

Bone Marrow Aspirate Concentrate Augmentation for ACL Reconstruction: A Double-Blinded Randomized Control Trial

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The Evolution of ACL Surgery:

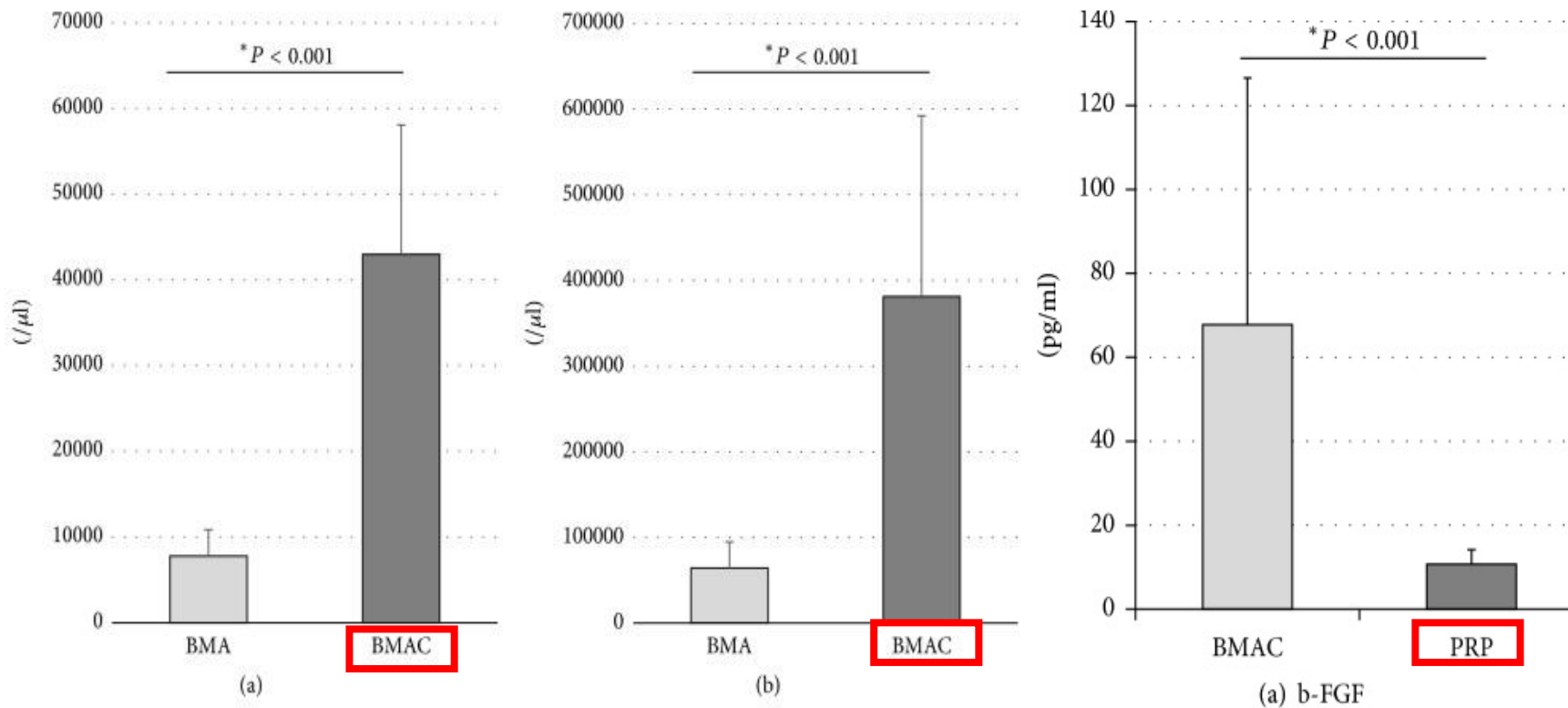
- Primary ACL Repairs
- Lateral Extraarticular Tenodesis, Reconstruction
- Intraarticular ACLR: Transtibial => Medial Portal
- Double Bundle ACLR
- Intraarticular Primary ACL Repair
 - Internal Brace?
 - Collagen Scaffolds?
- LET Augmentation with Primary, Revision intraarticular ACLR
- **ACL Reconstruction with BMAC!**

BMAC: What's in it?

Bone Marrow Res. 2018 Feb 25;2018:1549826. doi: 10.1155/2018/1549826. eCollection 2018.

