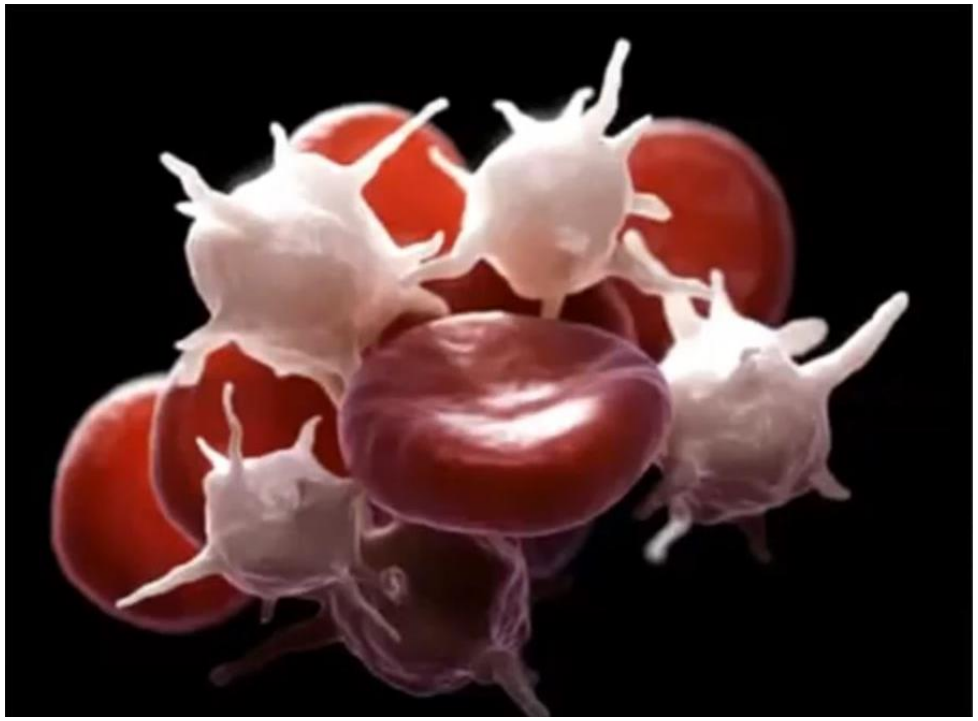
Orthobiologics



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ΚΛΙΝΙΚΗ ΑΓΙΟΣ ΛΟΥΚΑΣ

OSTEON

ORTHOPEDIC & SPINE CLINIC

Diclosures

- No Conflict of Interest
- Not an expert in Orthobiologics

St Luke's Hospital

Private practice, Thessaloniki

Osteon Clinic, Athens

Material taken from W.Berrigan review, "Orthobiologics in Orthopaedics"

Orthobiologics

- Platelet-rich plasma (PRP)
- Autologous “Stem Cells” (?)
  - *Bone Marrow Aspirate Concentrate (BMAC)*
  - *Adipose-derived Stromal Vascular Fraction*
- Amniotic Membrane allograft
- Umbilical cord-derived products

What are Orthobiologics?

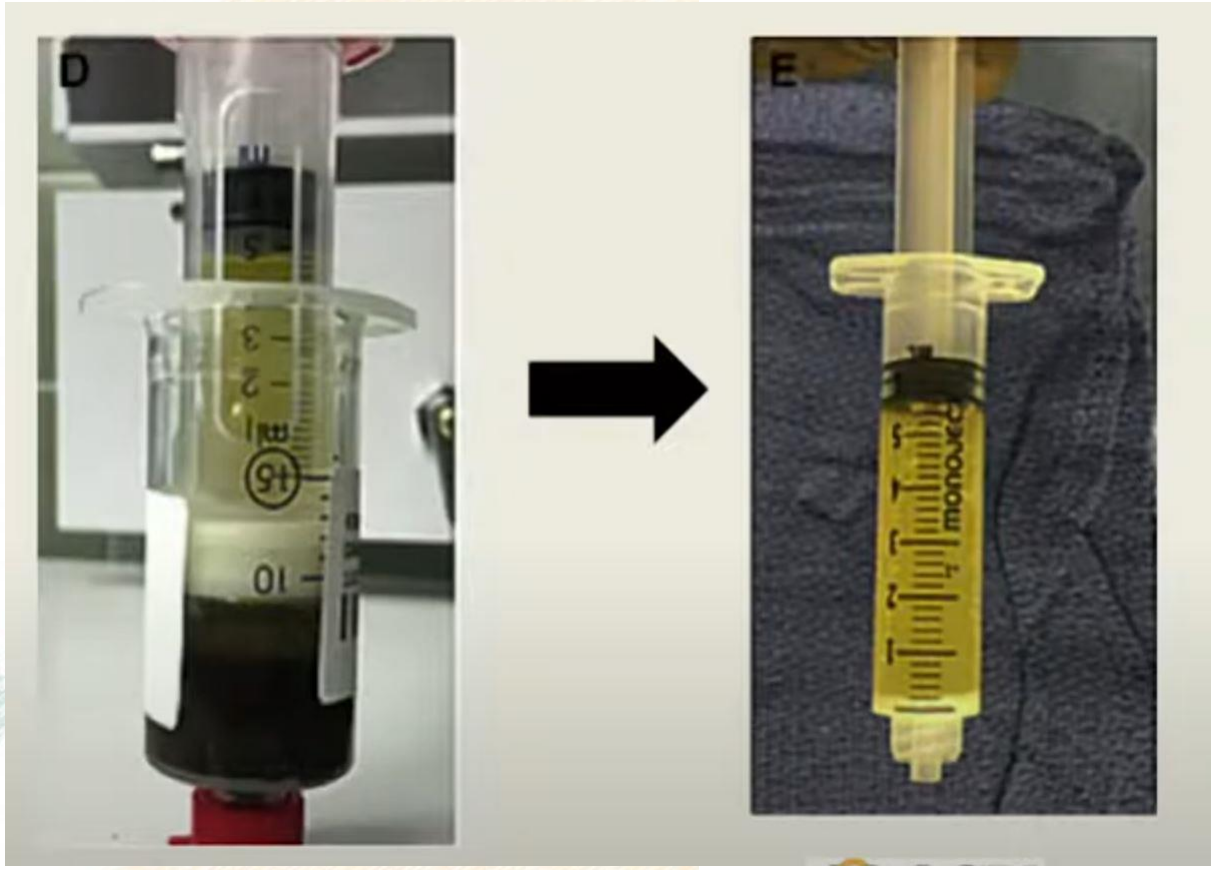
- A treatment that utilizes the body's native cellular components to promote the healing of damaged or diseased tissues
- 4 generations
    - Platelet Rich Plasma (PRP)
    - Bone Marrow Aspirate Concentrate (BMAC)
    - Lipoaspirate (Microfragmented adipose tissue, Nanofat, Stromal Vascular Fraction)
    - Amniotic tissue and umbilical products

Platelet Rich Plasma

- Concentrated cellular milieu of growth factors from venous blood following concentration
- The autologous blood concentration must be above baseline

  1.5x, 5x, 10x debate

- Deliver a supraphysiological level of growth factors to stimulate the body to heal



Call to Standardization

Two main standardization protocols

PLRA (Mautner et al 2015)

MARSPILL (Lana et al 2017)

		Criteria	
P	Platelet count	_____P Volume Injected	_____M Concentration/ uL
L	Leukocyte Concentration [1]	>1%	+
		<1%	-
R	Red Blood Cell Concentration	> 1%	+
		< 1%	-
A	Activation [2]	Yes	+
		No	-

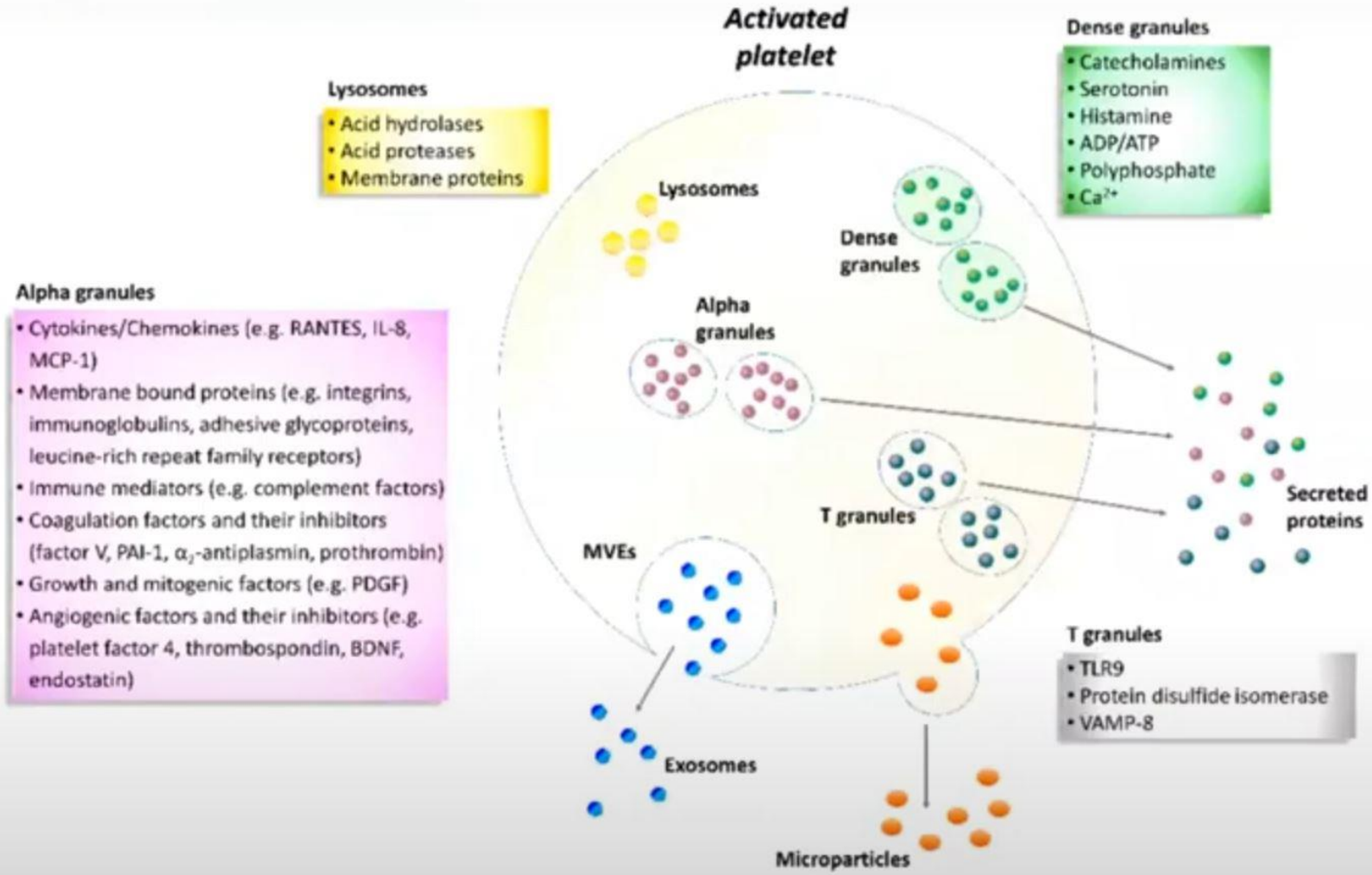
Letter	Relates to	Type
M	Method	Handmade (H) Machine (M)
A	Activation	Activated (A+) Not activated (A-)
R	Red blood cells	Rich (RBC-R) Poor (RBC-P)
S	Spin	One spin (Sp1) Two spins (Sp2)
P	Platelet number (folds basal)	PL 2–3 PL 6–8 PL 4–6 PL 8–10
I	Image guided	Guided (G+) Not guided (G-)
L	Leukocyte concentration	Rich (Lc-R) Poor (Lc-P)
L	Light activation	Activated (A+) Not activated (A-)

