

2023 Clinical Research Award

HIP CHONDROLABRAL DYSFUNCTION: THE ROAD FROM EXCISION TO REPAIR, REPLACEMENT AND REGENERATION

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DISCLOSURES

Research Support: National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institute of Aging, U.S. Department of Defense, Smith + Nephew, Inc., Ossur, Arthrex, Siemens

Shareholder: Arthrosurface, MIS, Vail Valley Surgery Center, Steadman Philippon Surgery Center, Dillon Surgery Center, Vail MSO Holdings LLC, Effrx, MJP Innovations, LLC, Olatec, iBalance (Arthrex), Stryker, Trimble, Grocery Outlet, 3M, Bristol Myers Squibb, Pfizer, AbbVie, Johnson & Johnson, DocBuddy

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Ownership: MJP Innovations, LLC

Investor: Manna Tree Partners

Inventor: “Methods for treating disease associated with senescence” (patent pending) and “Optimized surgery protocols and kits” (patent pending)

Profits Interest Units: NICE Recovery Systems

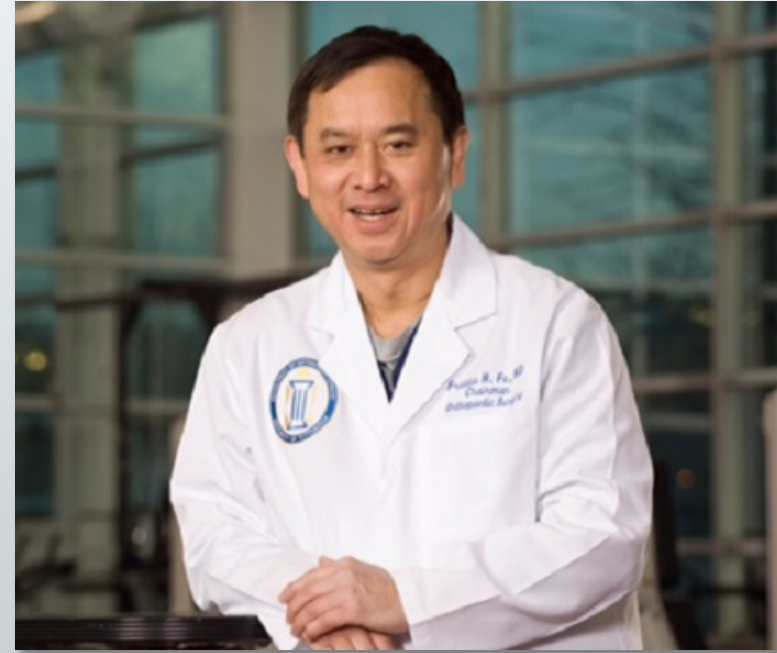
Faculty/Speaker Compensation: Synthes GmbH

Hospitality Payments: Siemens

Move from Florida to UPMC: 2001

Dr. Freddie Fu

- Visionary in arthroscopy
- Understood importance of treating the athlete
- Will be missed greatly in sports medicine, education and innovation



UPMC
LIFE CHANGING MEDICINE

Move from UPMC to Vail: 2005

Need for validation of hip arthroscopy procedure

“Head west, young man”



Goal in Vail

- Collect Data
- Publish Outcomes



Patients From Around the Globe



OUR APPROACH TO EVIDENCE-BASED PRACTICE

COOR: Center for Outcomes-Based Orthopaedic Research

Biomechanical Engineering

- Biomotion Laboratory
- Biomechanical Testing Laboratory

CRPM: Center for Regenerative and Personalized Medicine



Short-term

Mid-term

Long-term

"All the News
That's Fit to Print"

The New York Times

National Edition

Colorado: Partly sunny. 3
snow in Wyoming, Nebras
north Colorado. Highs in
northwest to around 50
Weather map is on Pg

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Hip Procedure Grows Popular Despite Doubt

Researchers Wonder if
Bone Shaving Helps

By GINA KOLODIA

It is one of the most popular operations in sports medicine. It comes in various forms, all with the same name: Hip impingement or bone shaving surgery. World-renowned athletes have had the operation — the Yankees' third baseman Alex Rodriguez had it about two years ago and the sprinter Tyson Gay had it last summer.

But some sports medicine researchers are asking: where is the evidence that shaving bone helps? Might the bumps or irregular shapes they call impingement be just normal variations? Does the shaved bone grow back?

And it is not just professional athletes who are having the oper-

THE ATHLETE'S PAIN

A Rush to Treatment

ation. Now some surgeons are even operating on teenage athletes with hip pain.

The idea is that bone that has rough edges or an irregular

SPARED IN WAR, LIBYA'S OIL FLOW IS SURGING BACK

← SHIELDED BY BOTH SIDES

Return to Huge Yield
Hinges on Avoiding
New Violence

By CLIFFORD KRAUSS

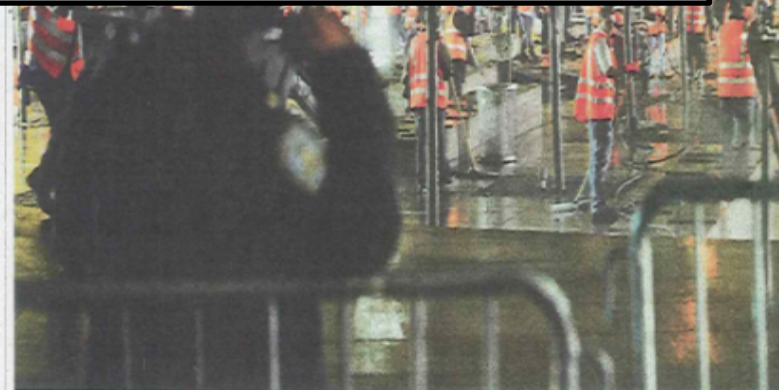
ZAWIYAH, Libya — The bullet holes in the oil tanks have been patched, the damaged backup generator is being repaired, and most important, the pipeline that feeds the giant oil refinery here has been reopened.

Oil production is quickly being restored in Zawiya and around the country, in large part because both the Qaddafi regime and the former rebels, now the interim leaders of Libya, took pains to avoid permanently crippling the country's most important industry during their six-month civil war.

"Qaddafi wanted to keep the refinery going because he needed the fuel, and the rebels wanted the refinery safe because it belongs to the Libyan people," said Khaled Rashed, shift coordinator at the Zawiya refinery's control room.

2011

"It is one of the most popular operations in sports medicine"



Workers power-washed Zuccotti Park on Tuesday, hours after protesters were evicted and hours before they were allowed to return.

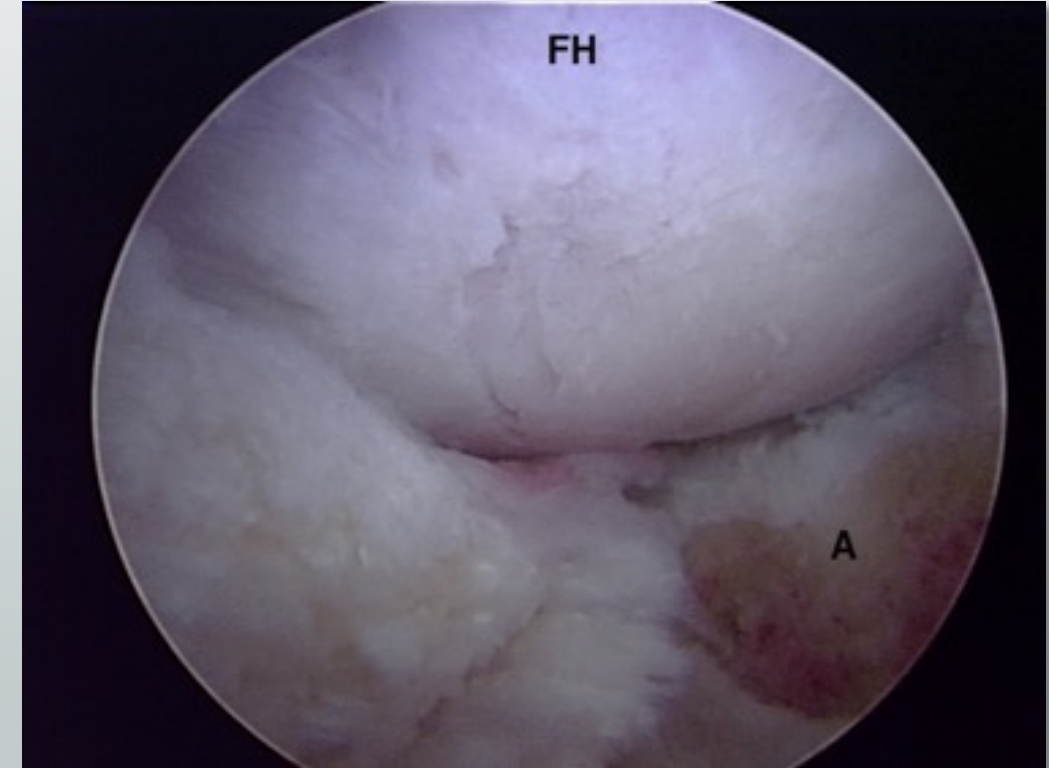
Movement Looks for Ways to Extend Influence Evicted by Po

SPORTS MEDICINE/HIP DISORDERS

Hip Arthroscopy 1995–Present

Experience

- >9200 hip arthroscopies
- 6,376 in Vail
 - 80% athletes
 - 20% elite athletes
- Over 1,228 presentations
- Over 408 published articles



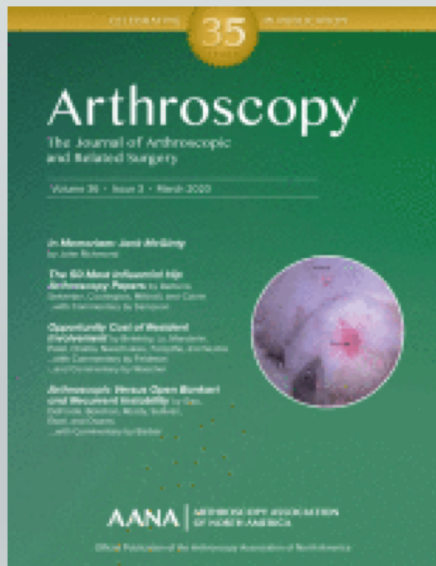
SPRI OUTCOMES RESEARCH IMPACT ON FIELD OF HIP ARTHROSCOPY

The Top 50 Most Influential Articles in Hip Arthroscopy

Table 1. Top 50 Cited Hip Arthroscopy Articles

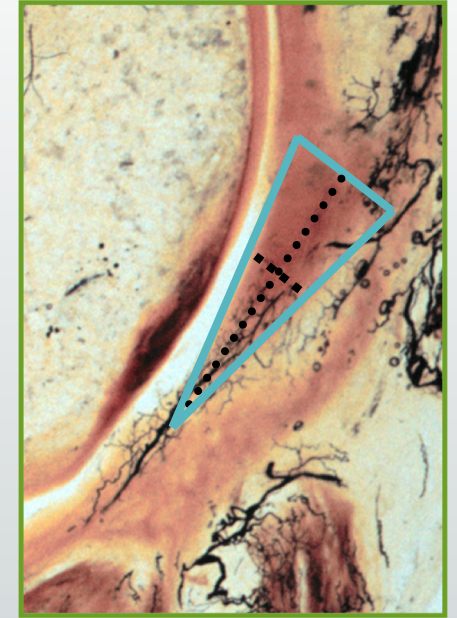
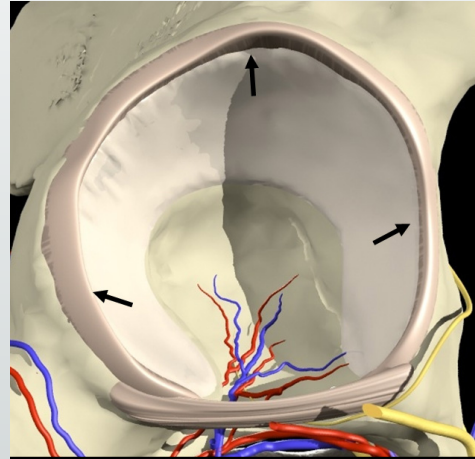
Rank	Article	No. of Citations (Citation Density ^a)
1	Philippon MJ, Briggs KK, Yen YM, Kuppersmith DA. Outcomes following hip arthroscopy for femoroacetabular impingement with associated chondrolabral dysfunction: Minimum two-year follow-up. <i>J Bone Joint Surg Br</i> 2009;91:16-23.	464 (46.4)
2	Byrd JW, Jones KS. Prospective analysis of hip arthroscopy with 2-year follow-up. <i>Arthroscopy</i> 2000;16:578-587.	318 (16.7)
3	Philippon M, Schenker M, Briggs K, Kuppersmith D. Femoroacetabular impingement in 45 professional athletes: Associated pathologies and return to sport following arthroscopic decompression. <i>Knee Surg Sports Traumatol Arthrosc</i> 2007;15:908-914.	273 (22.8)
4	Kelly BT, Weiland DE, Schenker ML, Philippon MJ. Arthroscopic labral repair in the hip: Surgical technique and review of the literature. <i>Arthroscopy</i> 2005;21:1496-1504.	244 (17.4)
5	Larson CM, Giveans MR. Arthroscopic debridement versus refixation of the acetabular labrum associated with femoroacetabular impingement. <i>Arthroscopy</i> 2009;25:369-376.	230 (23.0)
6	Philippon MJ, Stubbs AJ, Schenker ML, Maxwell RB, Ganz R, Leunig M. Arthroscopic management of femoroacetabular impingement: Osteoplasty technique and literature review. <i>Am J Sports Med</i> 2007;35:1571-1580.	227 (18.9)
7	Farjo LA, Glick JM, Sampson TG. Hip arthroscopy for acetabular labral tears. <i>Arthroscopy</i> 1999;15:132-137.	219 (11.0)
8	Philippon MJ, Schenker ML, Briggs KK, Kuppersmith DA, Maxwell RB, Stubbs AJ. Revision hip arthroscopy. <i>Am J Sports Med</i> 2007;35:1918-1921.	211 (17.6)
9	Larson CM, Giveans MR. Arthroscopic management of femoroacetabular impingement: Early outcomes measures. <i>Arthroscopy</i> 2008;24:540-546.	209 (19.0)
10	Kelly BT, Williams RJ, Philippon MJ. Hip arthroscopy: Current indications, treatment options, and management issues. <i>Am J Sports Med</i> 2003;31:1020-1037.	203 (12.7)

Recent
independent
bibliometric
analysis of
the most
cited papers
in the history
of hip
arthroscopy
research



ACETABULAR LABRUM

- Extends the acetabulum beyond the bony socket
- Is present around the entire lunate surface of the acetabulum
- Is continuous with the transverse acetabular ligament inferiorly



