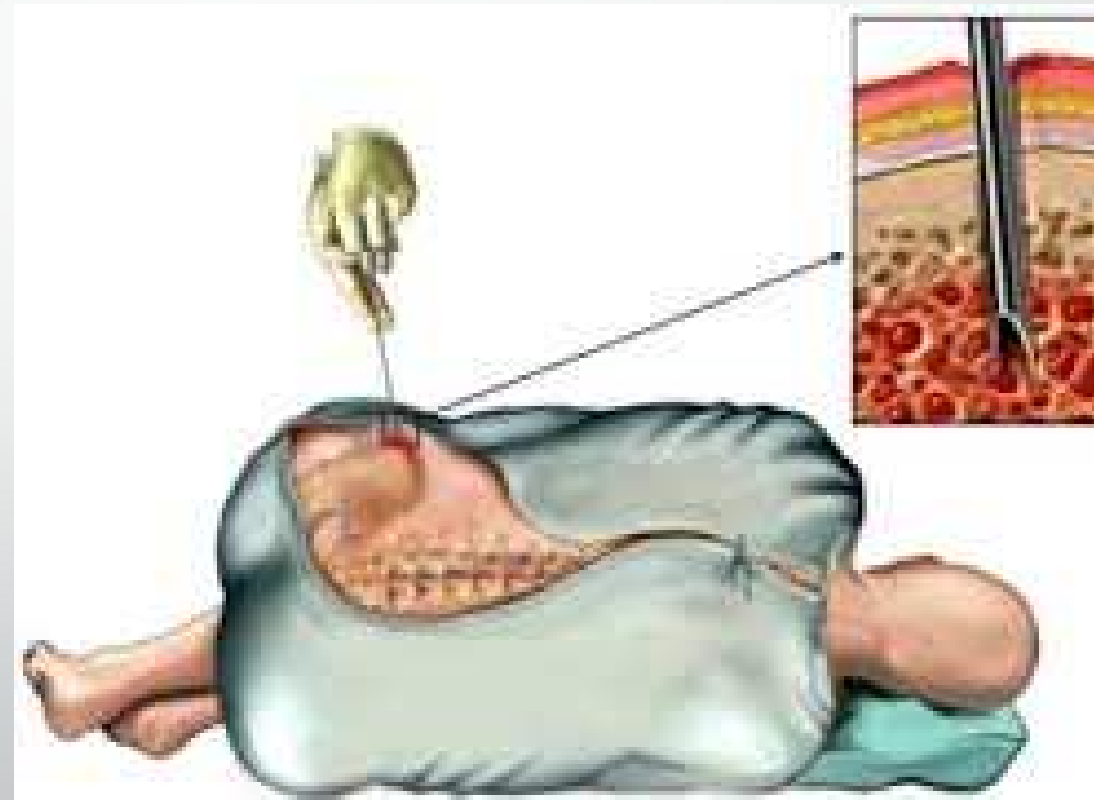
- 76 patients w/ lateral epicondylitis (tennis elbow) randomized to receive either 2mL of PRP (LR 4.8X baseline) vs 2mL AWB
- Compared at 0,4,8, weeks, and 6 and 12 months
- No difference → both showed improvement
- 28 patients with lateral epicondylitis randomized to receive single injection of 3mL autologous blood vs 3mL of PRP
- More improvement in the PRP group
 - Only statistically significant at 6 weeks point

Mesenchymal Stem Cell Injections

- Mechanism:
 - MSCs are multipotent stromal cells that can differentiate into a variety of cell types (including tenocytes)
 - Increases rate of healing



Mesenchymal Stem Cells



Prolotherapy

“you have to crack some eggs to make an omelette”

- Mechanism:
 - Dextrose-containing solution is hypertonic
 - Osmotic cell rupture
 - Phenol-glycerine-glucose
 - Local cellular irritation
 - Morrhuate Sodium
 - Chemotactic attraction of inflammatory mediators



Prolotherapy

Does it work?

- Zeisig et al looked at 32 patients w/ chronic lateral epicondylitis symptoms (9)
- Ultrasound-guided blinded injection of polidocanol or lidocaine plus epinephrine
- At 3 months, if they still had pain, they were offered another injection of polidocanol.
- At 3 and 12 months: a significant improvement in patient satisfaction and in VAS grip pain from baseline for both groups.
- However, there was no significant difference between the groups.