Comparative Analysis of Cellular and Growth Factor Composition in Bone Marrow Aspirate Concentrate and Platelet-Rich Plasma.

Sugaya H¹, Yoshioka T¹, Kato T², Taniguchi Y³, Kumagai H³, Hyodo K³, Ohneda O², Yamazaki M³, Mishima H³.



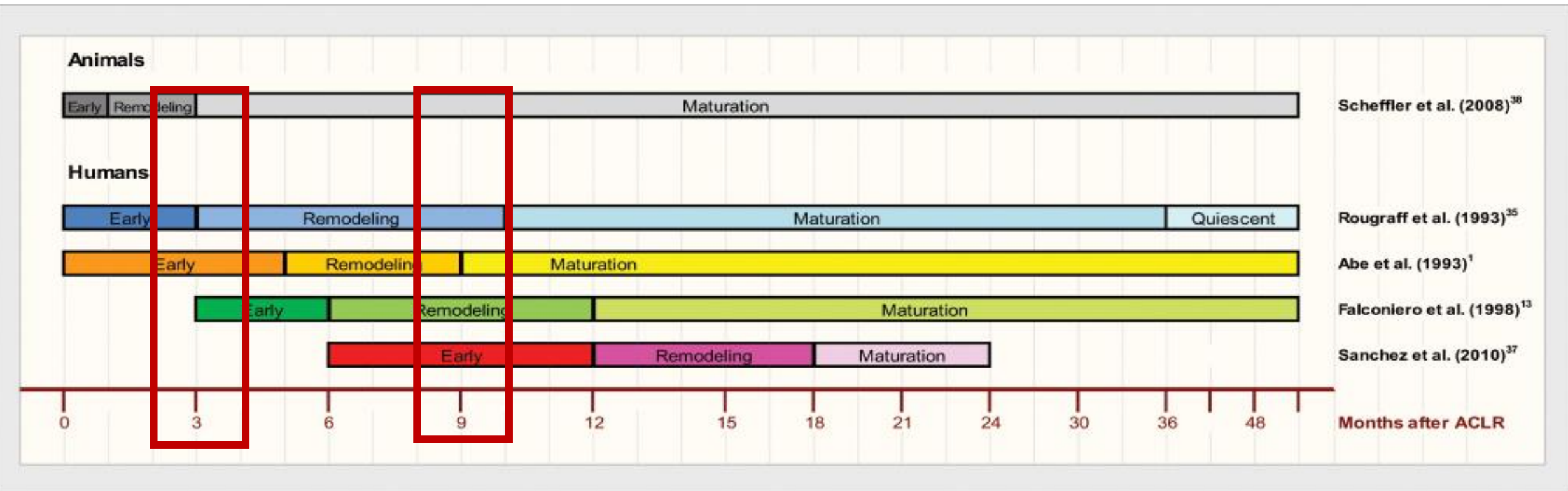
- 5x nucleated cells (0 in PRP)
- High WBCs
- 1.9% CD34+ Pluripotent Cells
- High **b-FGF**

Primary ACLR Healing

Am J Sports Med. 2011 Nov;39(11):2476-83. doi: 10.1177/0363546511402662. Epub 2011 Apr 22.

The "ligamentization" process in anterior cruciate ligament reconstruction: what happens to the human graft? A systematic review of the literature.

Claes S¹, Verdonk P, Forsyth R, Bellemans J.



Biological ACL Graft Healing:

Avascular Necrosis

- Hypocellularity, centrally
- Necrosis => Cytokine release => GF's
 - Cell migration, Proliferation, Revascularization

Remodeling:

- **Cell Mediated Restructuring** of the ECM
- Adaptive response to Mechanical Loading of graft

Ligamentization:

