

Care of the Elite Athlete: *The Bio-Psycho-Social Model*

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14 August 2016

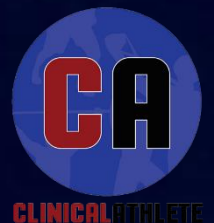
MAHEC Primary Care Sports Medicine Fellowship Director

Strength and Performance Summit



CLINICALATHLETE

Disclosures



Objectives

- ⌘ Focus your therapies
 - ⌘ Understand the underlying process, treat accordingly
- ⌘ Corticosteroids are not Evil
- ⌘ There are other options than stopping what you're doing

Elite



Olympic Athlete

Elite (cont)

⌘ What does it take to be elite?

⌘ Ericsson 3 Stages of Expert

⌘ Start at an early age

⌘ Specialize and increase participation

⌘ Dedicate full-time commitment

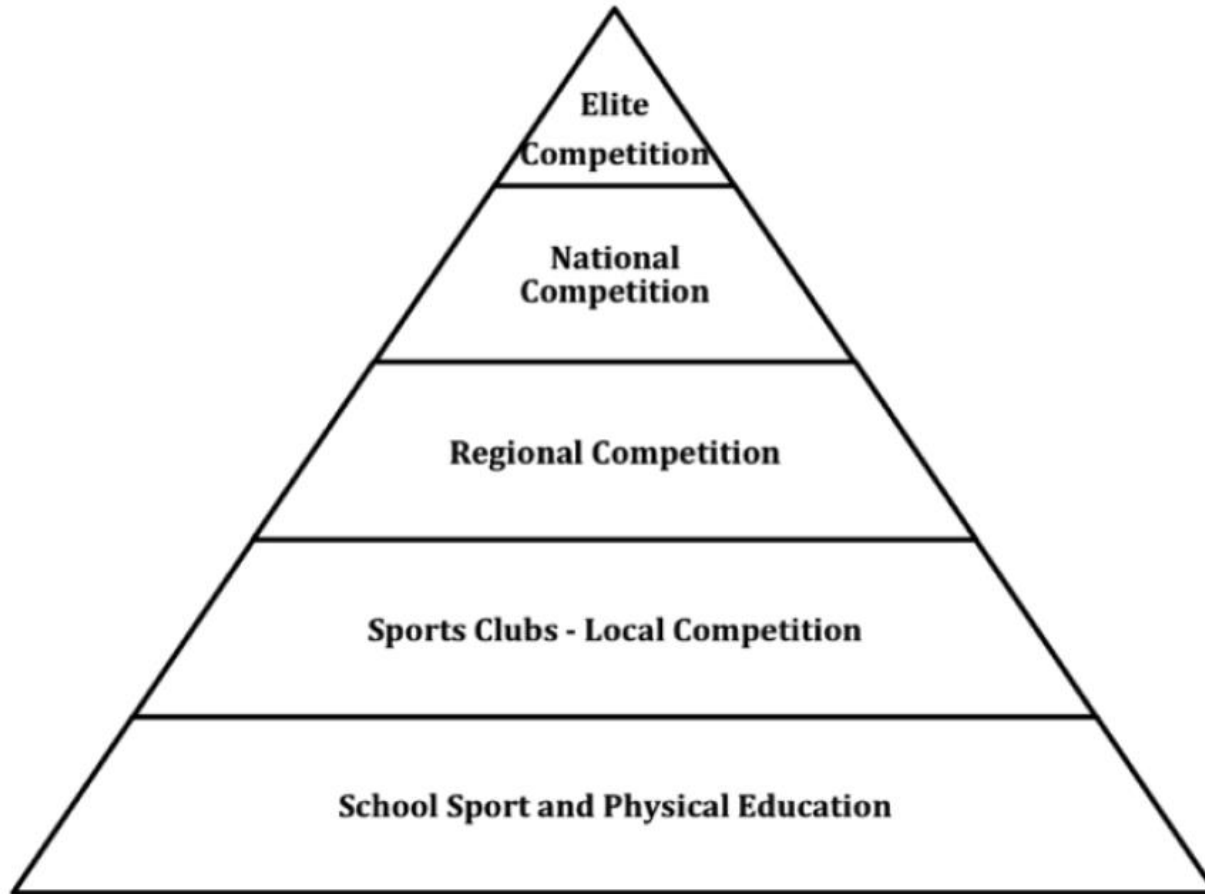
⌘ 10 Years/10k hour rule



Elite (cont)

Student-Athletes	Men's Basketball	Women's Basketball	Football	Baseball	Men's Ice Hockey	Men's Soccer
High School Student-Athletes	538,676	433,120	1,086,627	474,791	35,198	410,982
High School Senior Student-Athletes	153,907	123,749	310,465	135,655	10,057	117,423
NCAA Student-Athletes	17,984	16,186	70,147	32,450	3,964	23,365
NCAA Freshman Roster Positions	5,138	4,625	20,042	9,271	1,133	6,676
NCAA Senior Student-Athletes	3,996	3,597	15,588	7,211	881	5,192
NCAA Student-Athletes Drafted	46	32	254	678	7	101
Percent High School to NCAA	3.3%	3.7%	6.5%	6.8%	11.3%	5.7%
Percent NCAA to Professional	1.2%	0.9%	1.6%	9.4%	0.8%	1.9%
Percent High School to Professional	0.03%	0.03%	0.08%	0.50%	0.07%	0.09%

Elite (cont)



Elite (cont)

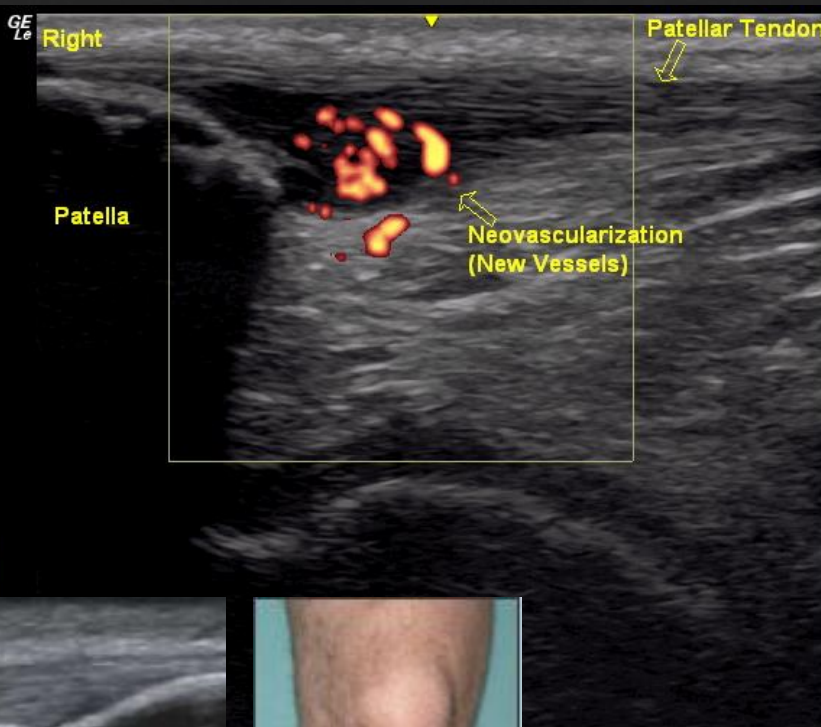
↳ Benefits of Specialization

- ⌘ Self-determination, commitment and motivation (psychosocial development)
- ⌘ Exploration of physical abilities (physical development & motor skills)
- ⌘ Engagement in “play”
- ⌘ Improving adult habits

↳ Risks

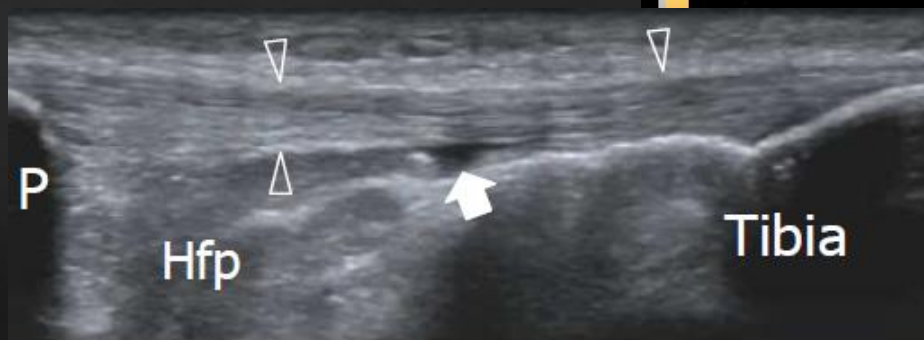
- ⌘ Sports-related injury
- ⌘ Disordered eating
- ⌘ Psychologic stress (low self-confidence/esteem)
- ⌘ Burnout

Case Presentation



- B CHI
Frq 10.0 MHz
Gn 56
E/A 3/2
Map H/0
D 3.5 cm
DR 90
FR 8 Hz
1- AO 100 %
XBea m On
BStr + Off

CF
Frq 8.0 MHz
Gn 11
2- L/A 2/2
AO 100 %
PRF 0.6 kHz
WF 67 Hz
S/P 2/16



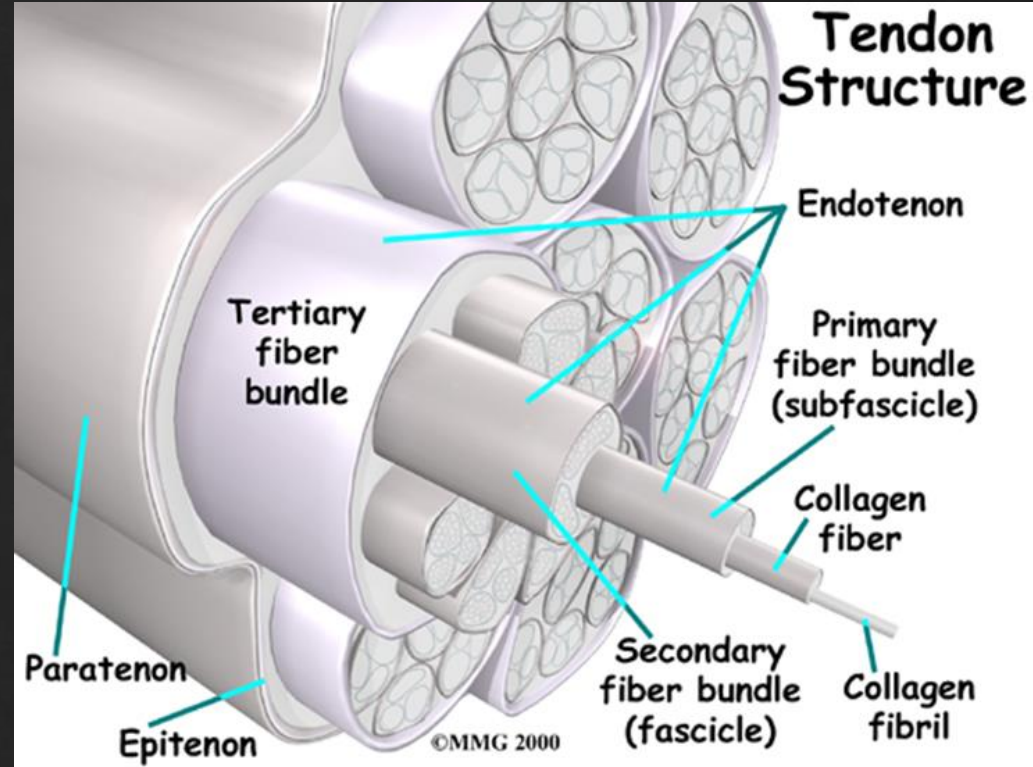
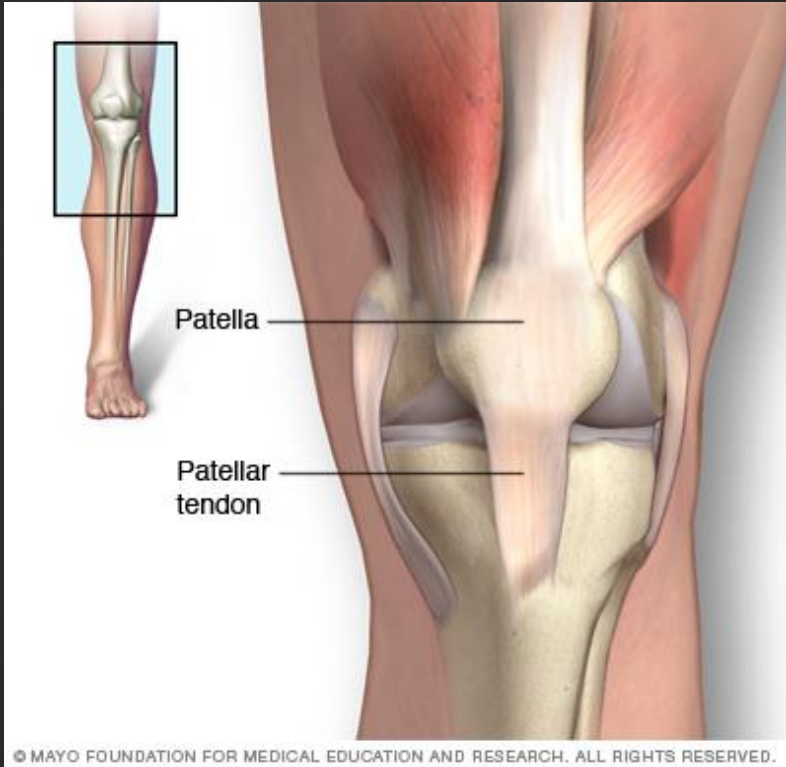
Legend: arrowheads, patellar tendon; arrow, deep infrapatellar bursa; Hfp, Hoffa fat pad; P, patella

Case Presentation (cont)

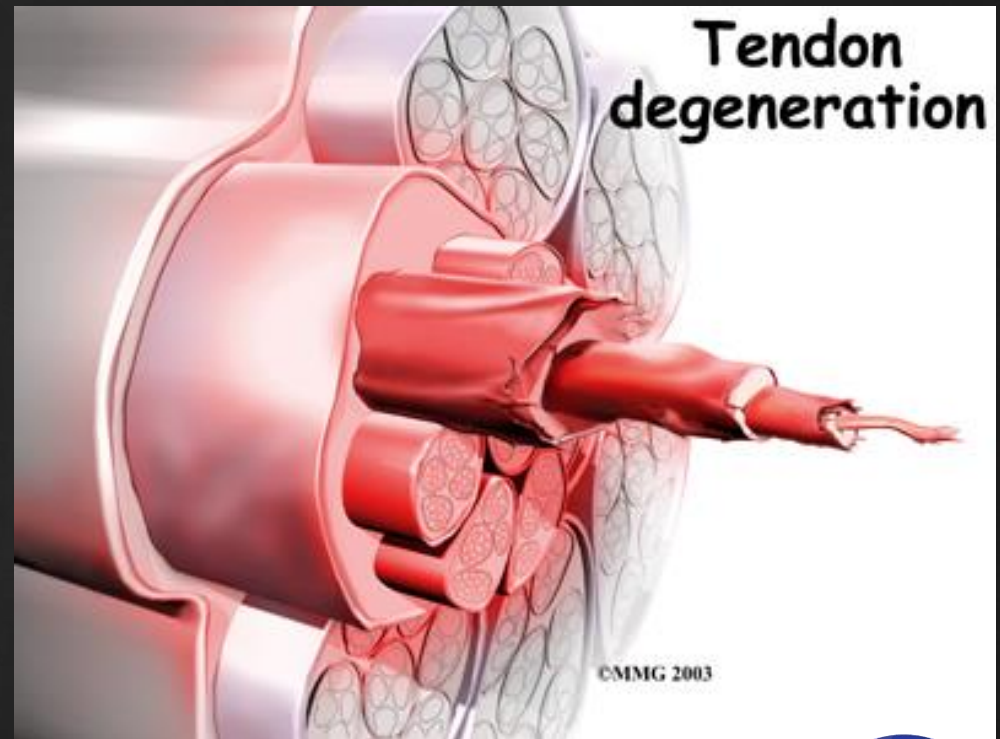
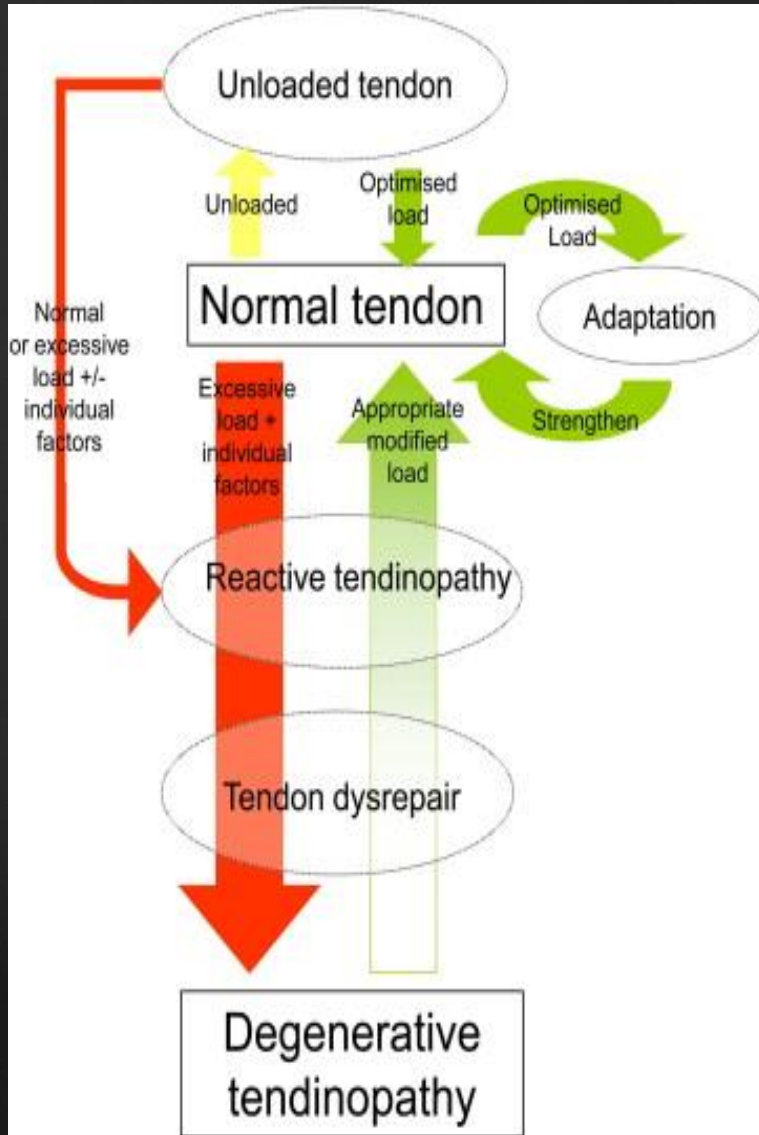
↳ Treatment:

- ∅ Corticosteroid; Oral vs Injectable
- ∅ NSAIDs; Oral vs Topical
- ∅ Eccentric Strengthening
- ∅ Ice/Heat
- ∅ Compression/KT taping
- ∅ Dry Needling vs Tendon Fenestration
- ∅ Biologic Therapies: PRP, Prolotherapy, Stem Cells
- ∅ Testosterone
- ∅ Nitroglycerin
- ∅ Viscosupplementation
- ∅ Tenex
- ∅ Surgery
- ∅ Narcotics
- ∅ Kitchen Sink

Injury/Pathology

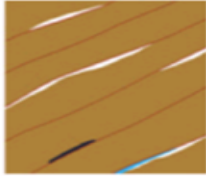
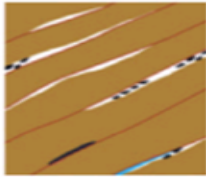
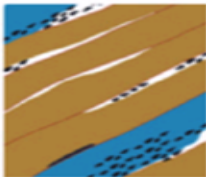
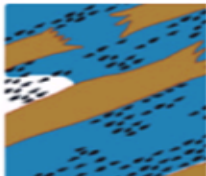



Injury/Pathology (cont)

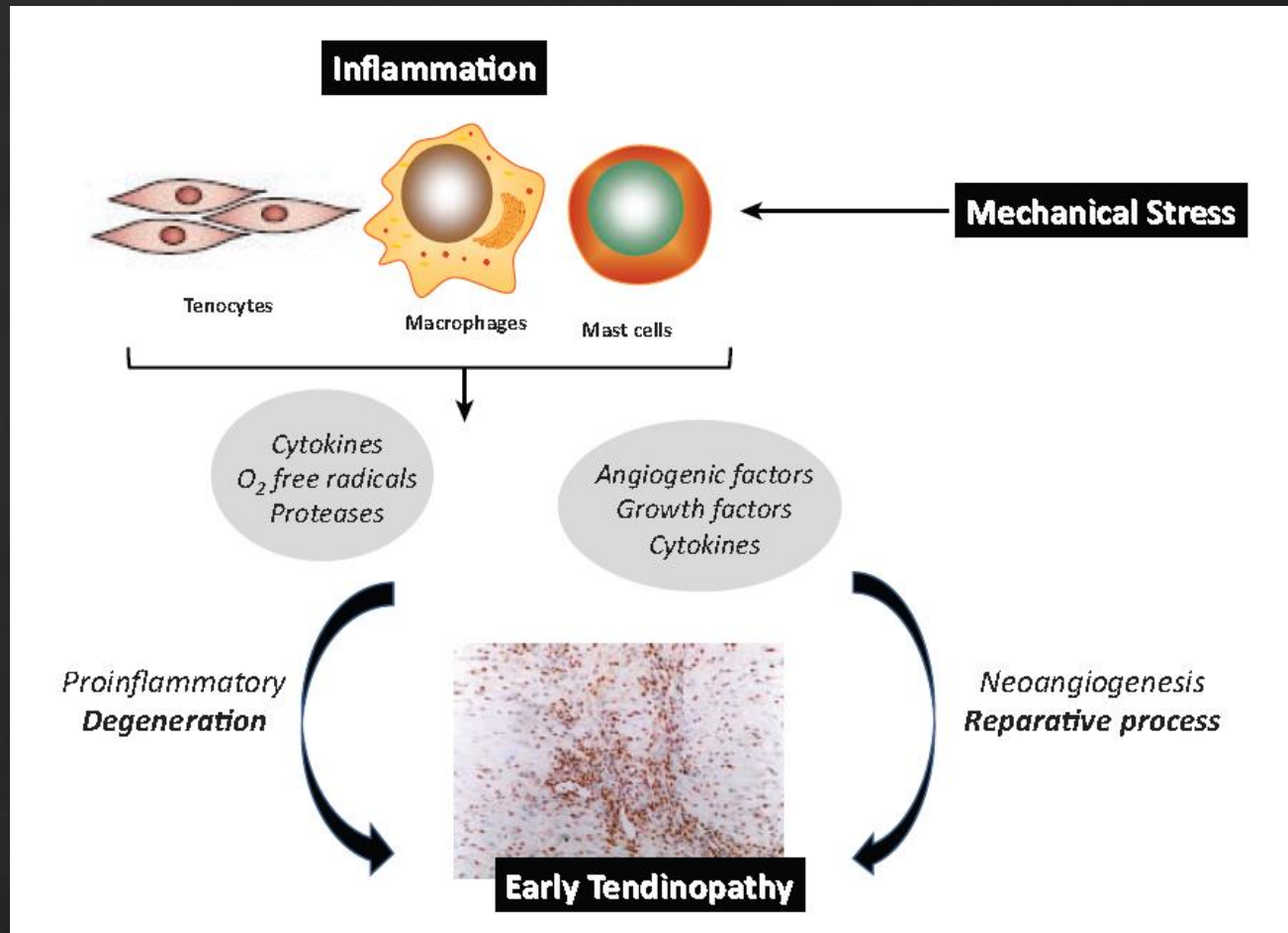


Injury/Pathology (cont)

Summary of tendinosis pathology

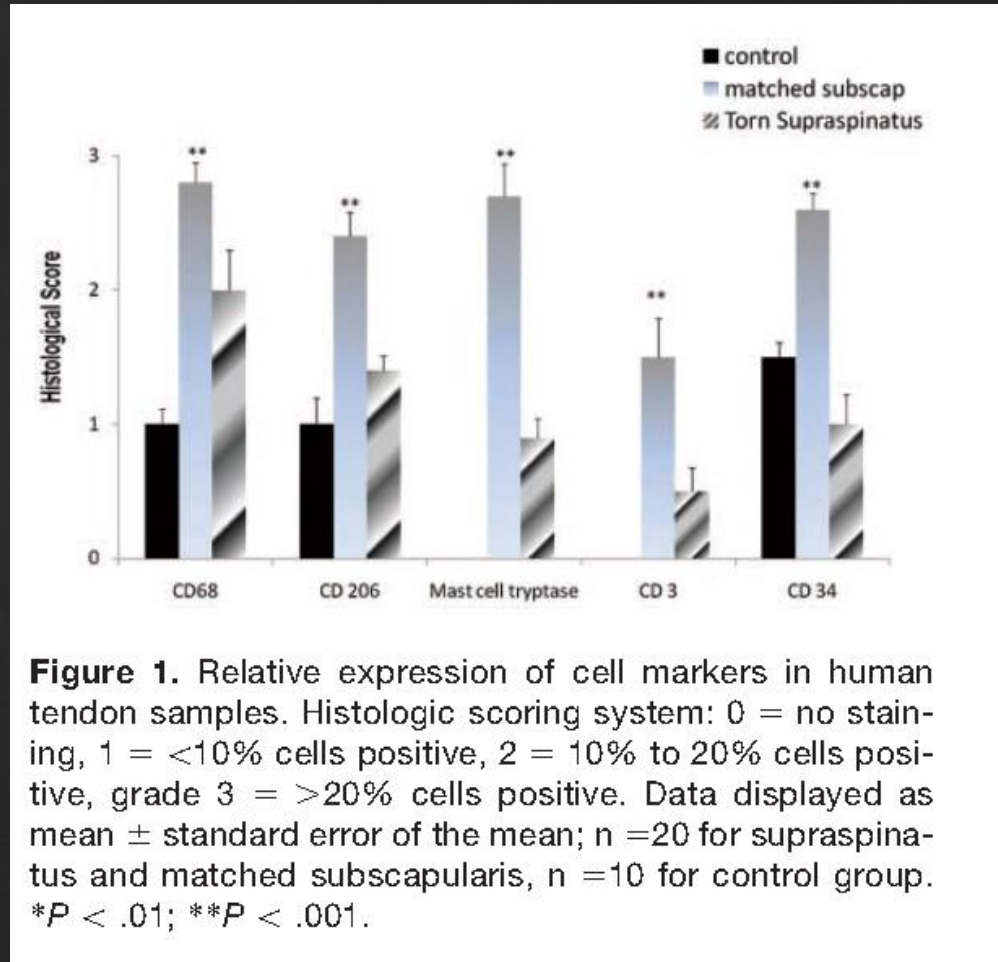
Feature	Morphological changes	Biochemical changes	
Normal tendon	Normal, elongated fibroblasts Intact collagen Sparse proteoglycan and vessels	-	
Tenocytes (tendon fibroblasts)	Abnormal distribution of tenocytes Less elongated tenocytes Mitotic or pyknotic nuclei	↑ DNA content ↑ Tenocyte turnover (death and proliferation) ↑ Lipid	
Extracellular matrix	Mucinous degeneration Fibrocartilage metaplasia	↑ Sulphated proteoglycan content ↑ Calcium	
Collagen	Separation Disorganization/scarring Fibril breaks/tears ↓ Fibril diameter	↓ Total collagen content ↑ Percent of Type III collagen ↓ Resistance to enzymatic degradation ↑ Collagenase activity	
Vessels/nerves	Vascular hyperplasia Neural sprouting Edema Increased blood flow Mast cells	↑ Substance P	

Histology [Tendinopathy]



Millar NL et al. Inflammation is present in early human tendinopathy. *Am J Sports Med.* 2010 Oct; 38(10): 2085-91.

Histology [Tendinopathy]



Millar NL et al. Inflammation is present in early human tendinopathy. Am J Sports Med. 2010 Oct; 38(10): 2085-91.

Histology [Tendinopathy]

TABLE 2
Histologic Features in Control, Matched Subscapularis, and Torn Supraspinatus Tendon Samples

Feature	Control (n = 10)	Matched Subscapularis (n = 20)	Torn Supraspinatus				
			Overall (n = 20)	Small (n = 6)	Medium (n = 6)	Large (n = 4)	Massive (n = 4)
Mean vessel count ^a	6 + 1	38 + 2	15 + 3	28 + 2	17 + 2	6 + 1	1 + 1
Inflammatory cell count ^b							
Macrophages	4 + 1	30 + 4	13 + 2	23 + 1	14 + 2	5 + 1	3 + 1
Mast cells	0 + 0.5	25 + 3	10 + 3	18 + 4	11 + 1	4 + 1	4 + 2
M ₂ macrophages	2 + 1	26 + 3	9 + 2	15 + 2	13 + 2	7 + 2	2 + 1
T cells	1 + 1	12 + 2	6 + 2	9 + 2	7 + 1	3 + 1	2 + 1

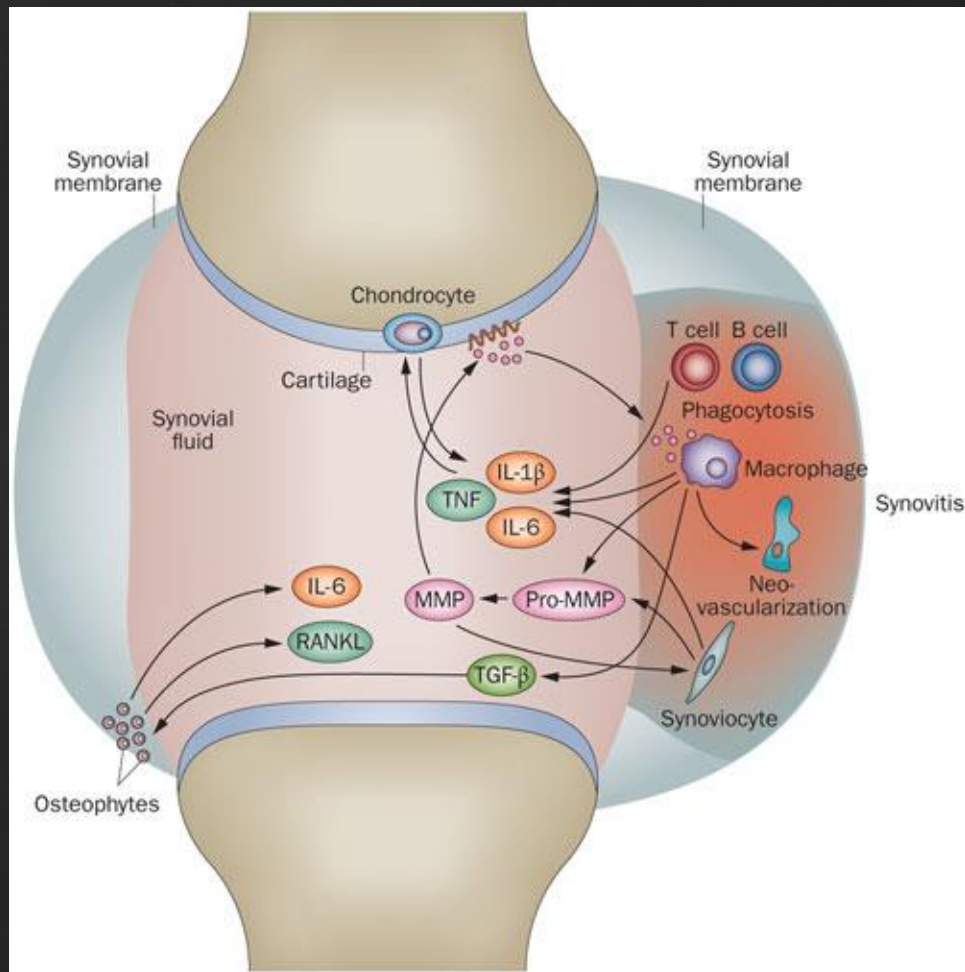
^aMean number of vessels in 10 high-power fields of view (magnification ×400).

^bMean number of cells in 10 high-power fields of view (magnification ×400).

Millar NL et al. Inflammation is present in early human tendinopathy. *Am J Sports Med.* 2010 Oct; 38(10): 2085-91.



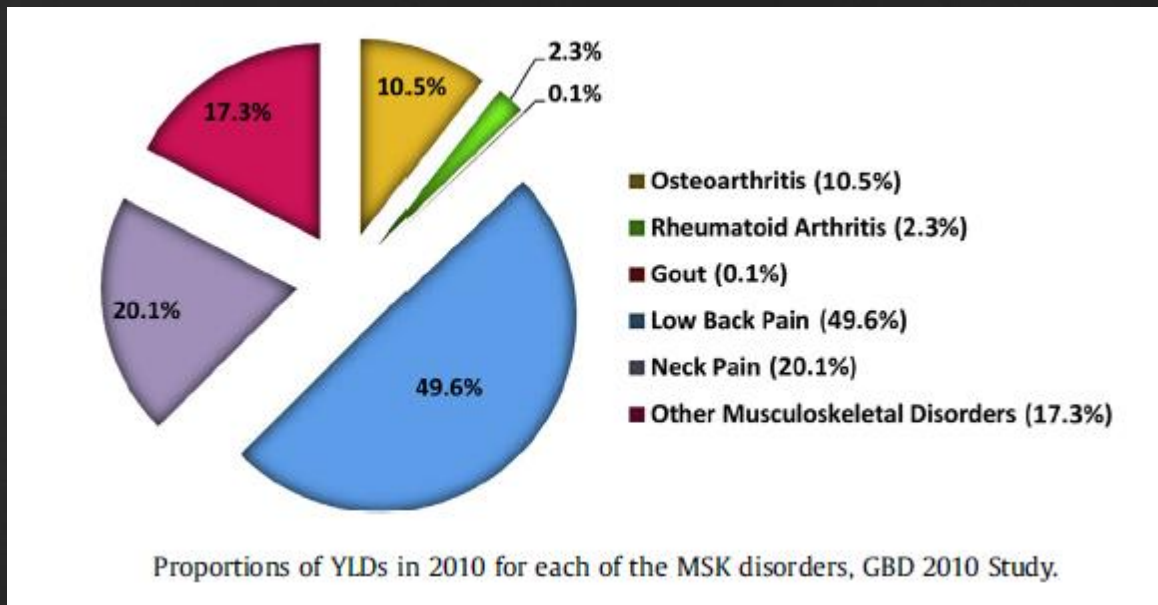
Histology [Osteoarthritis]



Chevalier X et al. *Biologic agents in osteoarthritis: hopes and disappointments*. Nature Reviews Rheumatology 9, 400-410 (July 2013).