Amniotic Membrane Injection

- Use of human and bovine amniotic membrane first reported in orthopaedic use around 1927
- Wound healing
- Tendon repair
- Muscle repair



- Amniotic membrane
 - Contains collagen types I, III, IV, V, and VII.
 - Composed of structural extracellular matrix (ECM) that also contains specialized proteins fibronectin, laminins, proteoglycans and glycosaminoglycans.
 - Also contains essential, active, healing growth factors such as epidermal growth factor (EGF), transforming growth factor beta (TGF- β), fibroblast growth factor (FGF), and platelet derived growth factor (PDGF).

High Volume Image Guided Injection

- Mechanically disrupt neovessels / neoverves through injection of a high volume of fluid
 - Typically between tendon and associated fat pad
- Limited well controlled studies, but seems to be effective



Tendon Scraping

- Mechanically disrupt neo-vessels / neo-erves
- Typically at interface between a tendon and associated fat pad
- Studies have been done comparing percutaneous to open surgical scraping
 - Similar outcomes



“Non-surgical Surgical treatment”

**“If plan 'A'
didn't work
the alphabet
has 25 more
letters”**

jakejenkins
29 July 2013 3:12 pm



Percutaneous Ultrasound Tenotomy

- Similar to Percutaneous Needle Tenotomy, but additional benefit of removal of degenerative tissue
- Tenex



TENEX
HEALTH

Tenex FAST Procedure

- Ultrasound guided percutaneous needle tenotomy / fasciotomy
- Outpatient
- Local anesthetic
- <20 minutes
- Rapid recovery
- High success rate

Tenex FAST Procedure

- Treating the “source of the tendon pain”
 - Degenerative frayed tendon
- Remove the damaged tissue allowing the body to heal
- Minimal downtime – quick return to ADLs
- Quick return to sport
 - 6 weeks typical

Tendinopathy Summary

- Tendinopathy is a common problem with a complex etiology and many treatment options
- There is no one size fits all treatment plan
- Start conservative and progress as necessary
- Correct the underlying etiology
- Corticosteroids are not a “magic bullet”
- There are minimally invasive highly effective treatment options even for chronic tendinopathy

Treatment Approach

- Stage 1

- Activity Modification
- Training program eval & modification
- Technique eval & modification
- Equipment / gear eval & modification
- Physical Therapy – eccentric strengthening program

- Stage 2

- Topicals (Nitrates)
- Maybe FSWT

- Stage 3

- Injections
 - PRP, Amniotic Membrane, AWB
 - Mesencymal Stem Cell (\$\$\$)
- Procedures
 - Tendon Scraping + HVIGI
 - Tenotomy (percutaneous vs ultrasound)
 - Surgery