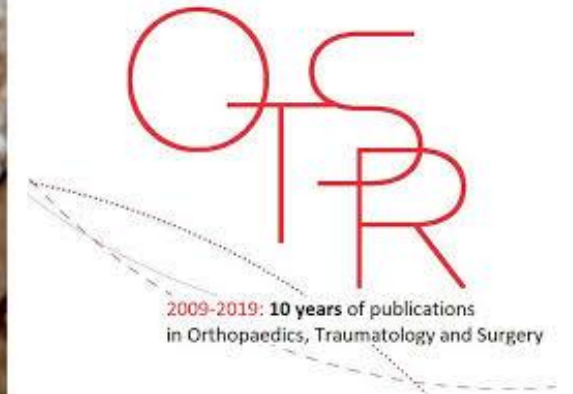
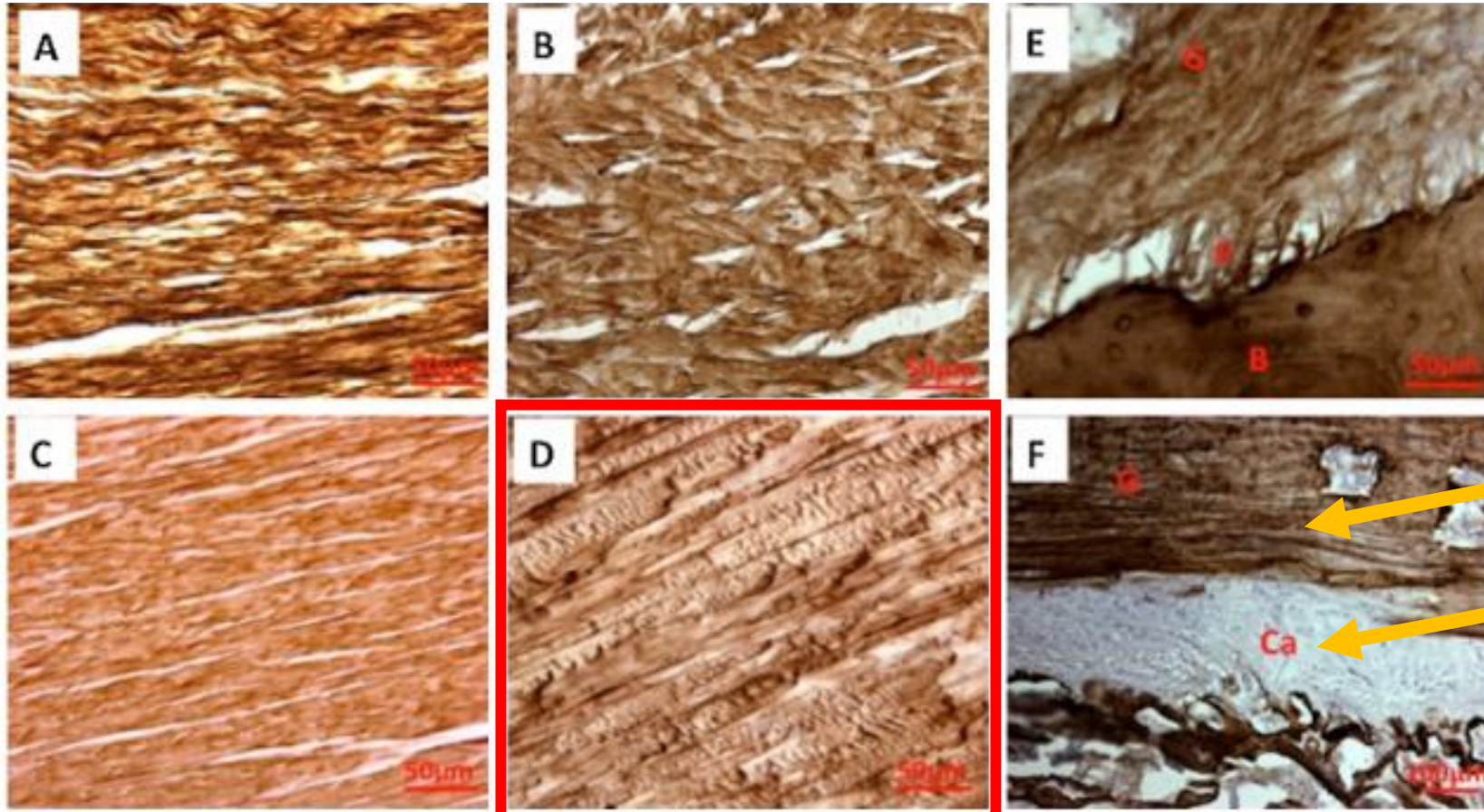
- Acquisition of histologic, biomechanical properties of native ACL

Primary ACLR Ligamentization: ECM

Orthop Traumatol Surg Res. 2016 Apr;102(2):189-95. doi: 10.1016/j.otsr.2015.12.007. Epub 2016 Jan 13.