Lc: Leukocyte concentration; PL: Platelet concentration; RBC: Red blood cell.

Leucocytes rich vs poor

- LR-PRP (increased inflammatory mediators):
  - *TNF-α*
  - *IL-6*
  - *IFN-γ*
  - *IL-1β*
- LP-PRP (antiinflammatory mediators)
  - *IL-4*
  - *IL-10*

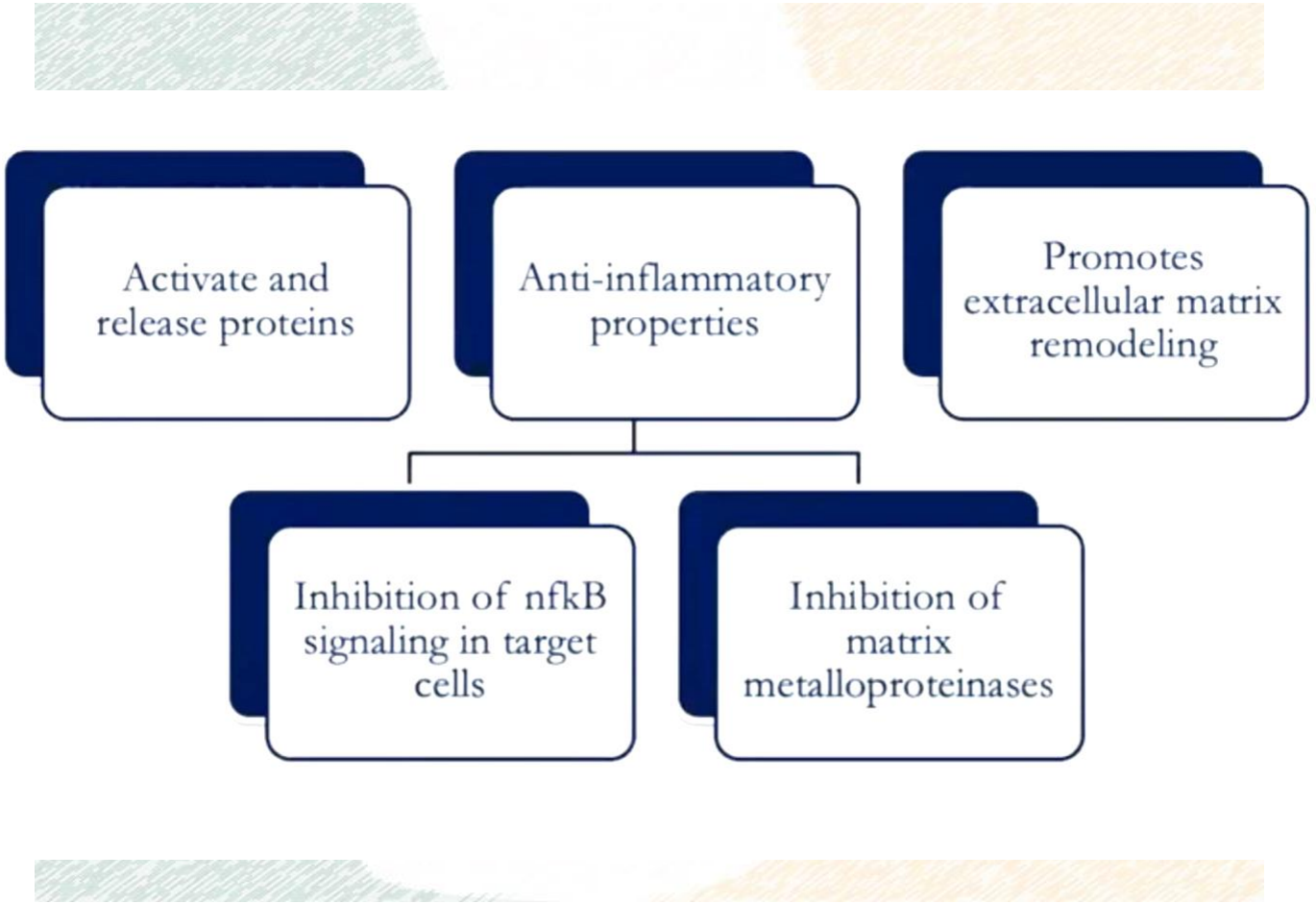
Platelet Rich Plasma: How Does it Work?



Growth Factors

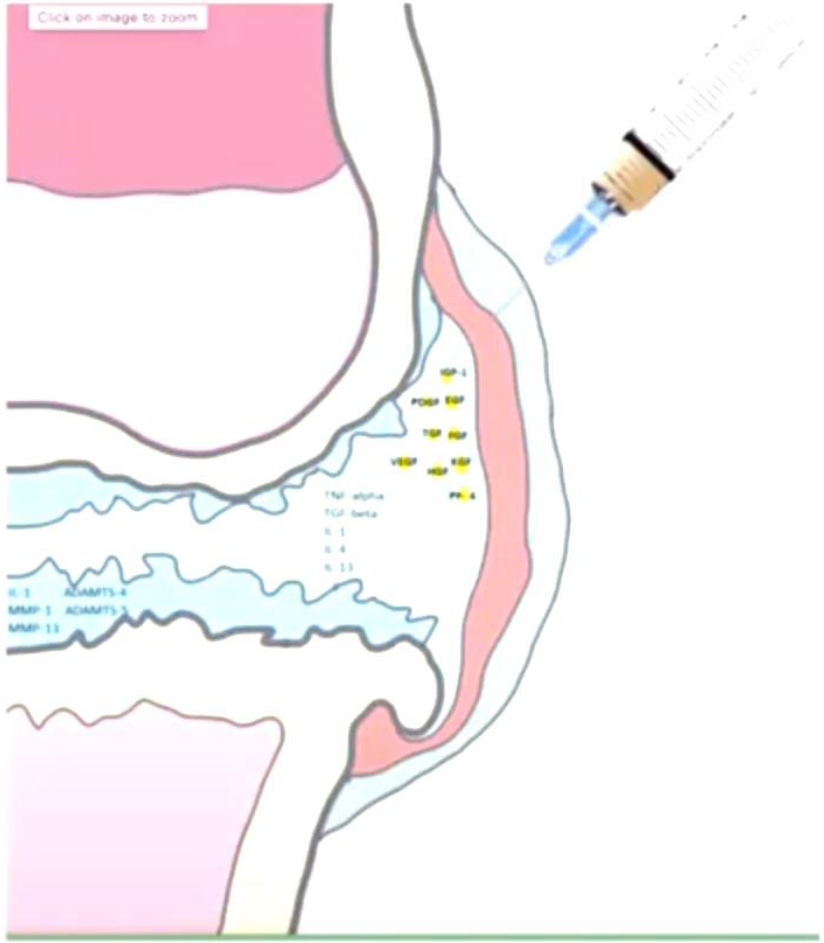
Platelet-derived growth factor (PDGF)	Stimulates cell replication
	Promotes angiogenesis
	Promotes epithelialization
	Promotes granulation tissue formation
Transforming growth factor (TGF)	Promotes formation of extracellular matrix
	Regulates bone cell metabolism
Vascular endothelial growth factor (VEGF)r	Promotes angiogenesis
Epidermal growth factor (EGF)	Promotes cell differentiation and stimulates re-epithelialisation, angiogenesis and collagenase activity
Fibroblast growth factor (FGF)	Promotes proliferation of endothelial cells and fibroblasts
	Stimulates angiogenesis

Sampson S, Gerhardt M, Mandelbaum B. Platelet rich plasma injection grafts for musculoskeletal injuries: a review. Curr Rev Musculoskelet Med. 2008 Dec;1(3-4):165-74. doi: 10.1007/s12178-008-9032-5. PMID: 19468902; PMCID: PMC2682411.