Injury/Pathology (cont)

& Prevalence and burden of Msk issues is high



March L et al. *Burden of Disability due to Musculoskeletal (Msk) Disorders*. *Best Practice & Research Clinical Rheumatology* 28 (2014) 353-366.

Objectives (revisited)

- ⌘ Focus your therapies
 - ⌘ Understand the underlying process, treat accordingly
- ⌘ Corticosteroids are not Evil
- ⌘ There are other options than stopping what you're doing

Therapeutics

⌘ Historical approach

- ⌘ Corticosteroids
- ⌘ NSAIDs
- ⌘ Tylenol
- ⌘ IA CS
- ⌘ IA Viscosupplementation

⌘ Novel

- ⌘ Nitroglycerin
- ⌘ Biologic Therapies: PRP, Prolotherapy, Stem Cells
- ⌘ Testosterone

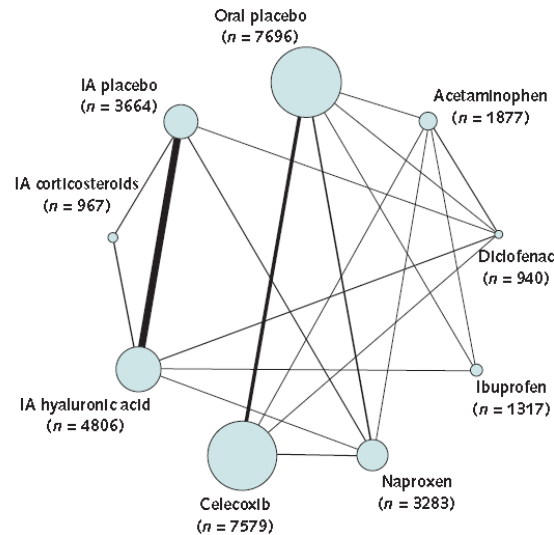
⌘ Surgical

- ⌘ Tenex



Therapeutics (Knee OA)

Figure 1. Network of treatment comparisons for pain.



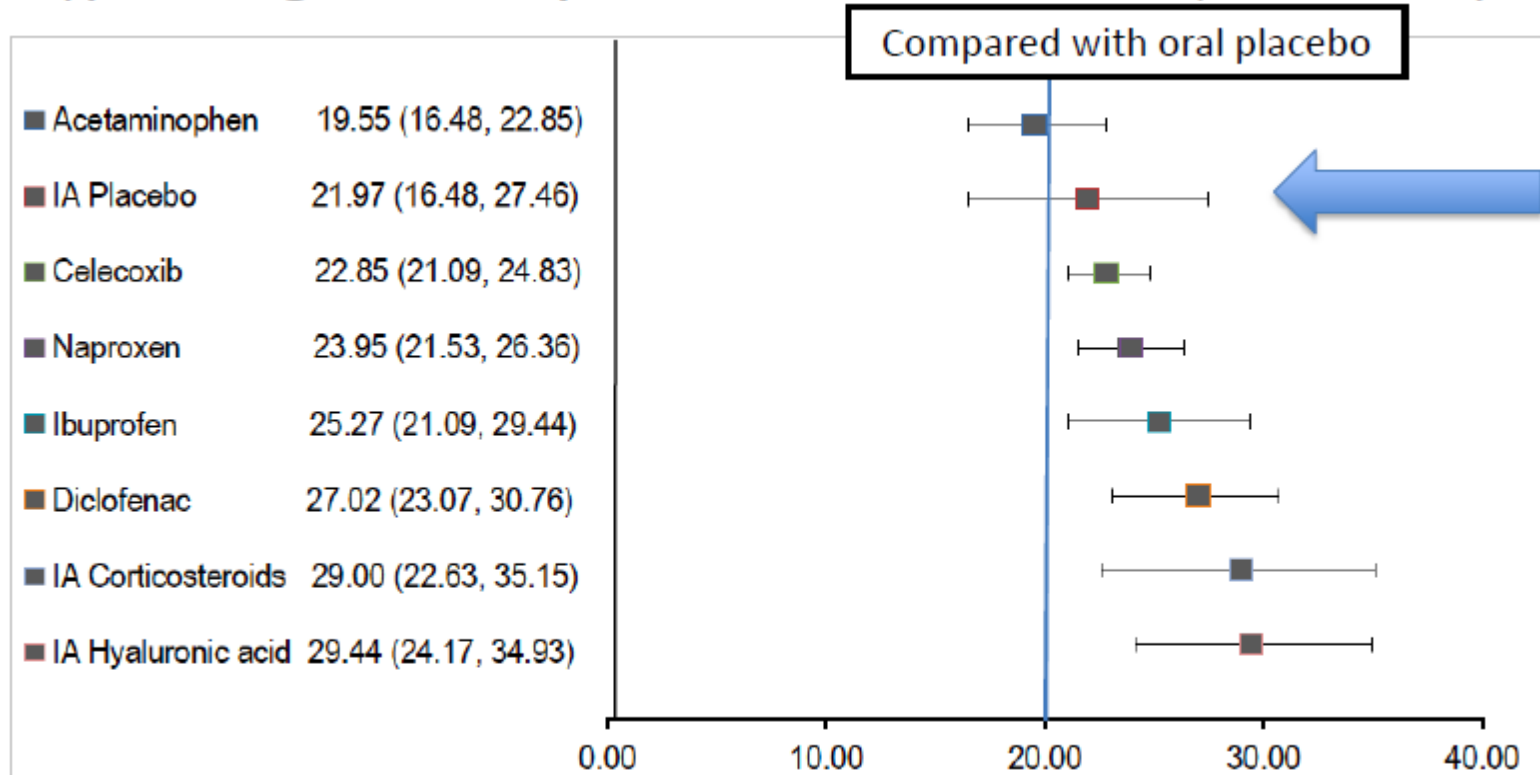
Comparisons	Trials, <i>n</i>
Oral placebo vs. acetaminophen	6
Oral placebo vs. diclofenac	6
Oral placebo vs. ibuprofen	5
Oral placebo vs. naproxen	14
Oral placebo vs. celecoxib	28
Acetaminophen vs. diclofenac	2
Acetaminophen vs. ibuprofen	2
Acetaminophen vs. naproxen	1
Acetaminophen vs. celecoxib	4
Diclofenac vs. celecoxib	1
Diclofenac vs. IA hyaluronic acid	2
Diclofenac vs. IA placebo	2
Ibuprofen vs. IA hyaluronic acid	1
Naproxen vs. celecoxib	7
Naproxen vs. IA haluronic acid	1
Naproxen vs. IA placebo	2
IA Hyaluronic acid vs. IA corticosteroids	12
IA Hyaluronic acid vs. IA placebo	52
IA Corticosteroids vs. IA placebo	7

Circle size reflects number of participants, and the line width reflects the number of direct comparisons. No connecting line between 2 treatments indicates that there was no direct comparison. IA = intra-articular.

Therapeutics (Knee OA)

⌘ Pharmacologic Management Oral/Injectable Pain Improvement

Supplement Figure 1: Forest plot of absolute treatment effects (WOMAC 0-100)

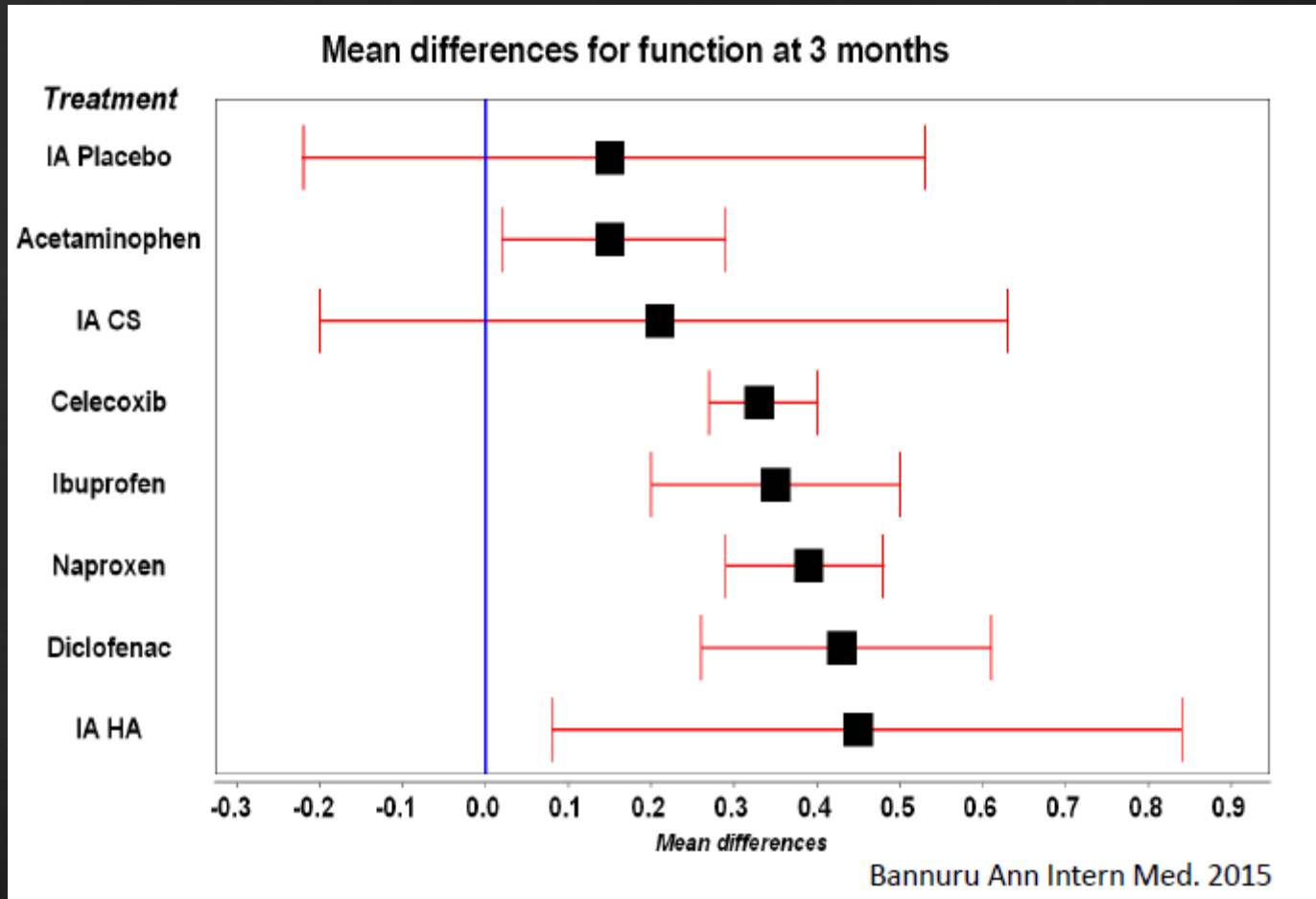


Blue line at 20.00 represents the line of clinical significance

Bannuru Ann Intern Med. 2015

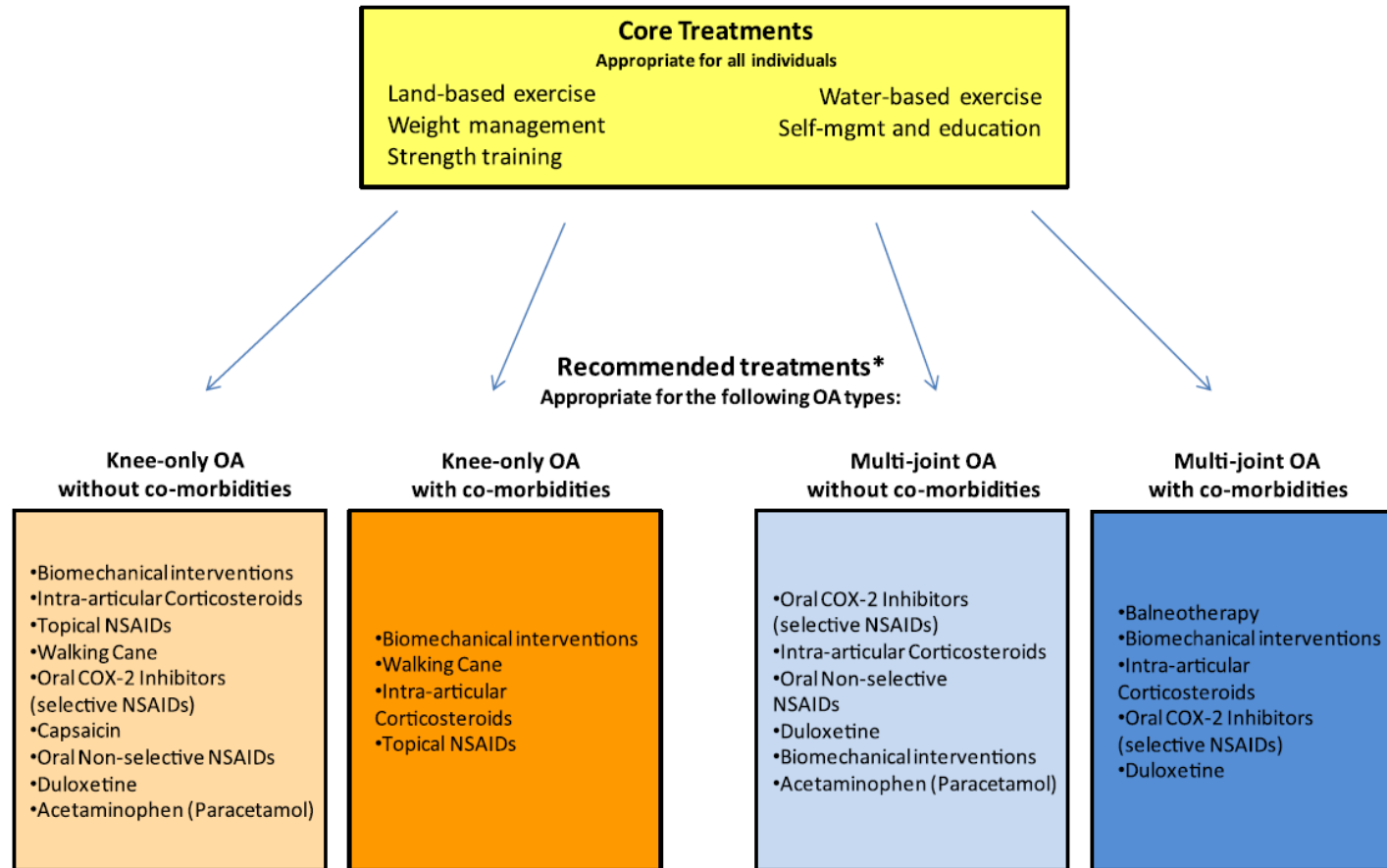
Therapeutics (Knee OA)

⌘ Pharmacologic Management Oral/Injectable Function



Therapeutics (Knee OA)

OARSI Guidelines for the Non-surgical Management of Knee OA

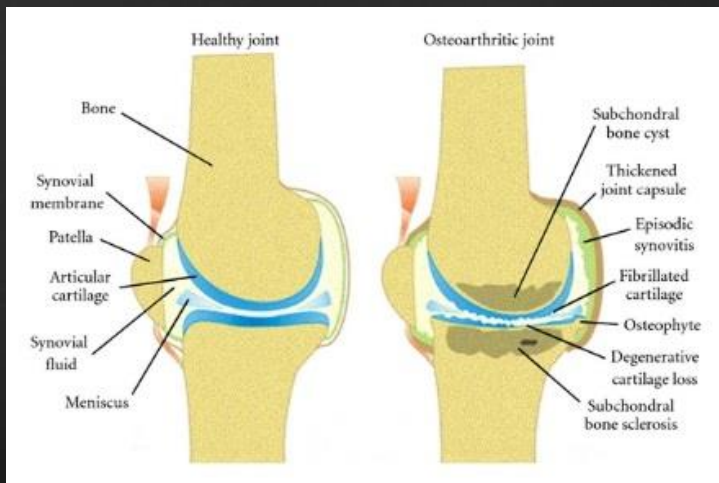


*OARSI also recommends referral for consideration of open orthopedic surgery if more conservative treatment modalities are found ineffective.

Therapeutics (Knee OA)

↳ Osteocytes

- ↳ Mechano-sensing cells that influence osteoclast and osteoblast activity
- ↳ Various cytokines and growth factors secreted by osteoclast/osteoblasts of OA sclerotic bone promote cartilage loss (proteoglycans)



- ↳ Osteocyte deaths confirmed in OA subchondral bone → increased subchondral bone remodeling
 - ↳ → dysregulation of osteoclast/osteoblasts → subchondral bone osteoporotic changes



Iijima H, Aoyama T, Ito A, Yamaguchi S, Nagai M, Tajino J, Zhang X, Kuroki H, Effects of short-term gentle treadmill walking on subchondral bone in a rat model of instability-induced osteoarthritis, *Osteoarthritis and Cartilage* (2015), doi: 10.1016/j.joca.2015.04.015.

Therapeutics (Knee OA)

↳ **Optimal Management of Symptomatic OA requires a combination of pharmacologic and non-pharmacologic therapies**

↻ **Activity:**

- ↻ **Strength training (isometric knee extensions in sitting for each leg 5x/wk)**
- ↻ **Cardiovascular land exercise**
- ↻ **Aquatic exercise**
- ↻ **Weak evidence of stretching/balance**

↻ **Therapy:**

- ↻ **Manual therapy + Supervised exercise plan**

↻ **Weight Loss**

- ↻ **Weight loss**



Zhang W et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis and Cartilage* (2008) 16, 137-62.

