


Platelet-Rich Plasma Treatment for Joint Conditions: Evidence Update

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*Allina Health Sports Medicine Conference
August 5th 2022*



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Disclosures

- None



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Goals and Objectives

• Goals

- Provide a brief overview of PRP and it's mechanism
- Review evidence for PRP injections in various joints

• Objectives

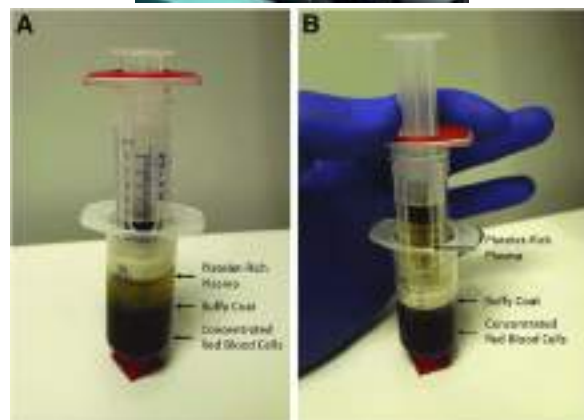
- Be able to explain the basics of a PRP injection
- Understand the limitations of PRP research
- Have a rationale to include or exclude PRP as a potential therapeutic option

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What is PRP?

- Platelet Rich Plasma
- Federally regulated as a “Minimally Manipulated therapy”
- Autologous blood sample
- Platelets isolated through centrifugation
- Injected into area of choice
- Various platelet and leukocyte concentrations
 - System dependent
 - Patient dependent



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Mechanism



- **Alpha granules released from activated platelets**
- **Growth factors and proteins released**
 - **Transforming growth factor (TGF- β):** regulates inflammation and healing.
 - **Platelet derived growth factor (PDGF):** angiogenesis, promotes cell differentiation.
 - **Insulin-like growth factor (IGF):** angiogenesis, proliferation keratinocytes and fibroblasts
 - **Vascular endothelial growth factor (VEGF):** angiogenesis
 - **Others**
- **Believed to induce healing, control inflammation, and decrease joint breakdown.**

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• **Simple version:**

- control the inflammatory state
- try to use the mechanisms for acute injury healing to treat chronic “dormant” problems.

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Why do we do it?

- **Because it works! (maybe)**
- **Biologic that feels like a more “natural option”**
- **Potentially less side effects**
- **Failure of other conservative treatment options**
- **Trying to avoid surgery**

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Well what's the Evidence?

Various factors study comparison difficult:


- Platelet concentration
- Centrifuge speed
- RBCs and WBCs
- Volume injected
- Number of injections
- Use of local anesthetic
- Anticoagulant
- Platelet activator
- Rehab protocol



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Let's Dive in



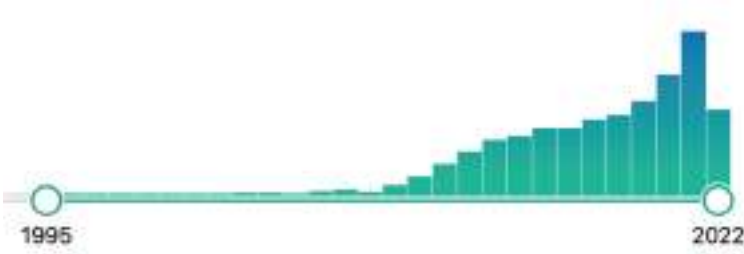
A photograph of a man in dark shorts jumping into a large body of water under a blue sky with scattered white clouds. The man is captured mid-air with his arms outstretched. The water is dark blue with some ripples. In the background, there is a line of green trees.

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Pub Med Search

- **“Platelet rich plasma knee”**
- **1043 results**



A bar chart showing the number of search results for "Platelet rich plasma knee" from 1995 to 2022. The x-axis is labeled with 1995 and 2022. The y-axis represents the number of results. The chart shows a steady increase in results over time, with a significant spike in 2022. The bars are colored in shades of green and blue.

