

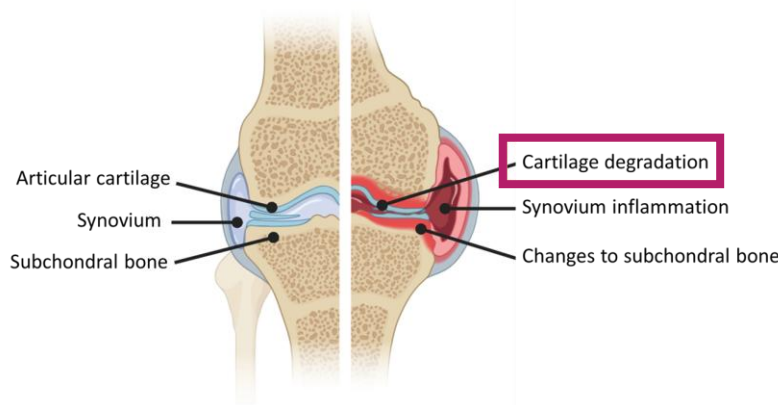
3D degradable hydrogels unlock enhanced contractility of osteoarthritic chondrocytes

Nele Vaes^{a 1}, Maxim Vovchenko^{a b 1}, Jorge Barrasa-Fano^a, Apeksha Shapeti^a, Rocío Castro-Viñuelas^{c d}, Laurens Kimps^a, Christ Glorieux^b, Ilse Jonkers^{c d e}, Hans Van Oosterwyck^{a f}

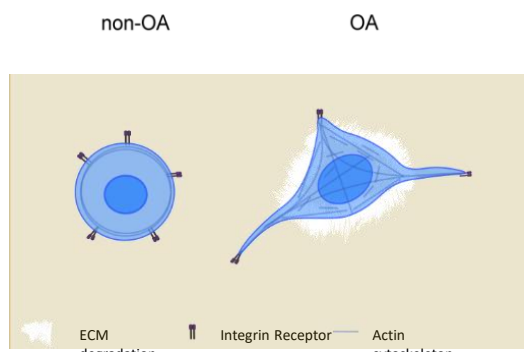
^a Biomechanics Section, Department of Mechanical Engineering, KU Leuven, ^b Laboratory for Soft Matter and Biophysics, KU Leuven, ^c Human Movement Biomechanics Research Group, KU Leuven, ^d Skeletal Biology and Engineering Research Centre, KU Leuven, ^e Institute for Physics-Based Modeling for In Silico Health, KU Leuven, ^f Prometheus Division of Skeletal Tissue Engineering, KU Leuven

Osteoarthritis

- 57 million Europeans
- Loadbearing** joints
- No cure**
- therapy for symptom relief
- Huge societal cost

