



ORTHOBIOLOGICS – FACT OR FICTION

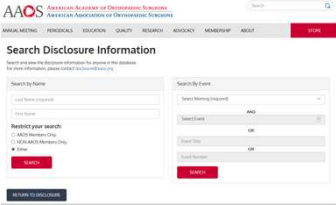
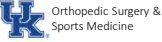
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 Division of Sports Medicine
 Department of Orthopaedic Surgery & Sports Medicine
 Team Physician for Eastern Kentucky University

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Disclosures

Institutional – Fellowship Support: Smith & Nephew, LLC, Arthrex, Inc.

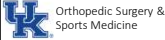
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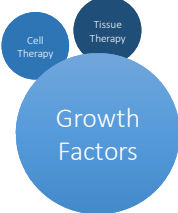
3

*biologics refers to natural products that are harvested and used to **augment** a medical process and/or the biology of healing*

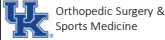
Anz+ JAAOS 2014



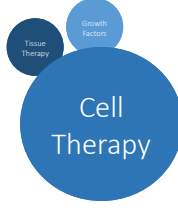
4



isolated growth factor therapy
platelet-rich plasma
autologous conditioned plasma



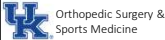
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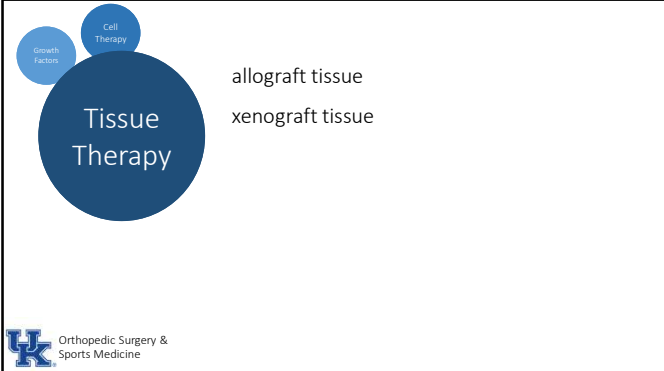
bone marrow aspirate concentrate (BMAC)
chondrocyte implantation
stem cell therapy

autologous Marrow-derived
Adipose-derived
Synovial-derived
Peripheral blood-derived

allogenic Mesenchymal adult stem cells
Amniotic-derived stem cells



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A diagram titled "Tissue Therapy" in a large blue circle. To its left are two smaller blue circles: "Growth Factors" and "Cell Therapy". To the right of the main circle are the terms "allograft tissue" and "xenograft tissue". At the bottom left is the logo for "Orthopedic Surgery & Sports Medicine".

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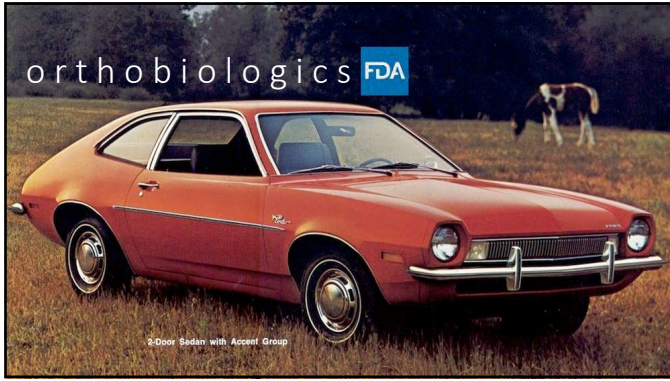
A slide featuring the FDA logo on the left. To the right, the text reads: "Not all are market approved", "Challenges beyond understanding orthopaedic applications", and "Regulatory oversight and compliance". At the bottom left is the logo for "Orthopedic Surgery & Sports Medicine".