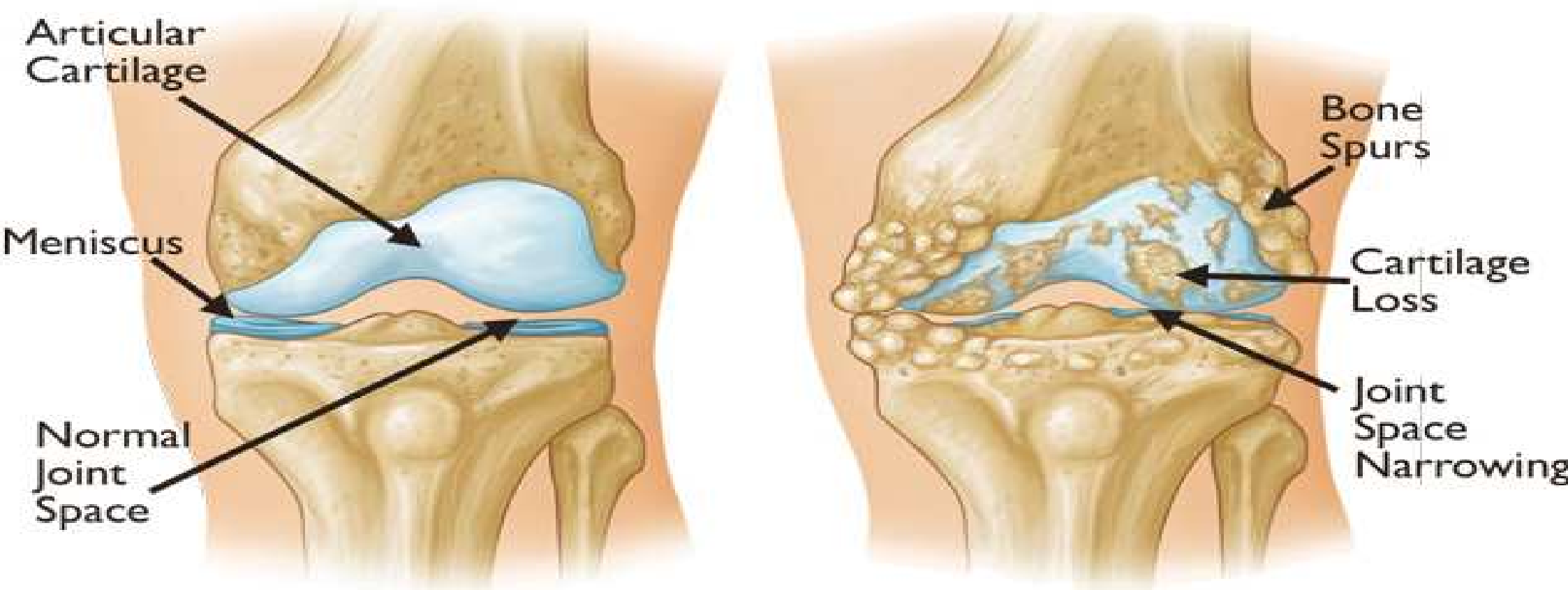


Osteoarthritis

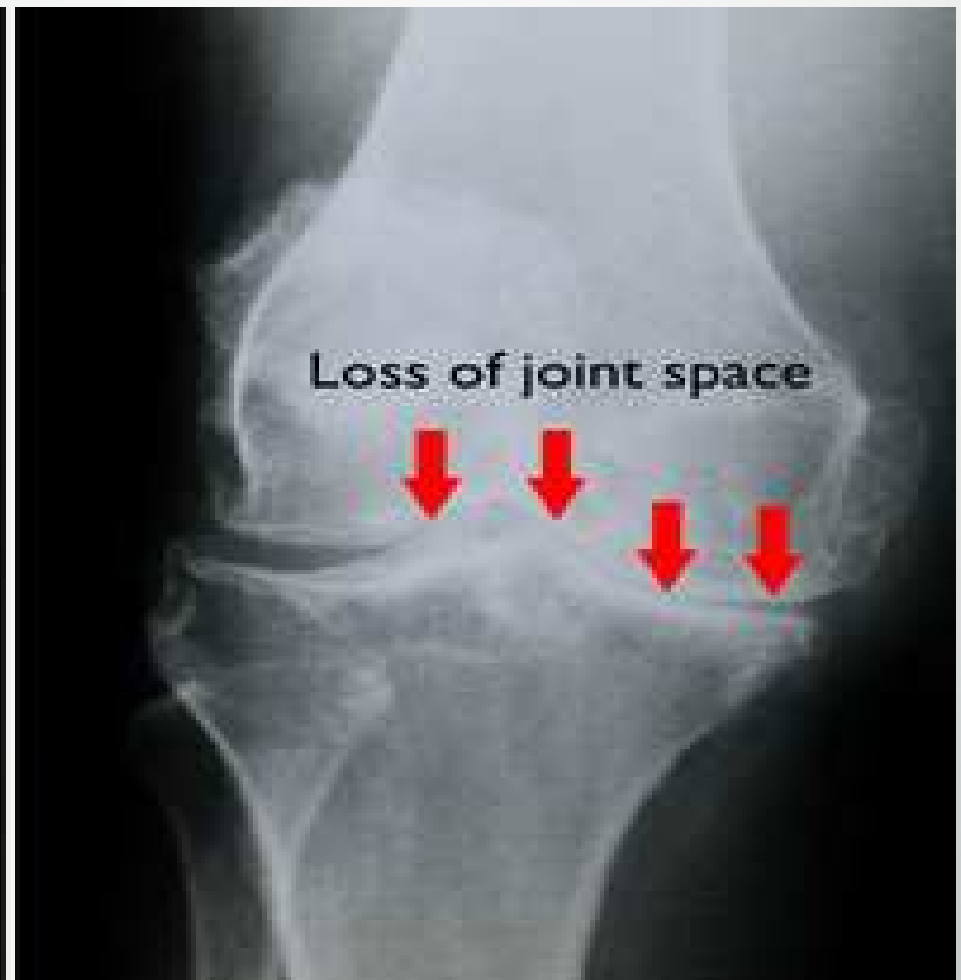
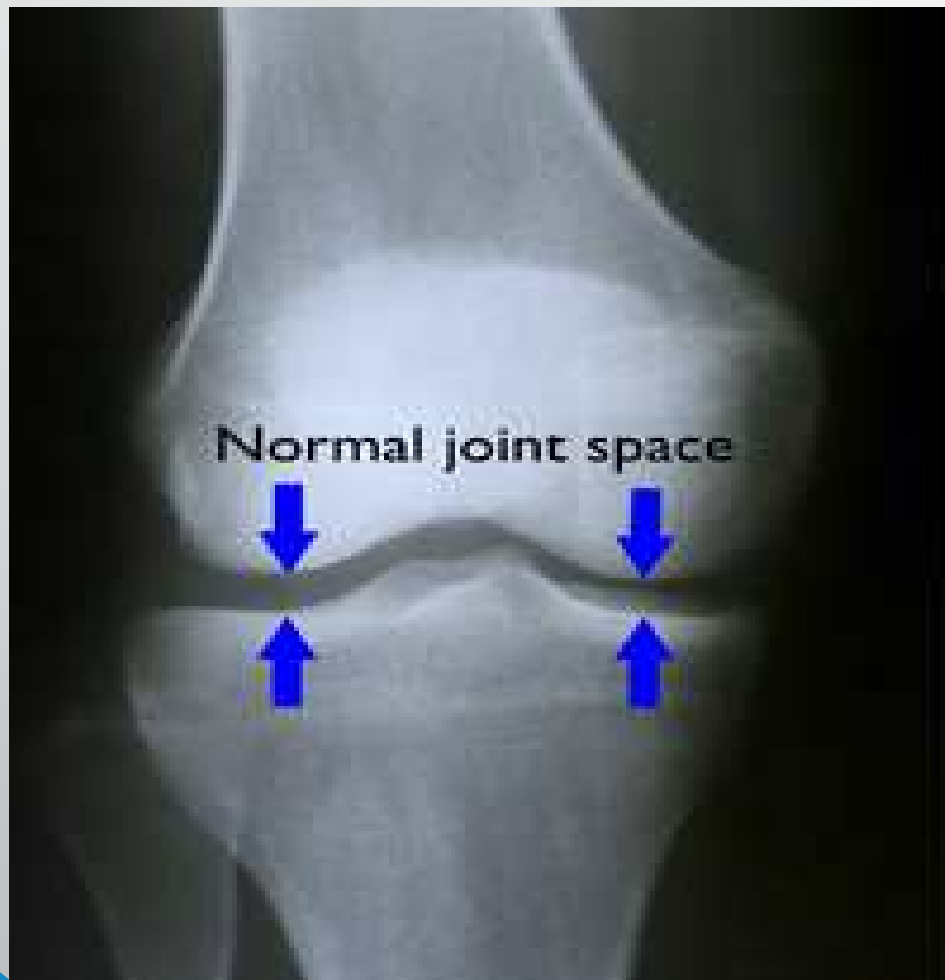
Osteoarthritis

- Osteoarthritis: Wear and tear or trauma causing thinning and ultimately loss of cartilage in a joint, resulting in pain, swelling, and loss of function
- Rheumatoid arthritis: An auto-immune disease causing joint pain, swelling, and loss of function

Osteoarthritic Knee X-Ray



X-ray Findings in Osteoarthritis



Statistics

- OA affects 27 million Americans
- OA accounts for 25% of visits to primary care physicians
- 80% of us will have x-ray evidence of OA by age 60
 - But only 60% of us will feel pain
- >600,000 knee replacement surgeries are performed every year in the US

Nonsurgical Options for Knee OA: Exercise

- Keep Moving!
- Weight loss: Losing 1 lb. equates to 2 lb. decrease in force through the knee joint when walking, 4 lb. decrease in force when running
- Strength: Optimizing leg/core muscles helps to support the joint