- The fibrocartilaginous labrum was contiguous with the acetabular cartilage through a 1-2 mm zone of transition
- Microvasculature of the acetabular labrum consists of a group of small vessels located in the substance of the labrum at its attachment site on the outer surface of the bony acetabular extension

Vascularity of the Labrum

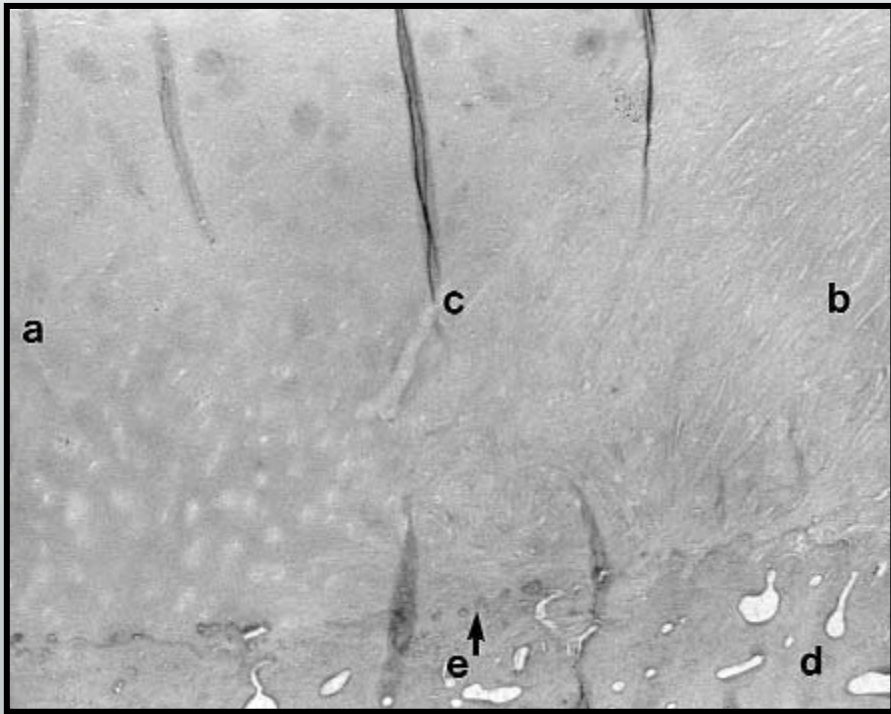
Capsular side of the labrum demonstrated significantly more vascularity than the articular side ($p < 0.005$)

Seldes RM, et al. Clin Orthop Relat Res. 2001;382(232-240)

Kelly et al. Arthroscopy 2005

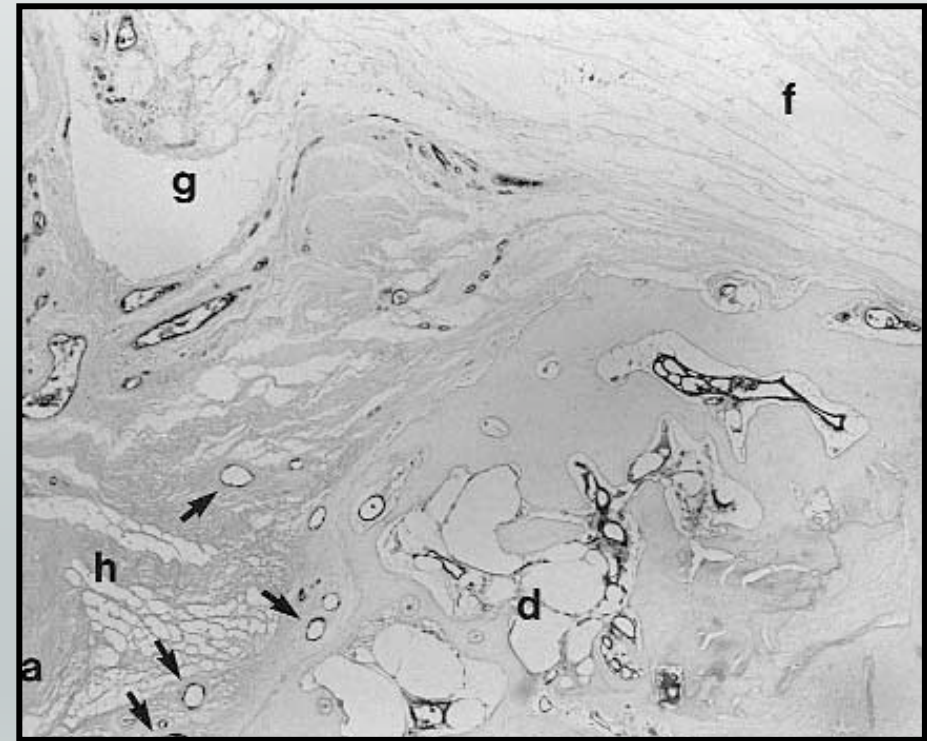
LABRAL ANATOMY

- Labrum attachment (b)
- Bony acetabulum (d)
- Transition zone (c) between labrum and articular cartilage (a)
- Tidemark zone is visible (e)

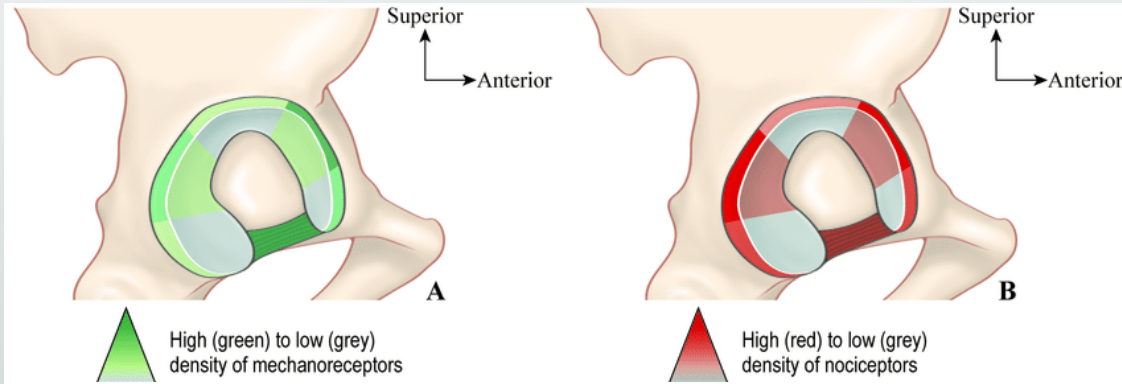


Seldes RM, et al. Clin Orthop Relat Res. 2001;382(232-240)

- Group of vessels (h, arrows) within the labrum (a)
- Hypervascular synovium
- Capsular recess (g) & capsule (f)
- The bony acetabulum (d)

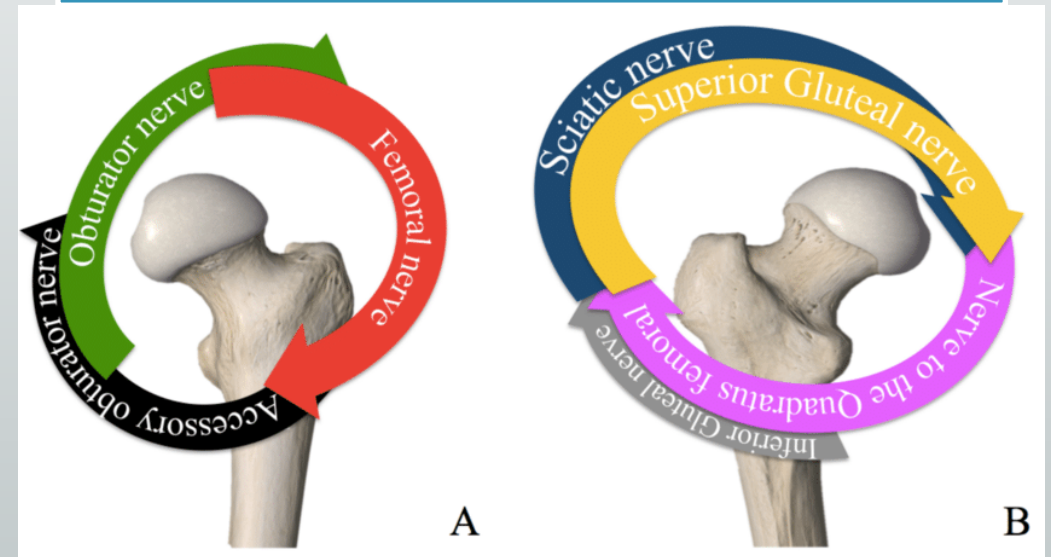


INNERVATION OF ACETABULAR LABRUM



- Majority of nociceptive and mechanoreceptive nerve endings are in the antero-superior and postero-superior labrum

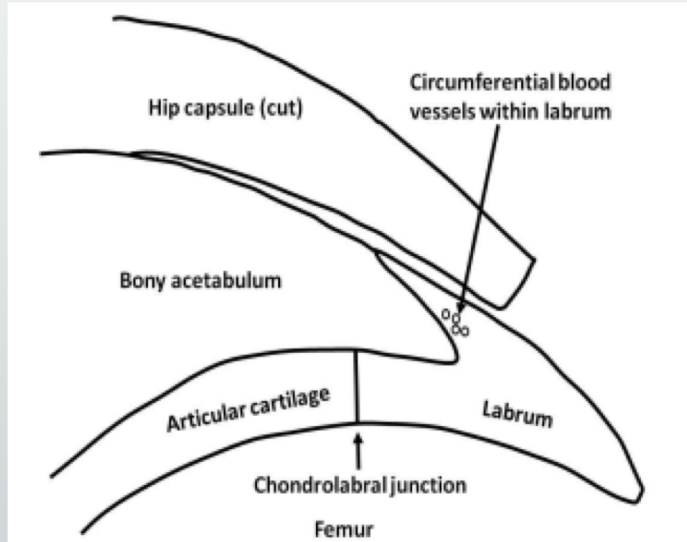
Primary source of innervation to the hip capsule and labrum



A. Anterior B. Posterior

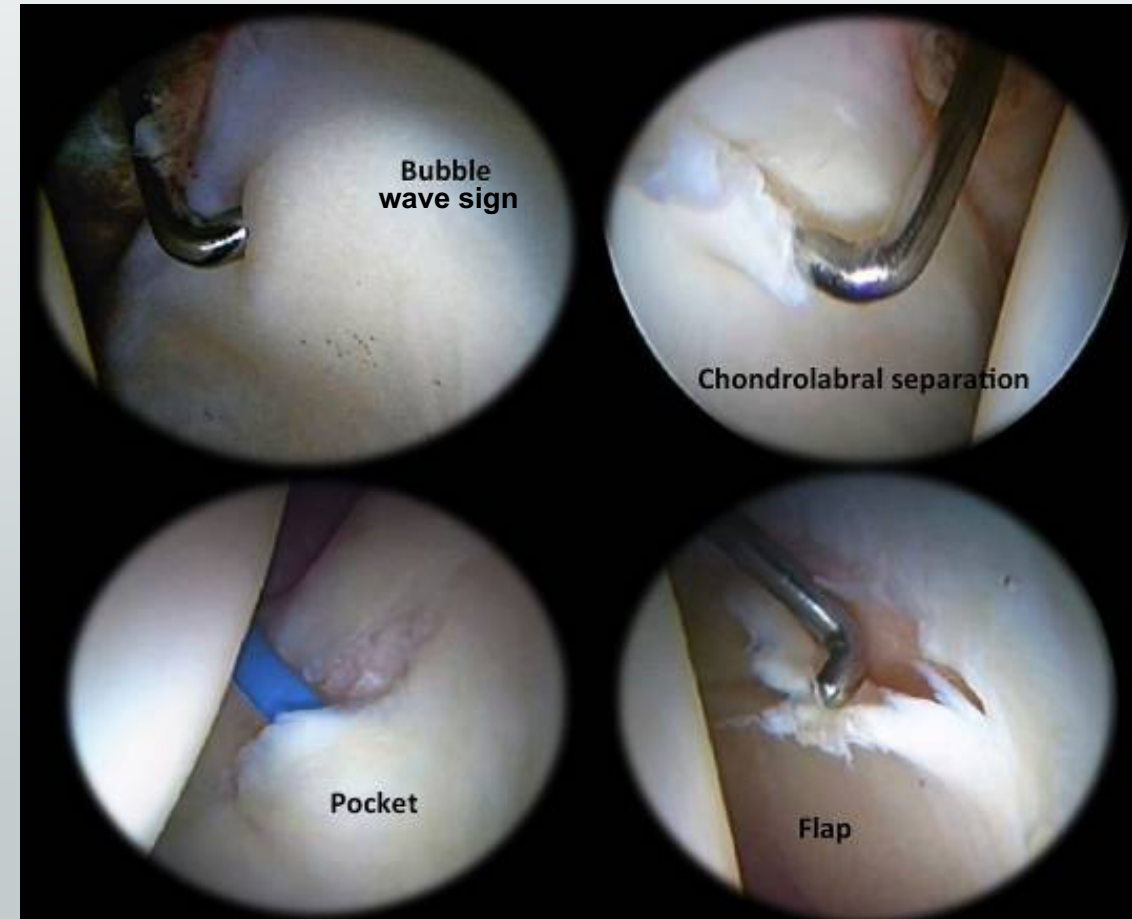
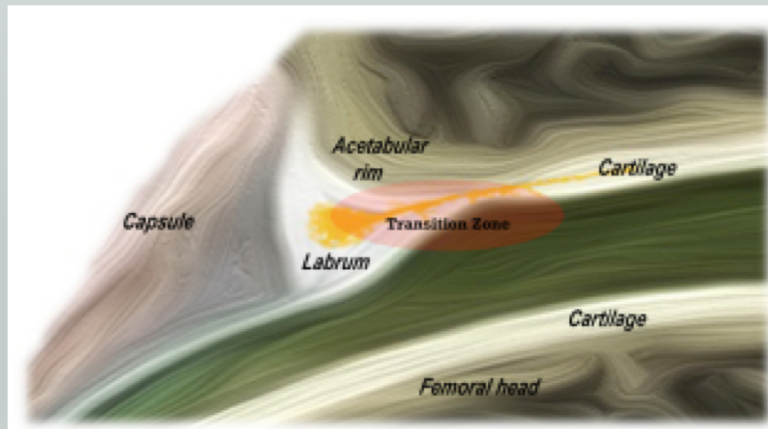
Laumonerie et. Al. (2021). SENSORY INNERVATION OF THE HIP JOINT AND REFERRED PAIN. A Systematic Review of the literature.. Pain Medicine. 10.1093/pm/pnab061/6132248.

