



# **Title: Comparison of the Tissue Molecular Profile Of ACL Repair, ACL Reconstruction, and Native ACL**

**Authors: Edoardo Monaco<sup>1</sup>, Danilo Ranieri<sup>2</sup>, Alessandro Annibaldi<sup>1</sup>, Alessandro Carrozzo<sup>1</sup>, Fabio Marzilli<sup>1</sup>, Vincenzo Visco<sup>2</sup>, Andrea Ferretti<sup>1</sup>**

<sup>1</sup> Orthopedic Unit and "Kirk Kilgour" Sports Injury Centre, S. Andrea Hospital, University of Rome "Sapienza," Rome, Italy

<sup>2</sup> Department of Clinical and Molecular Medicine, Faculty of Medicine and Psychology, "Sapienza" University of Rome, Rome, Italy.







**ISAKOS**  
CONGRESS  
2023



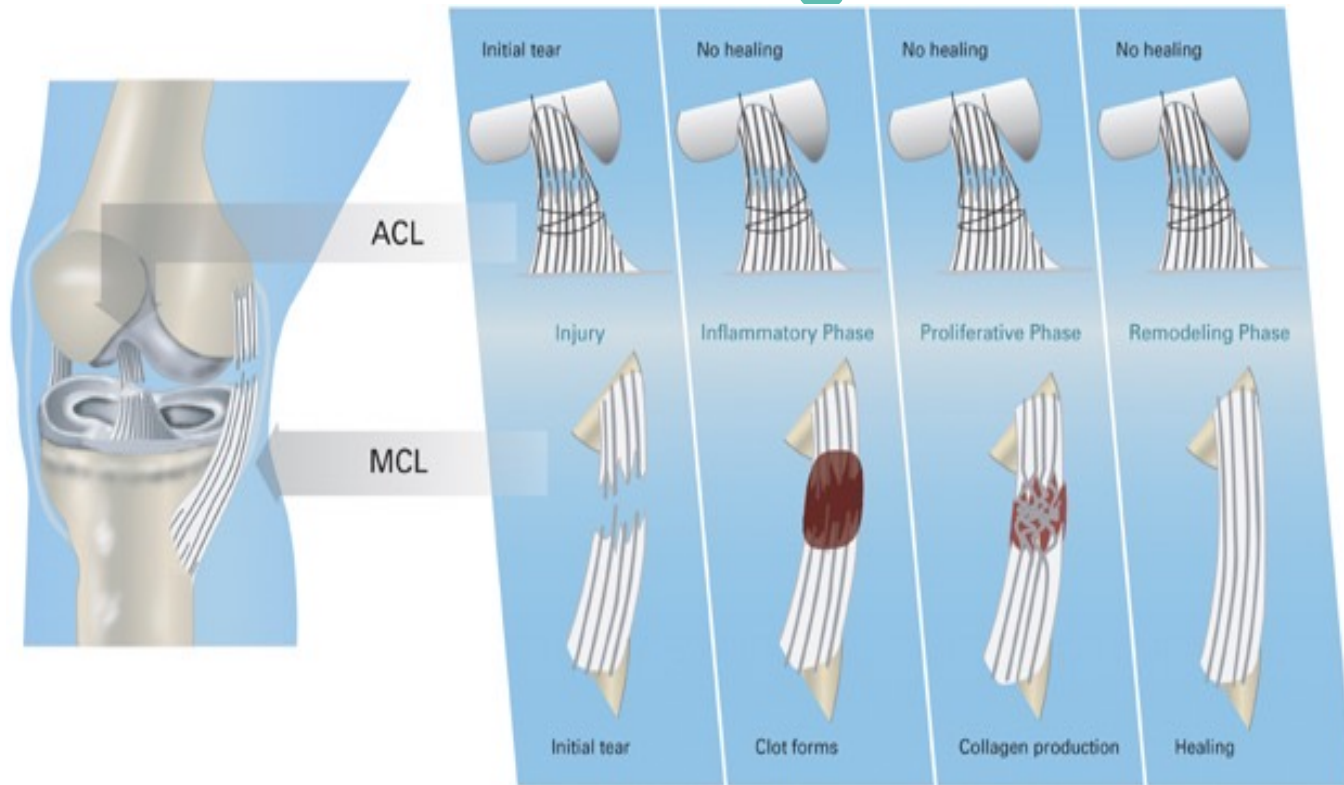
**Boston**  
Massachusetts  
June 18–June 21