Nonsurgical Options for Knee OA: Exercise

- Flexibility: A normal range of motion will reduce stiffness and prolong the lifespan of your cartilage
- Non-ballistic exercise is best:
 - Walking & cycling >> hiking, running, tennis



Nonsurgical Options for Knee OA: Medications

- Glucosamine/Chondroitin: Insufficient definitive evidence
- Tylenol: Underappreciated
- NSAIDs: Motrin/Advil/Aleve/Celebrex/Mobic, etc: Short term effect, many known and dangerous side effects
- Curcumin/Turmeric/etc: Insufficient evidence



Nonsurgical Options for Knee OA: Bracing

- Simple compression sleeve often helpful
- No evidence that copper braces are better
- Unloader Brace: Proven benefit when the OA is confined to one side of the joint



Nonsurgical Options for Knee OA: Steroid Injections

- Helpful for short-term relief
- Benefit wanes over time
- Ultimately is harmful to the cartilage cells
- Side effects: elevated blood sugar, fat atrophy, low infectious risk
- My take: Use them sparingly when in severe pain, need temporary relief, pre-vacation, etc...
- Max use is 3-4 per year

Nonsurgical Options for Knee OA: Viscosupplement Injections

- Better than steroids: Not a chemical
- Examples: Synvisc, Orthovisc, Suparz, Euflexxa, Hyalgan, Gel-one, etc...
- Large molecule protein that is nutritious and supportive for the joint
- Covered by most insurance including Medicare
 - State dependent
- Less effective in severe OA

Painful (& not effective) if not accurately injected

Ultrasound is key

Knee Replacement

- >600,000 performed yearly in US
- With projected growth of 673% per year, forecast is for 3.4 million surgeries in 2030
- Overnight hospital stay in almost every case, average length 3.4 days
- Cost, complication rate, and hospital stay go up if both knees are replaced
- 90-95% of replacements will last 10 years, 80-85% of replacements will last 20 years

Knee Replacement Statistics

(www.healthline.com)

- Cost: Average US knee replacement \$57,000 (pre-insurance)
- Outpatient costs not included: physical therapy average \$2600 (pre-insurance)
- Complications:
 - Mortality rate 0.25%
 - Infection rate 2% at 90 days
 - Others: blood clot/component failure/allergy/anesthesia complication/nerve injury/wound complication/etc....
- Significant pain and discomfort ~ 3-6 weeks

Sakellariou et al, Orthopedics 2016

- More than 1/3 of patients reported persistent pain for more than one year after knee replacement surgery
- Risk Factors: Female sex, diabetes, operative time, etc...

Nonsurgical Options for Knee OA: What is left?

- Typical orthopedic surgery management will offer all non-operative treatment options and then move to a knee replacement
 - “Come back when you can’t handle the pain anymore”
 - “you will know when it is time”
- What if the patient doesn’t want that?
- What if the patient cannot have surgery?
- Is there something else that can be done?

Nonsurgical Options for Knee OA: Autologous Stem Cell Injections

- Autologous=Your own cells
- Stem cells regenerate tissue
- Safe: No risk of rejection, minimal risk of infection (same as any other injection, 1:20,000)
- Effective: Case series reports
 - Ongoing studies

Clinical Outcome of Bone Marrow Concentrate in Knee Osteoarthritis

Kristin S. Oliver, MD, Matthew Bayes, MD, David Crane, MD, Chakrapani Pathikonda

ABSTRACT

Background: Knee osteoarthritis is an increasing health concern in the adult population. Nonsurgical treatment options for pain reduction and function improvement are limited in number and provide only short-term relief. The potential of regenerative therapies to go beyond temporary symptom reduction and delay or negate the need for total knee joint arthroplasty is enticing to both patients and providers.

Purpose: This study evaluated the clinical efficacy of autologous intra-articular bone marrow concentrate with autologous lipoaspirate as a treatment option for osteoarthritis of the knee. Additionally, bone marrow concentrate samples from a patient population subset not necessarily enrolled in this study, but IRB approved, were sent for outside laboratory analysis.

Study design: This study is a prospective case series.

Methods: Treatment registry data for 70 patients diagnosed with Kellgren-Lawrence Stage 2–4 knee osteoarthritis were analyzed. Data regarding adverse events and Knee Injury and Osteoarthritis Outcome Score metrics were obtained at baseline, 90 days, and 180 days. Samples of bone marrow concentrate from 11 patients were sent to an outside source for laboratory analysis.