CHONDROLABRAL JUNCTION



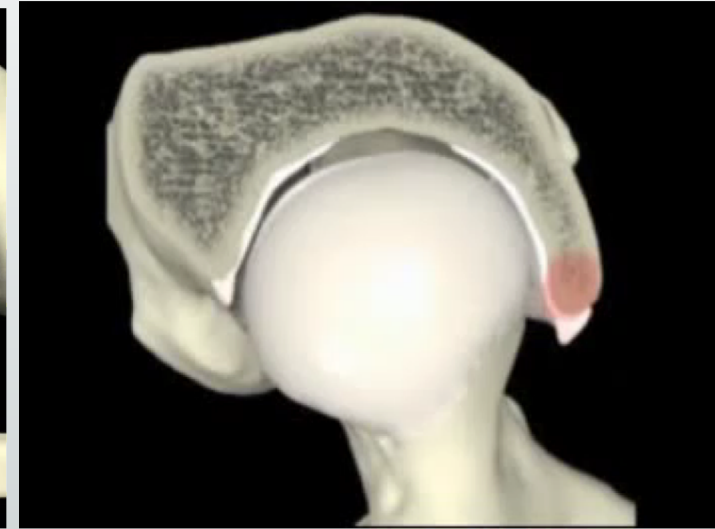
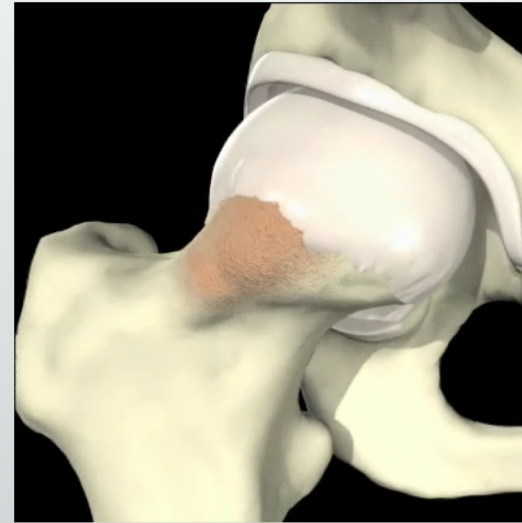
Transition zone (weak)
between the acetabular
labrum and the acetabular
articular cartilage

- Often area of injury



WHAT IS CHONDROLABRAL DYSFUNCTION?

- Damage to the chondrolabral junction due to FAI
- Labrum no longer can maintain the seal between the acetabulum and femoral head



WHY PRESERVE THE LABRUM?

- Intra-articular fluid pressurization
- Hip stability
- Proprioception/ Nociception
- Load distribution

compressive
load



Intra-articular + interstitial
fluid is pressurized within the
cartilage



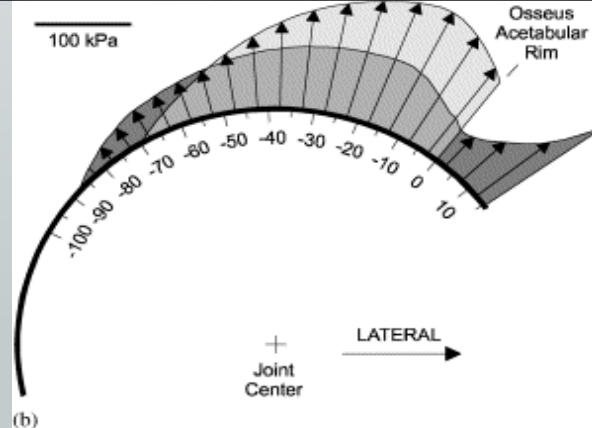
Cartilage matrix load (90%)

Surface friction

ROLE OF LABRUM

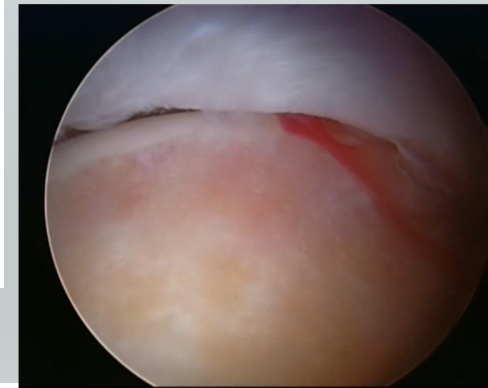
Ferguson et al. J. Biomech 2000

- Cartilage contact stress plotted at $t=1000$ s and $t=10000$ s after load of 0.75 times bodyweight.
- Dark grey – intact labrum
Light grey – without labrum
- Contact stresses in acetabular cartilage increase with time, and up to **92% higher** in the absence of the labrum



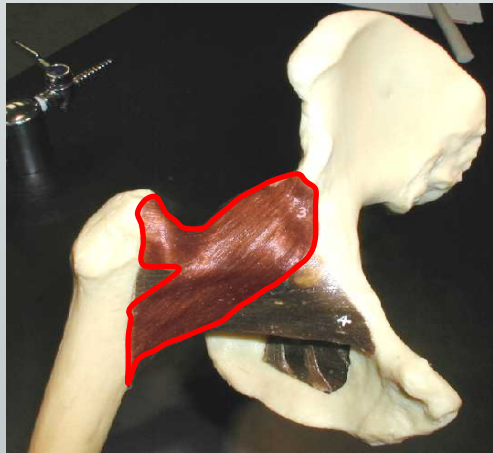
Importance of the suction seal

- The joint fluid provides nutrients to chondrocytes
- The seal mechanism maintains the hydrostatic joint pressure which affects load distribution
- Provides joint stabilization and proper joint function



CONSEQUENCES OF LABRAL TEARS

- Labral tears lead to microinstability, i.e., excessive translation of femoral head to labral rim



Primary restraint against extension and external rotation

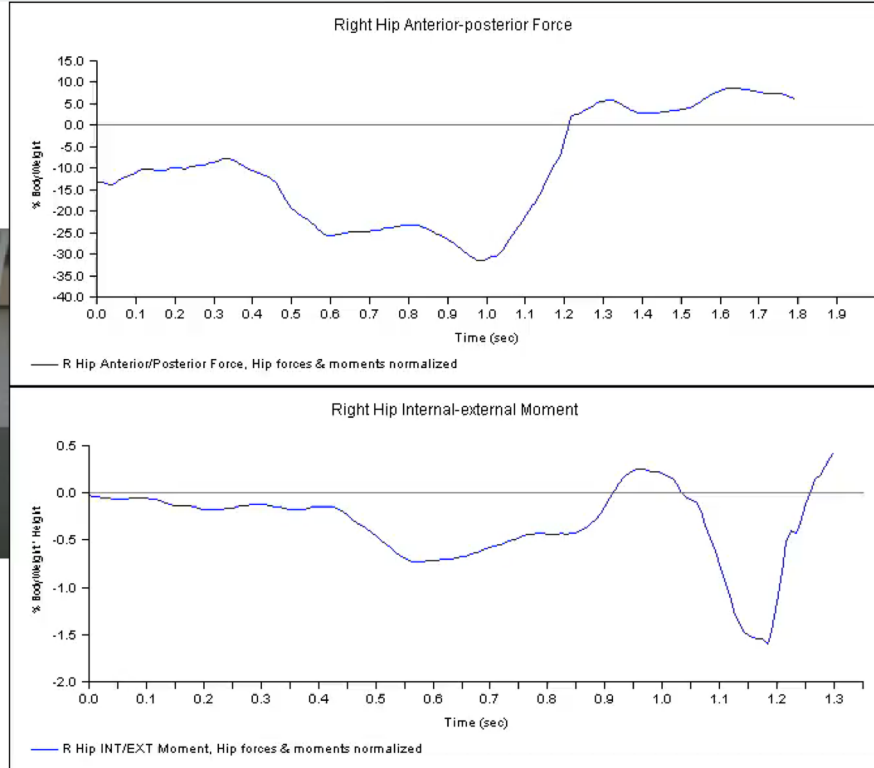
- Deficient labrum can lead to elongation of Iliofemoral Ligament



- Iliopsoas is dynamic stabilizer of the hip. Resting tone increases to compensate for the elongated IFL

MY EARLY EXPERIENCE

- Labral debridement
- Capsular redundancy
 - Microinstability
- Rotational athletes
 - Baseball players
 - Ballerinas
 - Golfers



HIP ARTHROSCOPY 0278-5919/01 \$15.00 + .00

THE ROLE OF ARTHROSCOPIC THERMAL CAPSULORRHAPHY IN THE HIP

Marc J. Philippon, MD

Instability in the hip joint is much less common than in the shoulder, but can be a source of great disability. The hip joint relies much less on its adjacent soft tissue for stability because of its intrinsic osseous stability in the hip. It is apparent that any deviation from "normal" bony anatomy will lead to more dependence on capsular tissue and labrum for stability. The author began to recognize and treat hip instability arthroscopically in 1998. Early results are promising and the purpose of this article is to enlighten the reader on the role of arthroscopic thermal capsular shrinkage in the hip and its specific indications.

ANATOMIC FACTORS IN HIP INSTABILITY

The hip (ox coxae) is an articulation between the head of the femur and the acetabulum. It is a ball and socket joint (enarthrosis). The femoral head forms two thirds of a sphere, and it is flattened (bean shaped) where the acetabulum applies its greatest load. Its anterior part is not engaged in the acetabulum when the body is in the anatomic position. The union of the ilium, ischium, and pubis forms the acetabulum. The acetabular surface is oriented approximately 45° caudally and 15° to 20° anteriorly. The lowest part of the acetabulum never rests upon the femur. The peripheral part of the acetabulum is horseshoe shaped and is covered with cartilage to allow for the articulation with the femoral head.

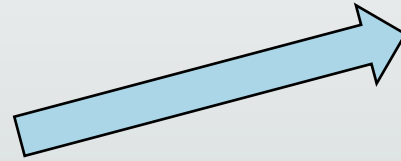
From the Orthopaedic Surgery Section, Holy Cross Hospital, Fort Lauderdale, Florida; and the UPMC Center for Sports Medicine, Department of Orthopaedic Surgery, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

CLINICS IN SPORTS MEDICINE

VOLUME 20 • NUMBER 4 • OCTOBER 2001

817

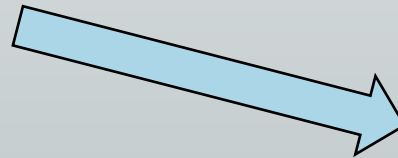
Treatment of
labral tears
evolved into
addressing
concomitant
pathology



FAI



Cartilage
Injury



Hip
Capsule

The Hip Suction Seal, Part I: The Role of Acetabular Labral Height on Hip Distractive Stability

Hunter W Storaci¹, Hajime Utsunomiya¹, Bryson R Kemler¹, Samuel I Rosenberg¹, Grant J Dornan¹, Alex W Brady¹, Marc J Philippon^{1 2}



The Hip Suction Seal, Part II: The Effect of Rim Trimming, Chondrolabral Junction Separation, and Labral Repair/Refixation on Hip Distractive Stability

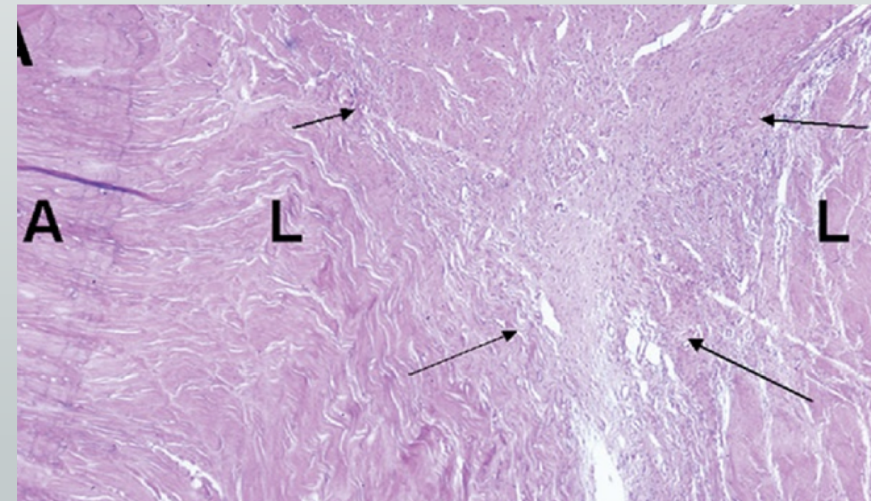
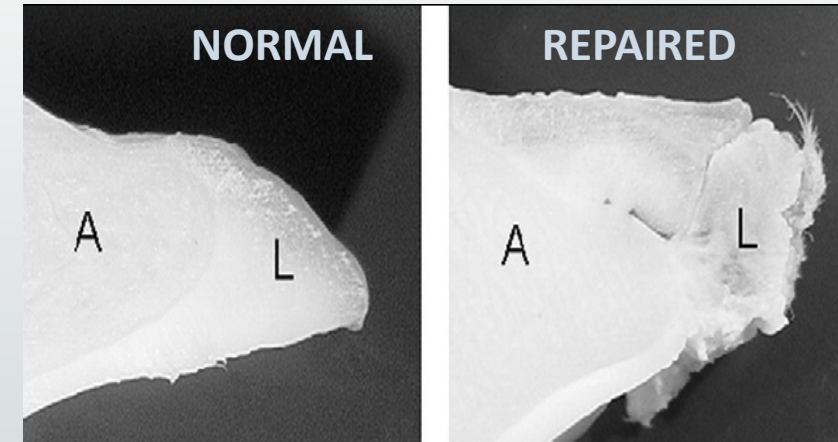
Hajime Utsunomiya¹, Hunter W Storaci¹, Samuel I Rosenberg¹, Bryson R Kemler¹, Grant J Dornan¹, Alex W Brady¹, Marc J Philippon^{1 2}

- Labral height was correlated with all suction seal parameters (maximum distraction force, distance to suction seal rupture and peak negative pressure)
- Smaller height (<6mm) labrum was significantly associated with decreased distance to suction seal rupture and decreased peak negative pressure
- Labral volume is important in hip suction seal

- Rim trimming did not affect any suction seal parameters
- In chondrolabral junction separation, larger distance to break the seal
- Labral refixation reduced labral mobility
- Max distraction force and peak negative pressure of the labral repair were lower than the native state

ANIMAL MODEL TO STUDY LABRAL REPAIR

- Ovine model
- Unilateral arthroscopic labral repair
- 1.5-cm-long incision made at the junction of the labrum and acetabulum
- The labral detachment then repaired arthroscopically with a single suture anchor.
- No form of postoperative immobilization was used