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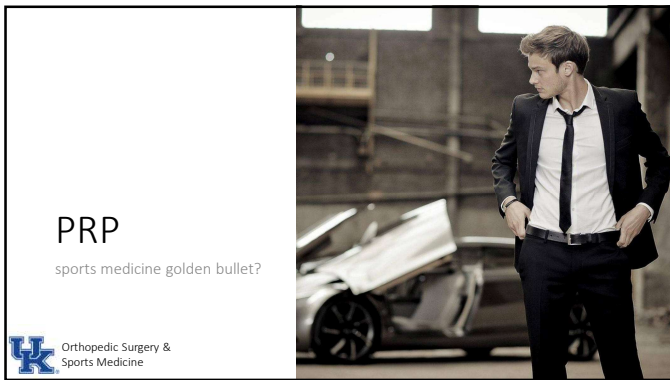


An advertisement for "orthobiologics" featuring a red sports car on a winding road at sunset. The word "orthobiologics" is written in a lowercase, sans-serif font across the middle of the image.

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platelet rich plasma

platelet rich plasma injection

Web Images Videos Maps News Explore

523,000 RESULTS Any time

Platelet Rich Plasma Injection (PRP): - AAOS - OrthoInfo
 orthoinfo.aaos.org/topic.cfm?topic=A00648
 During the past several years, much has been written about a preparation called platelet-rich plasma (PRP) and its potential effectiveness in the treatment of injuries.

| Year | Clinical studies | In Vivo studies | In Vitro studies |
|------|------------------|-----------------|------------------|
| 2000 | 0 | 0 | 0 |
| 2001 | 0 | 0 | 0 |
| 2002 | 0 | 0 | 0 |
| 2003 | 0 | 0 | 0 |
| 2004 | 0 | 0 | 0 |
| 2005 | 0 | 0 | 0 |
| 2006 | 0 | 0 | 0 |
| 2007 | 0 | 0 | 0 |
| 2008 | 0 | 0 | 0 |
| 2009 | 0 | 0 | 0 |
| 2010 | 0 | 0 | 0 |
| 2011 | 0 | 0 | 0 |
| 2012 | 0 | 0 | 0 |

Filardo+ KSSTA 2015


Orthopedic Surgery & Sports Medicine

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platelet rich plasma



Obtained from patient's blood
 Processed with spin speed to produce sample
 May be leukocyte-rich or leukocyte poor