Therapeutics: Novel

⌘ Topical Nitroglycerin (Shoulder)

Topical Glyceryl Trinitrate Application in the Treatment of Chronic Supraspinatus Tendinopathy

A Randomized, Double-Blinded, Placebo-Controlled Clinical Trial

Justin A. Paoloni,[†] MBBS, PhD, Richard C. Appleyard,[†] PhD, Janis Nelson,[‡] BPharm, and George A. C. Murrell,[†] MBBS, DPhil

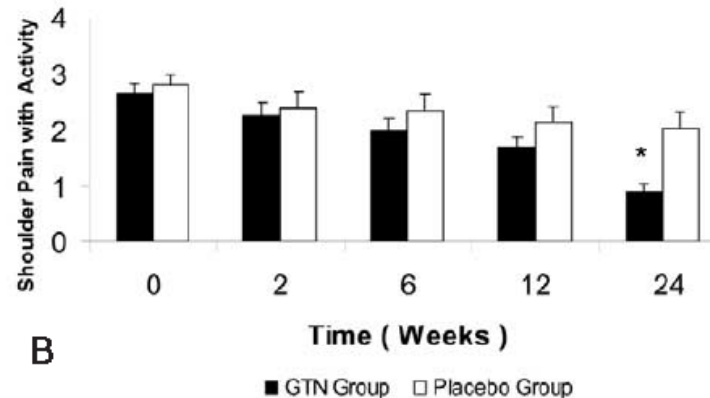
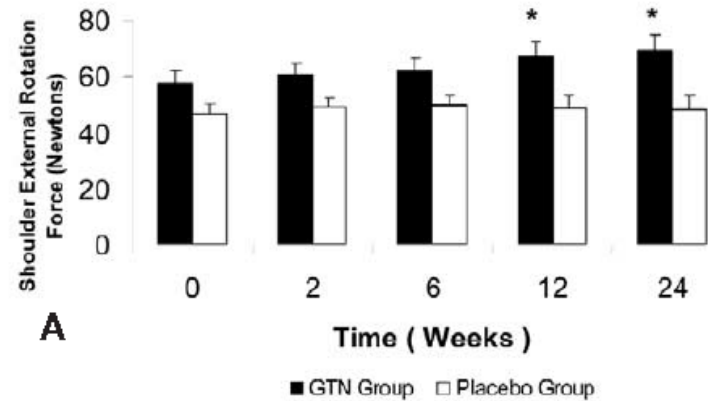
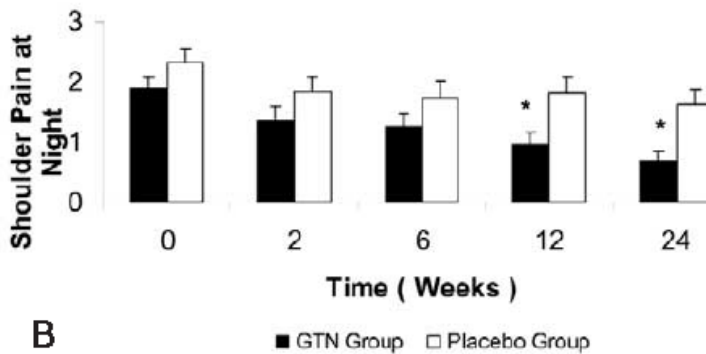
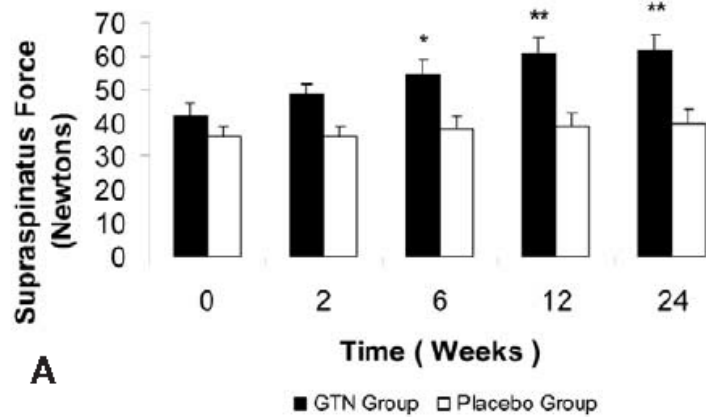
From the [†]Orthopaedic Research Institute, Research and Education Centre, St George Hospital, Kogarah, Sydney, Australia, and [‡]St George Public Hospital Pharmacy, Kogarah, Sydney, Australia



CLINICAL ATHLETE

Therapeutics: Novel

Topical Nitroglycerin (Shoulder)



CLINICAL ATHLETE

Therapeutics: Novel

& Topical Nitroglycerin (Shoulder)

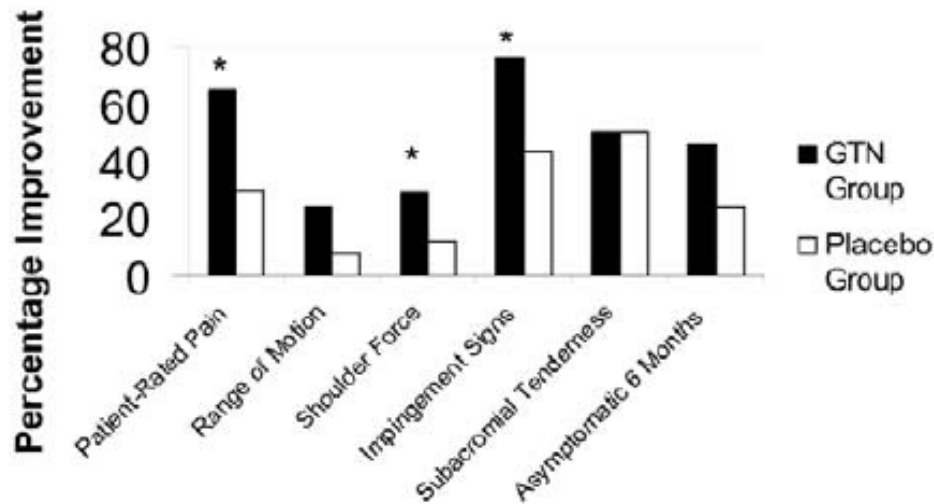


TABLE 2
Numerical Breakdown of Side Effects
and Paracetamol Use in the
Glyceryl Trinitrate Group and the Placebo Group^a

Side Effect	Glyceryl Trinitrate Group (n = 26)		Placebo Group (n = 27)	
	n	%	n	%
Headache	15	58***	9	33
Rash	3	12	1	4
No adverse effects	9	35	18	67



CLINICAL ATHLETE

Therapeutics: Novel

& Topical Nitroglycerin (Achilles)

TOPICAL GLYCERYL TRINITRATE TREATMENT OF CHRONIC NONINSERTIONAL ACHILLES TENDINOPATHY

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

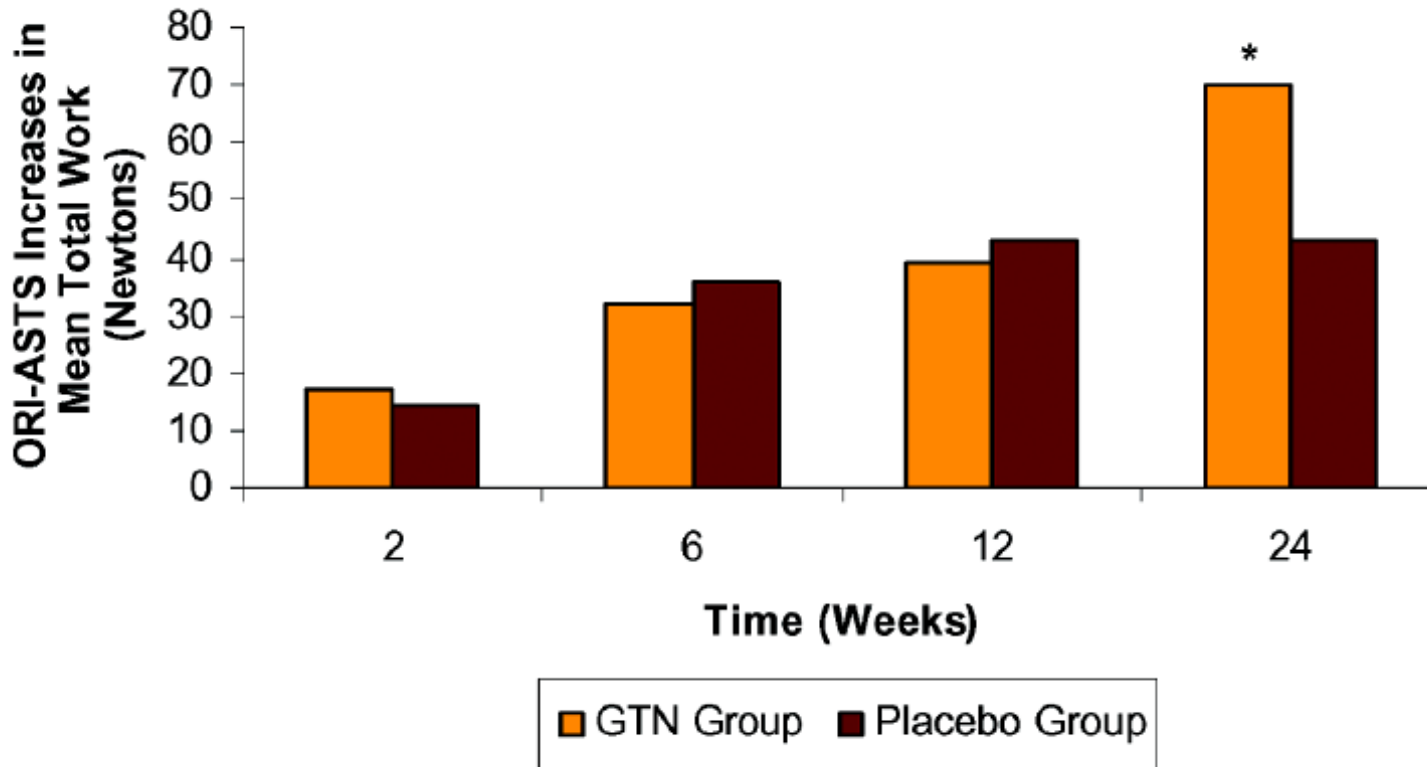
BY JUSTIN A. PAOLONI, MBBS, RICHARD C. APPLEYARD, PhD,
JANIS NELSON, MCLINPHARM, AND GEORGE A.C. MURRELL, MBBS, DPHIL



CLINICAL ATHLETE

Therapeutics: Novel

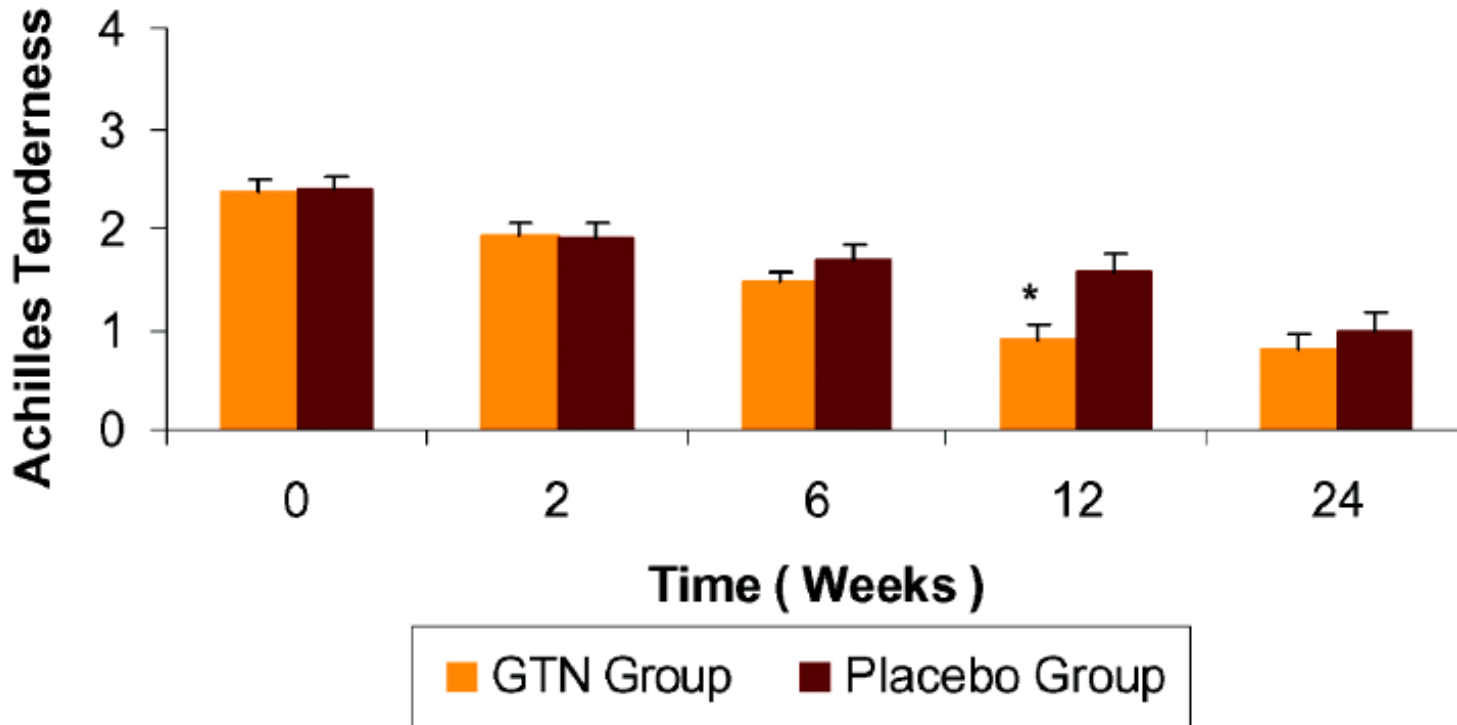
& Topical Nitroglycerin (Achilles)



CLINICAL ATHLETE

Therapeutics: Novel

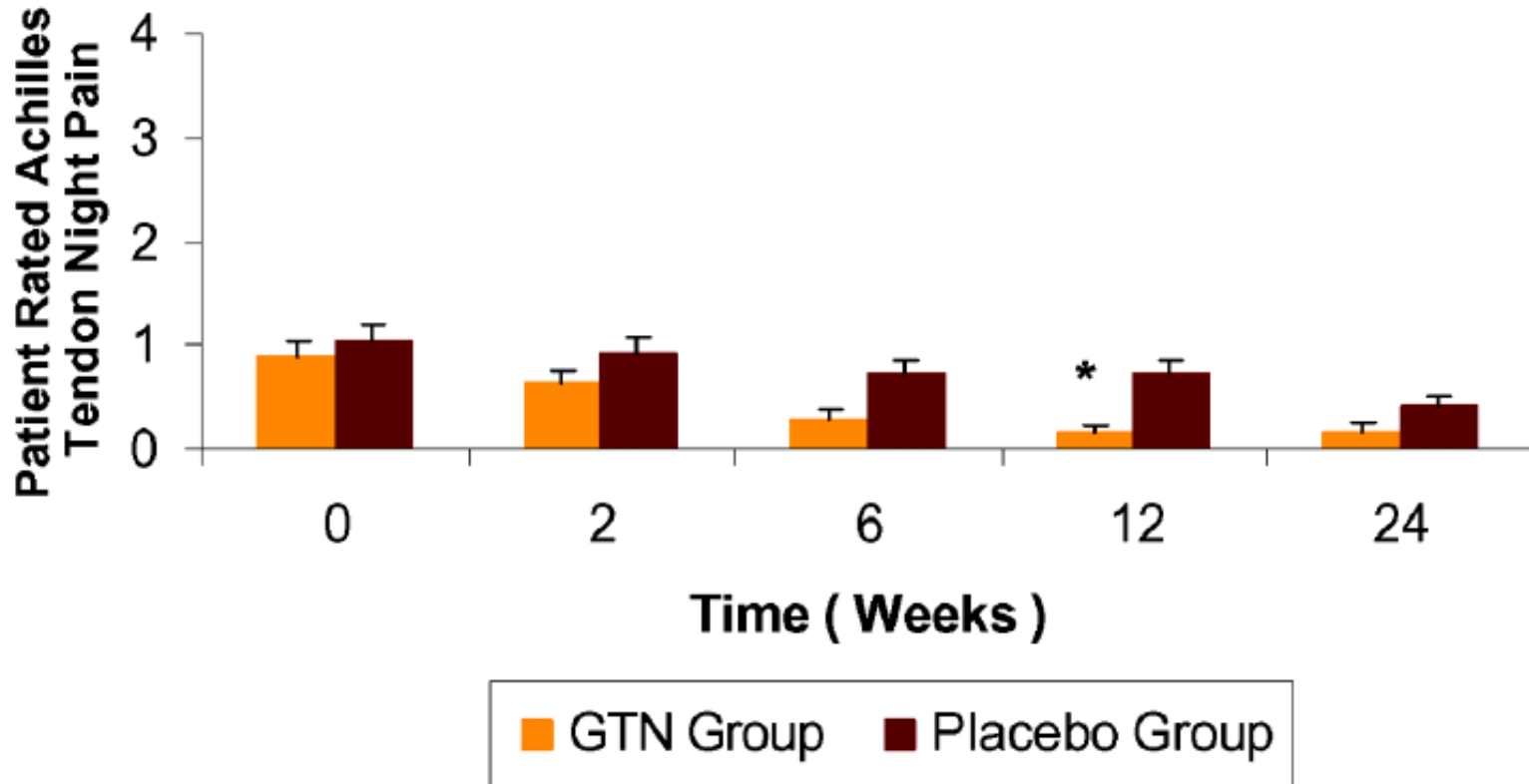
⌘ Topical Nitroglycerin (Achilles)