Activate and release proteins
Anti-inflammatory properties
Promotes extracellular matrix remodeling
Inhibition of nfkB signaling in target cells
Inhibition of matrix metalloproteinases

Mechanism of Action: Osteoarthritis

- Catabolic factors: IL-1B and TNF-Alpha
  - Matrix Metalloproteinases (MMPs)
  - Elastases
  - Chondrocyte apoptosis
- Growth factors that enhance cartilage repair and counteract this process
  - Enhance IL1-RA, TIMP, Type II collagen
  - Downregulate IL-1 receptor
  - Enhance chondrocyte proliferation



A. Joints - intraarticular

AMSSM
AMERICAN MEDICAL SOCIETY FOR SPORTS MEDICINE

American Medical Society for Sports Medicine Position Statement: Principles for the Responsible Use of Regenerative Medicine in Sports Medicine

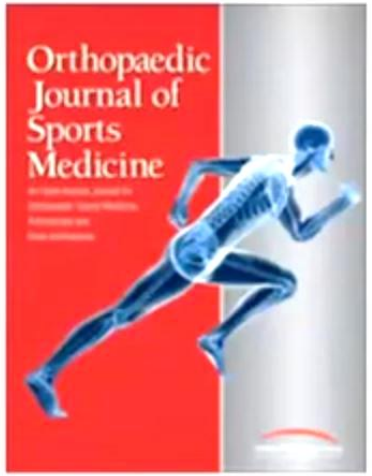
Jonathan T. Finnoff, DO,* Tariq M. Awan, DO,† Joanne Borg-Stein, MD,‡ Kimberly G. Harmon, MD,§ Daniel C. Herman, MD, PhD,¶ Gerard A. Malanga, MD,|| Zubin Master, PhD,** Kenneth R. Mautner, MD,†††‡‡‡ and Shane A. Shapiro, MD§§

TABLE 4. Summary of Meta-Analyses and Systematic Reviews Evaluating the Efficacy and Major Adverse Events of Platelet-Rich Plasma Injections for OA From 2019 to 2020

OA	Treatment Effective	Treatment Ineffective	Treatment Mixed Efficacy	Major Adverse Events
Unspecified location	1 study[33]	1 study[34]	0 studies	0 studies
Ankle	1 study[35]	0 studies	0 studies	0 studies
Foot	1 study[36]	0 studies	0 studies	0 studies
Hand	1 study[36]	0 studies	0 studies	0 studies
Hip	3 studies[11,37,38]	1 study[39]	0 studies	1 study[39]
Knee	14 studies[11,12,19,40–50]	0 studies	0 studies	1 study[46]
Temporo-mandibular	4 studies[51–54]	0 studies	0 studies	0 studies

OA, osteoarthritis.

Knee



Effectiveness of Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis

A Meta-analysis of Randomized Controlled Clinical Trials

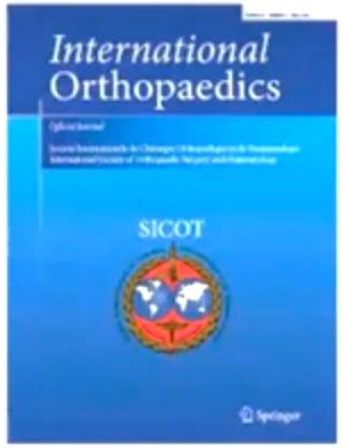
Liu-yan Nie,* MBBS, Kun Zhao,† MBBS, Jiaqi Ruan,† MBBS, and Jing Xue,*‡ PhD

Investigation performed at The Department of Rheumatology, the Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, P.R. China

21 trials included

PRP compared to corticosteroid, saline, HADF

"PRP injections are beneficial for pain relief and functional improvement in knee osteoarthritis."



Platelet-rich plasma injections delay the need for knee arthroplasty: a retrospective study and survival analysis

Mikel Sánchez [1 2], Cristina Jorquera [2], Pello Sánchez [2], Maider Beitia [2], Beatriz García-Cano [1], Jorge Guadilla [1], Diego Delgado [3 4]

- Retrospective analysis and survival analysis from 2014-2019
- 1084 Patients, 667 met the inclusion criteria
- KL 3-4 Osteoarthritis eligible for TKA
- 74.1% of patients achieved a delay in TKA of more than 1.5 years with a median delay of 5.3 years
- 85.7% of patients did not undergo TKA during five years follow up

Platelet-Rich Plasma Versus Hyaluronic Acid for Knee Osteoarthritis

CME

A Systematic Review and Meta-analysis of Randomized Controlled Trials

John W. Belk,*† BA, Matthew J. Kraeutler,‡ MD, Darby A. Houck,† BA, Jesse A. Goodrich,† BA, Jason L. Dragoo,† MD, and Eric C. McCarty,† MD
Investigation performed at Department of Orthopedics, University of Colorado School of Medicine, Aurora, Colorado, USA

- Level 1 Studies Comparing HA and PRP
- 18 Studies 811 Patients PRP, 797 HA
- Mean Follow-up 11.1 Months
- Improvement was higher in the PRP group (44.7%) than the HA group (12.6%) for WOMAC
- Of 11 studies based on the VAS, 6 reported PRP patients to have significantly less pain at latest follow-up when compared with HA patients

SYSTEMATIC REVIEW Open Access

Efficacy and safety of platelet-rich plasma combined with hyaluronic acid versus platelet-rich plasma alone for knee osteoarthritis: a systematic review and meta-analysis

Qing Zhang, Tuodong Liu, Yuan Gu, Yongquan Gao and Jiangdong Ni*

- 13 articles, 1118 patients
- VAS scores, WOMAC, KOOS and IKDC
- Smallest treatment effect did not reach MCID
- PRP+HA therapy was not found to be superior to PRP alone therapy in pain relief and function improvement for patients with KOA

The effectiveness of leucocyte-poor platelet-rich plasma injections on symptomatic early osteoarthritis of the knee: the PEAK randomized controlled trial

Emma Lewis [1], Khalid Merghani [1], Iain Robertson [2 3], Jonathon Mulford [1], Ben Prentice [1], Ronnie Mathew [1], Peter Van Winden [1], Kathryn Ogden [2 3]

Affiliations + expand

PMID: 35638203 DOI: 10.1302/0301-620X.104B6.BJJ-2021-1109.R2

There is **no evidence that single or multiple PRP had any additional beneficial** effect compared to saline injection up to 12 months, follow-up after treatment of early stage symptomatic OA of the knee.

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JAMA | Original Investigation

Effect of Intra-articular Platelet-Rich Plasma vs Placebo Injection on Pain and Medial Tibial Cartilage Volume in Patients With Knee Osteoarthritis
The RESTORE Randomized Clinical Trial

Kim L. Bennell, PhD; Kade L. Paterson, PhD; Ben R. Metcalf, BSc; Vicky Duong, DPT; Jillian Eyles, PhD; Jessica Kasza, PhD; Yuanyuan Wang, PhD; Flavia Cicuttini, PhD; Rachelle Buchbinder, PhD; Andrew Forbes, PhD; Anthony Harris, MSc; Shirley P. Yu, MPH; David Connell, MMed; James Linklater, MBBS; Bing Hui Wang, PhD; Win Min Oo, PhD; David J. Hunter, PhD

Among patients with symptomatic mild to moderate radiographic knee OA, **intra-articular injection of PRP, compared with injection of saline placebo, did not result in a significant difference** in symptoms or joint structure at 12 months.

SCIENTIFIC REPORTS

EN

Platelet-rich plasma (PRP) in osteoarthritis (OA) knee: Correct dose critical for long term clinical efficacy

Himanshu Bansal[1], Jerry Leon[2], Jeremy L. Pont[3], David A. Wilson[3], Anupama Bansal[1], Diwaker Agarwal[4] & Iustin Preoteasa[5]

> 10 Billion platelets for the total dose of platelets

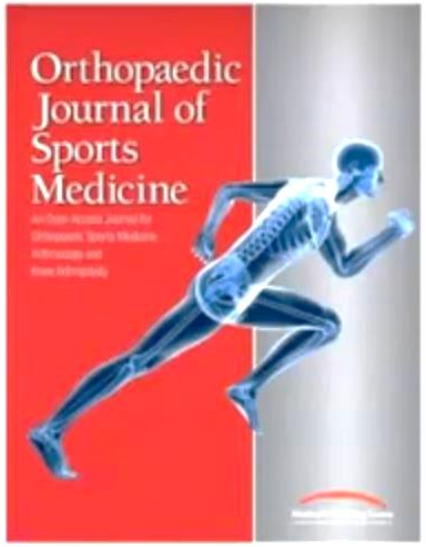
Leukocyte-Rich versus Leukocyte-Poor Platelet-Rich Plasma for the Treatment of Knee Osteoarthritis

A Double-Blind Randomized Trial

Alessandro Di Martino,* MD, Angelo Boffa,* MD, Luca Andriolo,* MD, Iacopo Romandini,*† MD, Sante Alessandro Altamura,* MD, Annarita Cenacchi,‡ MD, Veronica Roverini,‡ MLT, Stefano Zaffagnini,* MD, Prof., and Giuseppe Filardo,§ MD, PhD, Prof.
Investigation performed at IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy

> 5 Billion platelets per injection delivered in BOTH groups

Hip



Comparing Intra-articular Injections of Leukocyte-Poor Platelet-Rich Plasma Versus Low-Molecular Weight Hyaluronic Acid for the Treatment of Symptomatic Osteoarthritis of the Hip: A Double-Blind, Randomized Pilot Study