# Disclosures: Edoardo Monaco and Andrea Ferretti are consultant for Arthrex





# Background and purpose



Medial Collateral Ligament and Anterior Cruciate Ligament (ACL) cells within injured ligaments have comparable rates of proliferation;<sup>1</sup>

Each ligament is able to revascularize after rupture;

Comparable collagen production within the ligaments was observed up to one year after injury

Murray MM, Fleming BC. Biology of anterior cruciate ligament injury and repair: Kappa delta ann doner vaughn award paper 2013. J Orthop Res. 2013 Oct;31(10):1501-6

**The aim of this study was to evaluate and compare m-RNA collagen expression and cell activity in ACL repair, ACL reconstruction and native ACL**

**The hypothesis of the study is that the collagen expression and cellular senescence pattern of the repaired ACL are similar to the native ACL compared to the reconstructed ACL**

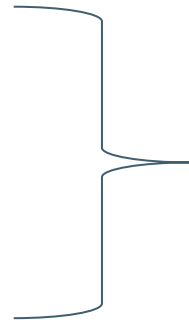
# Methods

## LOCATION:

Type I: >75%

Type II: 50-75%

Type III: <50%



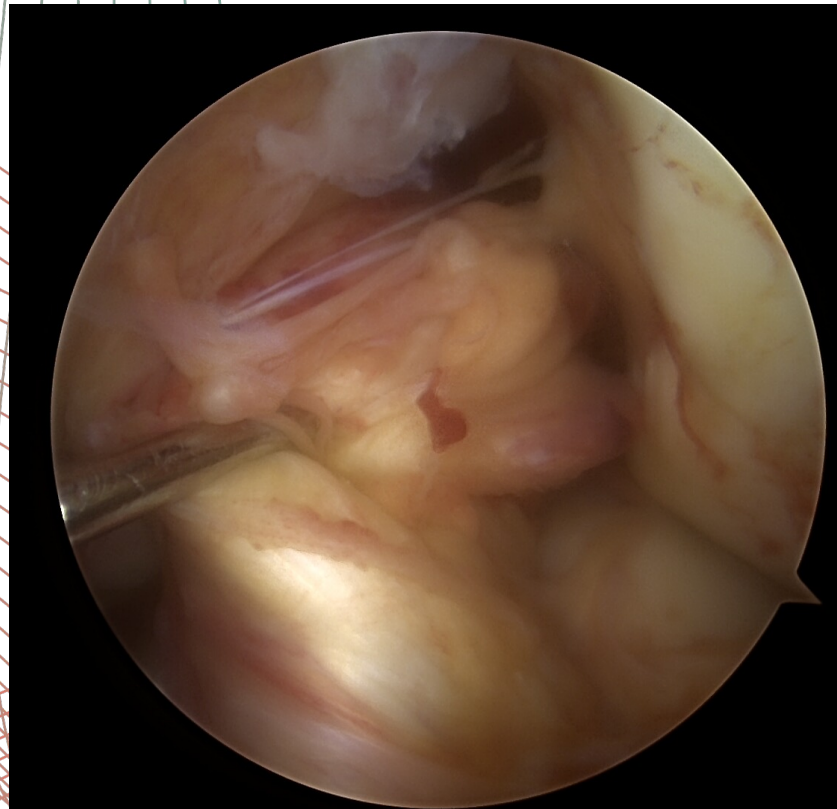
Our  
indication for  
ACL repair

## TISSUE QUALITY:

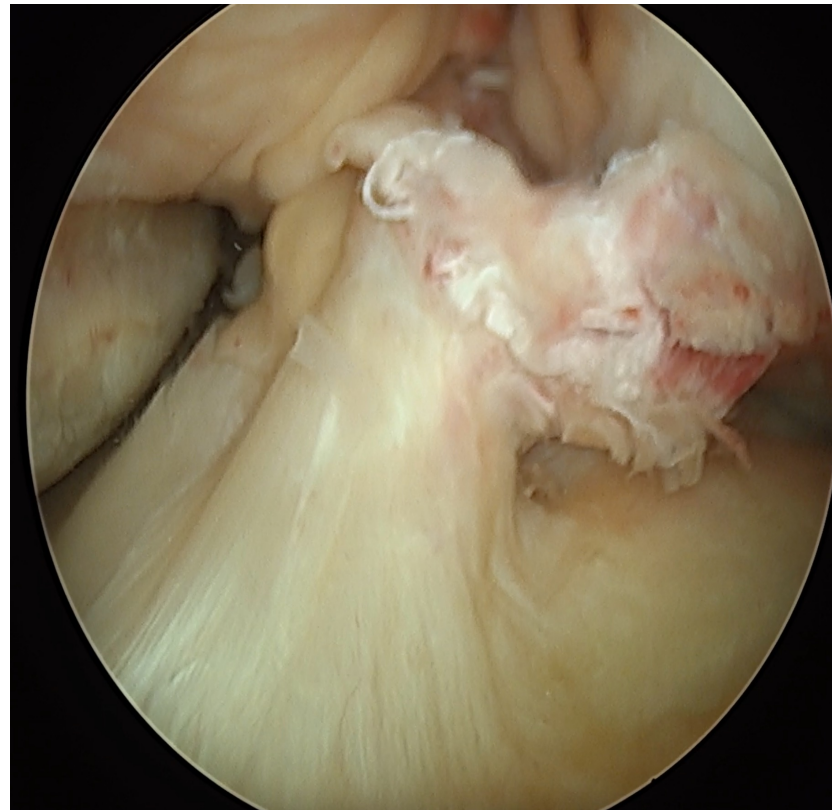
A: Excellent tissue quality

B: Good tissue quality

C: Poor tissue quality



Type I



Type II

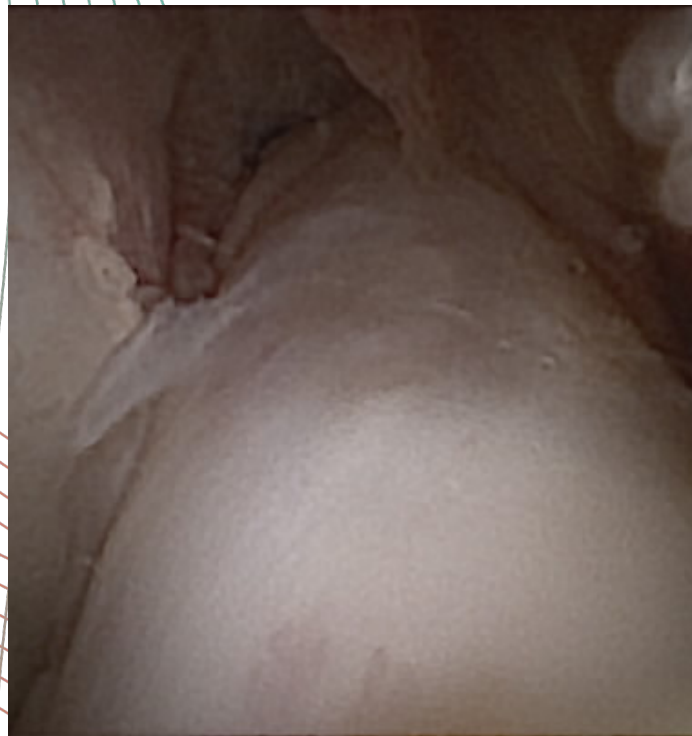


Type III



# Methods: three groups

Group A: 15 Acl repair



In-office needle arthroscopic view of an ACL repaired<sup>2</sup>

Group B: 10 Acl Reconstruction



Arthroscopic image of a graft with semitendinosus and gracilis

Group C: 15 fresh frozen knees



Knee arthroscopy in a fresh frozen knee

## Methods: tissue sampling

- A nanobiopsy with in-office needle arthroscopy was performed in patients who underwent ACL repair at a mean of 10 months of follow-up (Fig 3.)
- Patients who received an ACL Reconstruction and cadaveric specimens went for sampling of the ACL tissue during the performance of a standard arthroscopy.