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Platelet-Rich Plasma Intra-Articular Injection Versus Hyaluronic Acid Viscosupplementation as Treatments for Cartilage Pathology: From Early Degeneration to Osteoarthritis

Elizaveta Koc, M.D., Bert Mandelbaum, M.D., Roberto Buda, M.D., Giuseppe Filardo, M.D., Marco DeLuogiano, M.D., Antonio Timoncini, M.D., Pier Maria Fortasari, M.D., Sandro Giannini, M.D., and Maurizio Marcacci, M.D.

- 2011 Arthroscopy
- 150 patients, 50 each PRP, HW-HA, or LW-HA
- Center based, but not randomized and non-blinded
- 6 month follow up
- PRP showed better results in younger, more active patients, with lower degree of knee OA.

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Knee Surg Sports Traumatol Arthrosc
DOI 10.1007/s00167-015-3595-6



KNEE

Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial

Gökay Gürmelî¹ · Cemile Ayşe Gürmelî² · Baybars Ataslı¹ · Cemil Çelik⁴ · Okan Aslanlı¹ · Kadir Ertem¹

- 4 Groups: 1 PRP and 2 saline, 3 PRP, 3 HA, or 3 saline injections
- 6 months follow up: Multiple PRP injections showed significant improvement in EQ-Vas and IKDC scores compared to placebo, HA injections, and single PRP injections.

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> Arch Orthop Trauma Surg. 2021 Oct 27. doi: 10.1007/s00402-021-04230-2.
Online ahead of print.

Multiple platelet-rich plasma injections are superior to single PRP injections or saline in osteoarthritis of the knee: the 2-year results of a randomized, double-blind, placebo-controlled clinical trial

- 2021 study, multiple PRP vs single PRP vs saline
- Similar improvements at 12 months with multiple PRP injections.
- No difference at 24 months.

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Platelet-Rich Plasma Intra-articular Knee Injections Show No Superiority Versus Viscosupplementation

A Randomized Controlled Trial

Giuseppe Filardo,^{1*} MD, PhD, Berardo Di Matteo,^{2†} MD, Alessandro Di Martino,^{3*} MD, Maria Lefolia Merli,^{4*} MD, Annarita Cenacchi,⁵ MD, PierMaria Fomasari,⁶ MD, Maurizio Marcacci,^{7*} MD, Prof., and Elizaveta Kon,⁸ MD
Investigation performed at Rizzoli Orthopaedic Institute, Bologna, Italy

- 2015 AJSM
- 192 patients - DB, randomized (all underwent blood draw, covered syringe)
- 3 PRP injections vs 3 HW HA injections
- Leukocyte rich PRP
- Both groups saw improvement at 12 months in KOOS, IKDC, and EQ-VAS scores without significant difference between groups.
- Can't recommend over HA, but did show significant benefit from baseline.

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Platelet-Rich Plasma Versus Hyaluronic Acid Injections for the Treatment of Knee Osteoarthritis

Results at 5 Years of a Double-Blind, Randomized Controlled Trial

Alessandro Di Martino,^{*} MD, Berardo Di Matteo,^{††} MD, Tiziana Papio,^{‡‡} BScD, Francesco Tentoni,^{*} MD, Filippo Selleri,^{*} MD, Annarita Ceracchi,^{*} MD, Elizaveta Kon,^{††} MD, and Giuseppe Filardo,[§] MD, PhD
Investigation performed at the Orthopaedic Rizzoli Institute, Bologna, Italy

- Same group from 2015 study, but 5 year follow up.
- 167 patients made the final evaluation
- Age was significantly lower in the PRP group (52.7 vs 57.5, $P = .014$)
- Survival analysis of duration of beneficial effect was performed