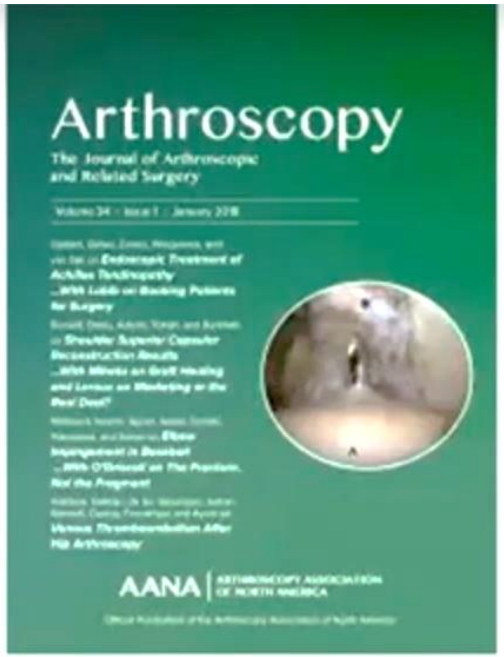
Matthew J Kraeutler [1], Darby A Houck [2], Tigran Garabekyan [3], Shannon L Miller [2], Jason L Dragoo [2], Omer Mei-Dan [2]

34 patients (36 Hips)

3 weekly IA injections of either PRP or HA

Conversion to either hip resurfacing or total hip arthroplasty over 2 years

50% of LMWHA converted to surgery vs 15.8% in the PRP group



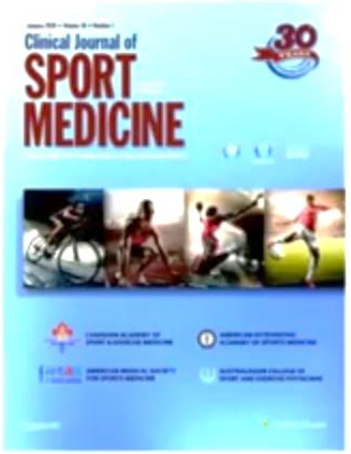
Systematic Review

Platelet-Rich Plasma Versus Hyaluronic Acid for Hip Osteoarthritis Yields Similarly Beneficial Short-Term Clinical Outcomes: A Systematic Review and Meta-analysis of Level I and II Randomized Controlled Trials

John W. Belk, B.A., Darby A. Houck, B.A., Connor P. Littlefield, B.A., Matthew J. Kraeutler, M.D., Andrew G. Potyk, B.S., Omer Mei-Dan, M.D., Jason L. Dragoo, M.D., Rachel M. Frank, M.D., and Eric C. McCarty, M.D.

- 6 Studies (5 Level 1, 1 Level 2), 211 patients PRP, 197 patients HA
- WOMAC, VAS, and Harris Hip Score
- No significant difference was found between HA and PRP
- Both showed improvement in outcome measures
- The average time to follow up is 12 months
- Large heterogeneity

Shoulder



Efficacy of Ultrasound-Guided Glenohumeral Joint Injections of Leukocyte-Poor Platelet-Rich Plasma Versus Hyaluronic Acid in the Treatment of Glenohumeral Osteoarthritis: A Randomized, Double-Blind Controlled Trial

Jonathan S Kirschner, MD,* Jennifer Cheng, PhD,* Andrew Creighton, DO,* Kristen Santiago, BA,* Nicole Hurwitz, BS,* Mark Dundas, MD,† Nicholas Beatty, DO,‡§ Dallas Kingsbury, MD,¶ Gabrielle Konin, MD,|| Zafir Abutalib, MHS,** and Richard Chang, MD, MPH‡

- 70 patients
- HA Group (36), LP-PRP (34)
- Shoulder Pain and Disability Index (SPADI), Numerical Rating Scale (NRS), satisfaction, side effects
- Improvement in both groups regardless of OA severity
- Similar satisfaction levels

Wrist

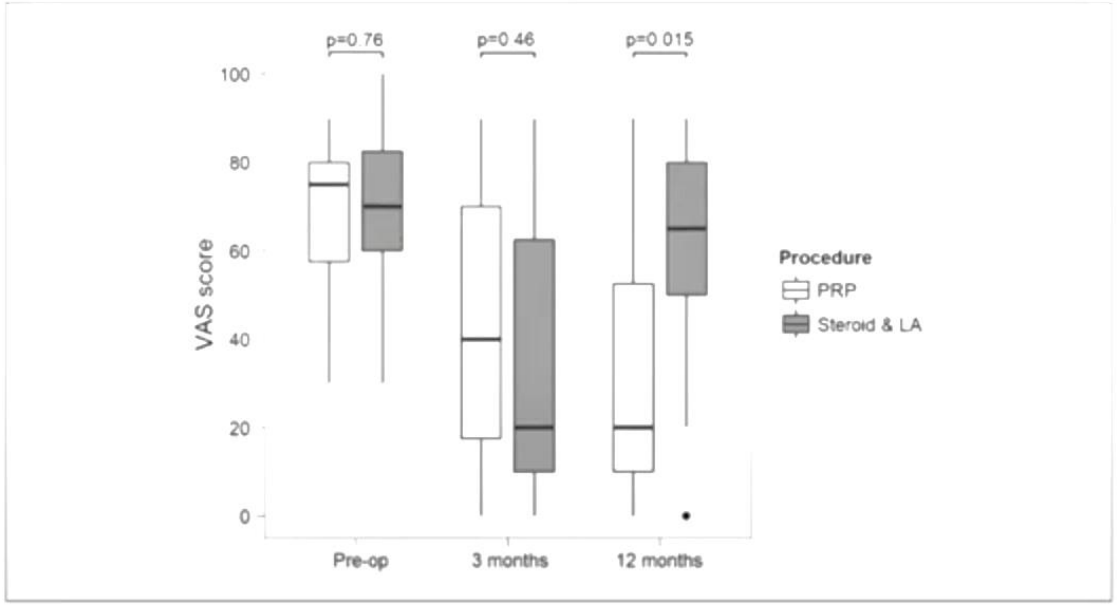
Orthobiologics

Platelet-Rich Plasma versus Corticosteroid Intra-Articular Injections for the Treatment of Trapeziometacarpal Arthritis: A Prospective Randomized Controlled Clinical Trial

CARTILAGE
2021, Vol. 12(1) 51–61

DOI: 10.1177/1947603518805230
journals.sagepub.com/home/CAR
SAGE

- 33 Patients
- 2 PRP injections vs 2 meythlprednisolone + lidocaine
- VAS, QDASH and satisfaction
- Satisfaction: 69.5% (PRP) vs 12.5% (Methylprednisolone)



Ankle

JAMA | Original Investigation

Effect of Platelet-Rich Plasma Injections vs Placebo on Ankle Symptoms and Function in Patients With Ankle Osteoarthritis

A Randomized Clinical Trial

Liam D. A. Paget, MD; Gustaaf Reurink, PhD; Robert-Jan de Vos, PhD; Adam Weir, PhD; Maarten H. Moen, PhD; Sita M. A. Bierma-Zeinstra, PhD; Sjoerd A. S. Stufkens, PhD; Gino M. M. J. Kerkhoffs, PhD; Johannes L. Tol, PhD; for the PRIMA Study Group

Among patients with ankle osteoarthritis, **intra-articular PRP injections, compared with placebo injections, did not significantly improve ankle symptoms and function over 26 weeks.** The results of this study do not support the use of PRP injections for ankle osteoarthritis.

B. Tendons

Tendinopathy

AMERICAN MEDICAL SOCIETY FOR SPORTS MEDICINE

American Medical Society for Sports Medicine Position Statement: Principles for the Responsible Use of Regenerative Medicine in Sports Medicine

Jonathan T. Finnoff, DO,* Tariq M. Awan, DO,† Joanne Borg-Stein, MD,‡ Kimberly G. Harmon, MD,§ Daniel C. Herman, MD, PhD,¶ Gerard A. Malanga, MD,|| Zubin Master, PhD,** Kenneth R. Mautner, MD,†††‡‡ and Shane A. Shapiro, MD§§

TABLE 3. Summary of Meta-Analyses and Systematic Reviews Evaluating the Efficacy and Major Adverse Events of Platelet-Rich Plasma Injections for Tendinopathy From 2019 to 2020

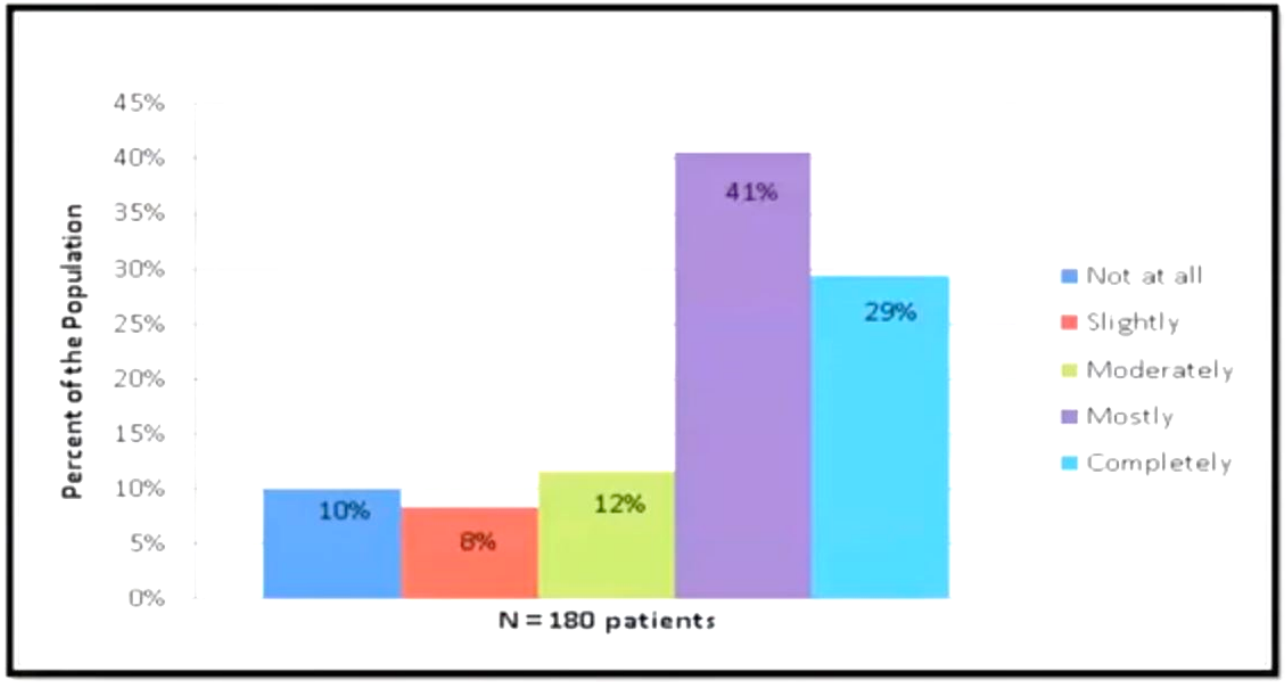
Tendinopathy	Treatment Effective	Treatment Ineffective	Treatment Mixed Efficacy	Major Adverse Events
Unspecified location	3 studies[10–12]	0 studies	0 studies	0 studies
Achilles tendinopathy	1 study[13]	2 studies[14,15]	2 studies[16,17]	0 studies
Lateral epicondylopathy	5 studies[18–22]	1 study[23]	1 study[24]	1 study[23]
Patellar tendinopathy	4 studies[25–28]	0 studies	0 studies	0 studies
Rotator cuff tendinopathy	3 studies[29–31]	0 studies	1 studies[32]	0 studies