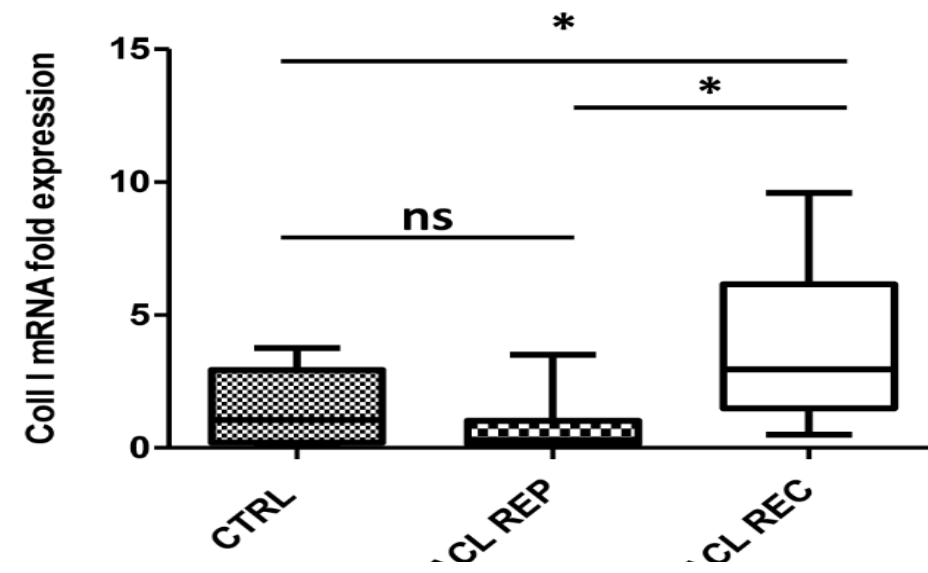
The gene expressions of the following proteins were taken into consideration:

1. Coll I, Coll III, and the ratio (Coll I/Coll III);<sup>3</sup>
2.  $\alpha$ -SMA isoform of actin identified and expressed in fibroblasts and myofibroblasts often present in scar tissues and with a central role in wound closure;<sup>4</sup>
3. Cyclin Dependent Kinase Inhibitor 2A/p16 (CDKN2A/p16), cellular aging marker responsible for the inactivation of replication and formation of new cells;<sup>5</sup>