CLINICAL ATHLETE

Therapeutics: Novel

& Topical Nitroglycerin (Achilles)



CLINICAL ATHLETE

Therapeutics: Novel

↳ Topical Nitroglycerin (Elbow)

Topical Nitric Oxide Application in the Treatment of Chronic Extensor Tendinosis at the Elbow

A Randomized, Double-Blinded, Placebo-Controlled Clinical Trial

Justin A. Paoloni, MBBS, Richard C. Appleyard, PhD, Janis Nelson, MClinPharm, and George A. C. Murrell,* MBBS, DPhil

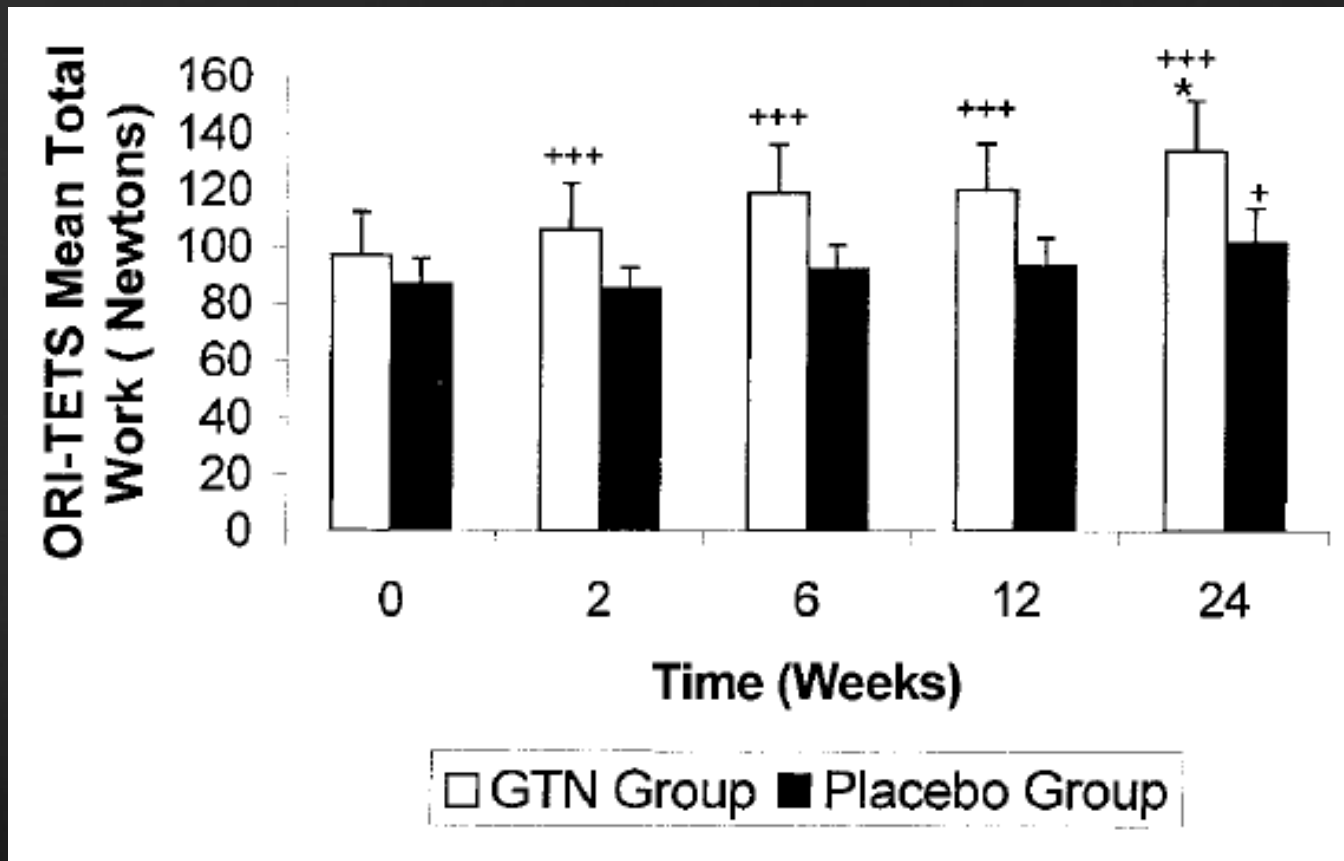
From the Orthopaedic Research Institute, St. George Hospital Campus, University of New South Wales, Sydney, New South Wales, Australia



CLINICAL ATHLETE

Therapeutics: Novel

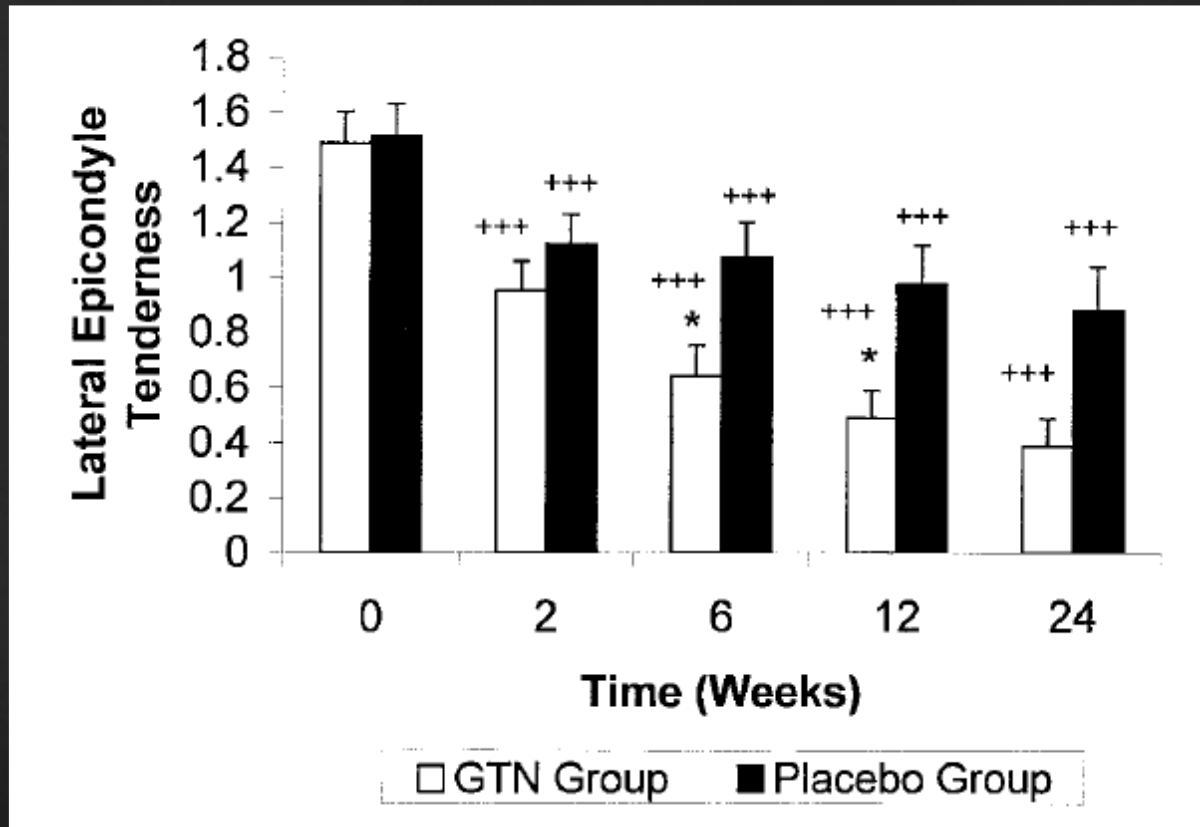
& Topical Nitroglycerin (Elbow)



CLINICAL ATHLETE

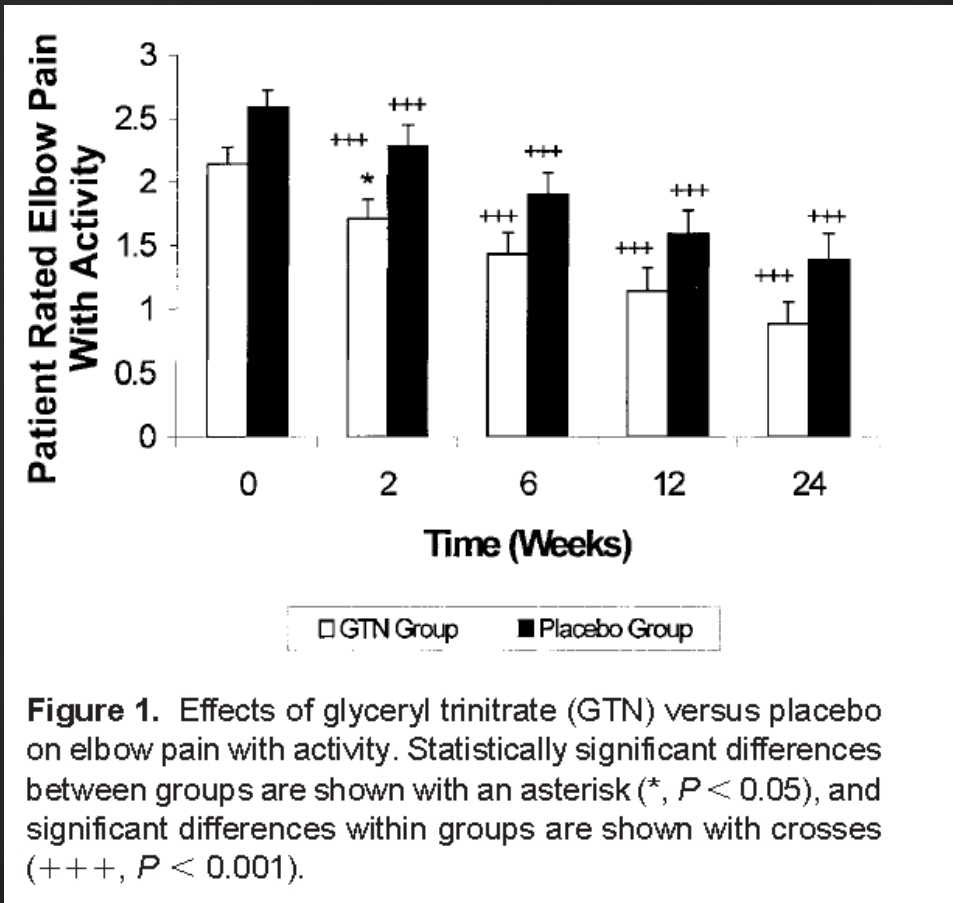
Therapeutics: Novel

& Topical Nitroglycerin (Elbow)



Therapeutics: Novel

& Topical Nitroglycerin (Elbow)



Therapeutics: Novel

PRP (Platelet Rich Plasma)

- ☞ Platelets promote blood clotting, tissue proliferation, healing and remodeling
- ☞ Triggering growth factors and cytokines within their alpha granules

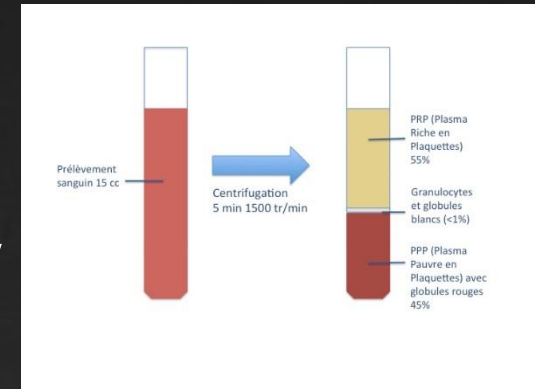


Table 1

Platelet growth factors present in platelet-rich plasma (PRP), with their main effects.

Growth factors	Role in the joint
Transforming growth factor beta (TGFβ)	Regulates collagen production and proteoglycan synthesis Promotes chondrocyte proliferation and differentiation Stimulates angiogenesis Regulates the release of other growth factors
Hepatocyte growth factor (HGF)	Inhibits the pro-inflammatory NF-κB pathway Stimulates angiogenesis
Vascular endothelial growth factor (VEGF)	Increases angiogenesis and blood vessel permeability Promotes endothelial cell proliferation
Platelet-derived growth factor (PDGF)	Increases angiogenesis Promotes fibroblast and osteoblast proliferation and differentiation Regulates collagen production and proteoglycan synthesis
Insulin-like growth factor (IGF)	Inhibits the pro-inflammatory NF-κB pathway Stimulates osteoblast and chondrocyte proliferation and differentiation Stimulates the production of extracellular matrix
Fibroblast Growth Factor-2 (FGF)	Promotes chondrocyte and mesenchymatous stem cell differentiation Stimulates chondrocyte proliferation Stimulates hyaluronic acid production by synovial cells Increases angiogenesis
Connective tissue growth factor (CTGF)	Stimulates angiogenesis Promotes chondrocyte differentiation Promotes platelet adhesion



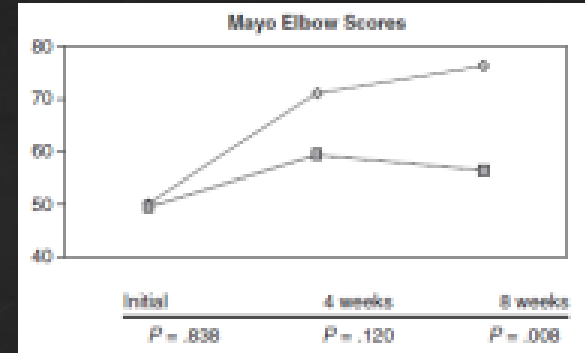
CLINICAL ATHLETE

PRP (cont)

Lateral Epicondylitis

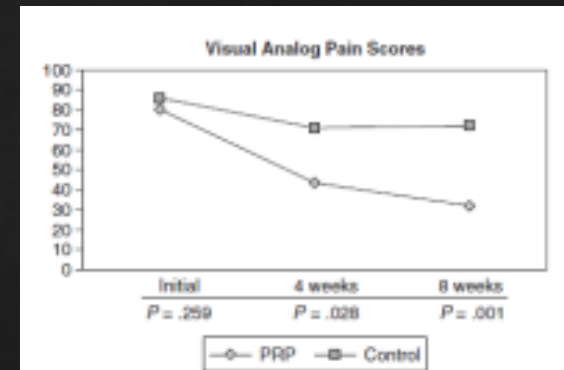
Mishra A and Pavelko T. AJSM. 2006:

- ⌘ Cohort Study [Level II]: 20 pts failed PT, non-operative care (~ 15 m)
- ⌘ PRP or bupivacaine → VAS, Mayo score
- ⌘ 4 wks: 46% improvement (vs. 17%)
- ⌘ 8 wks: PRP 60% improved VAS (vs. 16%)
- ⌘ 6 months: 81% improvement in VAS
- ⌘ ~ 25 m: 93% reduction in pain compared to pre-injection



Peerbooms J. AJSM. 2010

- ⌘ Double Blind Randomized Control Trial: 51 pts PRP vs 49 steroid → VAS, DASH
- ⌘ 49% Steroid group vs 73% of PRP successful at one year follow up
- ⌘ Steroid group initially did better but declined over the year



Therapeutics: Novel

& PRP (OA)

P. Ornetti et al. / Joint Bone Spine 83 (2016) 31–36

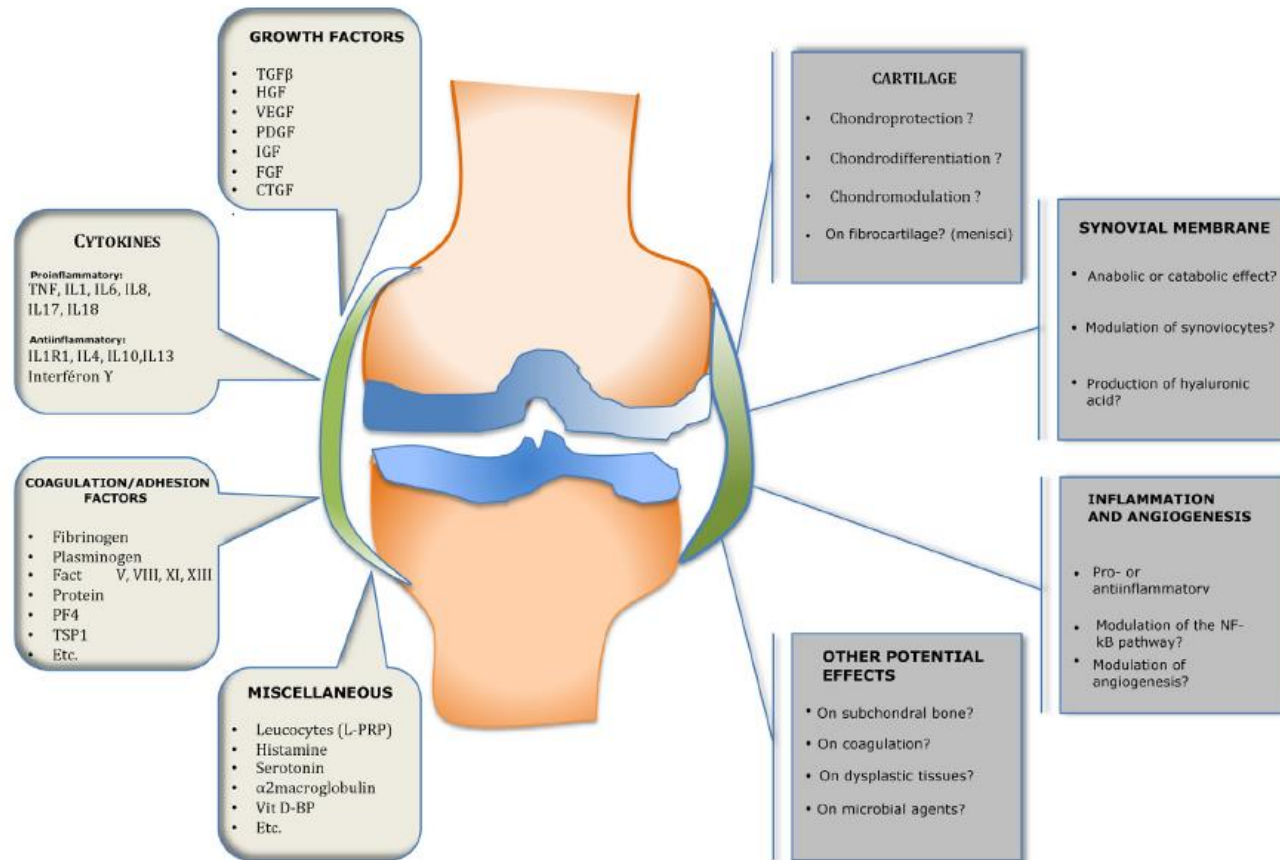


Fig. 1. Main components of platelet-rich plasma (PRP), with their potential effects on the osteoarthritis process.