Allograft integration in a rabbit transgenic model for anterior cruciate ligament reconstruction.

Bachy M¹, Sherifi I², Zedegan F³, Petite H⁴, Vialle R⁵, Hannouche D³.



Grafted tendon

New cartilage
deposition

OUR STUDY: RCT ACLR BTB Allograft + BMAC

The effects of BMAC on ACL reconstructions with Allograft tissue

- The **First** randomized controlled clinical trial

Autologous Bone Marrow Aspirate Concentrate in Patients Undergoing Anterior Cruciate Ligament Reconstruction

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Authorized Representative: Nikhil Verma MD

Co-Investigators: Nikhil Verma MD, Brian J. Cole MD MBA, Adam Yanke, MD PhD, Jorge Chahla, MD PhD, Bernard R Bach Jr MD

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Study Aim 1: ACLR + BTB allograft

To evaluate the effects of BMAC on graft **Ligamentization**:

- **T2* MR imaging** at 3 and 9 months.

T2* MR sequences:

- **Higher signals at 3 months:**
 - => Superior graft Remodeling
- **Lower signals at 9 months:**
 - => Superior graft Integration and Homeostasis



Study Aim 2: ACLR + BTB allograft

To evaluate the effect of BMAC on patient-reported outcome measures (**PROMs**) and **failure rates**

- 3, 6, 9, 12 & 24 months post-operatively

BMAC + BTB Allograft:

- Failure rates: => Similar or lower with BMAC
- PROMs (IKDC, KOOS Jr, and Tegner): No sig. diff. Study vs. Control.

Results: Demographics

- 80 patients met inclusion criteria
 - 1 withdrawal
 - 1 excluded: pregnancy
 - 1 re-rupture (control)
 - 4 Lost to follow up
- 80 → 73 patients data analyzed
 - **No significant differences pre-operatively**
 - 900 cells/ml

Table 1: Patient Demographics, Concomitant Procedures and Pre-operative PROs, Physical exam

Characteristic	Control (n = 37)	BMAC (n = 36)	P Value
Mean Age (SD), yr	36.6 (8.8)	36.3 (9.5)	0.84
Sex, n (%)			
Male	18 (42.9)	15 (38.5)	0.69
Female	24 (57.1)	24 (61.5)	
Laterality, n (%)			
Left	18 (42.9)	11 (28.2)	0.17
Right	24 (57.1)	28 (71.8)	
Mean BMI (SD)	27.6 (4.6)	27.9 (7.1)	0.83
Pre-operative PROs (SD)			
KOOS	64.3 (16.5)	66.8 (13.6)	0.59
Tegner	2.7 (1.6)	2.9 (1.4)	0.64
IKDC	48.6 (16.4)	51.4 (14.7)	0.47
Concomitant Procedures (%)			
Meniscal Repair	9 (24.3)	6 (16.7)	0.52
Partial meniscectomy	11 (29.7)	13 (36.1)	0.74
Patellar/Femoral Chondroplasty	4 (10.8)	1 (2.7)	0.36
Pre-operative Surgical Knee Flexion (SD), °	124.7 (12.6)	122.2 (13.8)	0.43
Pre-operative KT difference* (SD)	2.04 (1.99)	2.01 (2.01)	0.11

BMAC, Bone Marrow Aspirate Concentrate; BMI, Body Mass Index; SD, standard deviation; PROs, Patient reported outcomes; KOOS, Knee Injury and Osteoarthritis Score; IKDC, International Knee Documentation Committee

*KT Difference: Surgical knee KT score – Nonsurgical knee KT score

Results: T2 MRI

Table 2: MRI Signal Intensities at 3 and 9 Months Post-operatively

Timepoint	Signal Intensity	Control	BMAC ^a	P-values
3 Months Postop	SIR Superior Third vs Patellar Tendon ^b	3.7 ± 1.9	4.8 ± 3.9	0.17
	SIR Middle Third vs Patellar Tendon ^b	2.6 ± 2.1	3.4 ± 3.0	0.20
	SIR Inferior Third vs Patellar Tendon ^b	2.1 ± 1.5	3.2 ± 2.2	0.023
9 Months Postop	SIR Superior Third vs Patellar Tendon ^b	3.9 ± 2.4	4.6 ± 3.0	0.33
	SIR Middle Third vs Patellar Tendon ^b	3.3 ± 2.3	4.5 ± 3.3	0.12
	SIR Inferior Third vs Patellar Tendon ^b	3.5 ± 2.5	4.3 ± 2.9	0.26