Orthopedic Surgery &
Sports Medicine

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multiple systems available

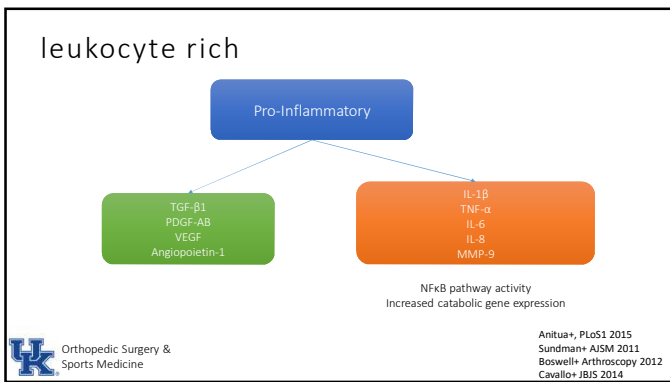


Orthopedic Surgery &
Sports Medicine

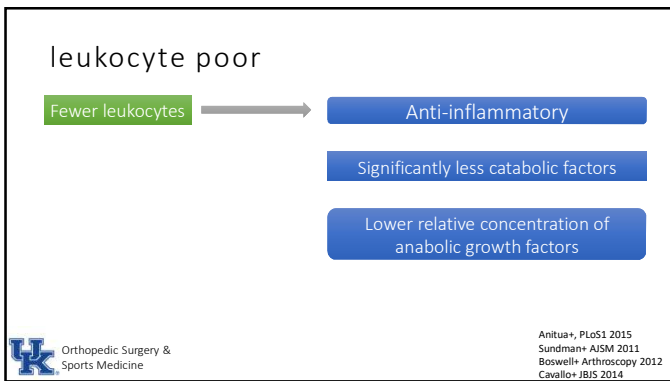
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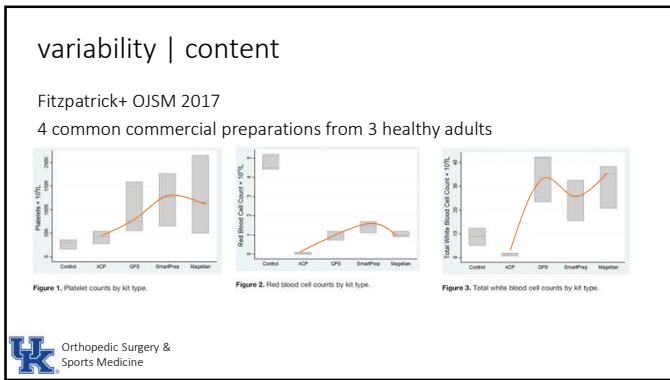
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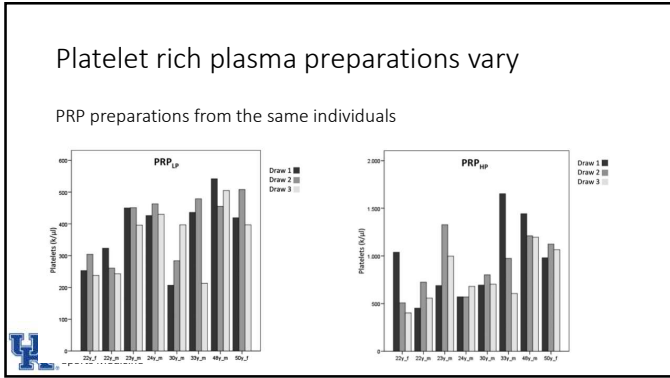
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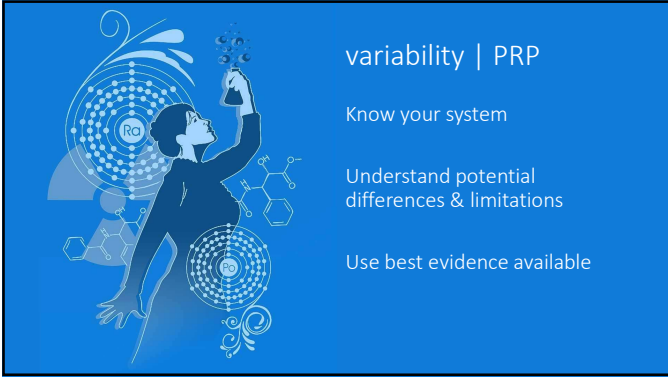


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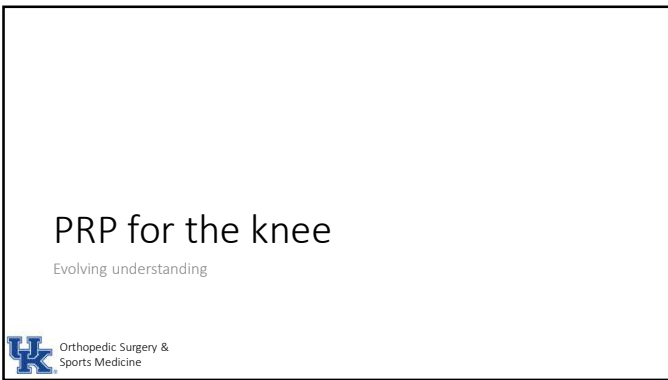
variability | PRP