Results: Adverse events were limited to transient pain and swelling of the treated joint. The mean reported KOOS changes from pre-procedure to 180 days post-procedure were as follows: Pain +18.1, Activities of Daily Living +15.6, Symptoms +17.3, Quality of Life +20.3, and Sports/Recreation +18.1. Laboratory analysis of the samples demonstrated statistically significant increases in concentration of platelets, interleukin-1 receptor antagonist and IL-1 β . The IL-1 α /IL-1 β ratio was also statistically significant at 193.54 when processed with a 2% Hct setting, and 720.62 when processed with a 15% Hct.

Conclusions: This study of intra-articular injection of autologous bone marrow concentrate and lipoaspirate in patients diagnosed with knee osteoarthritis demonstrates encouraging results for positive outcomes without complication. Further study with randomized controlled trials is warranted to prove the potential of this intervention. With laboratory analysis of samples of bone marrow concentrate we were able to identify the presence of statistically significant increases in the concentration of platelets and IL-1 α .

What is known about the subject: Bone marrow concentrate is known to contain a host of growth factors and stem cells and has been shown in animal studies to promote the regeneration of cartilage.^{22,46} There are two clinical studies published showing the efficacy of bone marrow concentrate in patients with knee osteoarthritis.^{12,22}

What this study adds to the existing knowledge: This study supports the findings of the two published clinical studies of bone marrow concentrate on patients with knee osteoarthritis. This alternative treatment option provides positive patients outcomes with low risk.

Journal of Prolotherapy. 2015;7:e937-e946.

KEYWORDS: Bone marrow concentrate, platelet-rich plasma, interleukin-1 receptor antagonist protein, knee osteoarthritis.

Introduction

Osteoarthritis is the most common cause of musculoskeletal pain and disability in the knee joint. Symptomatic knee OA occurs in 10% of men and 13% of women aged 60 or older.⁵⁷ In the third National Health and Nutrition Examination Survey approximately 37% of participants aged 60 or older had radiographic evidence of knee osteoarthritis.⁵⁸ By 2030, the demand for primary total knee arthroplasties is projected to grow by 673% to 3.48 million procedures.⁵⁵ The economic impact of knee OA is becoming an increasing concern. Estimated costs due to hospital expenditures of total knee joint replacements were \$28.5 billion in 2009 and are expected to continue to rapidly rise with our aging “baby-boomer” population.³⁹

Current nonsurgical treatment options for knee OA focus on short-term relief of symptoms. These interventions include physical therapy, activity modification, bracing, oral medications, and intra-articular use of steroids.

What is a stem cell?

- Stem cells are multipotent: Can grow new tissue
- This is how the body heals any injury
- We can use our own stem cells which are stored in our bone marrow and adipose tissue
- Easy to get: Simple outpatient procedure to obtain the cells, concentrate them in a centrifuge, and inject them into the joint

Stem Cells

- Have ability to self-renew
- Can continue to divide for a length of time
- Can be induced to differentiate into specialized cells with distinct functional characteristics (phenotypes)
 - Bone, cartilage, nerve, fat, connective tissue, cardiac, and liver cells

Stem Cells: Why do they work?

- We treat all of the sources of pain in and near the joint: nerve, soft tissue/capsule, tendon
- Known to decrease inflammation and increase anti-inflammatory effect
- Known to decrease nerve pain
- Known to increase HGH and testosterone within the joint: helps to improve healing
- Known to grow new cartilage in several studies