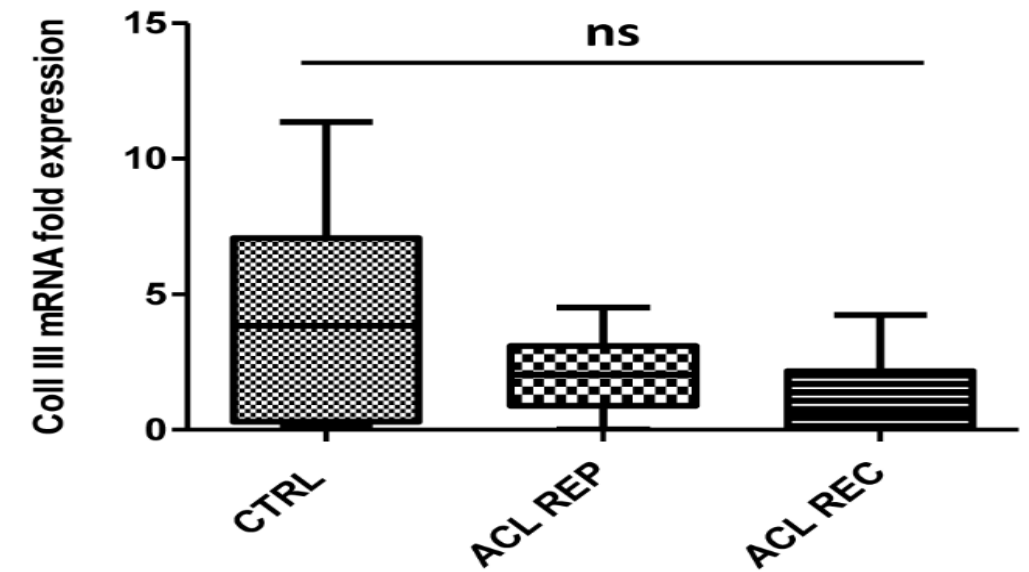


# Results

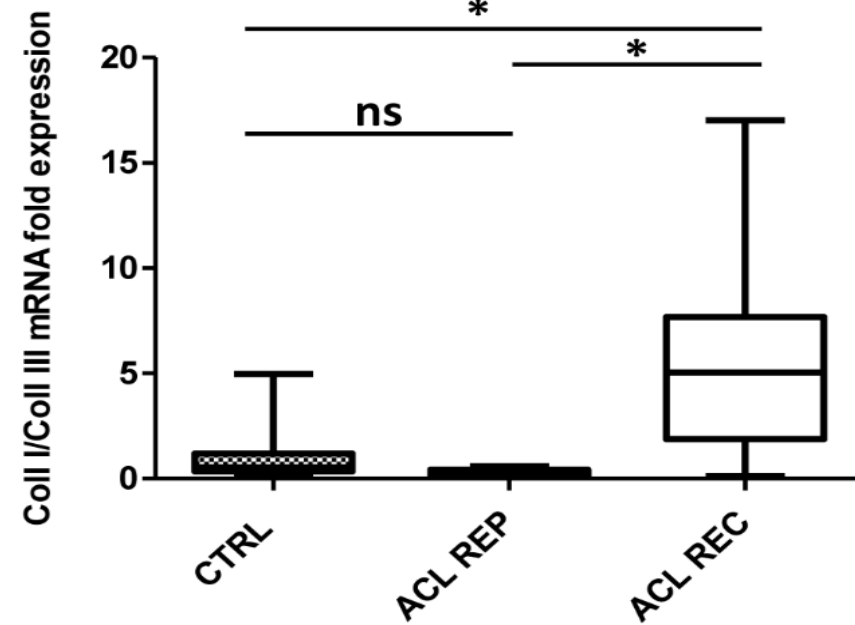
A



B



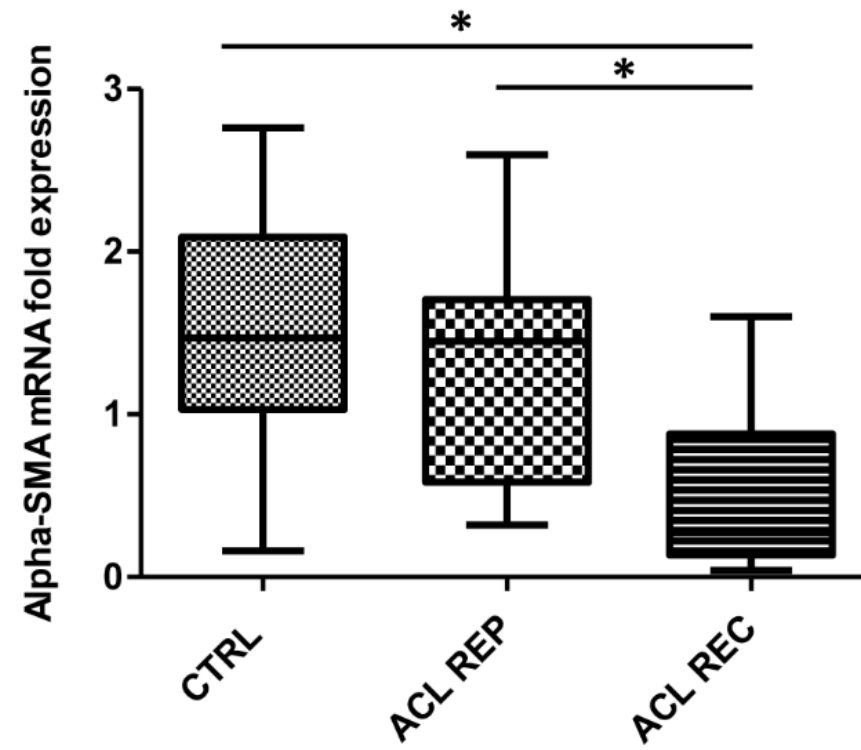
C



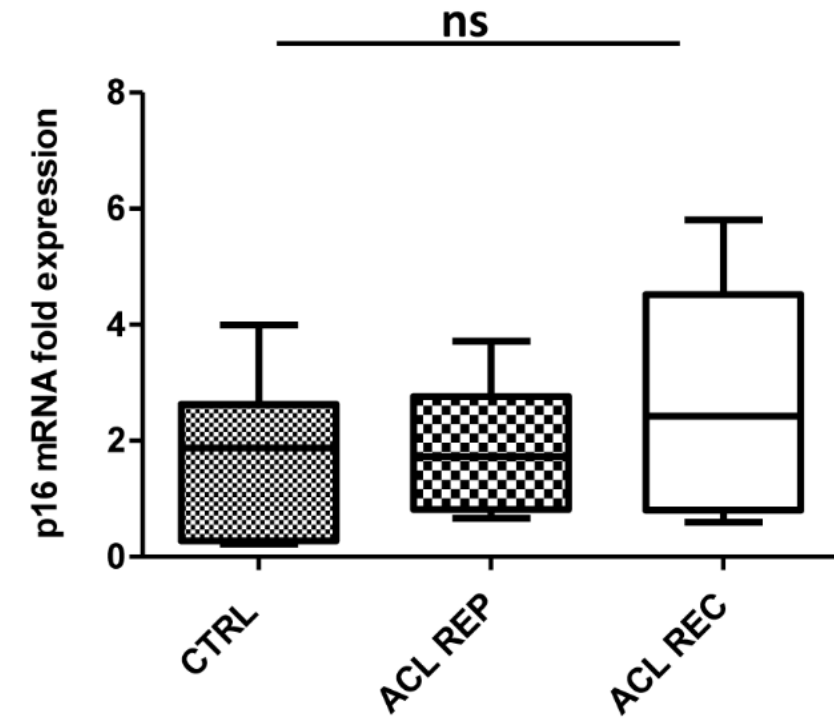
mRNA fold expression in the three groups: A Coll I expression; B Coll III expression; C Coll I / Coll III ratio;

# Results

D



E



mRNA fold expression in the three groups: D  $\alpha$ -SMA expression; E p16 expression.



**ISAKOS**  
CONGRESS  
2023



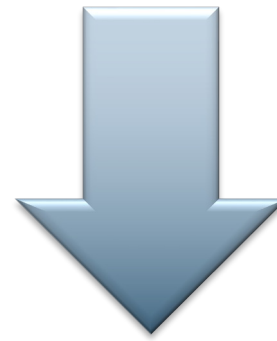
**Boston**  
Massachusetts  
June 18–June 21



## Conclusion

The main finding of this study is that, at a mean of 10 months after surgery, the repaired ACL have an m-RNA expression pattern that is closer to the native ACL than that resulted from a reconstructed ACL.

This similarity of expression profile was observed about collagen quality, degree of activation of cell differentiation process ( $\alpha$ -SMA) and degree of cell senescence (p16).



These results seem to support that the ACL heals as a normal ligament in terms of a collagen expression while an ACL reconstructed with hamstrings has different molecular expression