Know your system

Understand potential differences & limitations


Use best evidence available

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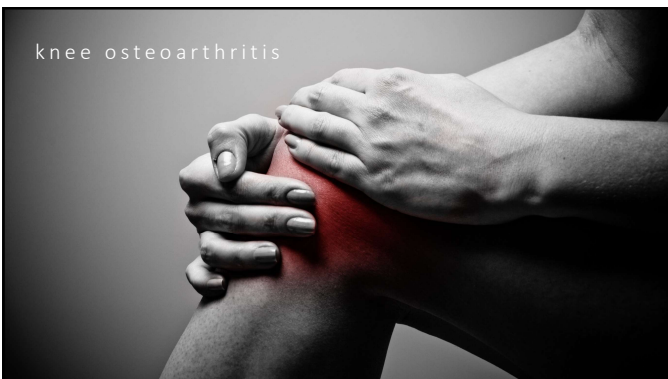


PRP for the knee

Evolving understanding


 Orthopedic Surgery & Sports Medicine

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knee osteoarthritis

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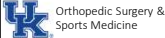


144 patients
Randomized to leukocyte poor or rich
3 injections for knee OA
IKDC primary outcome, VAS, Tegner

Filardo+ 2012

All patients improved at 3, 6 and 12 months
Less swelling with leukocyte poor PRP


Younger patients and less arthritis do best



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

A Randomized Controlled Trial

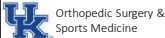


2016

Giuseppe Filardo,* MD, PhD, Berardo Di Matteo,*¹ MD, Alessandro Di Martino,* MD, Maria Leticia Merli,* MD, Annarita Cennacchi,* MD, PierMaria Fornasari,* MD, Maurizio Marcacci,* MD, Prof., and Elizaveta Kon,* MD
Investigation performed at Rizzoli Orthopaedic Institute, Bologna, Italy


192 patients received HA or leukocyte rich PRP

Both improved through 12 months
No difference between HA, LR-PRP



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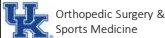
Intra-articular leukocyte poor PRP injection for knee OA




Smith 2016

12 months WOMAC improvement ↑

PRP 78% improvement
Saline 7% improvement

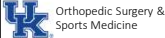



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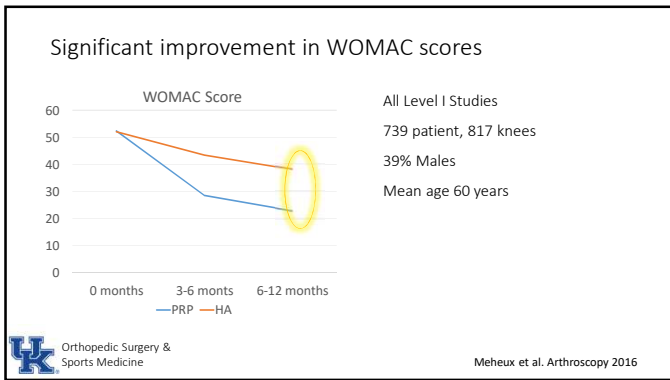


Meheux+ 2016

Systematic Review
All Level I Studies
739 patient, 817 knees
39% Males
Mean age 60 years




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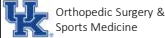
2019

PRP versus HA Meta-analysis of randomized controlled trials
1,314 patients evaluated



Both improved:
VAS-Pain
WOMAC pain
WOMAC function

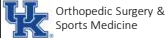
PRP slightly better



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where are we now?

| | |
|----------------------------|----------------------------|
| hyaluronic acid | PRP |
| covered by most insurances | not covered |
| easy to administer | more complex to administer |
| it works | it works |




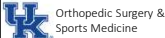
31

options

cortisone

high molecular weight, 3 injection hyaluronic acid

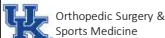
PRP – 1 or 3 based on cost

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Shoulder Applications

Treatment for Inflammatory Disease and Rotator Cuff Tears



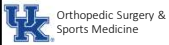
33

PRP | shoulder



Shams+ 2016

RCT – 40 Patients with symptomatic partial cuff tears
PRP versus cortisone
ASES, Constant, SST, VAS better with PRP @3 months
No group difference at 6 months but both improved



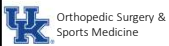
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PRP | rotator cuff tears