Outcomes after ultrasound-guided platelet-rich plasma injections for chronic tendinopathy: a multicenter, retrospective review

Kenneth Mautner [1], Ricardo E Colberg, Gerard Malanga, Joanne P Borg-Stein, Kimberly G Harmon, Aisha S Dharamsi, Samuel Chu, Paul Homer

- Pts age 16-70 (avg 48 yrs)
- Greater than 6 months of pain (avg 36 months)
- Diagnosed by clinical exam plus MRI or diagnostic US
- Failed conventional treatments
  - Medications, bracing , stretching, strengthening, modalities
- PRP was done under US guidance

Improvement



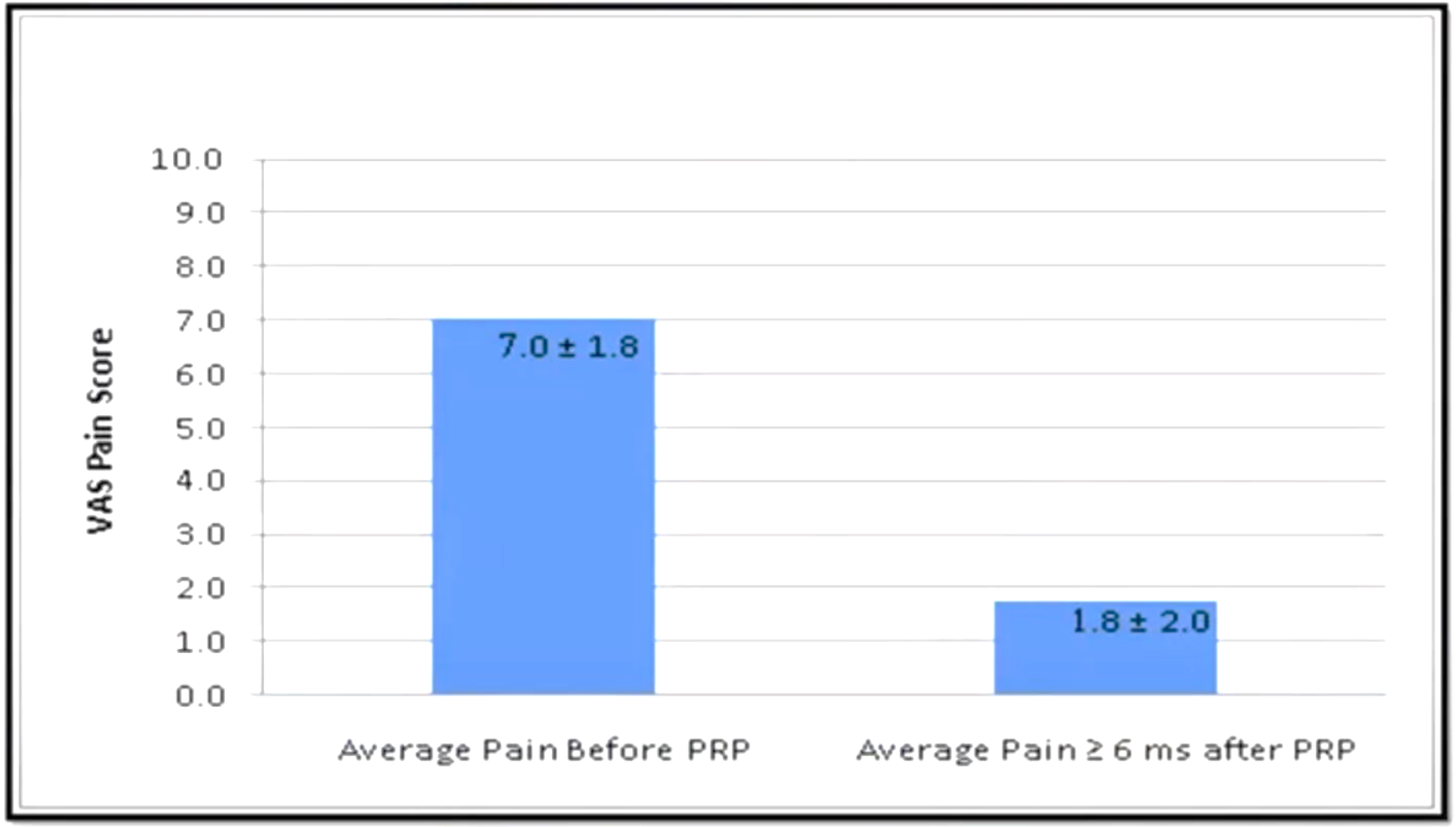
82% reported moderate to complete improvement

– 50%- 100% relief of symptoms

70 % reported mostly to complete improvement

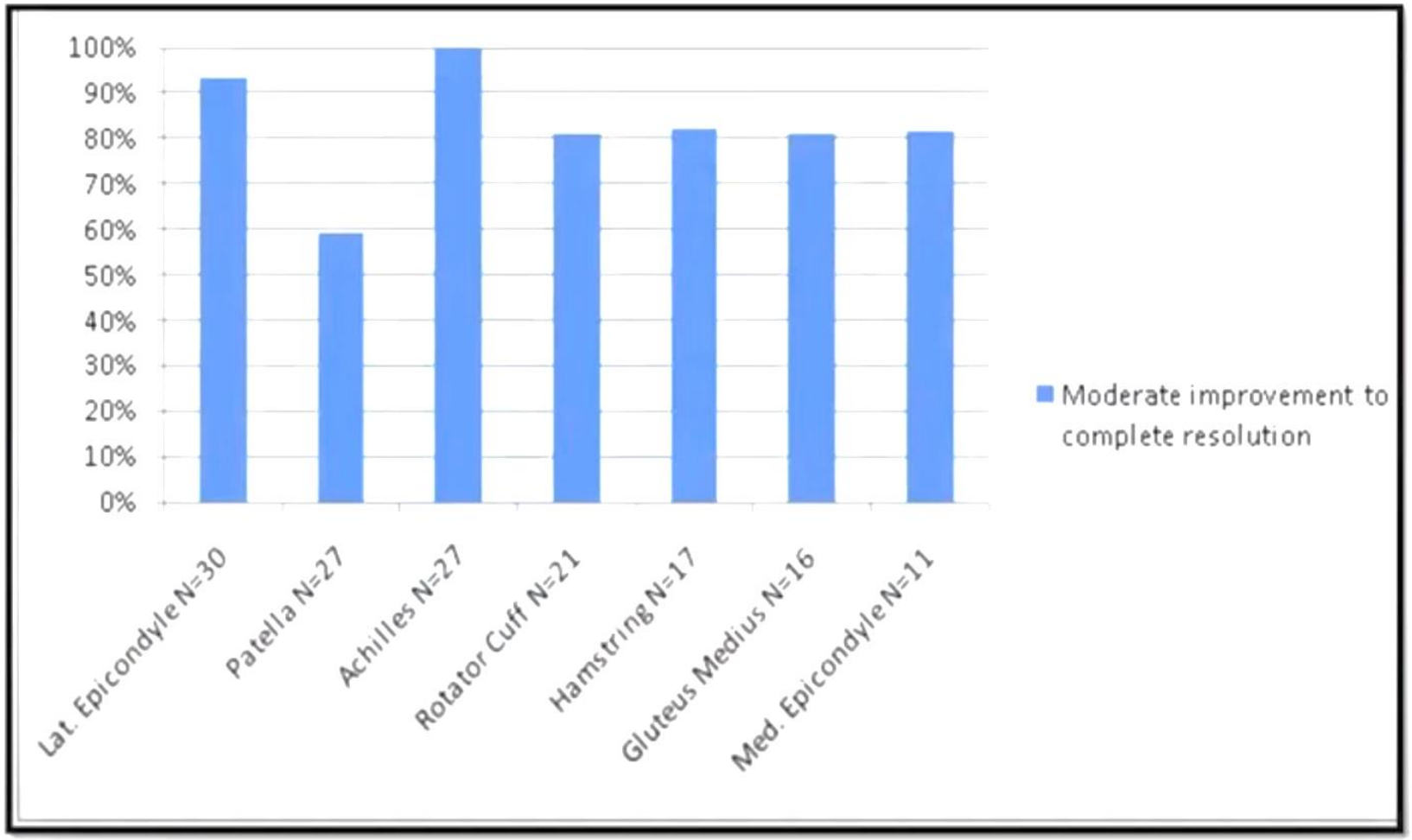
-- 75-100% relief of symptoms

Pain Score pre and post PRP



➤ 74% Reduction in VAS

% with > 50% Improvement



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JAMA | Original Investigation