^aBone Marrow Aspirate Concentrate (BMAC) containing Mesenchymal Stem Cells (MSCs); ^bSignal Intensity Ratio (SIR) of allograft in comparison to ipsilateral patellar tendon

Results: Physical Exam

- **No significant difference at any Timepoint**

Table 3: Physical Exam Findings

	Variables	Control	BMAC	P value
Pre-operative	Surgical Knee Flexion	124.7 (12.6)	122.2 (13.9)	0.43
	Knee Flexion Difference	5.2 (5.4)	5.6 (5.4)	0.48
	KT difference	2.0 (2.0)	2.0 (2.0)	0.11
6 weeks post-op	Surgical Knee Flexion	113.3 (15.2)	115.9 (13.5)	0.49
	Knee Flexion Difference	20.5 (14.2)	14.3 (14.0)	0.10
	KT difference	0.3 (1.2)	0.4 (1.0)	0.90
3 months post-op	Surgical Knee Flexion	125.4 (24.5)	124.1 (9.8)	0.79
	Knee Flexion Difference	6.1 (9.0)	5.7 (7.0)	0.82
	KT difference	0.2 (0.9)	0.3 (0.9)	0.84
6 months post-op	Surgical Knee Flexion	130.74 (9.0)	130.2 (8.1)	0.82
	Knee Flexion Difference	4.0 (5.7)	2.1 (7.4)	0.32
	KT difference	0.2 (0.9)	0.4 (0.9)	0.54
9 months post-op	Surgical Knee Flexion	129.4 (8.3)	133.2 (9.7)	0.22
	Knee Flexion Difference	2.1 (5.9)	0.5 (3.5)	0.29
	KT difference	0.2 (0.7)	0.3 (0.7)	0.41
1 year post-op	Surgical Knee Flexion	133.8 (9.5)	131.0 (11.1)	0.36
	Knee Flexion Difference	1.1 (4.0)	2.1 (3.2)	0.37
	KT difference	0.4 (0.9)	0.2 (0.7)	0.27

Knee Flexion Difference: Nonsurgical Knee Flexion – Surgical Knee Flexion; KT Difference: Surgical knee KT – Nonsurgical knee KT

Results: Patient Reported Outcomes

Table 4: Patient reported outcomes (PROs)

	Variables	Control	BMAC	P value
Pre-operative PROs	KOOS jr.	64.3 (16.5)	66.8 (13.6)	0.59
	Tegner	2.7 (1.6)	2.9 (1.4)	0.64
	IDKC	48.6 (16.4)	51.4 (14.7)	0.47
3 month follow up PROs	KOOS jr.	N/A	N/A	N/A
	Tegner	2.9 (1.1)	3.04 (1.0)	0.72
	IDKC	54.8 (16.0)	55.5 (13.3)	0.85
6 month follow up PROs	KOOS jr.	82.8 (12.5)	78.7 (10.1)	0.29
	Tegner	4.8 (1.5)	4.3 (1.2)	0.29
	IDKC	72.9 (13.9)	70.9 (11.7)	0.60
9 month follow up PROs	KOOS jr.	N/A	N/A	N/A
	Tegner	5.1 (1.5)	5.4 (1.9)	0.53
	IDKC	74.6 (14.2)	81.6 (10.5)	0.048
1 year follow up PROs	KOOS jr.	89.3 (9.3)	84.1 (10.7)	0.15
	Tegner	5.5 (1.3)	6.2 (1.9)	0.10
	IDKC	80.1 (13.0)	83.3 (11.5)	0.31

PROs, Patient reported outcomes; KOOS, Knee Injury and Osteoarthritis Score; IKDC, International Knee Documentation Committee

- **IKDC → significant difference @ 9 months**
- **Tegner → trend towards significance @ 1 yr**
- **KOOS Jr → no significant difference**

Conclusion:

In the first RCT evaluating BMAC Augmentation of Allograft ACL Reconstruction:

→ BMAC → Higher SIR on MRI at 3 months → increased revascularization

- (3.2 vs 2.1, $p=0.02$)

Other Superior outcomes at 9 months ($p<0.05$):

- IKDC

Thank You!