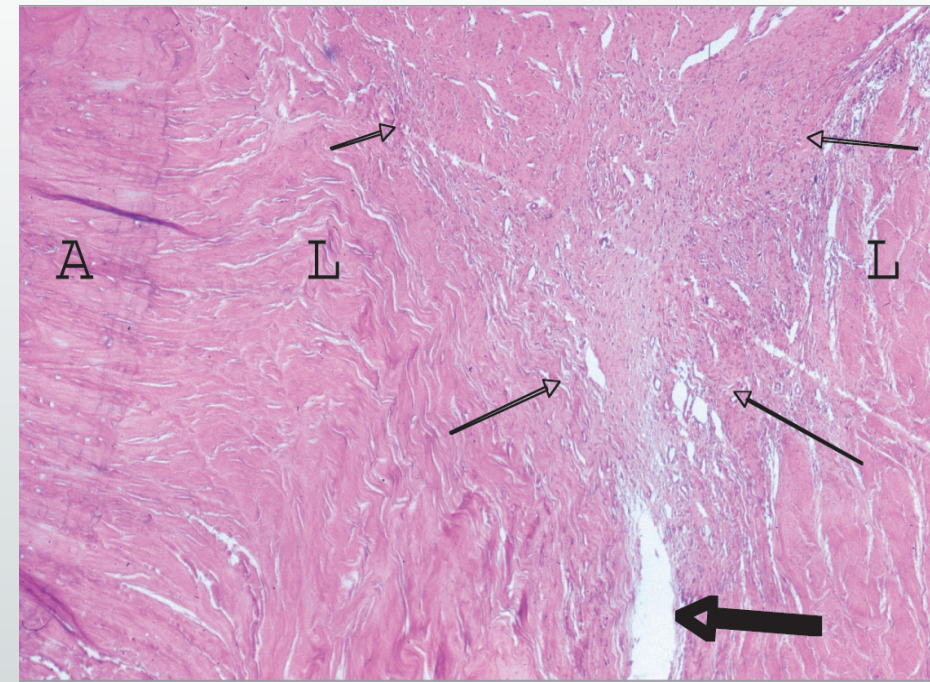
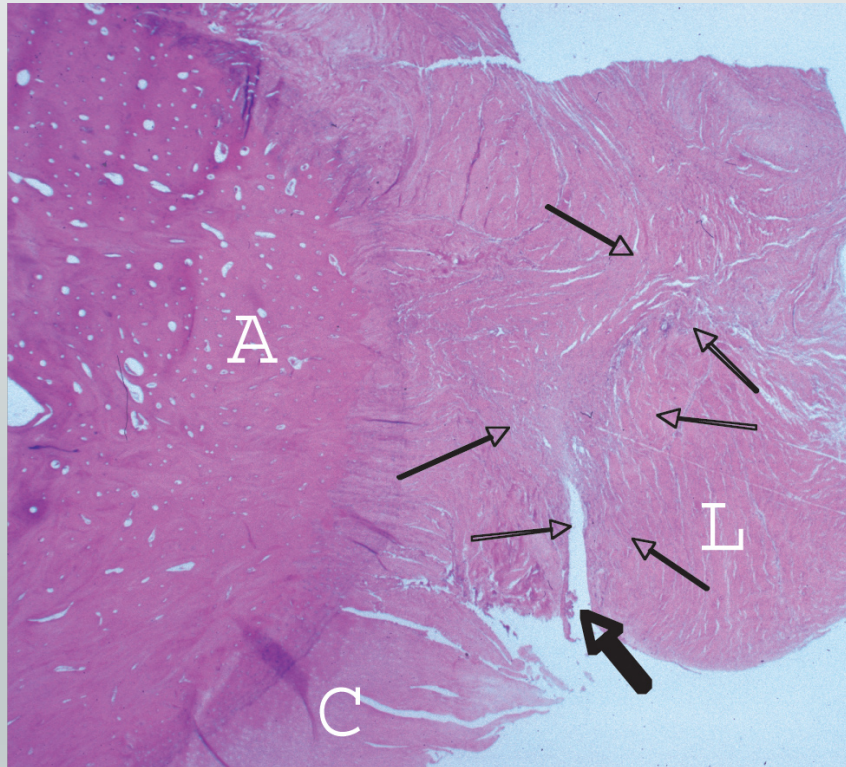
The lesion is being repaired by fibrovascular scar (small arrows) migrating from the capsular surface of the labrum.(A, acetabular bone; L, fibrocartilaginous labrum.)



Philippon, Arnoczky et al. Arthroscopy 2007 Apr;23(4):376-80

OVINE MODEL HISTOLOGY

- Acetabular articular surface with excised labrum showed signs of joint disease with reduced Safranin O staining for glycosaminoglycans (GAGs) in 33% of the animals at 12 weeks



- Acetabular cartilage for the labral repair group revealed that the main cell type were chondrocytes and some fibroblasts with minimal fibrocartilage at 12 weeks
- Safranin O staining revealed moderate GAGs on the articular cartilage.
- The joint surface showed no signs of inflammatory reaction or cartilage degeneration

Philippon, Arnoczky et al. Arthroscopy 2007 Apr;23(4):376-80

Survivorship and Outcomes 10 Years Following Hip Arthroscopy for Femoroacetabular Impingement

Labral Debridement Compared with Labral Repair

Travis J. Menge, MD, Karen K. Briggs, MPH, Grant J. Dornan, MSc, Shannen C. McNamara, BS,
and Marc J. Philippon, MD

Investigation performed at the Steadman Philippon Research Institute, Vail, Colorado

Background: Studies have demonstrated hip arthroscopy to be an effective treatment for femoroacetabular impingement (FAI) with associated labral tears. The purposes of this study were to report 10-year outcomes and hip survival following hip arthroscopy for FAI and to compare labral debridement with labral repair.

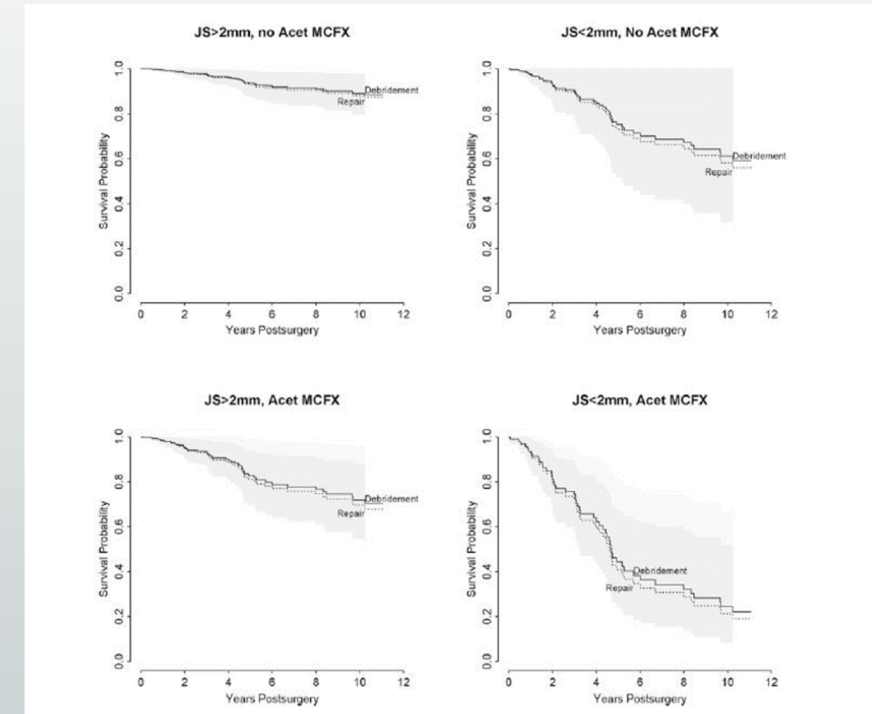
Methods: Prospectively collected data on patients followed for a minimum of 10 years after hip arthroscopy for FAI with either labral debridement or labral repair performed by a single surgeon were retrospectively analyzed. The primary patient-reported outcome measure was the Hip Outcome Score (HOS) Activities of Daily Living (ADL) subscale. Mann-Whitney U tests were used to compare outcomes between groups, and Wilcoxon signed-rank tests were used to compare preoperative with postoperative scores. Survival analysis was performed using a multivariate Cox proportional hazards model.

WHO ARE THE BEST CANDIDATES?

TABLE III Results of Multivariate Cox Model

Variable	Level 1	Level 2	HR*	95% CI	P Value†
Age at surgery	31 yr	51 yr	3.06	1.69-5.56	<0.001
Treatment	Repair	Debridement	1.10	0.59-2.05	0.762
Joint space ≤ 2 mm	No	Yes	4.26	1.98-9.21	<0.001
Acetabular microfracture	No	Yes	2.86	1.07-7.62	0.036

*HR is the hazard ratio for THA, interpreted as the change in the hazard rate when moving from Level 1 to Level 2 with all other predictors held constant. †P values calculated via the Wald z test.



When adjusted for microfracture labral repair was superior to labral debridement



10-year outcomes favor labral preservation as an effective treatment of labral pathology

JB & JS

Hip arthroscopy versus best conservative care for the treatment of femoroacetabular impingement syndrome (UK FASHIoN): a multicentre randomised controlled trial

*Damian R Griffin, Edward J Dickenson, Peter D H Wall, Felix Achana, Jenny L Donovan, James Griffin, Rachel Hobson, Charles E Hutchinson, Marcus Jepson, Nick R Parsons, Stavros Petrou, Alba Realpe, Joanna Smith, Nadine E Foster, on behalf of the UK FASHIoN Study Group**

THE LANCET

- Randomized controlled trial
- 348 patients
 - 171 allocated to hip arthroscopy and 177 received hip therapy
- iHOT33 was superior in hip arthroscopy patients at 12-month follow-up
- Treatment effect exceeded the minimum clinically important difference
- While both groups saw improvement, arthroscopy led to greater improvement

LEVEL 1 EVIDENCE

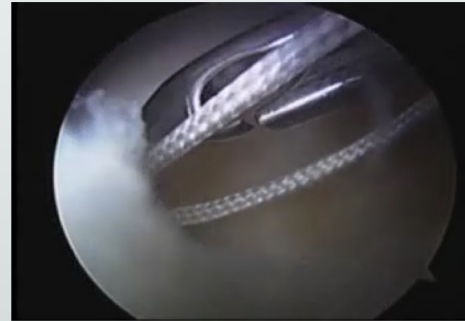
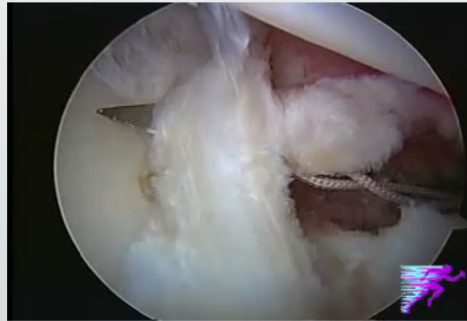
ADVANCES IN TREATING LABRUM

Repair

Through

Loop

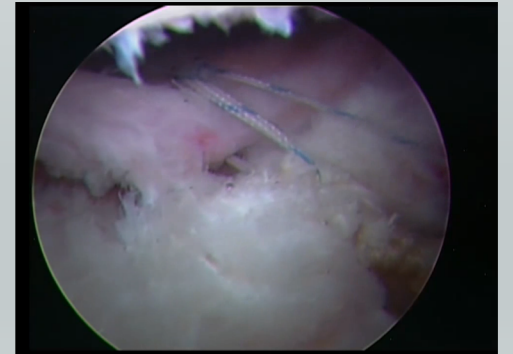
Debridement



Reconstruction



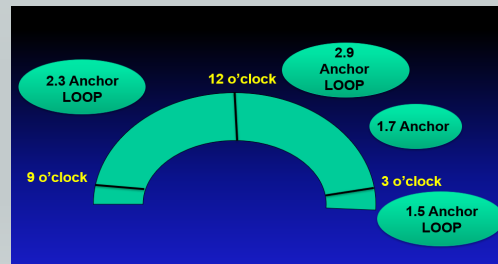
Augmentation



Clinical Outcomes After Arthroscopic Hip Labral Repair Using Looped Versus Pierced Suture Techniques

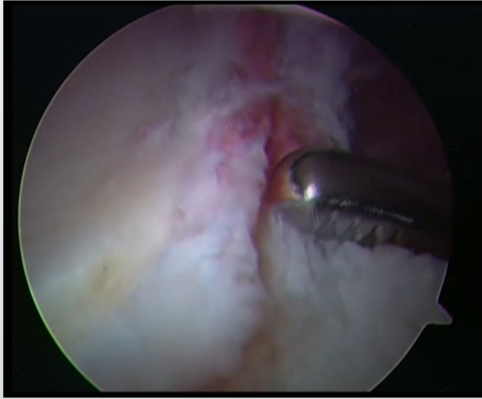
Gregory A. Sawyer, MD^{*}, Karen K. Briggs, MPH^{*}, Grant J. Dornan, MSc^{*}, N. Dawn Ommen, MD^{*}, and Marc J. Philippon, MD^{*,†}

Anatomic Repair

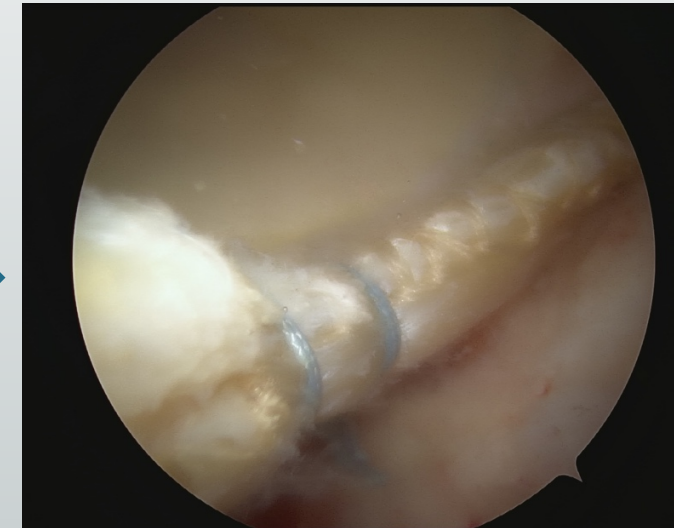
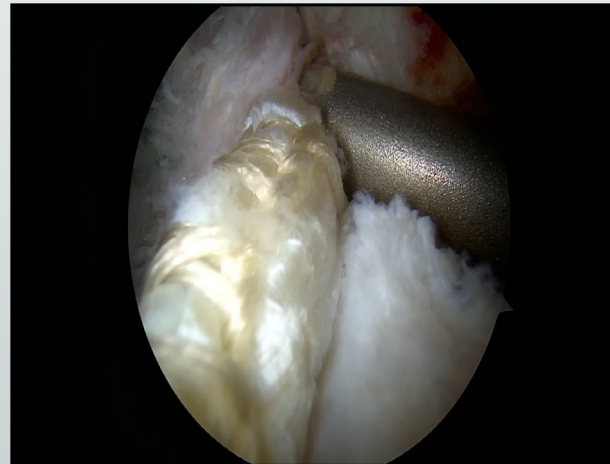