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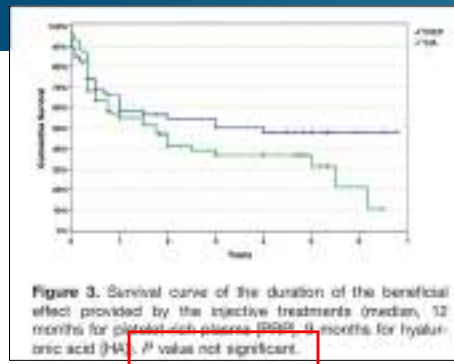
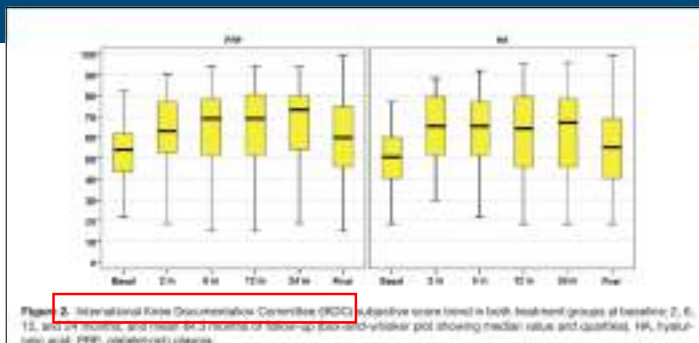


TABLE 2
EuroQol Visual Analog Scale (EQ-VAS) Scores at Different Follow-up Times in Both Treatment Groups^a

	Baseline	2 Months	6 Months	12 Months	24 Months	Final Evaluation
Platelet-rich plasma	72.7 \pm 12.3	76.5 \pm 12.7	76.9 \pm 12.2	77.6 \pm 10.5	79.4 \pm 13.4	71.9 \pm 13.6
Hyaluronic acid	71.2 \pm 13.3	74.6 \pm 12.8	73.8 \pm 15.6	72.5 \pm 16.3	74.3 \pm 17.3	66.6 \pm 14.2
P values	NS	NS	NS	NS	NS	NS

^aData are expressed as mean \pm SD. NS, not significant.

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Effect of Leukocyte Concentration on the Efficacy of Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis

Jonathan C. Riboh,^{1†} MD, Bryan M. Saltzman,¹ MD, Adam B. Yanke,¹ MD, Lisa Fortier,¹ DVM, PhD, and Brian J. Cole,¹ MD, MBA
Investigation performed at the Division of Sports Medicine, Rush University Medical Center, Chicago, Illinois, USA

- 2016 Network meta-analysis of 6 RCT's and 3 prospective comparative trials.
- LP-PRP demonstrated significantly more improvement in WOMAC scores than placebo and HA.
- LR-PRP did not demonstrate significant benefit over placebo and HA.
- Imbalance of baseline WOMAC scores between LR-PRP and LP-PRP
 - Could not provide direct comparison
 - Meta-regression did not detect a difference

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Randomized Controlled Trial > Am J Sports Med. 2022 Mar;50(3):609-617.
doi: 10.1177/03635465211064303. Epub 2022 Feb 1.

Leukocyte-Rich versus Leukocyte-Poor Platelet-Rich Plasma for the Treatment of Knee Osteoarthritis: A Double-Blind Randomized Trial

Alessandro Di Martino¹, Angelo Boffa¹, Luca Andriolo¹, Jacopo Romandini¹,
Santa Alessandro Altamura¹, Annarita Cesacchi², Veronica Rovarini², Stefano Zaffagnini¹,
Giuseppe Filardo³

- More recent study, 192 patients, DBRC trial, LR-PRP vs LP-PRP, 3 weekly injections.
- KL Grade 1-3.
- 12 month follow up, LR-PRP and LP-PRP injections both showed significant improvement in baseline IKDC.
- Neither was significantly better than the other.
- 15 mild adverse events (pain or swelling) in both groups total (p=.101).

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CME

Platelet-Rich Plasma Versus Hyaluronic Acid for Knee Osteoarthritis

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

- **18 level 1 studies, 811 patients PRP injections vs 797 with HA injections.**
- **WOMAC: 5 studies with at least 12 month follow up, PRP had significantly better scores (p<0.00001).**
 - $I^2=81%$, moderate to high heterogeneity and underpowered.
- **VAS: 5 studies with at least 12 month follow up, PRP no significant difference (p=0.07)**
 - $I^2=99%$, high heterogeneity and underpowered.
- **IKDC: 4 studies with at least 12 month follow up, PRP had significantly better scores (p=0.009).**
 - $I^2=99%$, moderate to high heterogeneity and underpowered.
- **LP-PRP resulted in better subjective IKDC scores than LR-PRP. No difference in WOMAC or VAS.**

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CME

Platelet-Rich Plasma Versus Hyaluronic Acid for Knee Osteoarthritis

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

- **Possible improvement in clinical outcomes at 12 months**
- **Need more high quality, similar studies, with longer follow up, to add more power to the analysis.**
- **LP-PRP might be better.**

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Randomized Controlled Trial > J Orthop Surg Res. 2020 Jul 10;15(1):257.
doi: 10.1186/s13018-020-01753-z.