Cait+ 2019

Blinded RCT – 200 Patients with symptomatic partial cuff tears <1 cm
4 group: saline, LP-PRP, hyaluronic acid, LP-PRP + HA
ASES, Constant, VAS-Pain significantly improved with PRP
and PRP + HA at 3, 6, 12 months
Improved healing on MRI for LP-PRP, LP-PRP+HA



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PRP | rotator cuff tears



Jo+ 2015

Medium to large tears
RCT: 37 PRP + repair, 37 repair only
PRP gel at repair site

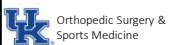
No difference in PROs
Decreased re-tear rate
Increased healing area



Wang+ 2015


DR repair of supraspinatus tears
RCT: 30 PRP+2 + repair, 30 repair only
PRP at repair site

No difference in PROs
for pain or function



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PRP | rotator cuff tears



Barber+ 2016

<3 cm tears
RCT: 20 SR and 20 SB repair
PRP fibrin at repair site

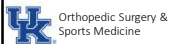
No difference in PROs
No change in re-tear rate



Flury+ 2016

DR repair of supraspinatus tears
RCT: 60 PRP + repair, 60 ropivacaine + repair
PRP at repair site

No difference in PROs
No change in re-tear rate
2 year follow-up, triple
blinded



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PRP | rotator cuff tears



Cait+ 2015



Holtby+ 2016







Meta-analyses
No difference
Pain or Function

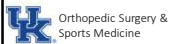
Decreased re-tear rate in small to medium size tears



38

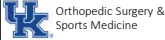
PRP | rotator cuff tears

| | partial | small-medium | large |
|----------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Efficacy |  |  |  |
| Value |  |  |  |




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PRP for Tendinopathy




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PRP | lateral epicondylitis

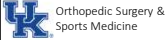

Mishra+ 2014

230 pts with lateral epicondylitis >3 months
LR-PRP with significantly better pain and residual tenderness
MCID achieved compared to control of local anesthetic


Peerbooms+ 2010
Gosens+2011


Double blind RCTs with 1- and 2-year follow-up
LR-PRP with longer continuous relief compared to cortisone

Good evidence





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PRP | patellar tendinopathy

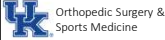

Dragoo+ 2014

23 pts with refractory patellar tendinopathy
Dry needling with or without LR-PRP
Earlier improvement in pain and symptoms but equivalent at >26 weeks


Vetrano+ 2013

Chronic refractory patellar tendinopathy
LR-PRP versus ECSWT
LR-PRP significant improvement in symptoms at 6 and 12 month follow-up
No difference detected prior to 6 months.

Decent evidence



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PRP | Achilles tendinopathy



Dragoo+ 2011

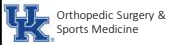
54 pts with refractory Achilles tendinopathy
Double blind RCT: LR-PRP versus Saline
No difference between groups although both improved
Improved tendon structure in both groups



Boesen+ 2017

Chronic Achilles tendinopathy
RCT: 4 injections of LR-PRP versus steroid or saline
PRP and steroid groups both improved
PRP results inferior to high volume steroid (caution!)

Not recommended



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PRP | plantar fasciitis

Medicine

Yang+ 2017

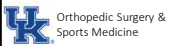
Meta-analysis of RCTs for PRP for plantar fasciitis
PRP superior to cortisone injections
Reduces risk associated with cortisone



Singh+ 2017

Meta-analysis of PRP for plantar fasciitis
PRP superior to cortisone at early time points
Similar outcomes at 6 and 12 months

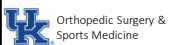
Decent evidence



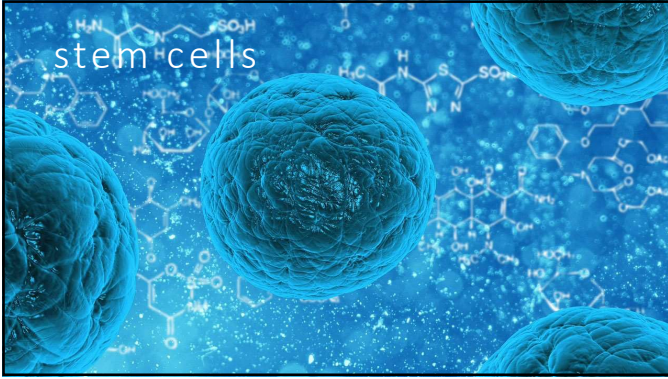
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PRP | best available evidence