WHAT IF THERE ISN'T ENOUGH LABRUM

RECONSTRUCTION vs. AUGMENT



labrum
<6mm



EVIDENCE TO SUPPORT ADVANCEMENT AND INNOVATION

• Labral Reconstruction

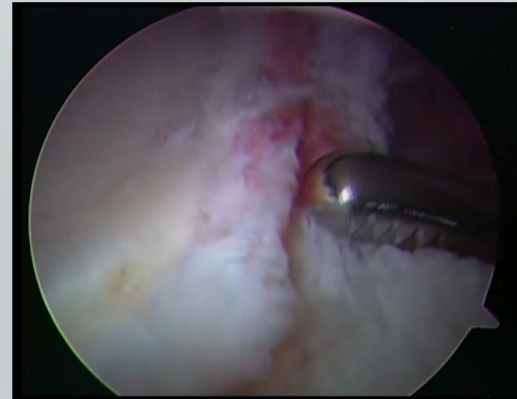
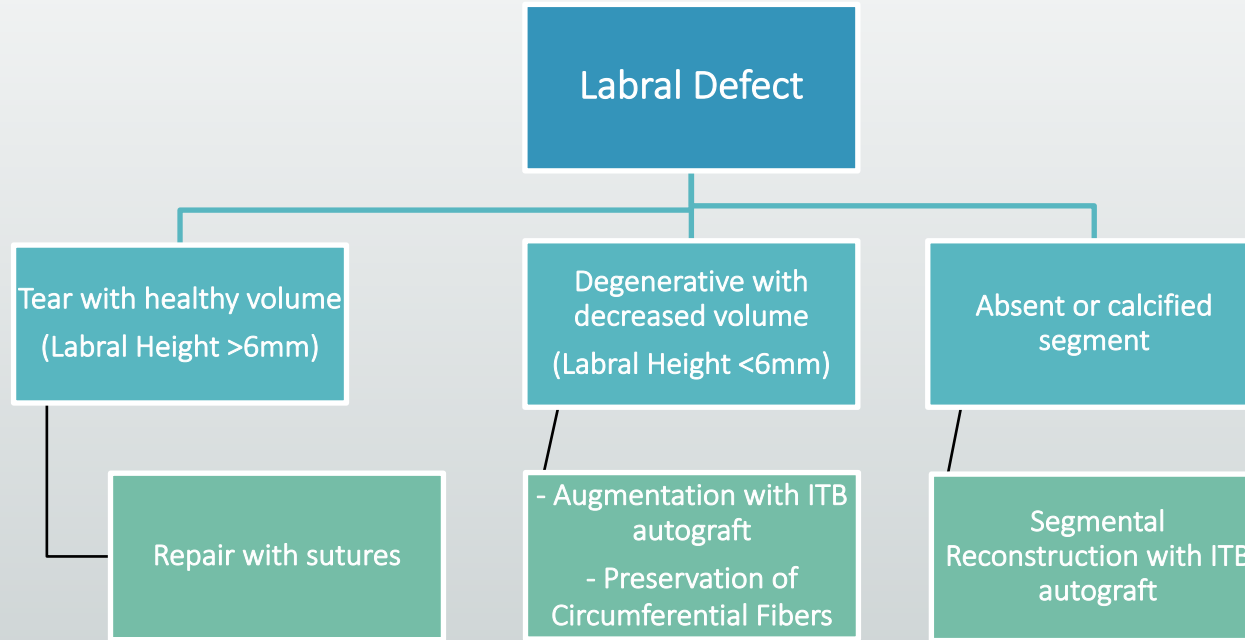
- Technique developed
- Biomechanics to support
- Outcomes to provide evidence of efficacy

• New Technique

- Preserve the remaining tissue
- Labral augmentation
- Augmentation outcomes better than reconstruction

<i>Arthroscopy</i>. 2010 Jun;26(6):750-6. doi: 10.1016/j.arthro.2009.10.016. Epub 2010 Apr 3. Arthroscopic labral reconstruction in the hip using iliotibial band autograft: technique and early outcomes. Philippon MJ¹, Briggs KK, Hay CJ, Kuppersmith DA, Dewing CB, Huang MJ.	
<i>Am J Sports Med</i>. 2013 Aug;41(8):1750-6. doi: 10.1177/0363546513487311. Epub 2013 May 3. Acetabular labral reconstruction with an iliotibial band autograft: outcome and survivorship analysis at minimum 3-year follow-up. Geyer MR¹, Philippon MJ, Fagrellius TS, Briggs KK.	
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<i>Am J Sports Med</i>. 2015 Jan;43(1):98-104. doi: 10.1177/0363546514553089. Epub 2014 Oct 31. Labral reconstruction with iliotibial band autografts and semitendinosus allografts improves hip joint contact area and contact pressure: an in vitro analysis. Lee S¹, Wuerz TH¹, Shewman E¹, McCormick FM², Salata MJ³, Philippon MJ⁴, Nho SJ⁵.	
<i>J Hip Preserv Surg</i>. 2017 Nov 22;5(1):73-77. doi: 10.1093/jhps/hnx033. eCollection 2018 Jan. Outcomes following arthroscopic hip segmental labral reconstruction using autologous capsule tissue or indirect head of the rectus tendon. Locks R^{1,2}, Chahla J², Bolia JK², Briggs KK², Philippon MJ^{1,2}.	
<i>Arthroscopy</i>. 2018 Apr;34(4):1244-1250. doi: 10.1016/j.arthro.2017.10.054. Epub 2018 Feb 15. Revision Hip Arthroscopy After Labral Reconstruction Using Iliotibial Band Autograft: Surgical Findings and Comparison of Outcomes With Labral Reconstructions Not Requiring Revision. Locks R¹, Bolia JK¹, Utsunomiya H¹, Briggs KK¹, Philippon MJ².	
<i>JBJS Case Connect</i>. 2018 Jan-Mar;8(1):e21. doi: 10.2106/JBJS.CC.17.00155. Labral Augmentation with Native Tissue Preservation with a 7.5-Year Follow-up: A Case Report. Godin JA¹, Fagotti L¹, Briggs KK¹, Philippon MJ¹.	 CASE CONNECTOR

EVIDENCE-BASED TREATMENT ALGORITHM



Acetabular Labral Reconstruction with Iliotibial Band Autograft

Outcome and Survivorship at a Minimum 10-Year Follow-up

Marc J. Philippon, MD, Justin W. Arner, MD, Matthew D. Crawford, MD, Ioanna K. Bolia, MD, and Karen K. Briggs, MPH

Investigation performed at the Steadman Philippon Research Institute, Vail, Colorado

Background: Labral reconstruction has been shown to result in improved patient-reported outcomes (PROs) at mid-term follow-up in patients with a deficient labrum. The purpose of this study was to determine survivorship and PROs at a minimum 10-year follow-up.

Methods: A retrospective evaluation of a prospectively collected single-surgeon database included 91 hips (89 patients) that underwent arthroscopic labral reconstruction with iliotibial band autograft between 2006 and 2008. The primary PRO was the Hip Outcome Score (HOS)-activities of daily living (ADL). The modified Harris hip score (mHHS), HOS-sports, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, and patient satisfaction (on a scale of 1 to 10) were also collected at a 10-year minimum follow-up. Survivorship analysis curves were evaluated.

Results: Eighty-two hips were evaluated at a 10-year minimum follow-up. Overall survivorship, with revision hip arthroscopy or total hip arthroplasty (THA) as the end point, was 70% at 5 years and 61% at 10 years, and the mean survival time was 9 years (95% confidence interval = 7.6 to 10 years). For the patients who did not undergo subsequent surgery, on average the mHHS increased from 60 preoperatively to 82 at the 10-year follow-up ($p = 0.001$), the HOS-ADL improved from 69 to 90 ($p = 0.004$), the HOS-sports improved from 43 to 76 ($p = 0.001$), and the median patient satisfaction was 10 of 10. Eighty percent of the patients achieved the minimal clinically important difference (MCID) in the HOS-ADL, and 87% obtained a patient acceptable symptom state (PASS).

Conclusions: Following arthroscopic labral reconstruction with iliotibial band autograft, 9% of the hips underwent revision arthroscopy and 27% underwent THA. At 10 years, the survival rate, with revision hip arthroscopy or THA as the end point, was 61%; however, for those with >2 mm of joint space, the current indication for labral reconstruction, the 10-year survival rate was 90%. Excellent PROs and patient satisfaction were reported by those who did not require revision or THA. With appropriate patient selection and prevention of postoperative adhesions, labral reconstruction results in excellent outcomes and high patient satisfaction that is sustained at a minimum 10-year follow-up.

Level of Evidence: Therapeutic Level IV. See Instructions for Authors for a complete description of levels of evidence.

JB&JS

THE Journal OF Bone
& Joint Surgery

82 Patients

10-year follow-up

Revision or THA endpoints

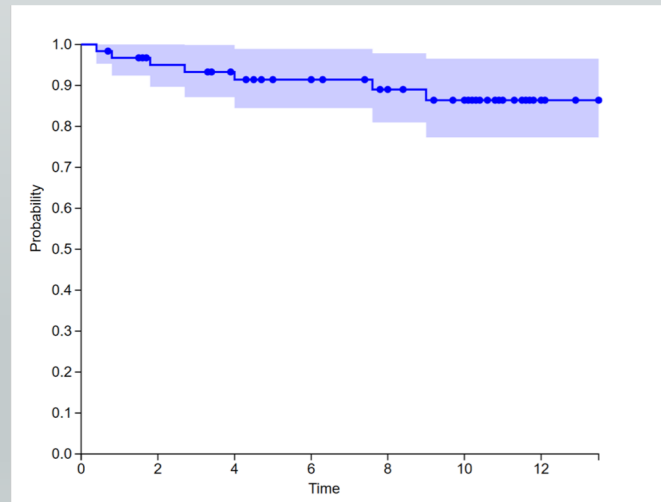
Overall survivorship: 5 yr=70%, 10 yr=61%

Mean survival: 9 years (95% ci 7.5-10)

Median satisfaction: 10

Significant improvement in hos-adl, hos-sss

Survivorship for >2 mm JS





INNOVATION THROUGH REGENERATIVE MEDICINE

SPRI's Regenerative & Translational Medicine Program

- 
- Adult stem cells
 - Muscle stem cells
 - Adipose stem cells
 - Bursa stem cells
 - PDGFR+ cells
 - IPS cells
 - OrthoBiologics
 - Platelet-Rich Plasma
 - Bone Marrow Concentrate

- 
- FDA-approved drugs
 - Telomerase activity
 - Senolytic drugs
 - Senomorphic drugs
 - mTOR inhibitors
 - Rapamycin
 - Metformin
 - Anti-fibrotic agent
 - Anti-angiogenic agent
 - Epigenetic drugs

Biologics

**Regenerative
Medicine
Approaches**

**Tissue Repair after
Injury, Disease &
Aging**

Therapeutics

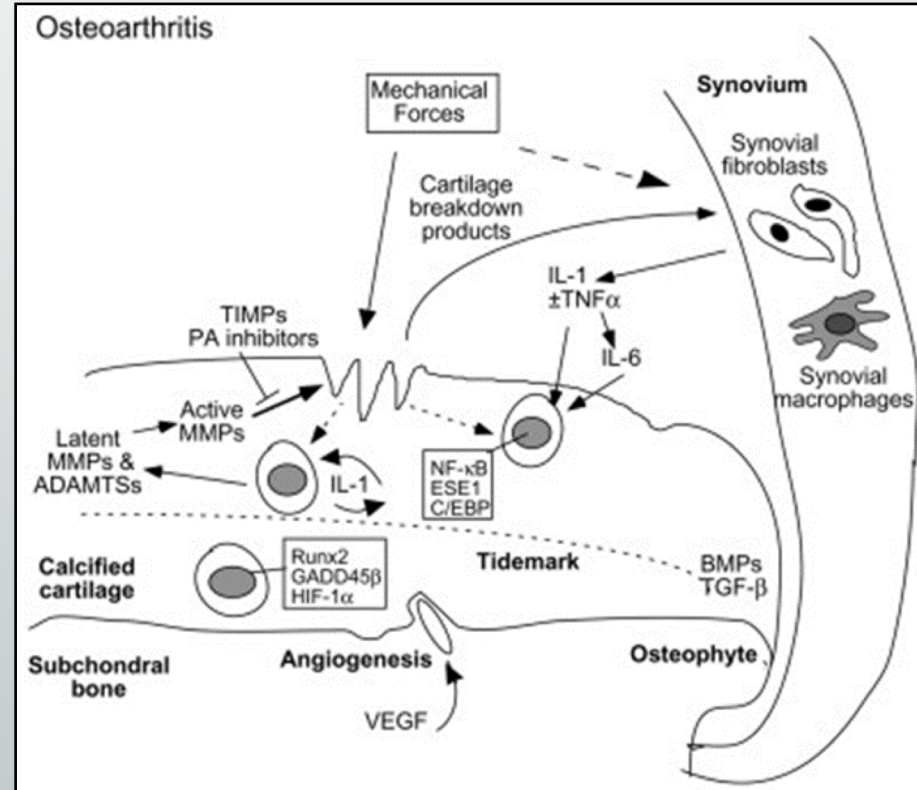
**Animal
modelling**

- Gene therapy
- CRISPR-CAS9 gene editing technology
- Exosomes/vesicles
- Coacervate
- Microspheres
- PA nanofibers
- Magnetic nanoparticles

- Dystrophic mice
 - Mdx, dKO
- Progeria mice
 - Z24, ERCC mice
- Wild-type mice
- Parabiosis/Pregnancy
- Super-healer (MRL/MpJ)
- Microfracture
- Osteoarthritis model
- Ligament reconstruction

BIOLOGICS

- PRP
- BMAC
- Stem cells



- Alter the joint/cell environment for ultimate healing

BIOLOGIC AUGMENTATION

- Bone marrow aspirate concentrate

- PRP



- Losartan to prevent adhesion formation



Blocking TGF- β 1 improve the effectiveness of PRP for muscle repair through a reduction in fibrosis

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

Lars Engebretsen,^{1–3} Kathrin Steffen,^{1,2}
Joseph Alsousou,⁴ Eduardo Anitua,⁵
Norbert Bachl,⁶ Roger Devilee,^{7,8} Peter Everts,^{8,9}
Bruce Hamilton,¹⁰ Johnny Huard,¹¹
Peter Jenoure,¹² Francois Kelberine,¹³ Elizaveta
Kon,¹⁴ Nicola Maffulli,^{15,16} Gordon Matheson,¹⁷
Omer Mei-Dan,¹⁸ Jacques Menetrey,^{19,20}
Marc Philippon,²¹ Pietro Randelli,²²
Patrick Schamasch,¹ Martin Schweltnus,²³
Alan Vernec,²⁴ Geoffrey Verrall²⁵