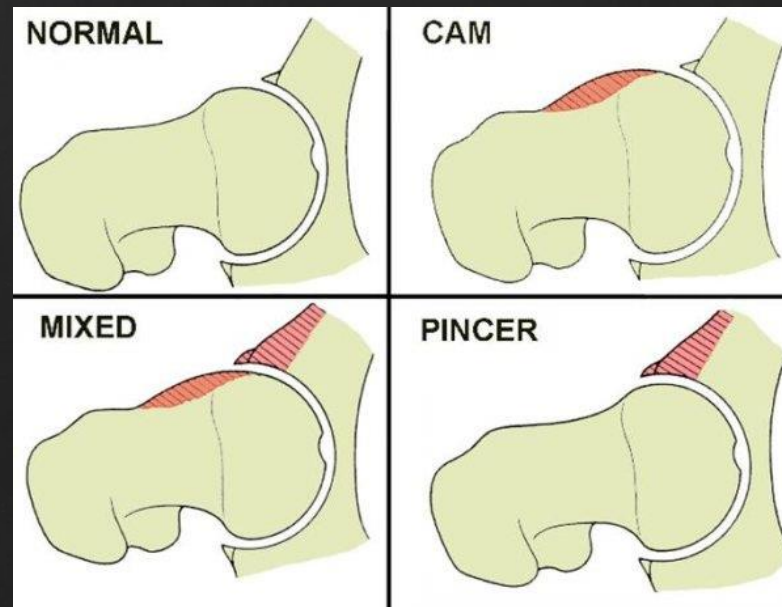
CLINICAL ATHLETE

Therapeutics: Novel

& PRP (OA)

Platelet-Rich Plasma Augmentation of Arthroscopic Hip Surgery for Femoroacetabular Impingement: A Prospective Study With 24-Month Follow-up

Claudio Rafols, M.D., Juan Eduardo Monckeberg, Ph.D., M.D., Jorge Numair, M.D.,
Julio Botello, M.D., and Julio Rosales, M.D.



Therapeutics: Novel

& PRP

Table 2. Operative Findings in Both Groups

	Mixed FAI, n	Cam FAI, n	Pincer FAI, n	Labral Tears, n	No. of Anchors Used in Surgery, Mean (Range)*
With PRP	16	14	0	30	2.9 (1-5)
Without PRP	17	10	0	27	2.7 (1-4)
<i>P</i> value	<i>P</i> = .43	<i>P</i> = .34		<i>P</i> = .11	<i>P</i> = .41

FAI, femoroacetabular impingement; PRP, platelet-rich plasma.

*The number of anchors indirectly reflects the size of the labral tear.

Table 3. Demographic Data and Radiologic Signs in Both Groups

	Age, yr	Alpha Angle, °		CE Angle, °	
		Preoperatively	Postoperatively	Preoperatively	Postoperatively
With PRP	34.18 (16-49)	62.57 (57-82)	40.83 (40-46)	35.8 (27-42)	30.32 (27-33)
Without PRP	36.5 (17-52)	60.51 (55-80)	40.6 (40-44)	39.29 (28-44)	30.11 (28-35)
<i>P</i> value	<i>P</i> = .32	<i>P</i> = .42	<i>P</i> = .31	<i>P</i> = .08	<i>P</i> = .43

NOTE. Data are presented as mean (range). The groups were shown to be comparable regarding all variables.

CE, center edge; PRP, platelet-rich plasma.



CLINICAL ATHLETE

Therapeutics: Novel

& PRP

Table 4. VAS and mHHS Results in Both Groups

	VAS Score				mHHS		
	Preop	2 d Postop	3 mo Postop	6 mo Postop	Preop	3 mo Postop	6 mo Postop
With PRP	5.04 (5-8)	3.04 (1-4)	1.22 (1-4)	0.71 (0-3)	70.79 (50-80)	91.79 (85-95)	94.8 (90-98)
Without PRP	4.94 (4-7)	5.2 (4-6)	1.2 (1-4)	0.77 (0-6)	71.48 (60-80)	90.97 (80-95)	94.0 (85-95)
<i>P</i> value	<i>P</i> = .45	<i>P</i> < .05	<i>P</i> = .54	<i>P</i> = .65	<i>P</i> = .32	<i>P</i> = .65	<i>P</i> = .65

NOTE. Data are presented as mean (range).

mHHS, modified Harris Hip Score; Postop, postoperatively; Preop, preoperatively; PRP, platelet-rich plasma; VAS, visual analog scale.



Therapeutics: Novel

↳ **Prolotherapy**

- ∞ Injury → attracts granulocytes which are then activated and release chemotactic factors to attract macrophages to the area of injury.
 - ∞ Macrophages serve to remove the cellular debris as well as secrete growth factors to attract fibroblasts to the injury site.
 - ∞ Granulation tissue is subsequently formed when the fibroblasts produce collagen fibers onto the area
- ∞ Several types of proliferant solutions have been identified in the initiation of this inflammatory cascade.
 - ∞ Irritants (ex. phenol), chemotactic agents, osmotic agents (e.g. dextrose) and particulates (e.g. pumice flour) are four types of prolotherapy solutions.
- ∞ Dextrose is thought to dehydrate cells and release cytokines which in turn attracts macrophages as well.



Therapeutics: Novel

↳ Prolotherapy (cont)

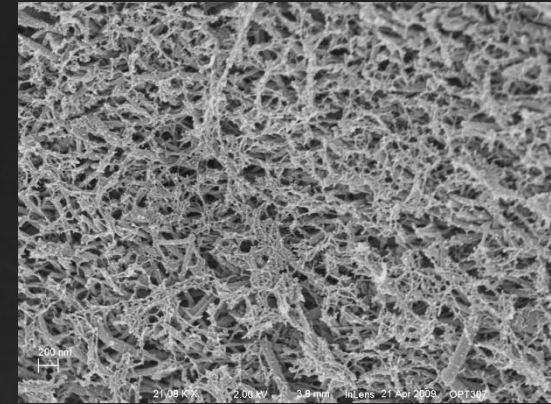
⌘ 2007 Maxwell

- ⌘ 36 patients w/ symptomatic Achilles tendinosis (midportion and insertional)
- ⌘ U/S demonstrated neovascularity, increased tendon thickness, mixed echogenicity, intratendinous calcifications.
- ⌘ 25% dextrose solution (1mL of 2% Lidocaine + 1mL 50% dextrose)
- ⌘ Injection q6wks until resolved
- ⌘ Mean treatment sessions: 4.0
- ⌘ Pain scales improved at 6wks and 12 months
- ⌘ U/S findings improved (except calcification)



CLINICAL ATHLETE

Therapeutics: Novel



↳ Stem Cells

⌘ Bone Marrow Aspirate

- ⌘ Bone marrow is composed of mesenchymal stem cells (hematopoietic and non-hematopoietic). The proliferation and differentiation of these stem cells are regulated by multiple factors, including cytokines, growth factors, systemic hormones and transcriptional regulators. Mesenchymal stem cells are multipotent cells capable of differentiation into several lineages including bone, fat, cartilage and muscle cells.
- ⌘ Usually obtained from iliac crest via biopsy (sometimes tibia, calcaneus)

⌘ Adipose Cells

- ⌘ Adipose derived stem cells were shown to be as effective as bone marrow stem cells by their multipotency and proliferative efficiency
- ⌘ Usually obtained from abdominal wall soft tissue



CLINICAL ATHLETE

Therapeutics: Novel

⌘ Stem Cells (cont)

- ⌘ Bone Marrow Aspirate

- ⌘ Fortier et al. (2010)

 - ⌘ 12 horses. 1.5cm cartilage defects; microfracture vs microfracture + BMAC

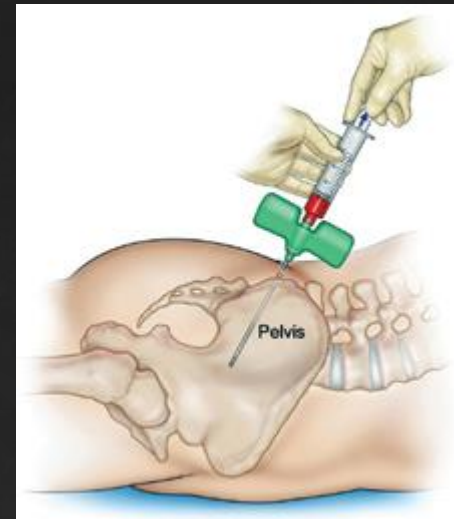
 - ⌘ @8 months, improved defect filling in the microfx + BMAC group

- ⌘ McIlwrath (2011)

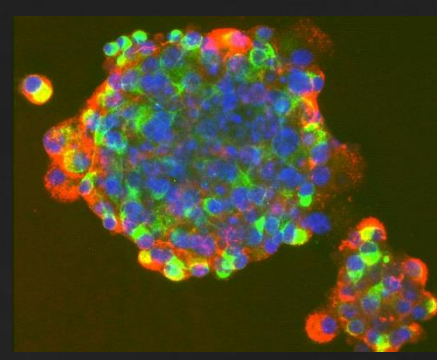
 - ⌘ Similar results in horses with 1.0cm cartilage defects @ 1 year

- ⌘ Many human subject studies using BMAC w/ hyaluronic acid scaffolding for the treatment of chondral defects in knee, talus

 - ⌘ Trend toward improvement but little statistical significance



Therapeutics: Novel



↳ Stem Cells (cont)

↳ Adipose Tissue

↳ **Clinical outcome of autologous bone marrow aspirates concentrate (BMAC) injection in degenerative arthritis of the knee.**

↳ **PURPOSE:**

- ↳ As a treatment method of degenerative arthritis of knee, this study evaluated the clinical efficacy of the intra-articular injection of autologous bone marrow aspirates concentrate (BMAC) with adipose tissue.

↳ **MATERIALS AND METHODS:**

- ↳ Between April 2011 and May 2012, 41 patients (75 knees) who were diagnosed as a degenerative knee arthritis and underwent the BMAC injection with adipose tissue were included in this study. Mean age was 60.7 years old (ranged 53-80). Kellgren-Lawrence grade was used for assessing radiologic degree of osteoarthritis; there were each 12, 24, 33, and 6 cases of grade I, II, III, and IV. At preoperative and postoperative 3, 6, and 12 months, pain score using visual analogue scale (VAS) and functional scales were used for evaluation.

↳ **RESULTS:**

- ↳ After the procedure, mean VAS score was decreased from 7.0 preoperatively to 4.1, 3.5, and 3.3 postoperatively 3, 6, and 12 months. And functional scores were also improved; International Knee Documentation Committee score (from 37.7 preoperatively to 59.3, 66.3, 69.3 postoperatively all increased after the procedure. When classified according to K-L grade, the improvement of VAS score in grade IV group was 8.2 preoperatively to 5.5, 5.3, and 5.7 postoperatively, which was significantly poorer than those of grade I-III groups. In the knee functional scales, similar pattern was checked.

↳ **CONCLUSIONS:**

- ↳ BMAC injection significantly improved both knee pain and functions in the patients with degenerative arthritis of knee. Also, the injection would be more effective in early to moderate phases.



CLINICAL ATHLETE

Therapeutics: Novel

⌘ Anabolics (Testosterone)

⌘ **BACKGROUND:**

- ⌘ To date, no studies document the effect of anabolic steroids on rotator cuff tendons.

⌘ **STUDY DESIGN:**

- ⌘ Controlled laboratory study.

⌘ **HYPOTHESIS:**

- ⌘ Anabolic steroids enhance remodeling and improve the biomechanical properties of bioartificially engineered human supraspinatus tendons.

⌘ **METHODS:**

- ⌘ Bioartificial tendons were treated with either nandrolone decanoate (nonload, steroid, n = 18), loading (load, nonsteroid, n = 18), or both (load, steroid, n = 18). A control group received no treatment (nonload, nonsteroid [NLNS], n = 18). Bioartificial tendons' remodeling was assessed by daily scanning, cytoskeletal organization by staining, matrix metalloproteinase-3 levels by ELISA assay, and biomechanical properties by load-to-failure testing.

⌘ **RESULTS:**

- ⌘ The load, steroid group showed the greatest remodeling and the best organized actin cytoskeleton. Matrix metalloproteinase-3 levels in the load, steroid group were greater than those of the nonload, nonsteroid group ($P < .05$). Ultimate stress and ultimate strain in the load, steroid group were greater than those of the nonload, nonsteroid and nonload, steroid groups ($P < .05$). The strain energy density in the load, steroid group was greater when compared to other groups ($P < .05$).

⌘ **CONCLUSIONS:**

- ⌘ Nandrolone decanoate and load acted synergistically to increase matrix remodeling and biomechanical properties of bioartificial tendons.

⌘ **CLINICAL RELEVANCE:**

- ⌘ Data suggest anabolic steroids may enhance production of bioartificial tendons and rotator cuff tendon healing in vitro. More research is necessary before such clinical use is recommended.



CLINICAL ATHLETE

Trianatafillopoulos et al. Nandrolone Decanoate and Load Increase Remodeling and Strength in Human Supraspinatus Bioartificial Tendons. Am J Sports Med 2004; 32(4). 934-43

Therapeutics: Novel

& Minimally Invasive Surgery (TENEX)

Peer-Reviewed Clinical Publications

Published/Accepted

- Koh et al – Am. Journal of Sports Medicine, 2013 (elbow)
- Hackel – Orthopedics Today 2013 (procedure overview / mixed tendons)
- Morrey – Techniques in Elbow and Hand Surgery 2013 (elbow)
- ElAttrache – Operative Techniques in Sports Medicine 2013 (knee)
- Barnes – Operative Techniques in Sports Medicine 2013 (procedure overview/mixed tendons)
- Khanna et al – Am Academy of Physical Med & Rehab Poster 2013 (mixed tendons)
- Traister et al – Am Med Society for Sports Medicine Presentation 2014 (mixed tendons)
- Barnes et al – accepted, Journal of Shoulder and Elbow Surgery 2014 (elbow)
- Patel – accepted, American Journal of Orthopedics 2014 (plantar fascia)
- Mayo Clinic Epidemiology study – accepted, American Journal of Sports Medicine 2014 (elbow)