# References

- <sup>1</sup> Murray MM, Fleming BC. Biology of anterior cruciate ligament injury and repair: Kappa delta ann doner vaughn award paper 2013. J Orthop Res. 2013 Oct;31(10):1501-6
- <sup>2</sup> Annibaldi A, Monaco E, Daggett M, Carrozzo A, Mazza D, Previ L, Rossi G, Orlandi P, Ferretti A. In-office needle arthroscopic assessment after primary ACL repair: short-term results in 15 patients. J Exp Orthop. 2022 Sep 7;9(1):89. doi: 10.1186/s40634-022-00528-1
- <sup>3</sup> López De Padilla CM, Coenen MJ, Tovar A, De la Vega RE, Evans CH, Müller SA. Picrosirius Red Staining: Revisiting Its Application to the Qualitative and Quantitative Assessment of Collagen Type I and Type III in Tendon. J Histochem Cytochem. 2021 Oct;69(10):633-643
- <sup>4</sup> Weiler A, Unterhauser FN, Bail HJ, Hüning M, Haas NP.  $\alpha$ -Smooth muscle actin is expressed by fibroblastic cells of the ovine anterior cruciate ligament and its free tendon graft during remodeling. J Orthop Res. 2002;20(2):310-317
- <sup>5</sup> Ashraf S, Cha B-H, Kim J-S, et al. Regulation of senescence associated signaling mechanisms in chondrocytes for cartilage tissue regeneration. Osteoarthr Cartil. 2016;24(2):196-205