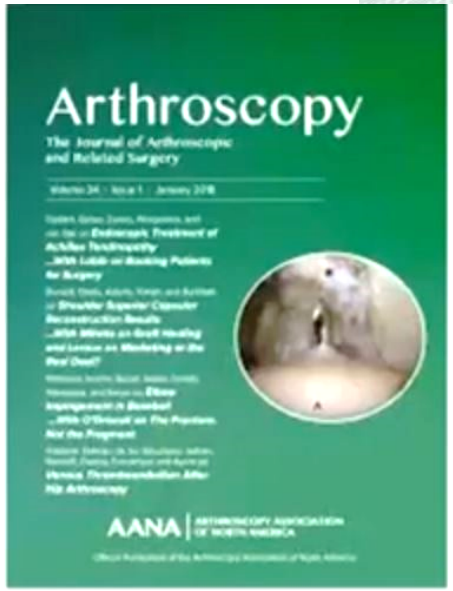
Effect of Platelet-Rich Plasma Injection vs Sham Injection on Tendon Dysfunction in Patients With Chronic Midportion Achilles Tendinopathy

A Randomized Clinical Trial

Rebecca S. Kearney, PhD; Chen Ji, PhD; Jane Warwick, PhD; Nicholas Parsons, PhD; Jaclyn Brown, BSc; Paul Harrison, PhD; Jonathan Young, MBChB; Matthew L. Costa, PhD; for the ATM Trial Collaborators

Among patients with chronic midportion Achilles tendinopathy, treatment with a single injection of intra-tendinous platelet-rich plasma, compared with insertion of a subcutaneous dry needle, did not reduce Achilles tendon dysfunction at 6 months. **These findings do not support the use of this treatment for chronic midportion Achilles tendinopathy**

3. Muscles



Does Platelet-Rich Plasma Lead to Earlier Return to Sport When Compared With Conservative Treatment in Acute Muscle Injuries? A Systematic Review and Meta-analysis

Ujash Sheth [1], Tim Dwyer [2], Ira Smith [3], David Wasserstein [4], John Theodoropoulos [2], Sachdeep Takhar [3], Jaskarndip Chahal [5]

Affiliations + expand

PMID: 28800920 DOI: 10.1016/j.arthro.2017.06.039

- Grade 1 or 2 Muscle Strains
- 5 RCTs, 268 patients
- Reduced return to play time and no difference in risk of reinjury
- No difference in RTP and Risk of reinjury in hamstring injuries alone

STEM CELLS

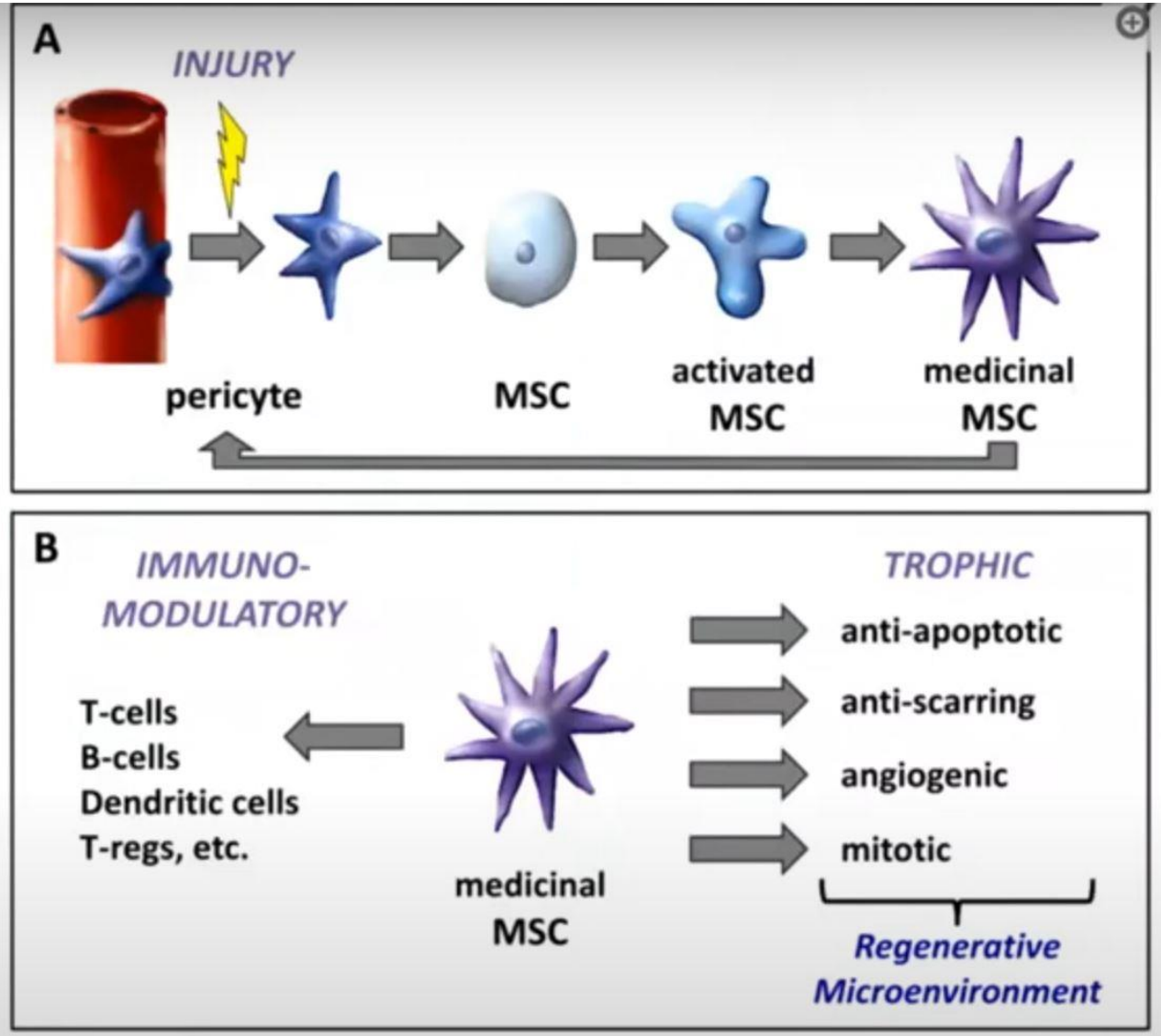
Mesenchymal Stem Cells (MSCs)

- Found in adipose, dermis, synovial fluid periosteum, umbilical cord blood, placenta and amniotic fluid

Hematopoetic Stem Cells (HSCs)

- Convert to MSCs and can orchestrate bone formation
- True driver?

MSCs

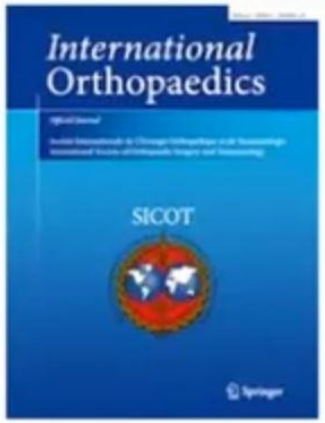

A
INJURY
pericyte
MSC
activated MSC
medicinal MSC
B
IMMUNO-MODULATORY
T-cells
B-cells
Dendritic cells
T-regs, etc.
medicinal MSC
TROPHIC
anti-apoptotic
anti-scarring
angiogenic
mitotic
Regenerative Microenvironment

Are these treatments safe?

ORIGINAL PAPER

A multi-center analysis of adverse events among two thousand, three hundred and seventy two adult patients undergoing adult autologous stem cell therapy for orthopaedic conditions

Christopher J. Centeno[1] · Hasan Al-Sayegh[2] · Michael D. Freeman[3,7] · Jay Smith[4] · William D. Murrell[5] · Rostyslav Bubnov[6]



- 3012 procedures performed on 2372 patients with follow-up 2.2 years, 18 Clinical Facilities

- 325 Adverse Events

- Pain post-procedure (3.9%), Pain from progressive degenerative disease (3.8%), 7 neoplasms (less than the general population)

- Lowest adverse events-BMC alone

Characteristics of Stem Cells, Culture-Expanded Connective Tissue Cells and Minimally Manipulated Cell Preparations

Cell Type	Definition	Examples
Stem cells[10]	Three minimum characteristics: (1) capable of division and self-renewal for long periods of time, (2) unspecialized, and (3) can give rise to specialized cell types	ES cells, induced pluripotent stem cells
Culture-expanded connective tissue cells	Culture-expanded tissue-derived cells	MSCs, muscle-derived cells, adipose-derived cells, cartilage-derived cells
	Plastic adherent	—
	Tend to differentiate or undergo senescence with prolonged culture	—
	Biological attributes and function dependent on and vary with tissue source and culture conditions	—
	Bioactivity varies between donors and batch, even with standardized processing	—
	Expansion makes cell banking and allograft sourcing an option	—
	Requires prospective FDA-approved clinical trials	—
Minimally manipulated autologous cell preparations	Cleared for homologous use	Bone marrow concentrate, adipose stromal or stromal vascular fraction, placenta tissue fragments
	Processing must not alter the relevant biological characteristics of cells or tissues	—
	Mixed cell populations, with variable composition	—
	Stem or progenitor cells may be present at lower prevalence	—
	Biological attributes and function highly variable	—