Studies revealed at least 90% patients pain-free within 6 weeks of treatment

No additional treatment – single minimally invasive procedure / well-tolerated

Strong safety profile

Submitted/In Preparation

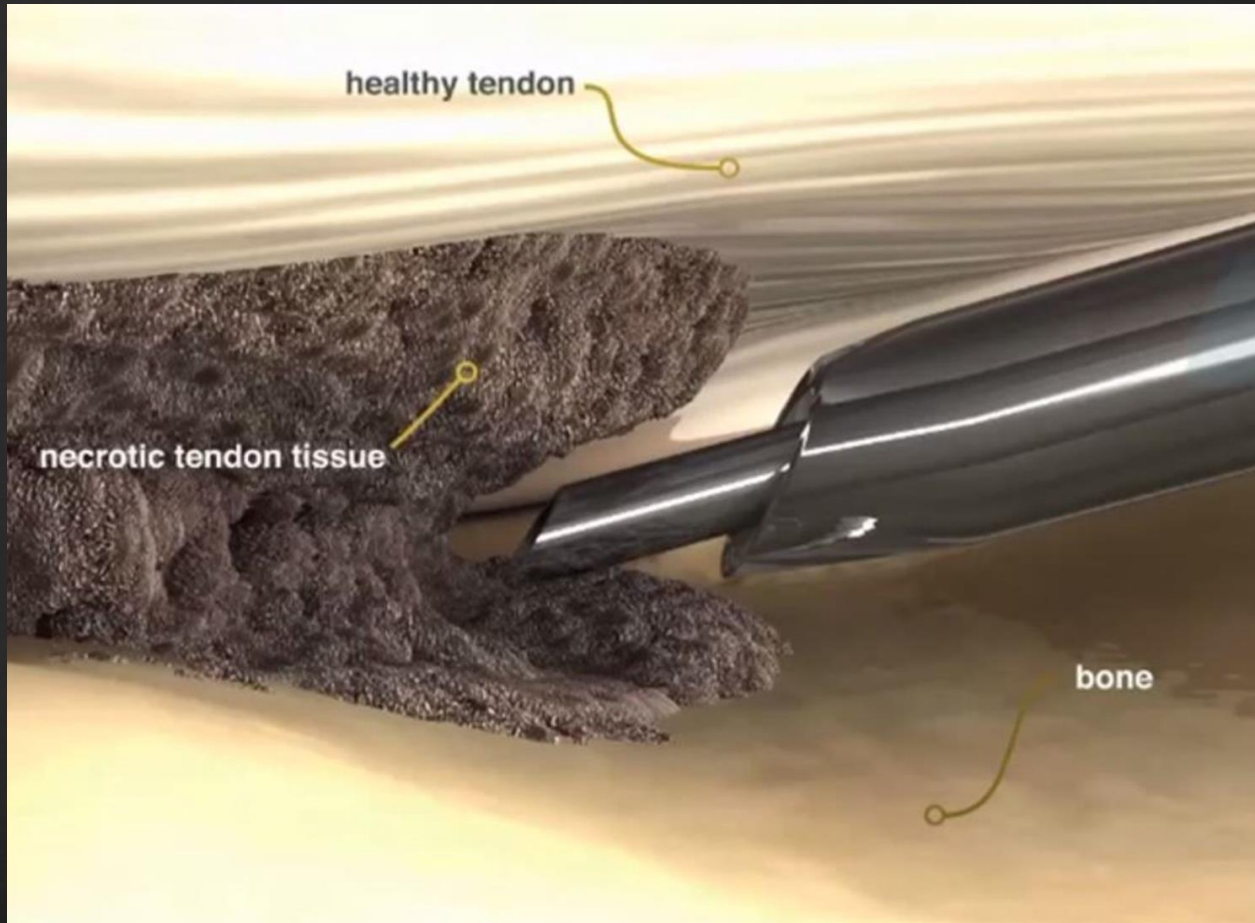
- Kamineni (Univ. of KY) – Controlled animal model study
- Koh et al (Singapore/Mayo) – Two year clinical efficacy and safety follow-up in elbow tendinosis
- Yanish (Des Moines, IA) – Cost effectiveness study: Tenex vs Surgery (elbow)
- Vanderwoude (Lincoln, NE) – Plantar fascia study
- Ellis et al (Phoenix, AZ) – Achilles tendon study
- Patel (Indianapolis) – Plantar fibroma study
- Stowers (Florida State) – Patellar tendon study



CLINICAL ATHLETE

Therapeutics: Novel

& Minimally Invasive Surgery (Tenex)



Objectives (revisited)

- ⌘ Focus your therapies
 - ⌘ Understand the underlying process, treat accordingly
- ⌘ Corticosteroids are not Evil
- ⌘ There are other options than stopping what you're doing

Bio-Psycho-Social Model

& Kent State University Athletics - The Gold Standard



Bio-Psycho-Social Model

⌘ Pending STUDY PROTOCOL

- ⌘ Psychological skills training and a mindfulness-based intervention to enhance functional athletic performance: design of a randomized controlled trial using ambulatory assessment



Bio-Psycho-Social Model

- ∞ Pilot Study Investigating changes in neural processing after mindfulness training in elite athletes
 - ∞ Athletes underwent mPEAK training (Mindful Performance Enhancement, Awareness and Knowledge)
 - ∞ Main results:
 - ∞ 1) Elite athletes self-reported higher levels of interoceptive awareness and mindfulness
 - ∞ 2) Greater insula and Anterior cingulate cortex activity
 - ∞ Training may lead to increased attention to bodily signals and greater neural processing during the anticipation and recovery from interoceptive perturbations (mindfulness tx)→greater adaptation
 - ∞ Seen on FMRI scans

Objectives (revisited)

- ⌘ Focus your therapies
 - ⌘ Understand the underlying process, treat accordingly
- ⌘ Corticosteroids are not Evil
- ⌘ There are other options than stopping what you're doing

Ultrasound: What we see first



Ultrasound (cont): With Ultrasound



Ultrasound (cont)

- ⌘ A mechanical, longitudinal wave with a frequency above the level of human hearing (>20 kHz)
- ⌘ Medical Diagnostic Ultrasound is 2MHz-20MHz



Ultrasound (cont)

- ⌘ Electric charge sent to transducer
- ⌘ Electric charge causes piezoelectric crystals to vibrate
- ⌘ Piezoelectric crystal vibration create sound wave that travels through tissue
- ⌘ Ultrasound waves travel through and reflect off structures in the body
- ⌘ Sound waves reflect back to the transducer → converted to an electric current → image



Ultrasound (cont)

- ⌘ 6-13 MHz transducer
 - ⌘ Very good resolution
 - ⌘ Less penetration
- ⌘ 2-5 MHz transducer
 - ⌘ Less resolution
 - ⌘ Deeper penetration

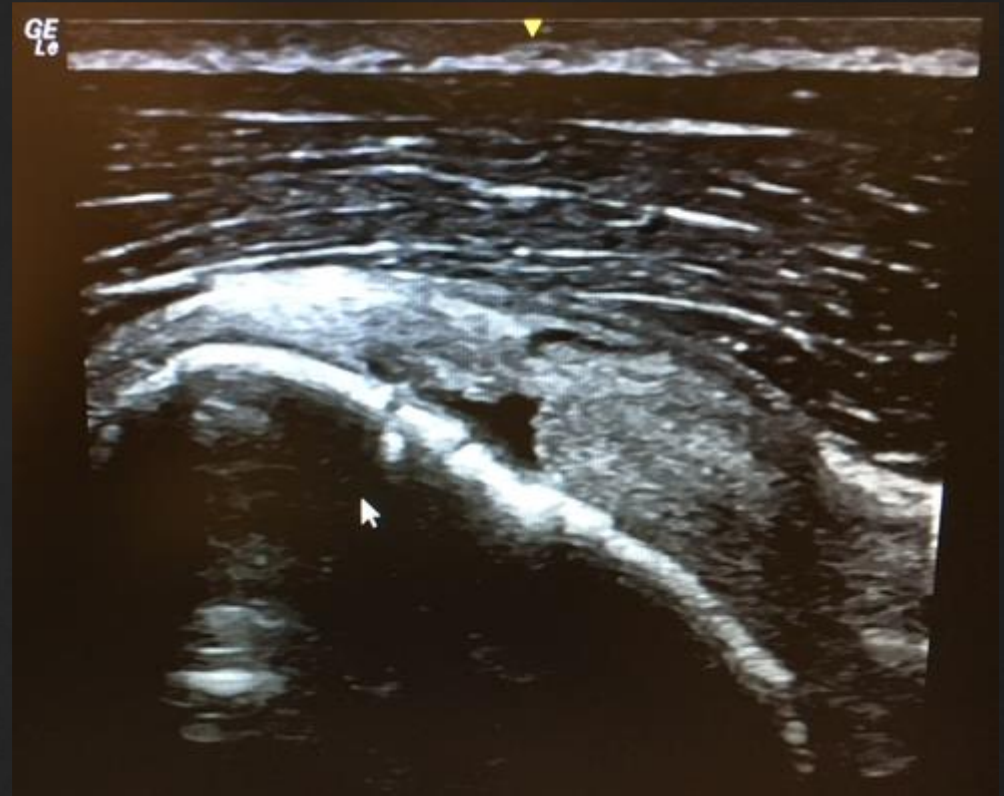


Ultrasound (cont)

- ⌘ Echogenicity
 - ⌘ Hypoechoic: less echogenic than surrounding tissue
 - ⌘ Hyperechoic: more echogenic than surrounding tissue
 - ⌘ Anechoic: absence of echoes
 - ⌘ Isoechoic: same echogenicity as surrounding tissue
- ⌘ Depth: Can't control depth of beam (frequency) but can control depth of displayed data (focus)
- ⌘ Gain: More tissue = more attenuation
 - ⌘ Compensate by gain; brighter/darker

Ultrasound (cont)

- ⌘ Diagnosis
 - ⌘ RTC pathology
 - ⌘ Achilles rupture
 - ⌘ Hamstring (muscle defects)
 - ⌘ Fracture
- ⌘ Injury Trending
- ⌘ Therapeutic
 - ⌘ Hip
 - ⌘ Glenohumeral
 - ⌘ Small joint
 - ⌘ Nerve
 - ⌘ Tendon
 - ⌘ Muscle



Ultrasound Evidence

& Diagnosis¹

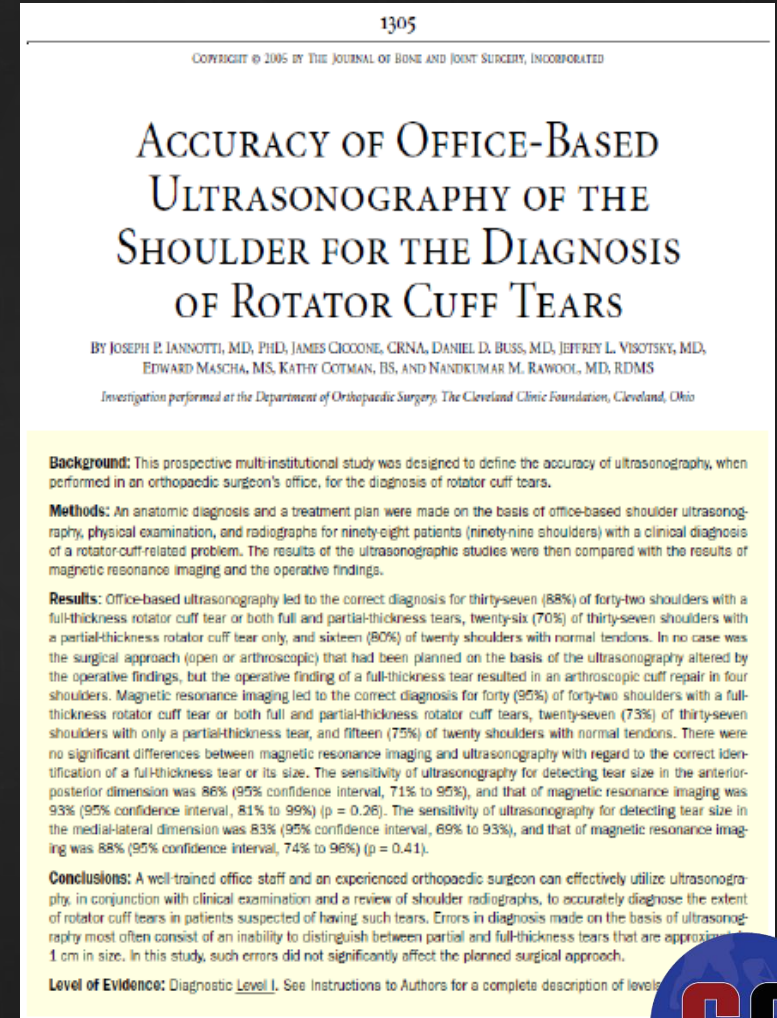
& Office-based U/S

⌘ Correct diagnosis for 37/42 (88%) shoulders with a full-thickness RCT

⌘ 26/37 (70%) shoulders with a partial-thickness RCT only

⌘ 16/20 (80%) shoulders with normal tendons

& MRI (95%, 73%, 75%) respectively



Ultrasound Evidence

Accuracy²

☞ Guided injections (shoulder) tend to be more accurate in placement as compared to blind injections

Subacromial corticosteroid injections

Konrad I. Gruson, MD, David E. Ruchelman, MD, and Joseph D. Zuckerman, MD, New York, NY

The use of subacromial injections to treat shoulder pain has remained one of the most common procedures for the practicing orthopedist, rheumatologist, and general practitioner. Despite this, many prospective studies have questioned the efficacy of corticosteroid injections compared with nonsteroidal anti-inflammatory drugs or injections of local anesthetics alone, or both, when used for the treatment of symptomatic rotator cuff disease. Accurate diagnosis of the etiology of a patient's shoulder pain and proper injection technique are important in achieving satisfactory clinical outcomes. Both extrinsic as well as intrinsic etiologies for rotator cuff disease should be considered and must be elucidated with appropriate physical examination techniques. Although subacromial injections appear straightforward, more recent cadaveric, radiographic, and clinical studies have demonstrated variable accuracy rates using the two common techniques. In addition, absolute sterile technique must be used because infections of the subacromial space after injections, although uncommon, have generally led to debilitating conditions. This article reviews the etiology and pathophysiology of rotator cuff disease and the indications and techniques for subacromial corticosteroid injections. (*J Shoulder Elbow Surg* 2008;17:1185-1305.)

Shoulder pain due to rotator cuff pathology accounts for many annual patient visits to orthopedists and rheumatologists, as well as general practitioners. An understanding of the complex shoulder anatomy, familiarity with a broad differential that may be responsible for the symptoms, and competence with shoulder physical examination are requisite for establishing a definitive diagnosis. Cervical spine pathology must be ruled out during history taking and

physical examination. Gorski and Schwartz¹⁷ reported a series of patients with subjective complaints of neck pain, positive impingement signs, and radiographic findings of a greater tuberosity pseudocyst or subacromial sclerosis. These patients responded to subacromial lidocaine and corticosteroid injections and behavior modification; the authors recommended adding shoulder impingement to the differential diagnosis of chronic neck pain.

Our comprehension of the complex etiology and pathophysiology of rotator cuff disease continues to evolve through contributions from basic science research and clinical data. Although subacromial impingement commonly affects the shoulder, it is important to recognize that outlet impingement implicitly establishes both a diagnosis of rotator cuff disease as well as the pathomechanics (ie, subacromial mechanical abutment) for the acquisition and progression of bursal-sided cuff pathology. In addition to extrinsic factors, intrinsic degenerative tendinopathy¹⁸ may be important in the etiology of the development of clinically significant rotator cuff disease and impingement; partial tears may allow subtle proximal humeral head migration, which may result in subacromial impingement and, ultimately, full-thickness cuff tears. Other causes for rotator cuff disease must also be considered, such as internal impingement,³⁴ which may culminate in articular-sided cuff pathology or labral lesions. This disorder is seen more often in younger, high-performance overhead athletes who subject their shoulders to repetitive and extreme external rotation. This patient population is less likely to respond to subacromial corticosteroid injections.

Compression of the supraspinatus tendon against the undersurface of the anterior acromion, as originally described by Neer, results in a spectrum of bursal-sided rotator cuff pathology and may manifest as subacromial bursitis, acute^{35,44} and chronic³⁶ tendonitis, and attritional degenerative tears.⁷ Neer described outlet impingement as occurring in a continuum of stages: early macroscopic changes may be limited to local edema and hemorrhage (stage 1); with chronic repetitive impingement, subacromial bursitis (stage 2) is followed by irreversible tendon disruption (stage 3; partial/complete tears).³³ Zlatos⁴³ proposed a staging system of subacromial impingement syndrome based on progressive logistic changes in the rotator cuff observed on magnetic resonance imaging (MRI; Table I).

From Department of Orthopaedic Surgery, New York University Hospital for Joint Diseases.

Reprint requests: Joseph D. Zuckerman, MD, NYU Hospital for Joint Diseases, Department of Orthopaedic Surgery, 301 E 17th St, Ste 1402, New York, NY 10003 (E-mail: Joseph.Zuckerman@nyumc.org).

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1058-2746/2008/\$34.00
doi:10.1016/j.jse.2007.07.009

1185



Ultrasound Evidence

⌘ Efficacy³

- ⌘ 2 RCTs pooled data
- ⌘ Improved pain and function at 6 weeks post-injection guided vs blind

RESEARCH ARTICLE

Open Access

Image-guided versus blind corticosteroid injections in adults with shoulder pain: A systematic review

Edmund Soh^{1*}, Wenyun Li^{2,3}, Keh Oon Ong¹, Wen Chen⁴ and Dianne Bautista^{2,3}

Abstract

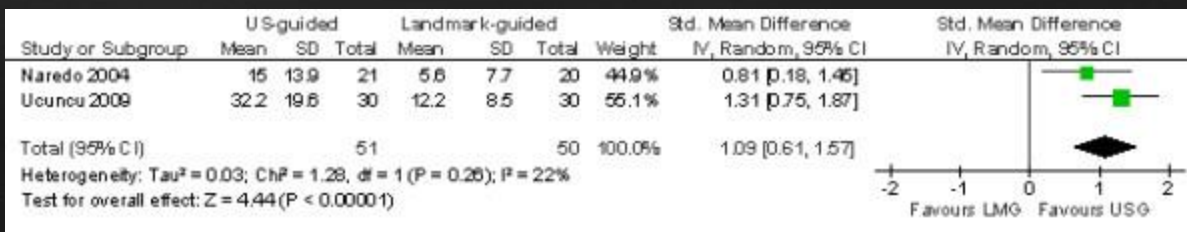
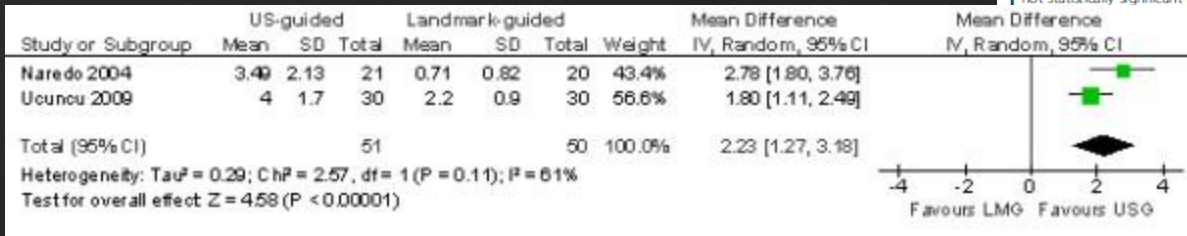
Background: Corticosteroid injections can be performed blind (landmark-guided) or with image guidance, and this may account for variable clinical outcomes. The objective of this study was to assess the effectiveness and safety of image-guided versus blind corticosteroid injections in improving pain and function among adults with shoulder pain.