INTRODUCTION

Acute and chronic musculoskeletal injuries in sports are common and problematic for both athletes and clinicians. A significant proportion of these injuries remain difficult to treat, and many athletes suffer from decreased performance

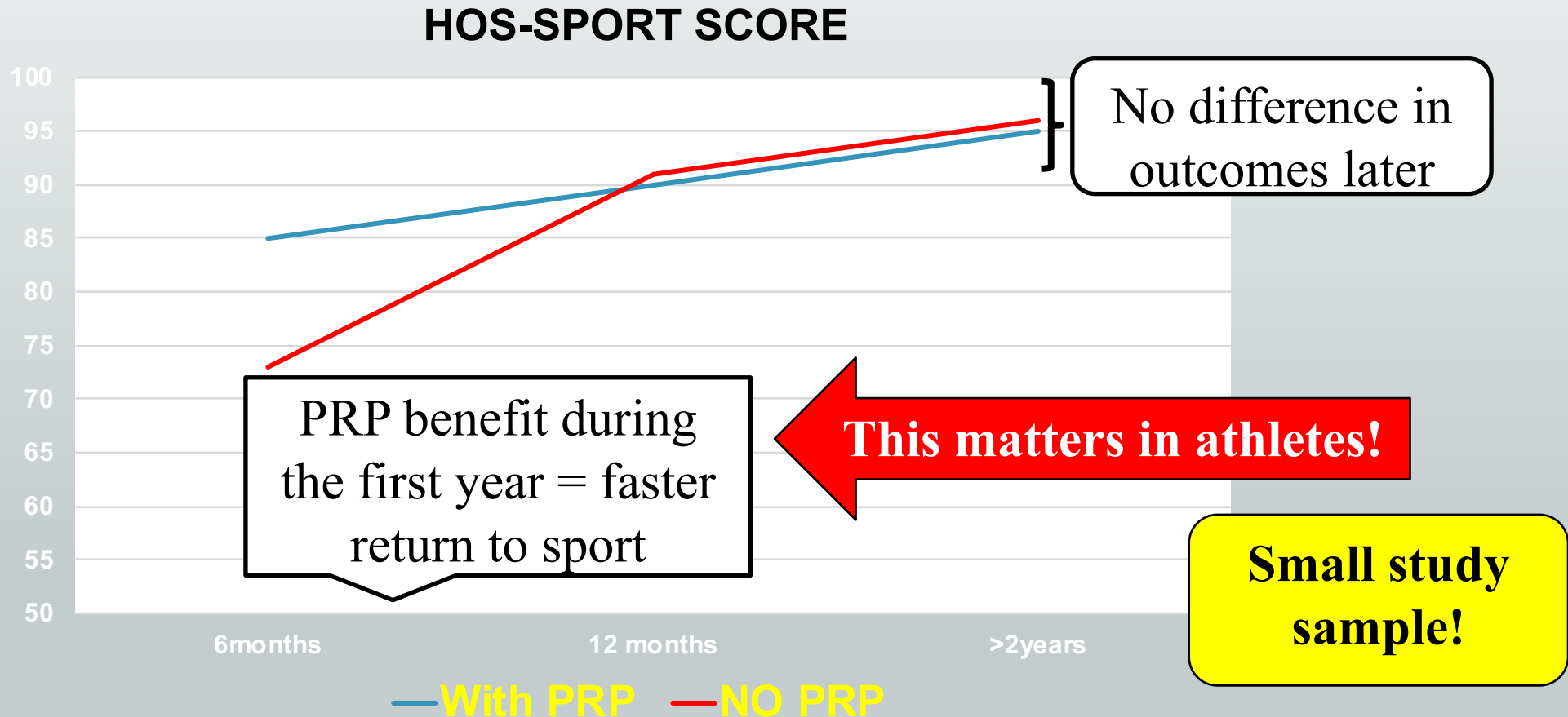
PRP and its variant forms were originally used in clinical practice as an adjunct to surgery to assist in the healing of various tissues. PRP has also been used in prosthetic surgery to promote tissue healing and implant integration, and to control blood loss.^{4,5} Furthermore, the application

state of PRP treatment among athletes, aiming to provide recommendations for clinicians, athletes and individual sports governing bodies. The purpose of this consensus paper is furthermore to review the evidence for the clinical effectiveness of PRP, its ergogenic potential and safety, and attempt to reconcile any possible disparity between its increasing popularity and the underlying science supporting its use. After an introduction into the basic science of PRP (i), the group considered the following issues regarding PRP use in clinical practice; (ii) the role of PRP in muscle injuries; (iii) the role of PRP in tendon injuries; (iv) the role of PRP in cartilage injuries and the healing of other tissues; (v) suggested techniques for the application of PRP and postinjection recommendations; (vi) potential adverse effects of PRP use; (vii) developing a randomised controlled trial (RCT) on PRP; (viii) PRP and antidoping regulations; and (ix) summary and recommendations.

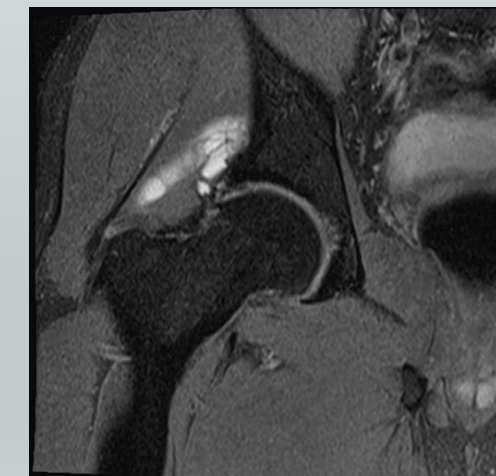
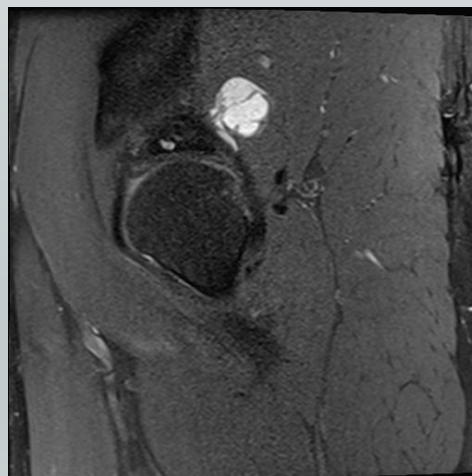
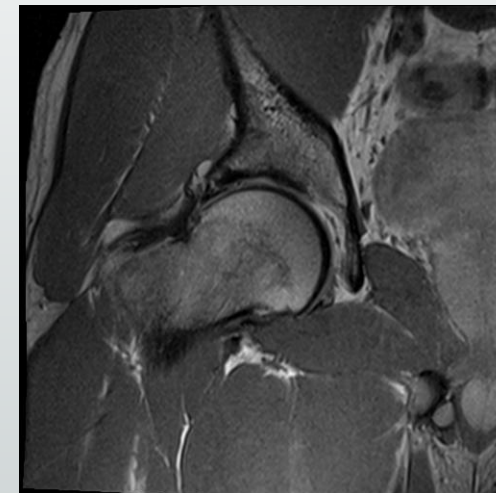
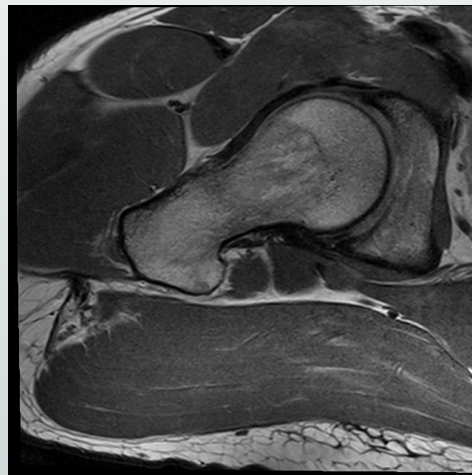
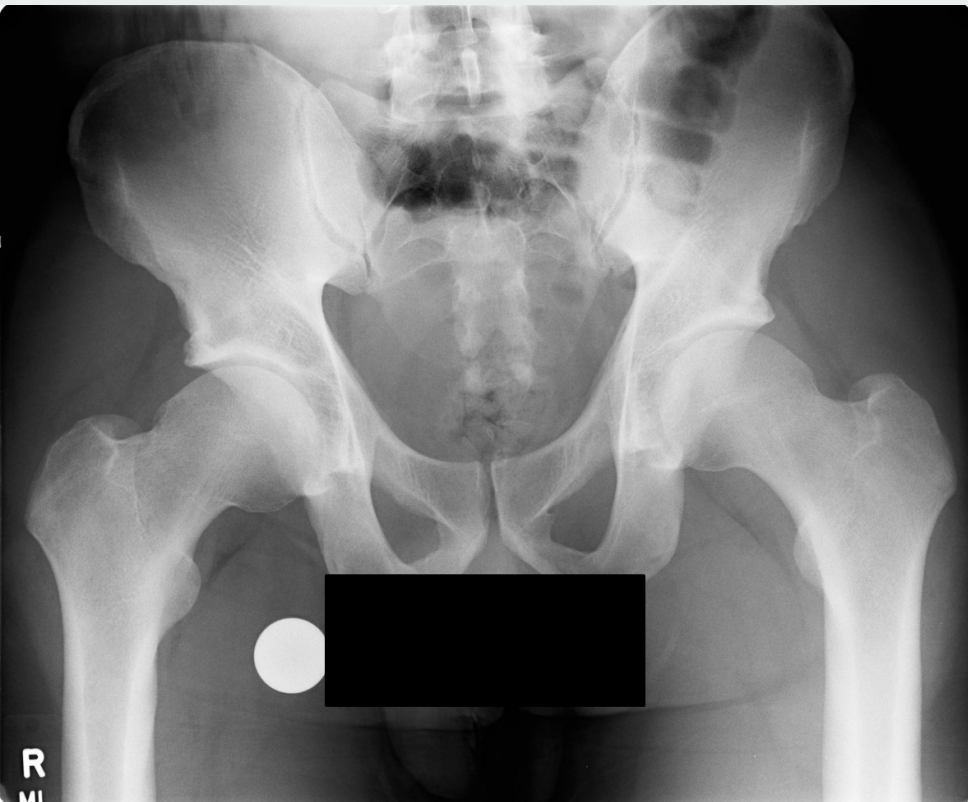
Basic science of PRP

In broad terms, PRP may be defined as a volume of the plasma fraction of autologous blood having a platelet concentration above baseline,⁷ and is therefore a concentrated source of autologous platelets. Platelets contain a number of growth

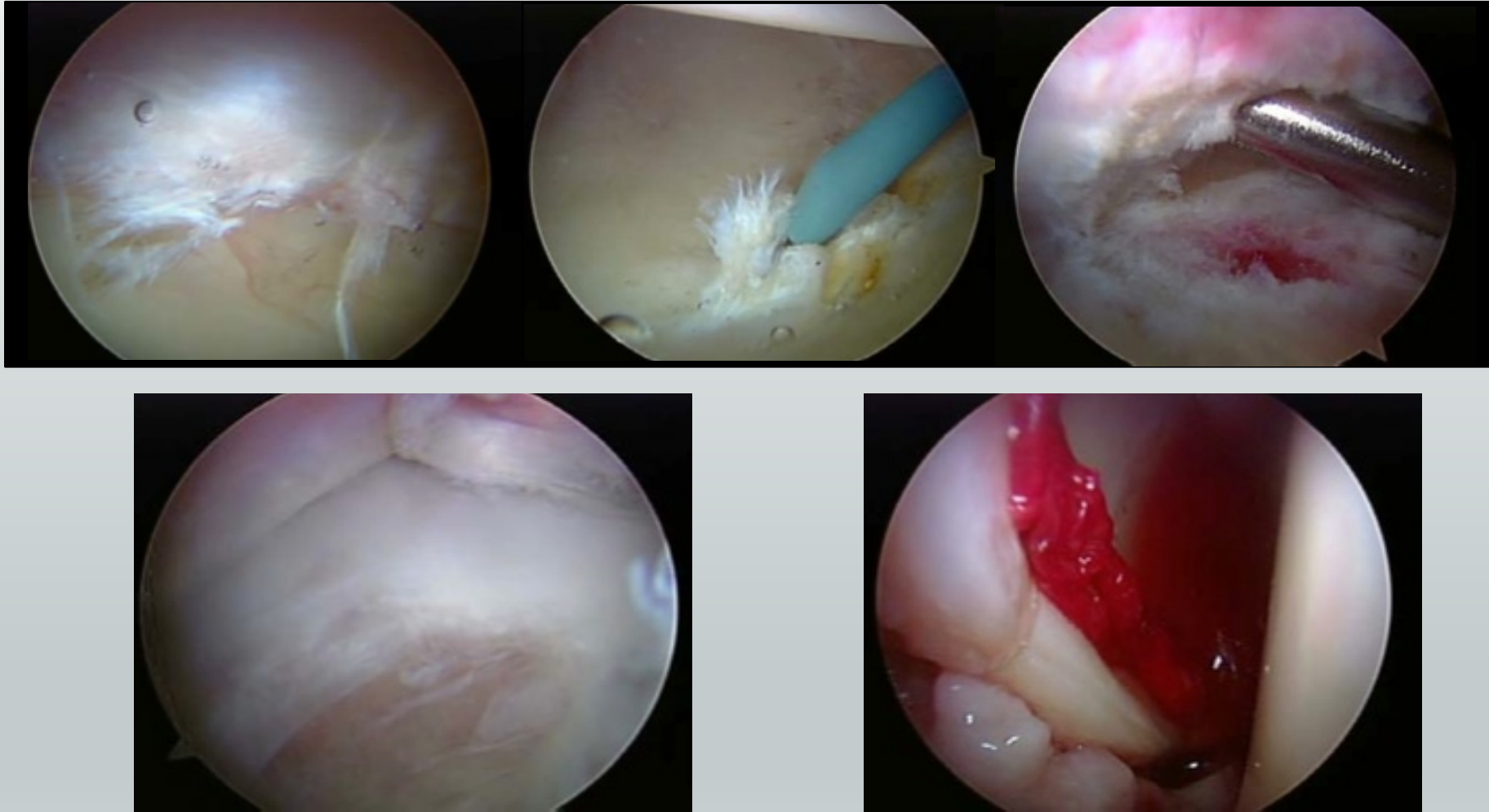
OLYMPIC ATHLETES (PRIOR TO CONSENSUS) COMPARED TO PRO ATHLETES