Intra-articular platelet-rich plasma vs corticosteroids in the treatment of moderate knee osteoarthritis: a single-center prospective randomized controlled study with a 1-year follow up

Andreja Elksenti-Firogejina ^{1,2}, Luis Vidal ², Andreja Peredatija ⁴

- **What about compared to cortisone?**
- KL grade 2-3.
- 20pts treated with 40mg kenalog and 20pts treated with PRP
- PRP shows significant improvement at 12 months in VAS, IKDC, and KSS scores.

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Effect on Medial Tibial Cartilage Volume?

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; Nicky Duong, DPT; Jillian Eyles, PhD; Jooika Koza, PhD; Yuanquan Wang, PhD; Hava Oudizhe, PhD; Rachel Buchbender, PhD; Andrew Forbes, PhD; Anthony Harris, MSc; Shihyong Yu, MPH; David Connell, MMed; James Linklater, MBBCh; Bing-Hui Wang, PhD; Win Min Do, PhD; David J Hunter, PhD

- **Randomized study, first large trial of it's kind, 288 participants**
- **Mild to moderate knee OA**
- **LP-PRP injections X3 vs saline placebo injections**
- **Commercial product 1.6 to 5x platelet concentration**
- **Well blinded study, PRP prep was done in a separate room**
- **12 month follow up**
- **No significant effect on pain scores or medial tibial cartilage volume on MRI**

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Biomedicine, 2022 May; 10(5): 561.
Published online 2022 Apr 25, doi: 10.3380/biomedicine10090991

PMCID: PMC9138292
PMD: 35825728

Intra-Articular Injection of Platelet-Rich Plasma Is More Effective than Hyaluronic Acid or Steroid Injection in the Treatment of Mild to Moderate Knee Osteoarthritis: A Prospective, Randomized, Triple-Parallel Clinical Trial

David Szewczowski,^{1,2*} Ak Moslesen,^{3,4,5,6} Andrzej Matuszko,⁷ Jan Zaleski,⁸ and Stawronik Jaka⁹

- What about steroid?
- non-blinded study
- 25pts in each group
- When compared head to head with cortisone and HA injections, PRP is more effective at 6 months (P<0.001).

The graph, titled 'Mean WOMAC Score', plots 'Points in WOMAC Score' on the y-axis (ranging from 0 to 70) against 'Time from the injection (in months)' on the x-axis (0, 1.5M, 3M, 6M). Three data series are shown: PRP (blue line), HA (red line), and CS (green line). All groups start at approximately 65 points at 0 months. The PRP group shows a significant decrease to about 25 points at 6 months. The HA and CS groups show a smaller decrease, ending at approximately 35 and 45 points respectively at 6 months. Error bars represent standard deviation.

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Review > Arch Orthop Trauma Surg. 2021 Sep;141(9):1473-1480.
doi: 10.1007/s00402-020-03551-y. Epub 2020 Jul 28.

Comparison between intra-articular infiltrations of placebo, steroids, hyaluronic and PRP for knee osteoarthritis: a Bayesian network meta-analysis

Filippo Migliorini¹, Arne Driessen², Valentin Quack³, Nadja Sippel², Brian Cooper², Yasser El Mansy², Markus Tingart², Jörg Eschweiler²

- 30 RCT's
- At 12 months PRP had significantly better VAS and WOMAC scores compared to steroid, HA, and placebo injections.

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Knee – Meniscus Tears

- Minimal studies, mostly centered around augmenting surgical repairing of the meniscus with PRP.



- 2020 Ukraine study showed 4-6 PRP injections was better than 3 injections in terms of WOMAC, VAS, and Oxford Knee scores at 2 years.