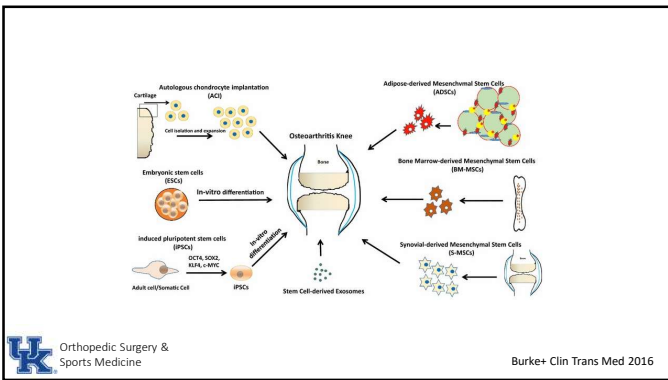
| | |
|-----------------------|----------------------|
| Inside the joint | leukocyte poor PRP |
| Rotator cuff | unclear |
| Lateral epicondylitis | leukocyte rich PRP |
| Patellar tendinopathy | leukocyte rich PRP |
| Achilles tendinopathy | Not recommended |
| Plantar fasciitis | PRP, ?leukocyte rich |



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bone marrow aspirate concentrate (BMAC)

Obtained from iliac crest, proximal tibia, humerus greater tuberosity

Safe for harvest and injection

May be combined with collagen scaffold/membrane

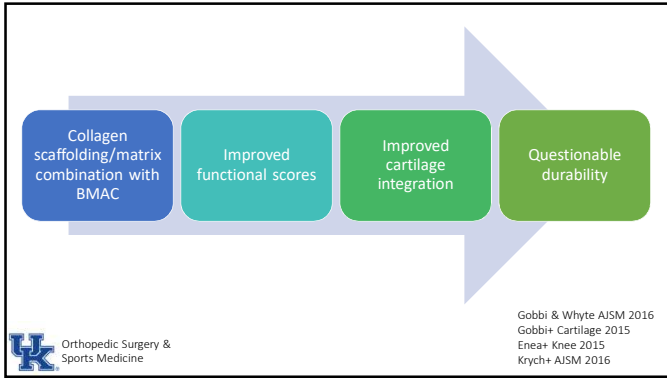
May be injected alone

 A photograph showing a medical professional performing a bone marrow aspiration procedure. A hand is holding a syringe and needle, drawing fluid from a patient's hip area.

Orthopedic Surgery & Sports Medicine

Chahla+ 2016, Gobbi+ 2015, Gobbi & Whyte 2016, Krych+ 2016, Centento+ 2014

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Cartilage
Gobbi+ 2015

MACI vs BMAC with collagen scaffold
2 year minimum follow-up
PROs and limited 2nd look arthroscopies

Both improved in PROs
BMAC slightly more durable at final follow-up

Low return to activity
31% in MACI
34% in BMAC
Older patients – mean age ~45 ± 7.5 years

MACI Trochlea
A
B
BMAC Patella

Orthopedic Surgery & Sports Medicine

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Sports Medicine
Gobbi & Whyte 2016

Microfracture versus BMAC with HA scaffold
5 year follow-up

A
B

BMAC with HA scaffold superior in PROs at 5 years
Results improved even in age >45 years, size >4 cm², multiple lesions

Orthopedic Surgery & Sports Medicine

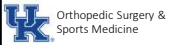
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BMAC injection for knee osteoarthritis