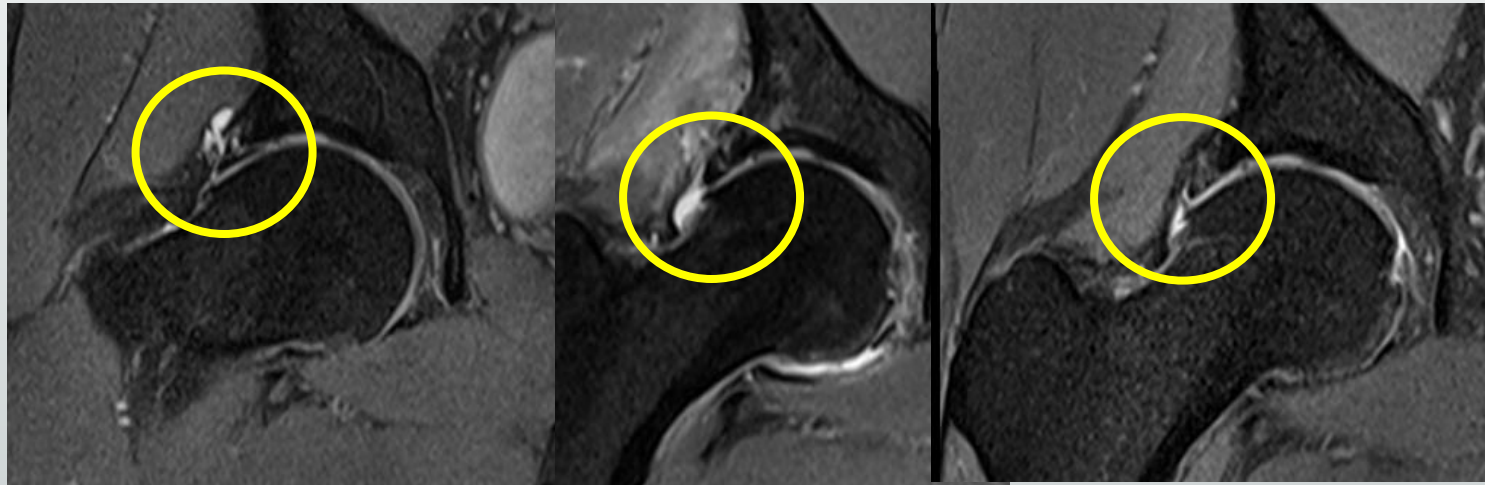
PROFESSIONAL BASEBALL PLAYER INSIDIOUS ONSET OF RIGHT HIP PAIN



RIGHT HIP ARTHROSCOPY



MRI FOLLOW-UP



Pre-op

16 d Post-Op

9 m Post-Op



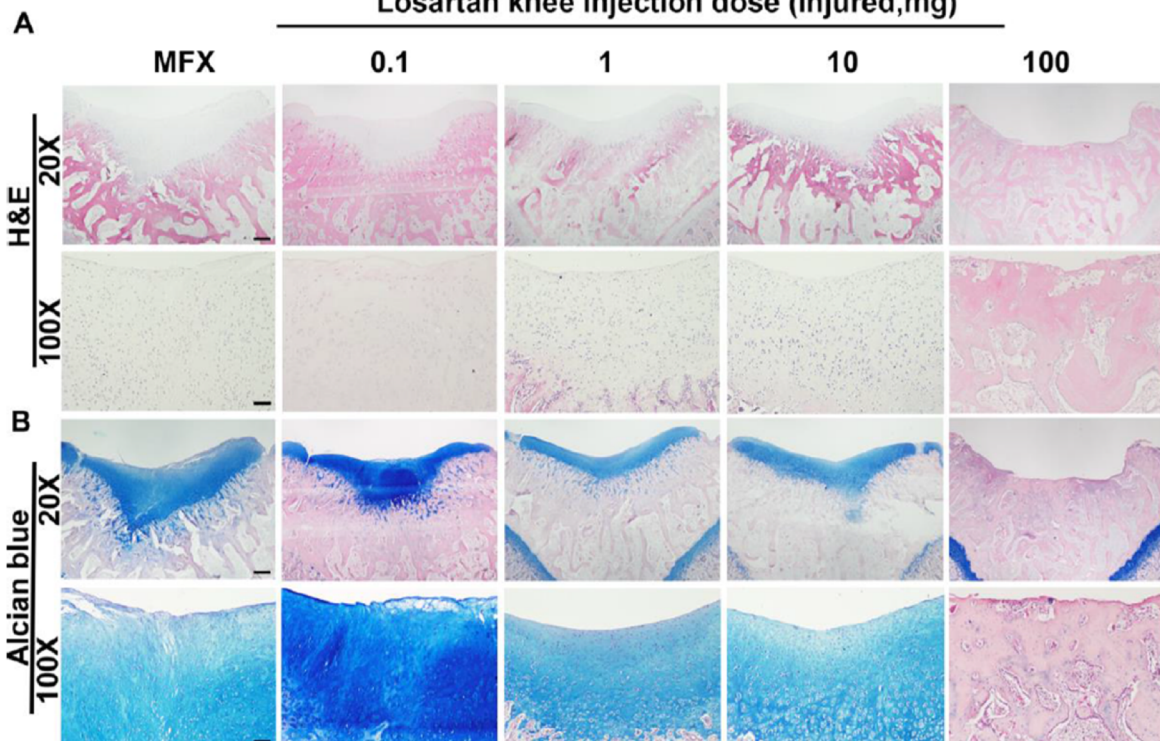
TGF- β 1 IS THE CAUSE OF FIBROSIS

- Blocking TGF- β 1 can inhibit fibrosis in muscle injury.
- Fibrocartilage is the problem with microfracture mediated cartilage repair.
Kobayashi, Huard Am J Sports Med 2016
- However, TGF- β 1 is an essential factor for chondrogenesis and joint cartilage homeostasis.
- Recently, the role of TGF- β 1 for cartilage repair has been challenged
- A protective effect on articular cartilage
 - Wild mice of DMM model (OA) with losartan (TGF- β 1 blocker) treatment.

Zhen. Nat Med 2013, Chen. Am J Pathol. 2015

Hypothesis: Blocking TGF- β 1 might be able to regulate fibrosis and improve cartilage healing.

Losartan knee injection dose (injured,mg)



IA injection of losartan demonstrates a dose-dependent effect on MFX-mediated cartilage repair

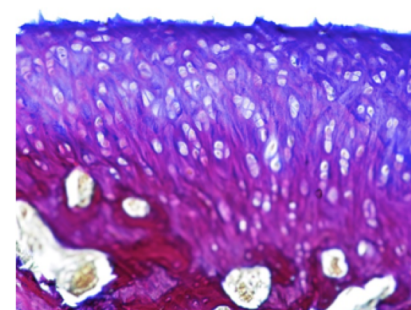
Winner of the Cabaud Award

Biologically Regulated Marrow Stimulation by Blocking TGF- β 1 With Losartan Oral Administration Results in Hyaline-like Cartilage Repair

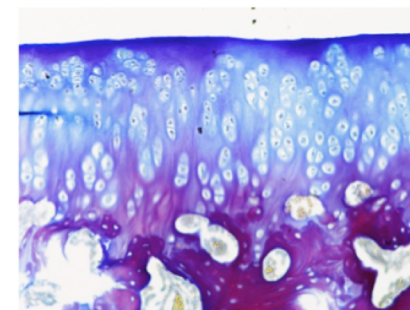
A Rabbit Osteochondral Defect Model

Hajime Utsunomiya, MD, PhD, Xueqin Gao, MD, PhD, Zhenhan Deng, MD, Haizi Cheng, MD, Gilberto Nakama, MD, Alex C. Scibetta, BA, Sudheer K. Ravuri, PhD, Walter R. Lowe, MD, William G. Rodkey, DVM, Tamara Alliston, PhD, Marc J. Philippon,* MD, and Johnny Huard,* PhD
Investigation performed at Center for Regenerative Sports Medicine, Steadman Philippon Research Institute, Vail, Colorado, USA

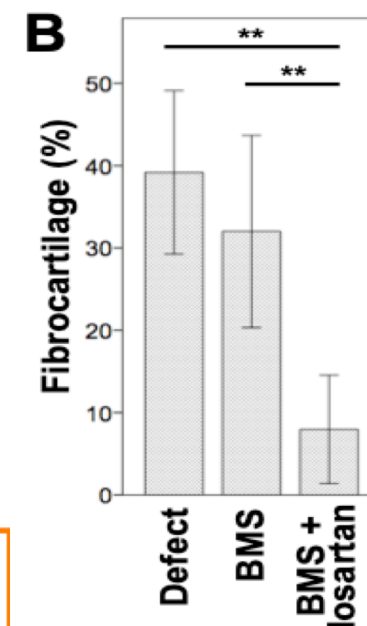
Herovici staining for cartilage evaluation: Dark purple = Collagen type 3 = Fibrosis



Bone marrow stimulation (BMS) only=> Fibrocartilage

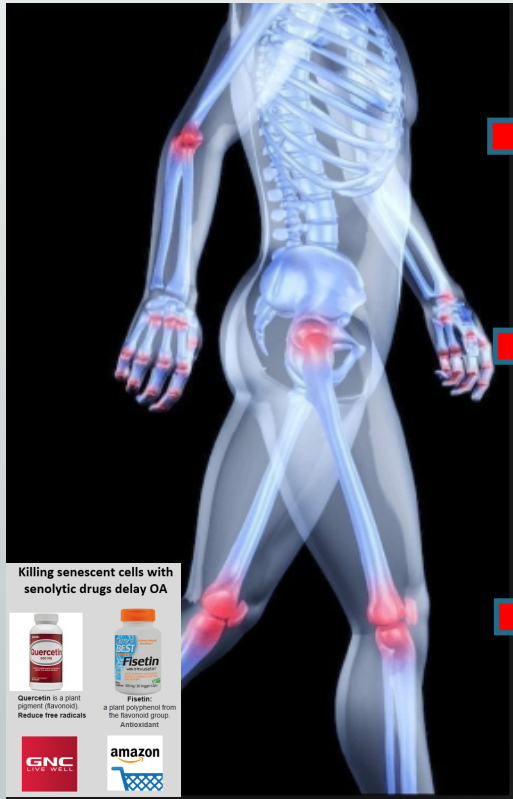


BRMS by oral losartan => Hyaline-like cartilage



Blocking TGF- β 1 by oral losartan significantly reduced fibrotic tissues in the repair site.

COMBINATION OF BIOLOGICS FOR OPTIMAL MUSCULOSKELETAL CARE

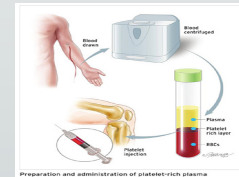


FDA U.S. FOOD & DRUG
ADMINISTRATION

Treating patients with senolytic agents prior to stem cell harvesting to eliminate pre-existing senescent cells in the body.



Bone marrow aspirate



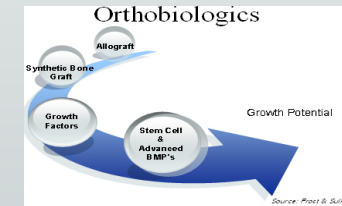
Platelet-Rich Plasma



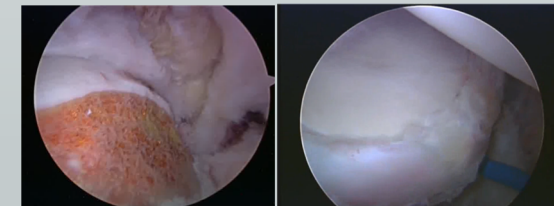
Orthopaedic Surgery



Improve stem cell banking



Improve Orthobiologics treatments



Improve Surgical Outcome

MODIFYING THE JOINT ENVIRONMENT

Losartan

- FDA approved angiotensin II type 1 receptor blocker
- Can be useful as an antifibrotic agent in humans
- Block TGF B1

Potential Usefulness of Losartan as an Antifibrotic Agent and Adjunct to Platelet-Rich Plasma Therapy to Improve Muscle Healing and Cartilage Repair and Prevent Adhesion Formation

JOHNNY HUARD, PHD; IOANNA BOLIA, MD, MSC; KAREN BRIGGS, MPH, MBA; HAJIME UTSUNOMIYA, MD, PHD; WALTER R. LOWE, MD; MARC J. PHILIPPON, MD

CASE WITH ADHESIONS

Intra-articular



Rectus Tendon

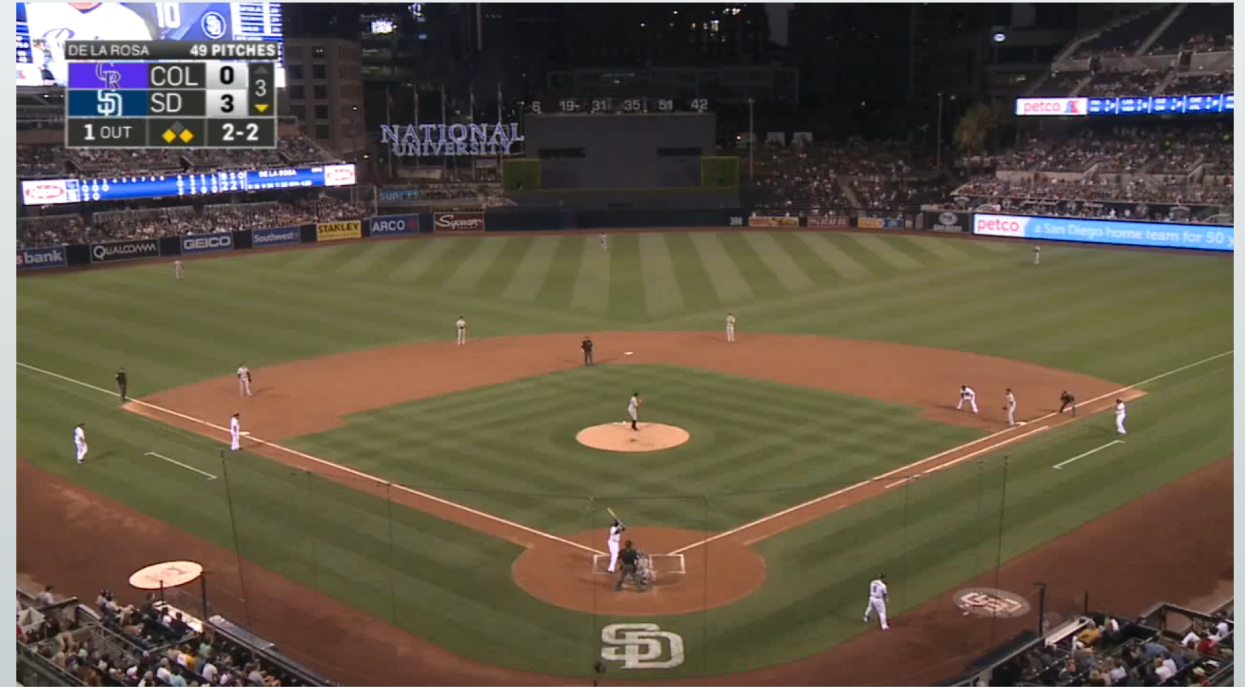


CLINICAL OUTCOME

- 5 months and 25 days
 - (-) pain, Hip ROM symmetric, FABER
 - distance (-), anterior impingement (-)
 - Sports test 17/20