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Int J Med Sci. 2019 Feb; 20(4): 858.
Published online 2019 Feb 16, doi: 10.1009/ijms20090858

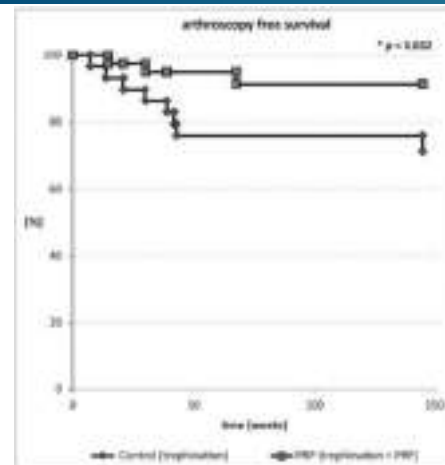
PMCID: PMC6412887
PMD: 30721883

Short-Term Outcomes of Percutaneous Trephination with a Platelet Rich Plasma Intrameniscal Injection for the Repair of Degenerative Meniscal Lesions. A Prospective, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study

Rafal Szemrak,^{1*} Mada Malyszewska-Wielik,² Krzysztof Sulinski,¹ Katarzyna Kozar-Kozimska,² Aneta Szafranska-Dobrowolska,³ and Stanislaw Ponsiackowski¹

Knee – Degenerative Meniscus Tears

- 72 patients, DBRC trial with placebo, LR-PRP injected with US guidance into degenerative meniscus tears.
- Average age 46 in control and 44 in PRP group
- Tears had to be chronic, horizontal, and in the vascular area.
- KL degenerative changes of >2 and chondral defects were excluded.
- 24 month follow up, improved VAS pain and KOOS – Symptoms compared to control. Significant only when looking at MCID.
- Significantly more healed meniscus in PRP group (P=0.04), evaluated by MRI and arthroscopy.
- Arthroscopy free survival was superior in control group.



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Hip Osteoarthritis and PRP injections



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Platelet rich plasma versus hyaluronic acid in patients with hip osteoarthritis: A meta-analysis of randomized controlled trials

Ye Ye^a, Xiang Zhou^{b,*}, Shuiwei Mao^b, Jun Zhang^b, Bingmin Lin^b

^a Hip Injury and Disease Centre, Henan Provincial Luoyang Orthopedic Hospital, Luoyang, 471002, China

^b Department of Orthopedics, Longquan People's Hospital, Longquan, 323700, China

- **2018 International Journal of Surgery**
- **4 RCTs met inclusion**
- **PRP showed benefit significant improvement in VAS score over HA at 2 months, but not significant better outcomes at 6 and 12 months.**

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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 trials total (4 from previous analysis and 2 newer studies).**
- **3 used LP- PRP and 1 used LR-PRP**
- **No significant difference in WOMAC, VAS, or HHS scores between groups.**
- **Overall similar improvement from baseline in both groups.**

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Other joints

- **Hip labral tears, shoulder OA, thumb basilar OA**
- **Case reports, limited series studies, and pilot studies.**
- **Paving the way for future studies, but clearly more research is needed to make any conclusions.**



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PRP safety

- No significant adverse effects noted in any of the reviewed studies.
- Though no known study has looked specifically at the safety profile as the primary outcome.
- No long term data (>5 years) was found.
- Probably very safe considering "biologic" treatment

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• Perfect study?

- Randomized, double blinded, multicenter, placebo controlled, appropriately powered, comparing LR and LP PRP with noted platelet concentrations, with long term MRI and functional outcome follow up.
- Does not exist and not likely in the near future



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Take home points

- **No perfect study and many variables to try to account for.**
- **Need more consistent protocols**
- **Evidence will probably swing for and against, until we can get a “perfect study”**
- **Probably beneficial for low grade knee OA, especially when trying to avoid potential chondrotoxicity of corticosteroid.**
- **Consider for more advanced OA when patient does not want surgery.**
- **No significant adverse effects noted.**
- **Consider extrapolating to other joints.**
- **Cost effectiveness needs to be considered.**
- **Art > science**



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Thank You!

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