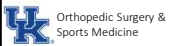
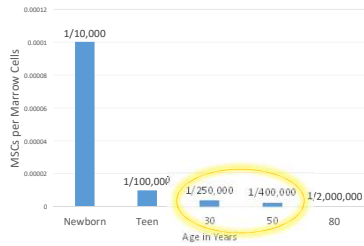
Single blind RCT 25 patients
One knee saline, one knee iliac crest BMAC
OARSI and VAS at 1 week, 3 & 6 months

Both knees significantly improved in pain from baseline for 6 months



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Indications not clear
Promising results in small trials
Age related decline in MSC activity



Caplan JCP 2007

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additional options for stem cells

- Adipose-derived MSCs— recent FDA approval
- Adipose derived and expanded MSCs— not FDA approved
- Amniotic derived – no current products with viable cells on the market

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Limited data available

Currently Level I RCT in place for osteoarthritis

Notable side effects – bruising, seroma, pain



LIPOGEMS® Granted New FDA 510k Clearance

As part of being a responsible company, we are excited to announce that Lipogems worked directly with the FDA to provide a new clearance that will be even more easily understood by the medical community.

Lipogems' new FDA clearance letter expands the indications for use to include the transfer of subglottic adipose tissue in arthroscopic surgery.

LIPOGEMS To learn more, contact your local representative or email us at info@lipogems.com

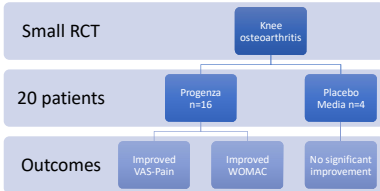



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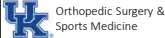
allogenic adipose MSCs | Progenza

Not approved in US

Phase Clinical 1 trials in Australia, Japan



Very limited data and not currently available



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amniotic derived cells & tissue


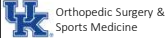
No viable cells

Cryopreservation techniques eliminate viability

Growth factors remain & some products have structures

Manipulation is under dispute

Many are still regulated under HCT/Ps with FDA

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proceed with caution when using allograft/biologics off label

ensure full understanding of the products

cell viability



Orthopedic Surgery & Sports Medicine

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Ensure transparency

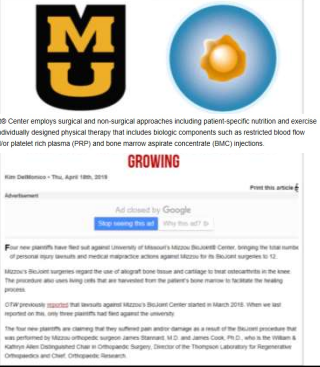
Manage expectations

Original suit filed in April 2018

Arthritic symptoms continued after two arthroscopies

Patient underwent TKA

11 subsequent suits all represented by one law firm



Orthopedic Surgery & Sports Medicine

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Summary

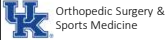
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|------|------------------------------------------------------------------------------------------------|
| PRP | Several applications demonstrating efficacy Relatively inexpensive Not regulated by FDA |
| BMAC | Some applications demonstrating efficacy More expensive and painful Not regulated by FDA |

Orthopedic Surgery & Sports Medicine

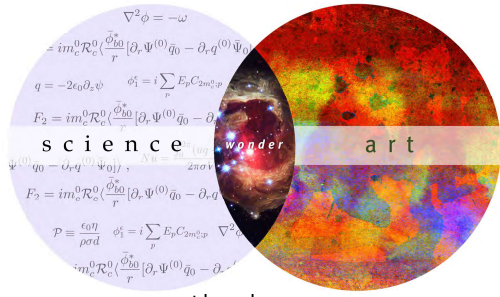
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Summary

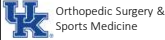
| | |
|-------------------|-----------------------------------------------------------------------------|
| MSCs | Limited data available Expensive Regulated by FDA to varying degrees |
| Amniotic Products | Exceedingly limited data Expensive Regulated by FDA, limited approval |



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thank you



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