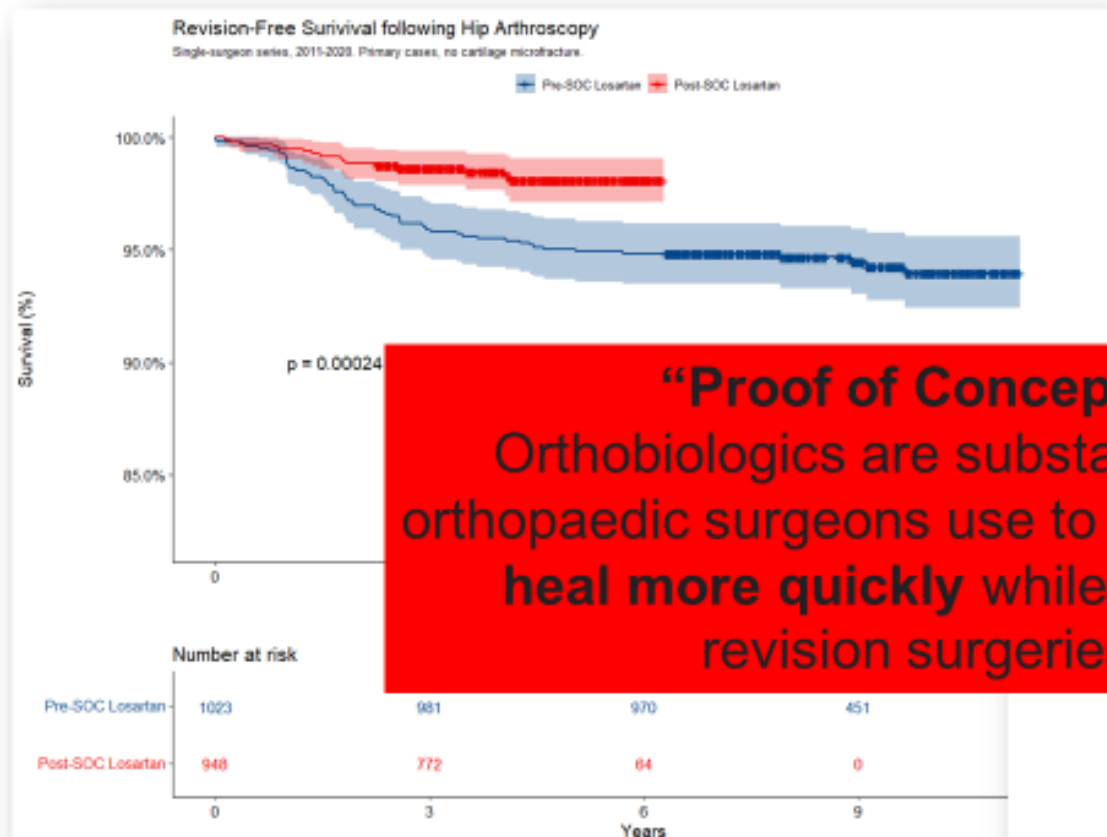
Returned Next Season

- 4th Most Games Ever Played
- 2nd Most at Bats
- 70 RBIs
- Hit 0.280
- Getting ready to complete 14th season



5 YEARS LATER: NO REVISION & NO ADHESIONS

Losartan results in a 64% reduction in the risk of requiring Hip revision surgery Now a standard of care for Dr. Marc Philippon



“Proof of Concept”:
Orthobiologics are substances that orthopaedic surgeons use to **help injuries heal more quickly** while reducing revision surgeries

Standard of Care
losartan administration
following primary hip
arthroscopy resulted in
a **64% reduction** in the
risk of requiring revision
surgery (HR = 0.36,
p<0.001).

for risk of revision hip scope at TSC

Characteristic	HR	95% CI	p-value
LOSARTAN			
Pre SOC Losartan	—	—	
Post SOC Losartan	0.36	0.21, 0.64	<0.001

¹ HR = Hazard Ratio, CI = Confidence Interval

ORTHOBIOLOGICS CLINICAL TRIAL

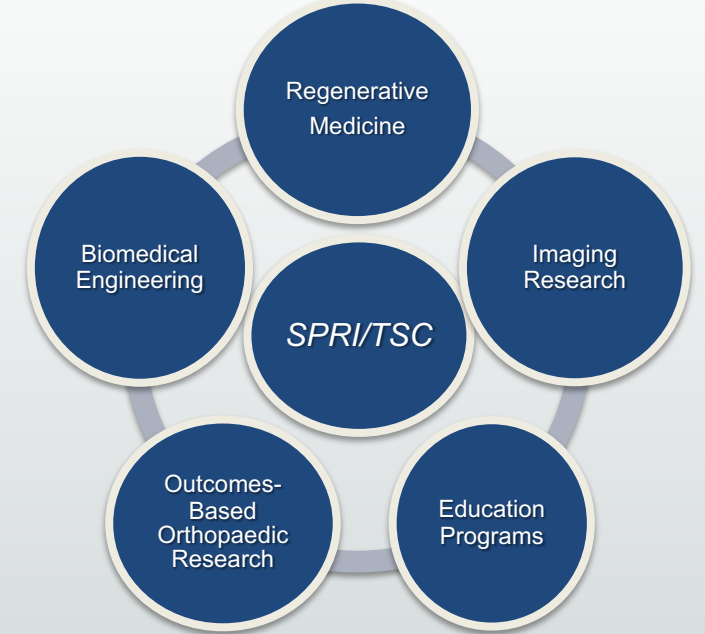
THE USE OF SENOLYTIC AGENT TO IMPROVE THE BENEFIT OF PLATELET-RICH PLASMA AND LOSARTAN FOR TREATMENT OF FEMOROACETABULAR IMPINGEMENT AND LABRAL TEAR: A PILOT STUDY

Enrolment began October 2021, funding allocated for 100 subjects total

Current Enrolment as of 8/1/2022: 24 Subjects

Objectives:

- 1.To determine whether pre- and post-operative Fisetin treatment when used in conjunction with hip arthroscopy and standard of care (PRP/Losartan) for the treatment of FAI and labral tears is safe.
- 2.To determine whether pre- and post-operative Fisetin will improve the benefits of PRP/Losartan when used in conjunction with hip arthroscopy and standard of care (PRP/Losartan) for the treatment of FAI and labral tears, based on patient-reported outcomes for pain and function, and quality of life.
- 3.To determine whether pre- and post-operative Fisetin will improve the benefits of PRP/Losartan when used in conjunction with hip arthroscopy and standard of care (PRP/Losartan) for the treatment of FAI and labral tears, based on serum biomarkers of osteoarthritis and inflammation.



U.S. DEPARTMENT OF DEFENSE

Dear Dr. Philippon:

We have received, on April 5, 2019, your submission dated April 3, 2019, for losartan. This submission contains a request for an exemption for your proposed study.

After reviewing the information contained in your submission, we have concluded that your study, entitled "*Biologically Regulated Marrow Stimulation by Blocking Fibrosis to improve Cartilage Repair: A Randomized, Double Blind, Placebo Controlled Study*", meets all of the requirements for exemption from the IND regulations and, therefore, an IND is not required to conduct your investigation.

After reviewing the information contained in your submission, we have concluded that your study, entitled "*Biologically Regulated Marrow Stimulation by Blocking Fibrosis to improve Cartilage Repair: A Randomized, Double Blind, Placebo Controlled Study*", meets all of the requirements for exemption from the IND regulations and, therefore, an IND is not required to conduct your investigation.

CONCLUSION

- Innovation in hip arthroscopy has been possible through:
 - Advancements in surgical techniques and devices
 - Collaboration between specialists
 - Integration of various modalities of research
- Future directions in hip arthroscopy and treatment of hip disorders:
 - Prevention program to optimize early intervention
 - Identify problem areas (revisions, adhesions, etc.)
 - Continue investigation of patient outcomes, biomechanics, and regenerative medicine

THANK YOU

- OREF
- AAOS Research Development Committee
- All our collaborators throughout the years
- Staff, fellows, interns and others who worked on these projects
- My Family for allowing me to dedicate my time to this effort

It takes a village to achieve our goals!

CLINICAL TEAM



Certified Athletic Trainer

- Sean Garvey, ATC



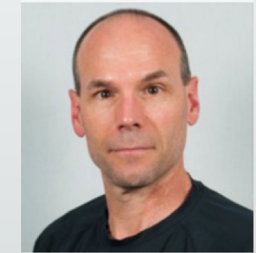
Practice Manager

- Heather Gilman, PA



Surgical Coordinator

- Meghan Giroux



Rehabilitation Coordinator

- Mark Ryan, ATC

RESEARCH TEAM



Director of COOR

- Grant Dornan, MS



Director of Hip Research

- Karen Briggs, MBA, MPH



Hip Research Assistant

- Jarrod Brown, MS, MD



Hip Research Assistant

- Spencer Comfort, BS



Marc J. Philippon, MD
Managing Partner, Sports Medicine, Hip Disorders, Hip Arthroscopy



Randy W. Viola, MD
Hand, Wrist, Elbow & Orthopaedic Trauma Specialist



David C. Karli, MBA, MD
Spine, Sports, Rehabilitation & Regenerative Medicine Specialist



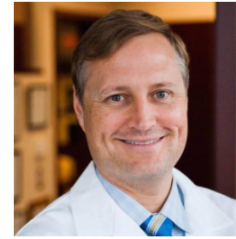
Tom R. Hackett, MD
Complex Knee, Shoulder & Elbow Surgeon



Peter J. Millett, MD, MSc
Shoulder, Knee, Elbow Surgery & Sports Medicine



Thos A. Evans, MD
Orthopaedic Interventionalist of Spine & Joint, Regenerative Medicine Specialist & Anesthesiologist



Matthew T. Provencher, MD
Complex Shoulder, Complex Knee & Sports Surgery



Raymond H. Kim, MD
Adult Joint Reconstruction, Knee & Hip Arthroplasty



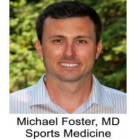
David A. Kuppersmith, MD
Internal Medicine



Joseph J. Ruzbarsky, MD
Shoulder, Knee, Elbow & Hip Preservation Surgery



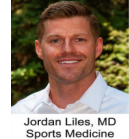
Kent Doan, MD
Sports Medicine



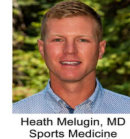
Michael Foster, MD
Sports Medicine



Toufic Jildeh, MD
Sports Medicine



Jordan Liles, MD
Sports Medicine



Heath Melugin, MD
Sports Medicine



Charles Su, MD
Sports Medicine



Matthew Vopat, MD
Sports Medicine



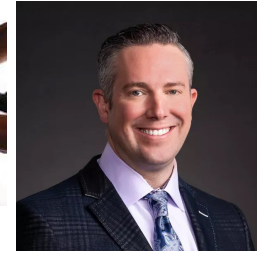
Stephen Yu, MD
Sports Medicine



Parker Duncan, MD
Foot & Ankle



Trevor Shelton, MD
Hip Preservation & Reconstruction



DR. MICHAEL GALLIZZI, MD
Robotic and Endoscopic Spine Surgeon



Dan Drawbaugh
CEO
Steadman Philippon Research Institute
The Steadman Clinic



Dr. Marc Philippon, MD
Hip Arthroscopy Pioneer
30 years of Treating Athletes
Managing Partner, The Steadman Clinic
Co-Chair of the Board of Directors
Steadman Philippon Research Institute



Dr. Johnny Huard, PhD
Principal Investigator
Chief Scientific Officer
Director of Center for Regenerative & Personalized Medicine
Steadman Philippon Research Institute
Director of Research, Proofpoint Biologics
The Steadman Clinic
Affiliate Faculty, Colorado State University



U.S. OLYMPIC & PARALYMPIC NATIONAL MEDICAL CENTER



Dr. Tom Clanton, MD
Healthy Aging Physician



Dustin Anderson, MD
Orthopaedic Interventionalist, Sports, Spine & Regenerative Medicine, PM&R and Pain Medicine



Robert Waltz, MD
TSC Fellow



Justin Ernat, MD
TSC Fellow



Simon Lee, MD
TSC Fellow



Hajime Utsunomiya, MD, PhD
International Fellow



Yoichi Murata, MD, PhD
International Fellow



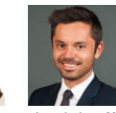
Naomasa Fukase, MD, PhD
International Fellow



Justin Arner, MD
TSC Fellow



Philip Nolte, MD
International Fellow



Ingrid Stake, MD
International Fellow



Luca Lacheta, MD
International Fellow



Haruki Nishimura, MD, PhD
International Fellow



Kohei Yamaura, MD, PhD
International Fellow



Maria D. Hazra, MD
International Fellow



Rony D. Hazra, MD
International Fellow



Joel M. Matta, MD
Hip Disorders: Preservation, Replacement & Fractures



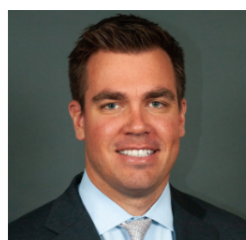
C. Thomas Haytmanek Jr, MD
Foot, Ankle & Trauma Surgery



Armando F. Vidal, MD
Complex Knee, Shoulder & Sports Medicine Specialist



Leslie B. Vidal, MD
Shoulder, Hip, Knee & Sports Medicine Specialist



Jonathan A. Godin, MBA, MD
Shoulder, Knee, Hip & Sports Medicine Surgeon



Kavi Sachar, MD
Hand, Wrist and Elbow Surgery



Jared T. Lee, MD
Aspen Medical Director, Shoulder, Hip, Knee & Sports Medicine



Waqqar Khan-Farooqi, MD
Foot, Ankle & Trauma Surgery



Thea Wojtkowski, MD
Hip Replacement & Trauma Surgery



Thank You!



J. Richard Steadman, MD

1937–2023

- Legend of orthopaedic surgery and clinical research
- Inventor of microfracture treatment and the “healing response”
- True innovator in physical therapy and rehabilitation, including movement and ambulation following surgery
- Founded the longest standing and most robust orthopaedic clinical outcomes database in the world
- Treated thousands of patients, including professional and Olympic athletes, many of whom went on to win titles and championships
- Served as Chief Physician for U.S. Ski Team for 9 consecutive Winter Games, beginning in 1976
- Legacy lives on in sports medicine and orthopaedic care at The Steadman Clinic, clinical outcomes research and innovative techniques and therapies developed at Steadman Philippon Research Institute (SPRI)