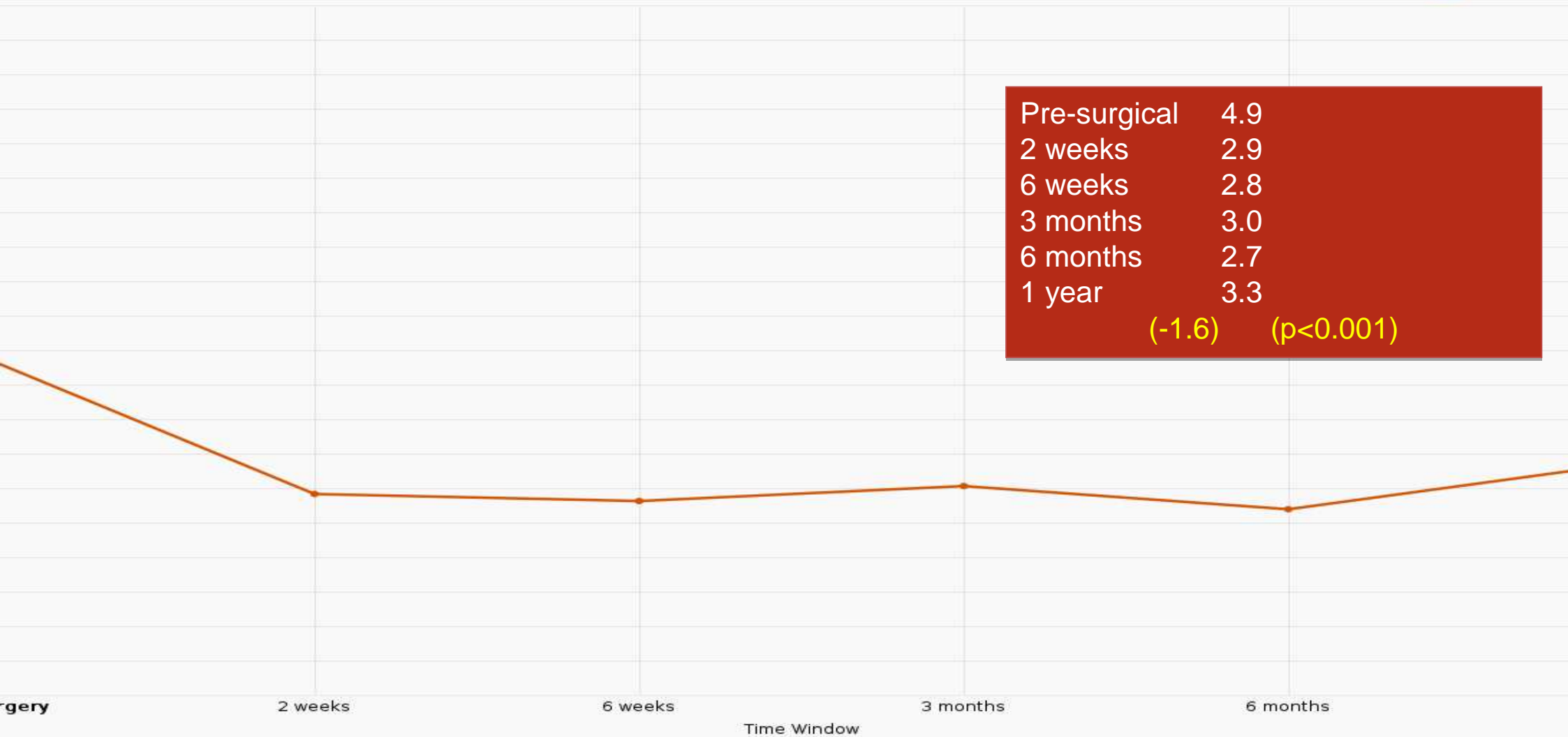
Stem Cells:

Is this too good to be true?