ES = embryonic stem, MSC = mesenchymal stromal cell

Characteristics of Stem Cells, Culture-Expanded Connective Tissue Cells and Minimally Manipulated Cell Preparations

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ES = embryonic stem, MSC = mesenchymal stromal cell

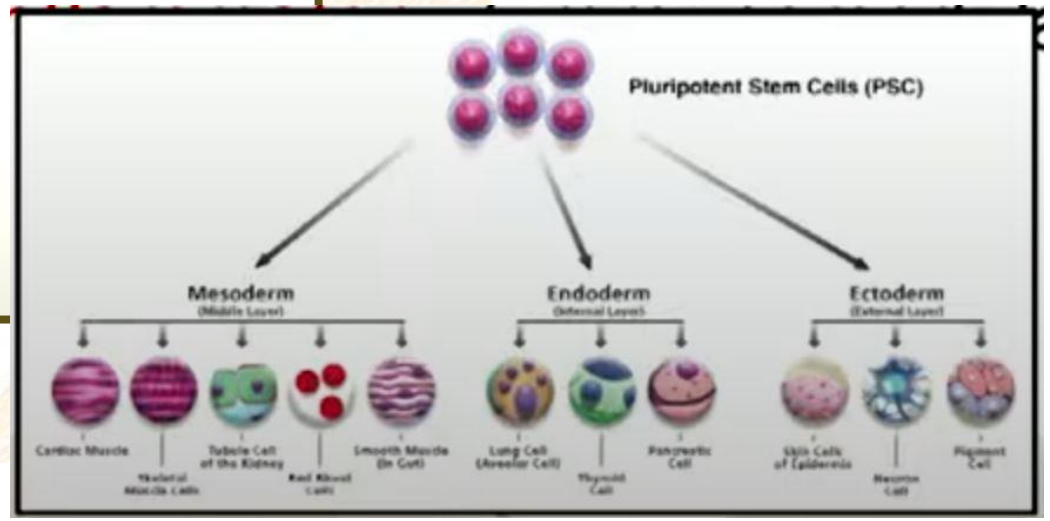
Harvested Tissue

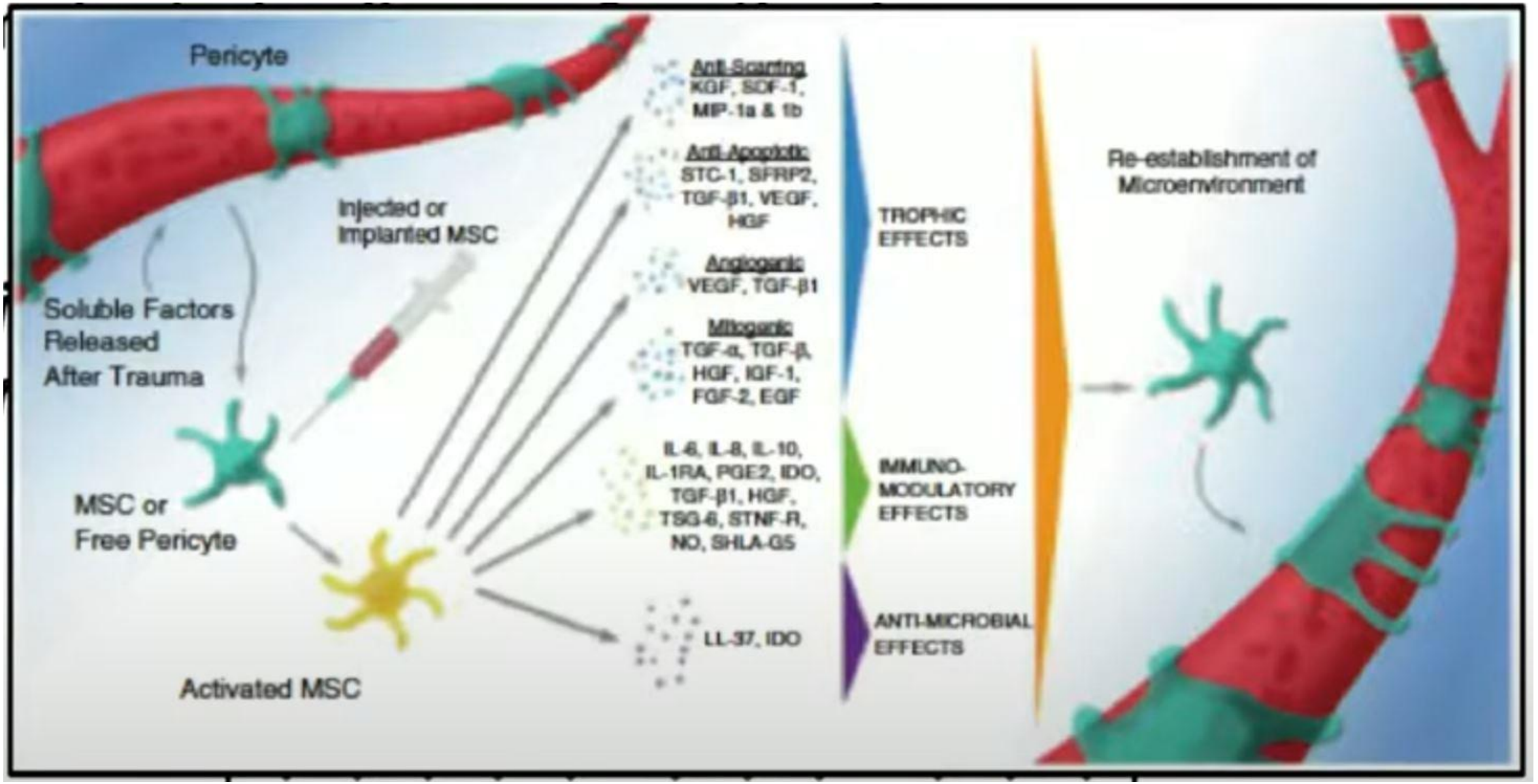
(i.e. blood, fat, bone marrow)

Other

(myelopoietic cells, erythropoietic ells, peripheral blood cells)

Stem cells (MSCs), progenitor cells (1/1000 – 1/1000000 cells)




Pericyte
Injected or Implanted MSC
Soluble Factors Released After Trauma
MSC or Free Pericyte
Activated MSC
Anti-Scarring
KGF, SDF-1, MIP-1a & 1b
Anti-Apoptotic
STC-1, SFRP2, TGF-β1, VEGF, HGF
Angiogenic
VEGF, TGF-β1
Mitogenic
TGF-α, TGF-β, HGF, IGF-1, FGF-2, EGF
IL-6, IL-8, IL-10, IL-1RA, PGE2, IDO, TGF-β1, HGF, TSG-6, STNF-R, NO, SHLA-G5
LL-37, IDO
TROPHIC EFFECTS
IMMUNO-MODULATORY EFFECTS
ANTI-MICROBIAL EFFECTS
Re-establishment of Microenvironment

Mesenchymal Stem cells

MSCs are pericytes that can be isolated from any vascularized tissue

MSCs secrete a large number of bioactive molecules and have immunomodulatory activities

Secrete pro or anti-inflammatory molecules based on the environment

Manage pain by secreting molecules that occupy opioid receptors

Secrete molecules that are mitogenic to tissue intrinsic stem cells

Caplan AI, Correa D. The MSC: an injury drugstore. Cell Stem Cell. 2011 Jul 8;9(1):11-5. doi: 10.1016/j.stem.2011.06.008. PMID: 21726829; PMCID: PMC3144500. Title

Bone Marrow Aspirate Concetrate

Harvest

BMAC

- 60 cc of bone marrow aspirate was harvested from the PSIS using ultrasound guidance
- 3 separate sites with 10cc syringes (20 cc per site)
- Processed with Centrifuge
- 8cc of pure BMAC