Methods: MEDLINE, the Cochrane Controlled Trials Register and EMBASE were searched to May 2010. Additional studies were identified by searching bibliographies of shortlisted articles. Search items included blind, landmark, anatomical, clinical exam, image-guided, ultrasound, fluoroscopy, steroid injection, frozen shoulder, random allocation, randomized controlled trial (RCT) and clinical trial.

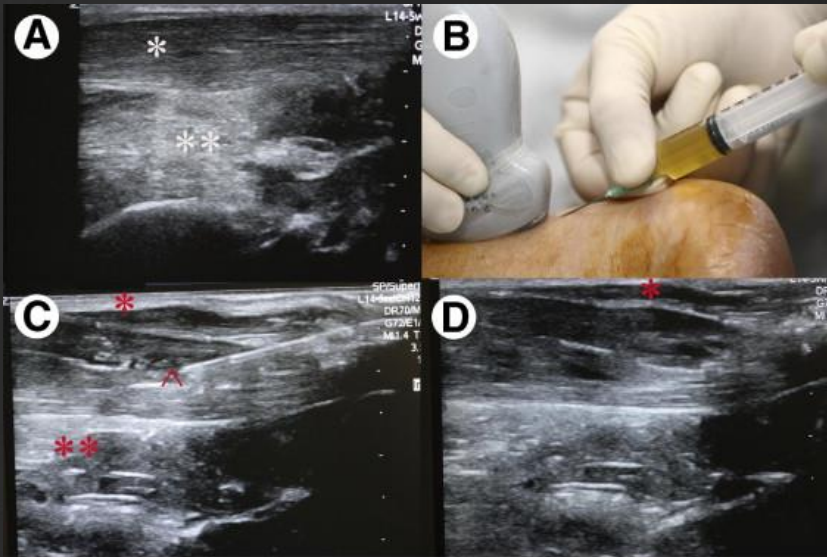
Randomized controlled studies comparing image-guided versus blind (landmark-guided) corticosteroid shoulder injections that examined pain, function and/or adverse events were included. Independent extraction was done by two authors using a form with pre-specified data fields, including risk of bias appraisal. Conflicts were resolved by discussion. The decision to pool data was based on assessment of clinical design homogeneity. When warranted, studies were pooled under a random-effects model.

Results: Two RCTs for pain, function and adverse events (n = 101) met eligibility criteria. No serious threats to validity were found. Both trials compared ultrasound-guided versus landmark-guided injections and were judged similar in clinical design. Low to moderate heterogeneity was observed: shoulder pain $I^2 = 60%$, function $I^2 = 22%$. A meta-analysis demonstrated greater improvement with ultrasound-guided injections at 6 weeks after injection in both pain (mean difference = 2.23 [95% CI: 1.27, 3.18]), as assessed with a 0 to 10 visual analogue scale, and shoulder function (standardised mean difference = 1.09 [95% CI: 0.61, 1.57]) as assessed with shoulder function scores. Although more adverse events (all mild) were reported with landmark-guided injections, the difference was not statistically significant (risk ratio = 0.20 [95% CI: 0.04, 1.13]).

In two moderate-sized trials. Blinding of patients was not performed in both trials, outcome assessment since primary endpoints were wholly or partially patient-reported. Quality of RCTs on image-guided versus landmark-guided corticosteroid shoulder injections and adverse events. In this review, patients who underwent image-guided (ultrasound) corticosteroid injections potentially offer a significantly greater clinical improvement in shoulder pain and function at 6 weeks after injection. However, this apparent benefit requires confirmation by adequately-powered and well-executed RCTs.



Ultrasound and Neovascularization



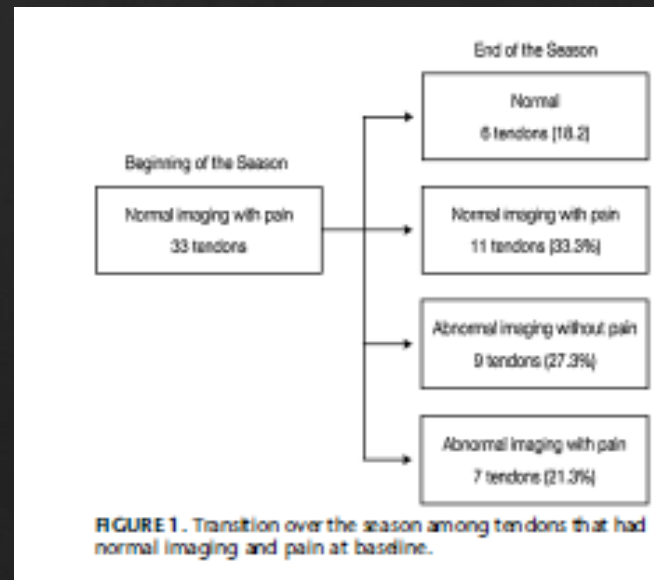
U/S and Neovascularization (cont)

- ⌘ Cook JL, et al. Vascularity and pain in the Patellar Tendon of Adult Jumping Athletes: A 5 Month Longitudinal Study. *Br J Sports Med* 2005; 39: 458-461.
 - ⌘ Study Design: Longitudinal Study
 - ⌘ Background: Study investigated changes in tendon vascularity in 102 (67 men, 35 women) volleyball players over a 6 mo competitive season
 - ⌘ Methods: Athletes examined with both grey scale U/S and color Doppler settings. Vessel length and pain measured each month on 5 occasions
 - ⌘ Vascular tendons: 1) 5/5 Persistent vascularity 2) >2, <5 occasions (intermittent)
 - ⌘ Results:
 - ⌘ 41/133 abnormal tendons were vascular on ≥ 2 occasions
 - ⌘ No significant gender difference
 - ⌘ Significant changes:
 - ⌘ Subjects with changes in both tendons more likely to have persistent vascularity ($p=0.045$)
 - ⌘ Vessels were larger in tendons with persistent vascularity ($p<0.000$)
 - ⌘ Pain greater in persistent rather than intermittent vascularity ($p=0.043$)
 - ⌘ Conclusions
 - ⌘ Presence of blood vessels more likely to be source of pain than flow in them
 - ⌘ Vascularity/Neovascularization \rightarrow Pain

U/S and Neovascularization (cont)

✧ Malliarus P, et al. Patellar Tendons with Normal Imaging and Pain: Change in Imaging and Pain Status over a Volleyball Season. *Clin J Sports Med* 2006; 16: 388-391.

- ✧ Study Design: Longitudinal Study
- ✧ Background: 101 male and female volleyball athletes. Investigate the behavior of tendons with normal imaging and pain over a volleyball season.
- ✧ Methods: Imaging and pain scores at beginning and end of competitive season. Imaging (ultrasound->hypoechoic regions, thickening). Pain scores: Single leg decline squat test.
- ✧ Results:



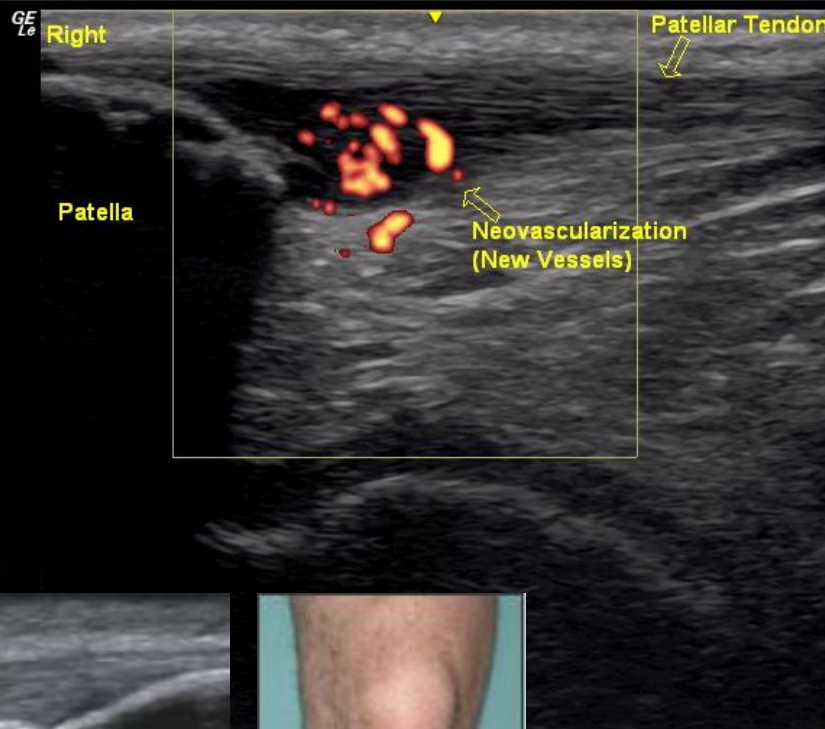
- ✧ Conclusion: Imaging cannot be used to determine whether pain in the region of the patellar tendon is tendon based.

Demonstration



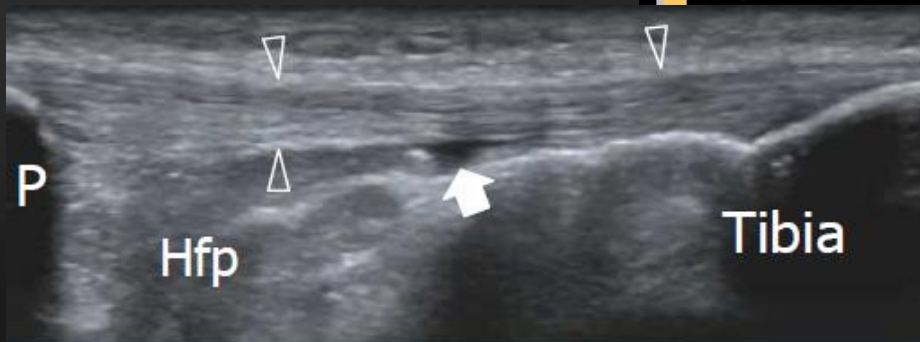
MAHEC Biltmore Campus
A beautiful education center!

Case Presentation (revisited)



- B CHI
Frq 10.0 MHz
Gn 56
E/A 3/2
Map H/0
D 3.5 cm
DR 90
FR 8 Hz
1- AO 100 %
XBea m On
BStr + Off

CF 8.0 MHz
Frq 11
Gn 11
2- L/A 2/2
AO 100 %
PRF 0.6 kHz
WF 67 Hz
S/P 2/16



Legend: arrowheads, patellar tendon; arrow, deep infrapatellar bursa; Hfp, Hoffa fat pad; P, patella

Other:

↳ Banned Substances

↳ International:

↳ <http://globaldro.com/Home>

↳ <http://list.wada-ama.org/>

↳ NCAA

↳ <http://www.ncaa.org/2016-17-ncaa-banned-drugs>

↳ State (NFHS)

↳ <https://www.nfhs.org/sports-resource-content/supplements-position-statement/>

↳ Micronutrient Testing

↳ <https://www.spectracell.com/patients/patient-micronutrient-testing/>



CLINICAL ATHLETE

Objectives (revisited)

- ⌘ Focus your therapies
 - ⌘ Understand the underlying process, treat accordingly
- ⌘ Corticosteroids are not Evil
- ⌘ There are other options than stopping what you're doing

Citations

- ⌘ Chevalier X et al. *Biologic agents in osteoarthritis: hopes and disappointments*. Nature Reviews Rheumatology 9, 400-410 (July 2013).
- ⌘ Cook JL, et al. *Vascularity and pain in the Patellar Tendon of Adult Jumping Athletes: A 5 Month Longitudinal Study*. *Br J Sports Med* 2005; 39: 458-461
- ⌘ Ericsson et al. Training history, deliberate practice and elite sports performance: an alysis in response to Tucker and Collins review- what makes champions? *Br J Sports Med*
- ⌘ Fortier LA, Potter HG, Rickey EJ, Schnabel LV, Foo LF, Chong LR, et al. Concentrated bone marrow aspirate improves full-thickness cartilage repair compared with microfracture in the equine model. *J Bone Joint Surg Am* (2010) 92(10):1927–37. doi:10.2106/JBJS.I.01284
- ⌘ Haase et al. A Pilot study investigating changes in neural processing after mindfulness training in elite athletes. *Front Behav Neurosci* Aug 2015.
- ⌘ Jayanthi et al. Sports Specialization in Young Athletes: Evidence-Based Recommendations. *Sports Health: A Multidisciplinary Approach*. 2012.
- ⌘ Joseph P. Iannotti, James Ciccone, Daniel D. Buss, Jeffrey L. Visotsky, Edward Mascha, Kathy Cotman, Nandkumar M. Rawool. Accuracy of Office-Based Ultrasonography of the Shoulder for the Diagnosis of Rotator Cuff Tears. *The Journal of Bone & Joint Surgery* Jun 2005, 87 (6) 1305-1311.
- ⌘ Kim J-D, Lee GW, Jung GH, Kim CK, Kim T, Park JH, et al. Clinical out-come of autologous bone marrow aspirates concentrate (BMAC) injection in degenerative arthritis of the knee. *Eur J Orthop Surg Traumatol* (2014) 24(8):1505–11. doi:10.1007/s00590-013-1393-9
- ⌘ Maxwell, N.J et al. Sonographically guided intratendinous injection of hyperosmolar dextrose to treat chronic tendinosis of the Achilles tendon: a pilot study. 2007. *AJR Am J Roentgenol* 189:215-220.
- ⌘ Konrad I. Gruson, David E. Ruchelsman, Joseph D. Zuckerman, Subacromial corticosteroid injections, *Journal of Shoulder and Elbow Surgery*, Volume 17, Issue 1, Supplement, January–February 2008, Pages S118-S130.
- ⌘ Malina et al. Early Sport specialization: roots, effectiveness, risks. *Curr Sports Med Rep*. 2010 Nov-Dec; 9(6): 364-71.
- ⌘ Malliarus P, et al. *Patellar Tendons with Normal Imaging and Pain: Change in Imaging and Pain Status over a Volleyball Season*. *Clin J Sports Med* 2006; 16: 388-391
- ⌘ March L et al. *Burden of Disability due to Musculoskeletal (Msk) Disorders*. *Best Practice & Research Clinical Rheumatology* 28 (2014) 353-366.
- ⌘ McIlwraith CW, Frisbie DD, Rodkey WG, Kisiday JD, Werpy NM, Kawcak CE, et al. Evaluation of intra-articular mesenchymal stem cells to augment healing of microfractured chondral defects. *Arthroscopy* (2011) 27(11):1552–61. doi:10.1016/j.arthro.2011.06.002
- ⌘ Millar NL et al. Inflammation is present in early human tendinopathy. *Am J Sports Med*. 2010 Oct; 38(10): 2085-91.
- ⌘ Mishra et al. Treatment of Chronic Elbow Tendinosis with Buffered Platelet-Rich Plasma. *Amer J of Sports Medicine*. 2006; 34(11): 1774-1778.

Citations

- ⌘ Ornetti, et al. Does platelet-rich plasma have a role in the treatment of osteoarthritis? *Joint Bone Spine*. 2016 (31-36).
- ⌘ Paoloni, et al. Topical Glyceryl Trinitrate Application in the Treatment of Chronic Supraspinatus Tendinopathy: A Randomized, Double-Blinded, Placebo-Controlled Clinical Trial; *Amer J of Sports Medicine* (33): 6. 806-13.
- ⌘ Paoloni, et al. Topical Glyceryl Trinitrate Treatment of Chronic Noninsertional Achilles Tendinopathy: A Randomized, Double-Blind, Placebo-Controlled Trial. *Journal of Bone and Joint Surgery*. 2004; 86(5): 916-22.
- ⌘ Paoloni, et al. Topical Nitric Oxide Application in the Treatment of Chronic Extensor Tendinosis at the Elbow: A Randomized, Double-Blinded, Placebo-Controlled Clinical Trial. *American Orthopaedic Society for Sports Med*. 2003; 31(6): 915-20.
- ⌘ Peerbooms et al. Positive effect of an Autologous Platelet Concentrate in Lateral Epicondylitis in a Double Blind Randomized Controlled Trial: Platelet-Rich Plasma vs Corticosteroid Injection with a 1-Year Follow-up. *Am J Sports Med*. 2010; 38: 255-61.
- ⌘ Rafols et al. Platelet-Rich Plasma Augmentation of Arthroscopic Hip Surgery for Femoroacetabular Impingement: A Prospective Study with 24-Month Follow-Up. *The Journal of Arthroscopic and Related Surgery*. 2015. 31(10). 1886-1892.
- ⌘ Rothlin et al. Psychological skills training and a mindfulness-based intervention to enhance functional athletic performance: design of a randomized controlled trial using ambulatory assessment. *BMC Psychol*. 2016 Jul 26; 4(1): 39.
- ⌘ Soh E, Li W, Ong KO, Chen W, Bautista D. Image-guided versus blind corticosteroid injections in adults with shoulder pain: a systematic review. *BMC Musculoskelet Disord*. 2011 Jun 25;12:137.
- ⌘ Triantafyllopoulos et al. Nandrolone Decanoate and Load Increase Remodeling and Strength in Human Supraspinatus Bioartificial Tendons. *Am J Sports Med* 2004; 32(4). 934-43
- ⌘ Zhang W et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis and Cartilage* (2008) 16, 137-62
- ⌘ <http://kentstatesports.com/sports/2014/7/28/Gold%20Standard.aspx>



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