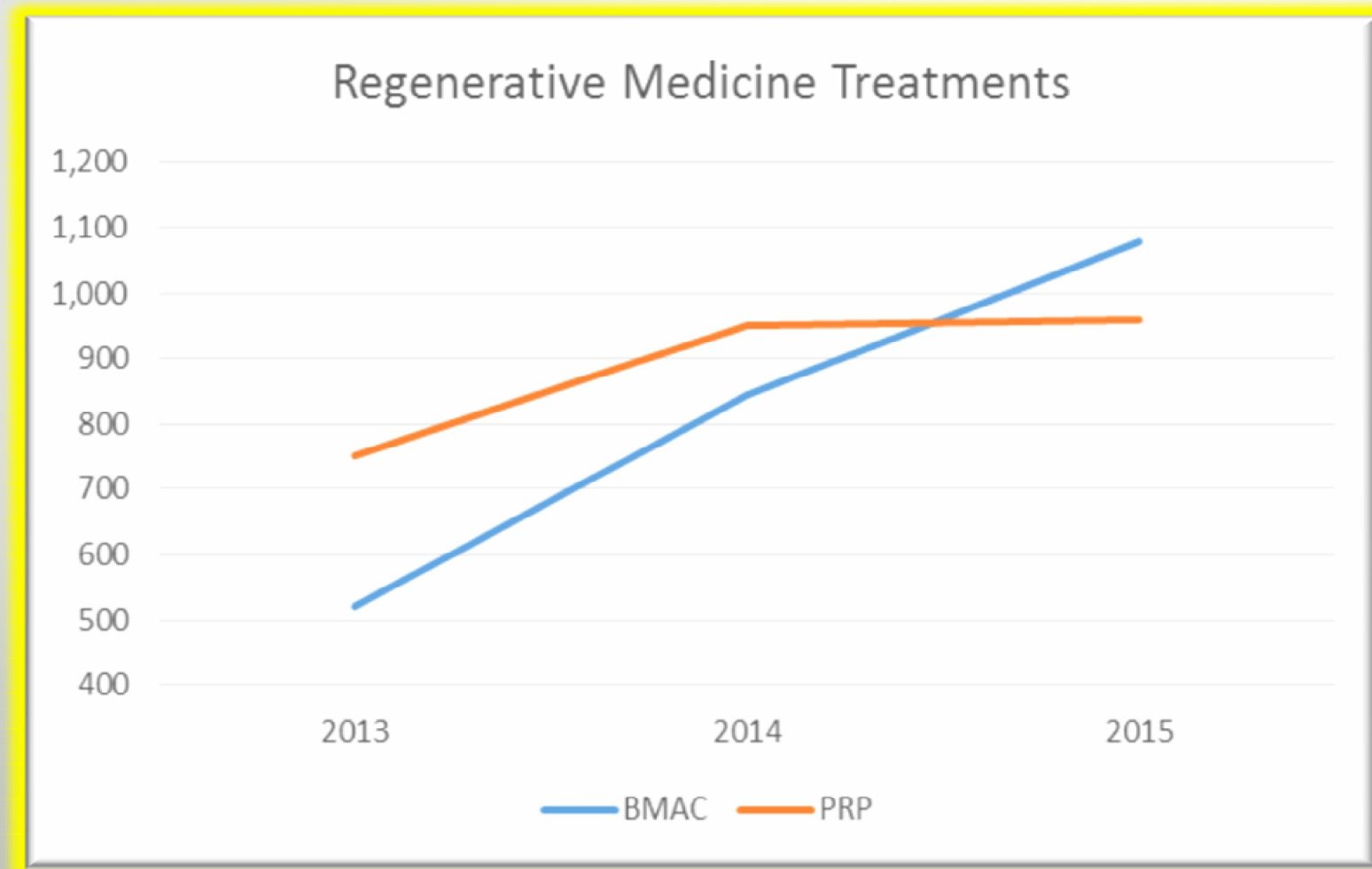
- Not necessarily
- Over 10 years of data being collected
- Case series supports: Pain relief can begin in 2 weeks, continues for many months
- More than one treatment may be needed
- Overall failure rate ~ 10%
- Risk: Age > 85, poorly controlled diabetes/heart failure, smoking, severity of OA

Stem Cells: Pain Scores over 1 year

Dr Oliver BMA



BlueTail Regenerative Treatment Data 2013-15



Bluetail Medical Group Biologics volume, 2013-2015 (projected)

Stem Cells and Knee OA: Initial Visit

- Physical Exam
- Weight bearing 4 view x-rays
- MSK Ultrasound: Defines soft tissue
- Review of all treatment options, including knee replacement or other surgery

Stem Cells and Knee OA: Treatment Day

- Treatment time avg 90-120 min
- Walk in, walk out
- Valium given if needed
- All injection sites are anesthetized using lidocaine to minimize pain, and ultrasound guided
- Typical response: It hurts more to inject the knee than to take the bone marrow &/or fat



Stem Cell Post-Care

- Post-injection pain
 - 3-7 days of increased pain
- Home Exercises
 - Primarily range of motion
- Physical Therapy
 - Begin at 2 weeks
- Resumption of activity
 - Once pain is back to normal



Post Procedure

- Ice
 - 15 min every 2-3 hours
 - What about anti-inflammatory effects?
 - Purist: No ice
 - Realist: Ice
- Analgesics
 - No NSAID's
 - Pain tolerance is unique
 - Narcotics vs acetaminophen
 - Start early and stay on top