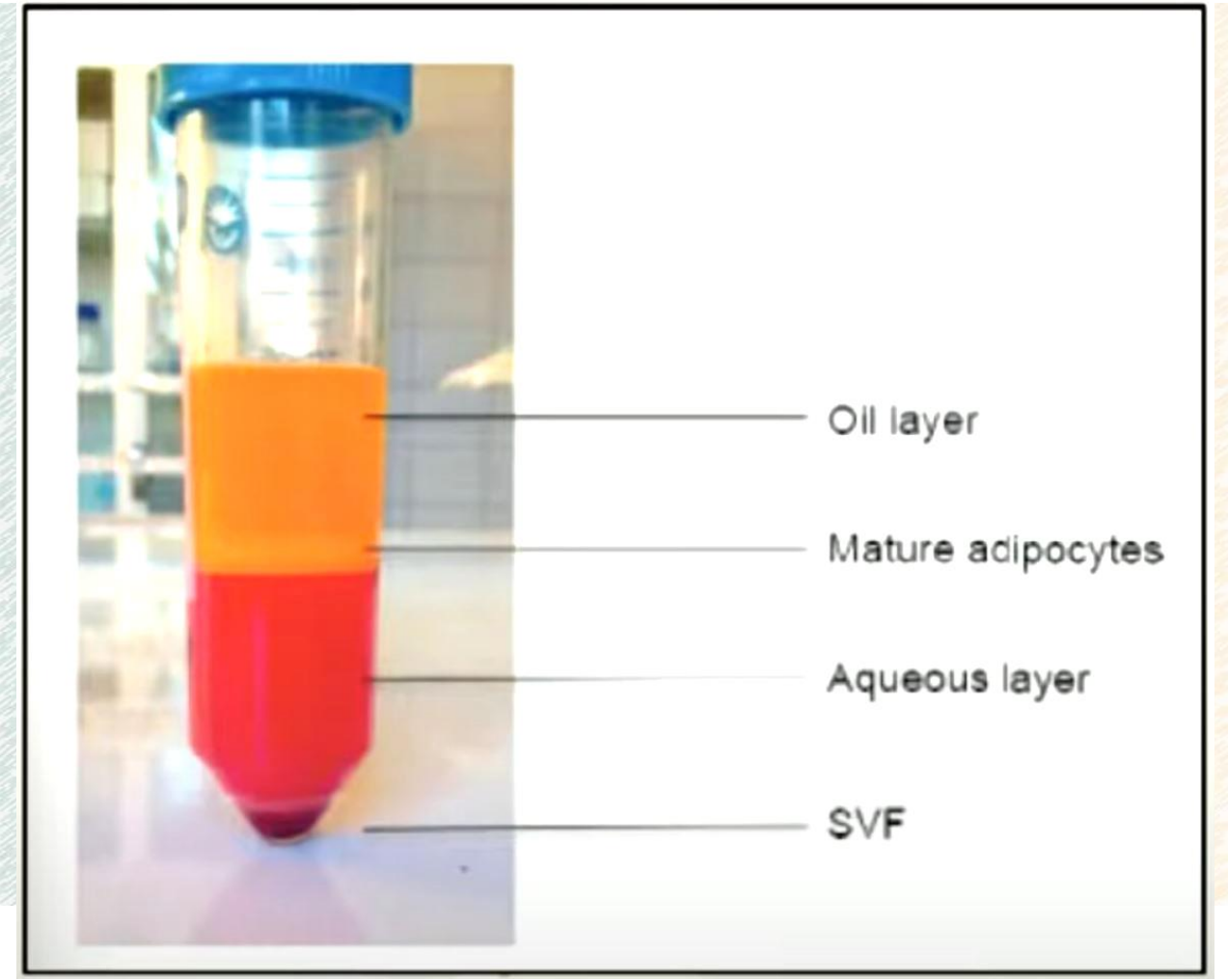
Microfragmented Adipose Tissue

Harvest

MFAT

- Harvested from the lower abdomen
- 60cc syringe to infiltrate 120cc of tumescent anesthesia
- 30 cc of lipoaspirate through a low-pressure vacuum using the lipoaspirate cannula
- Decanted, tumescent anesthesia removed, and transferred to a manual processing device
- 9cc MFAT

Stromal Vascular Fraction



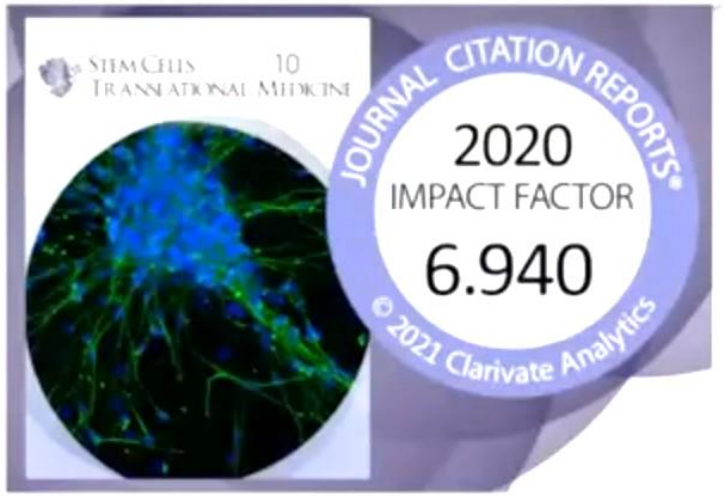
Bone Marrow vs Adipose

Adipose has more MSCs than bone marrow by concentration and volume (De Ugarte et al 2003)

- Up to 500x more stem cells/gram than bone marrow
- Mostly MSC
- Less decrease in number and activity with age compared to BMC

Adipose tissue MSC may have an inferior potential for both osteogenesis and chondrogenesis compared to BMC (Gun-ll et al)

- No clinical superiority between the two



Functional Outcomes Following Microfragmented Adipose Tissue Versus Bone Marrow Aspirate Concentrate Injections for Symptomatic Knee Osteoarthritis

KENNETH MAUTNER,[a,b] ROBERT BOWERS,[a,b] KIRK EASLEY,[c] ZACHARY FAUSEL,[b] RYAN ROBINSON[a]

- Retrospective review of prospectively collected data
- 110 Patients, 76 with adequate follow-up, 106 knees
- Follow Up: 1.8 years MFAT, 1.09 years BMAC
- Both groups improved in VAS, KOOS, and EQOL
- **No difference between groups**

MSCs Compared to PRP

Bone Marrow Aspirate Concentrate Is Equivalent to Platelet-Rich Plasma for the Treatment of Knee Osteoarthritis at 1 Year

A Prospective, Randomized Trial

Adam W. Anz,*† MD, Ryan Hubbard,† MD, Nicole K. Rendos,† PhD, Peter A. Everts,‡ PhD, FRSM, James R. Andrews,† MD, and Joshua G. Hackel,† MD

Investigation performed at the Andrews Research & Education Foundation, Gulf Breeze, Florida, USA

> Am J Sports Med. 2022 Sep;50(11):2881-2892. doi: 10.1177/03635465221115821. Epub 2022 Aug 19.

Microfragmented Adipose Tissue Versus Platelet-Rich Plasma for the Treatment of Knee Osteoarthritis: A Prospective Randomized Controlled Trial at 2-Year Follow-up

Stefano Zaffagnini [1], Luca Andriolo [1], Angelo Boffa [1], Alberto Poggi [1], Annarita Cenacchi [2], Maurizio Busacca [3], Elizaveta Kon [4,5], Giuseppe Filardo [6], Alessandro Di Martino [1]

Bone Marrow Aspirate Concentrate Is Equivalent to Platelet-Rich Plasma for the Treatment of Knee Osteoarthritis at 2 Years: A Prospective Randomized Trial.

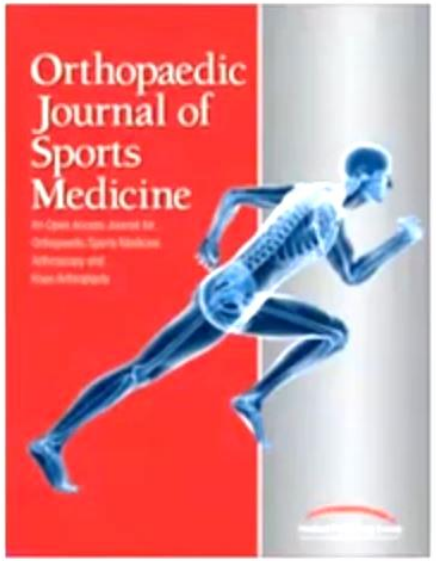
Anz AW[1], Plummer HA[1], Cohen A[2], Everts PA[3], Andrews JR[1], Hackel JG[1]

Article

Intra-Articular Injections of Autologous Adipose Tissue or Platelet-Rich Plasma Comparably Improve Clinical and Functional Outcomes in Patients with Knee Osteoarthritis

Jakub Kaszyński [1,†], Paweł Bąkowski [1,*,†], Bartosz Kiedrowski [1], Łukasz Stołowski [1], Anna Wasilewska-Burczyk [2], Kamilla Grzywacz [2] and Tomasz Piontek [1,3]

PRP v MFAT



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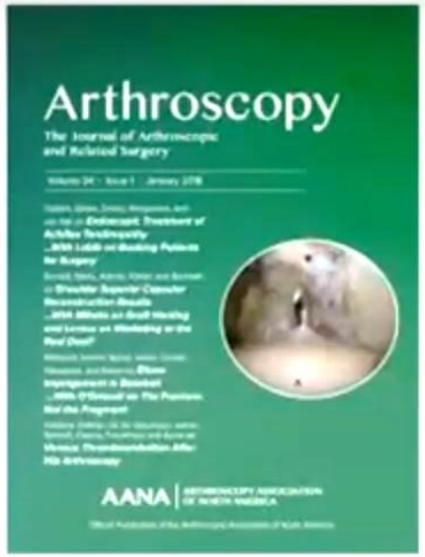
https://doi.org/10.1177/23259671221120678

SAGE journals

Platelet-Rich Plasma Versus Microfragmented Adipose Tissue for Knee Osteoarthritis: A Randomized Controlled Trial

Michael Baria, MD, MBA[†,*], Angela Pedroza, MPH[‡], Christopher Kaeding, MD[§], Sushmitha Durgam, PhD[‖], Robert Duerr, MD[§], David Flanigan, MD[§], James Borchers, MD, MPH[¶], and Robert Magnussen, MD, MPH[§]

- 58 patients KL1-4 Knee OA
- KOOS 1,3,6 months post-injection
- PRP – 2673 x10^3 platelets/microliter (12-17x) ; **13.68 billion cells**
- Both had a clinically meaningful improvement with no difference between groups



Meta-analysis

Intra-Articular Injections of Platelet-Rich Plasma, Adipose Mesenchymal Stem Cells, and Bone Marrow Mesenchymal Stem Cells Associated With Better Outcomes Than Hyaluronic Acid and Saline in Knee Osteoarthritis: A Systematic Review and Network Meta-analysis

Di Zhao, M.D., Jian-ke Pan, Ph.D., Wei-yi Yang, Ph.D., Yan-hong Han, M.D., Ling-feng Zeng, Ph.D., Gui-hong Liang, M.D., and Jun Liu, Ph.D.

- 43 Studies
- VAS score and WOMAC scores showed **Adipose-derived MSCs to be best treatment option**
- At 12 months only AD-SC were associated with improved VAS
- LR-PRP and LP-PRP were better than Placebo
- BMC studies were too highly variable for conclusions

Take home messages

- Orthobiologics are here to stay
- PRPs: Generic term (dose, leucocytes, activation, etc…)
- GOOD clinical evidence of PRP for mild to moderate knee OA
- ? Nr of injections needed

- MSCs: many questions unanswered
  - Trophic / Secretory effects
  - Effect on cartilage / Soft tissues

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Thank you!