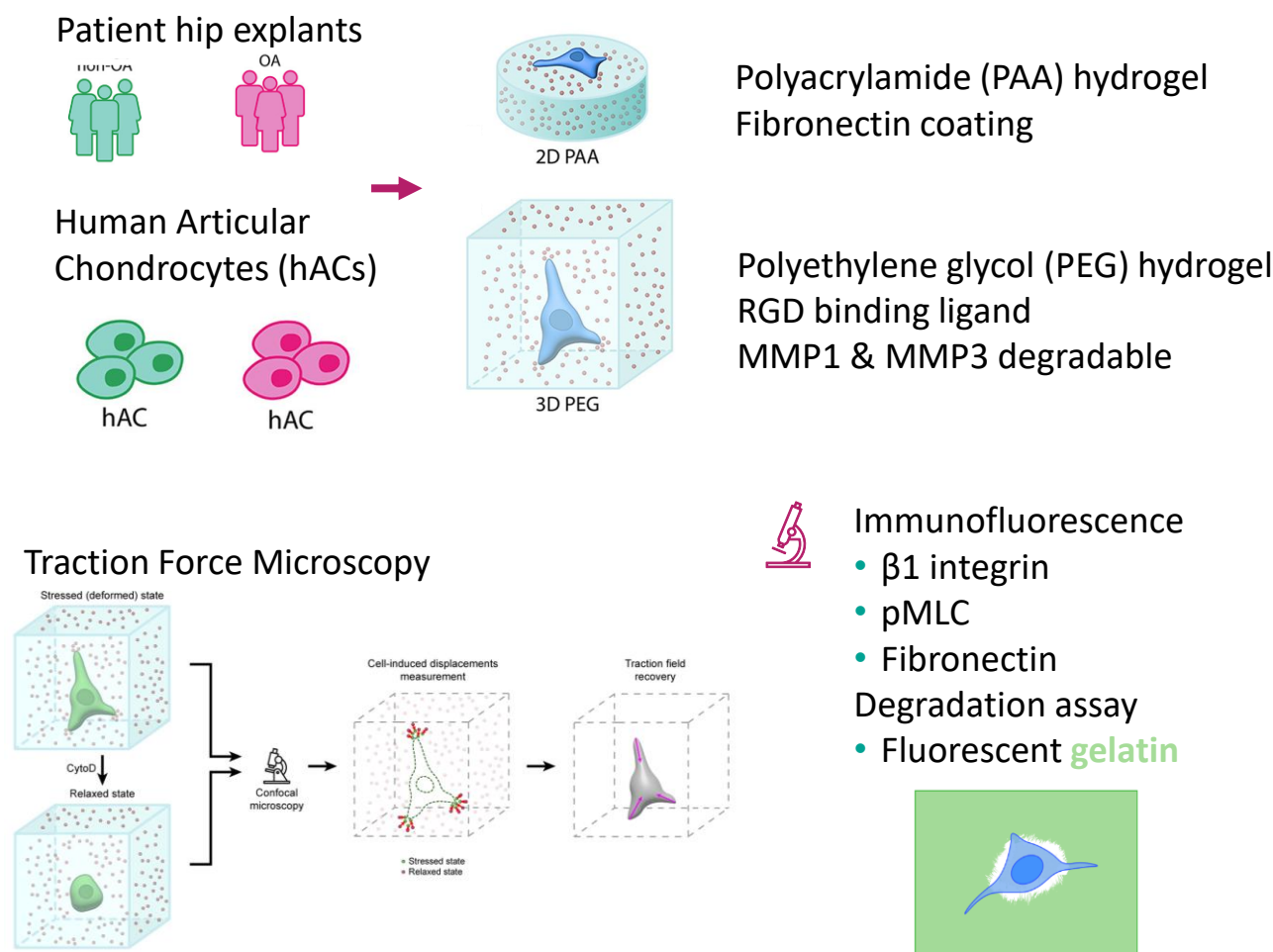


- Key force generation factors at cellular scale
- Disorganized and fragmented** cytoskeleton
 - Loss of round morphology**
 - Altered integrin** expression
 - Breakdown** of extracellular matrix proteins



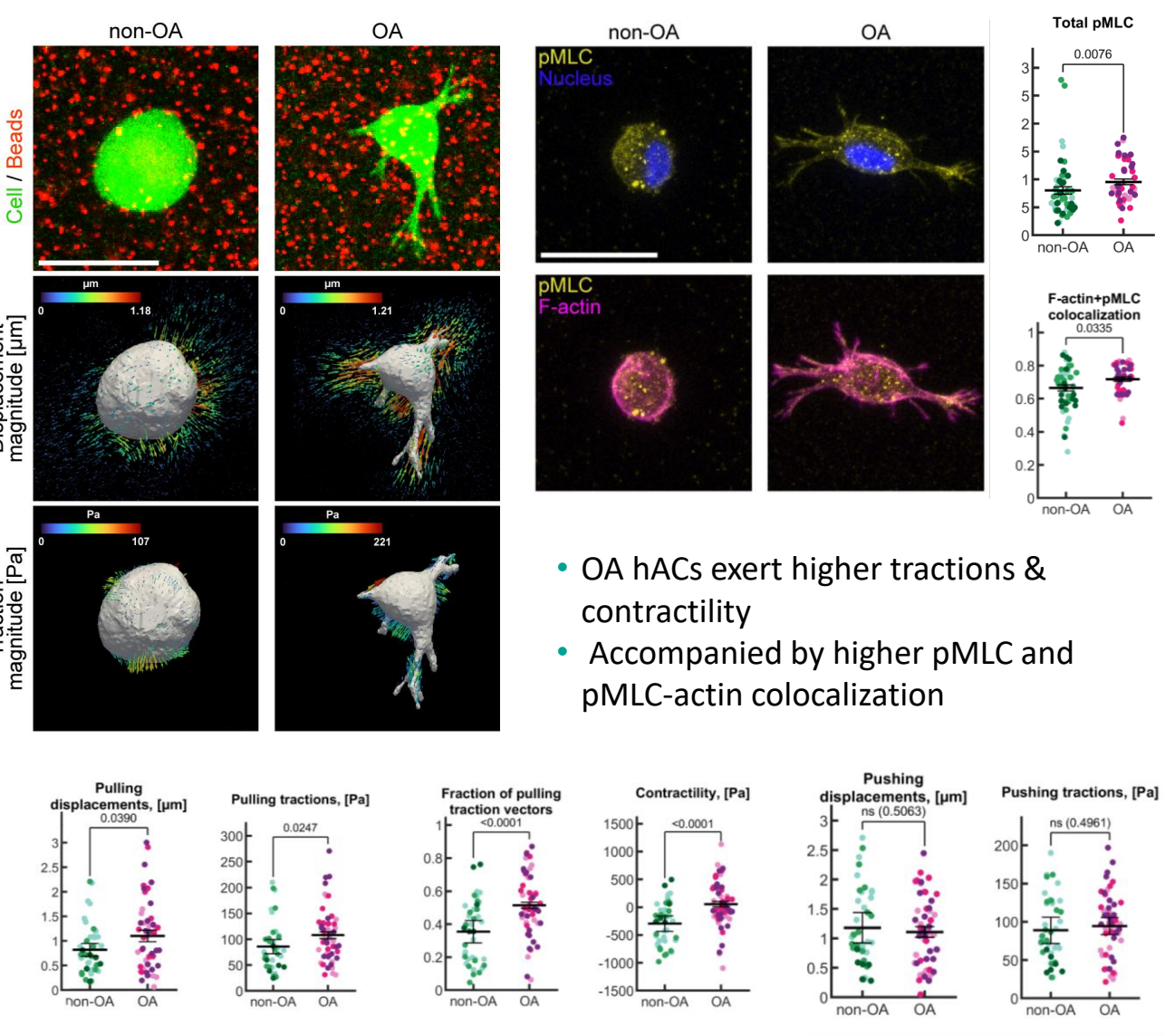
- Extrinsic mechanical loading important
- What is the role of intrinsic cell-generated forces in OA
- Inhibition contractile pathways → reduction MMP expression

Methods

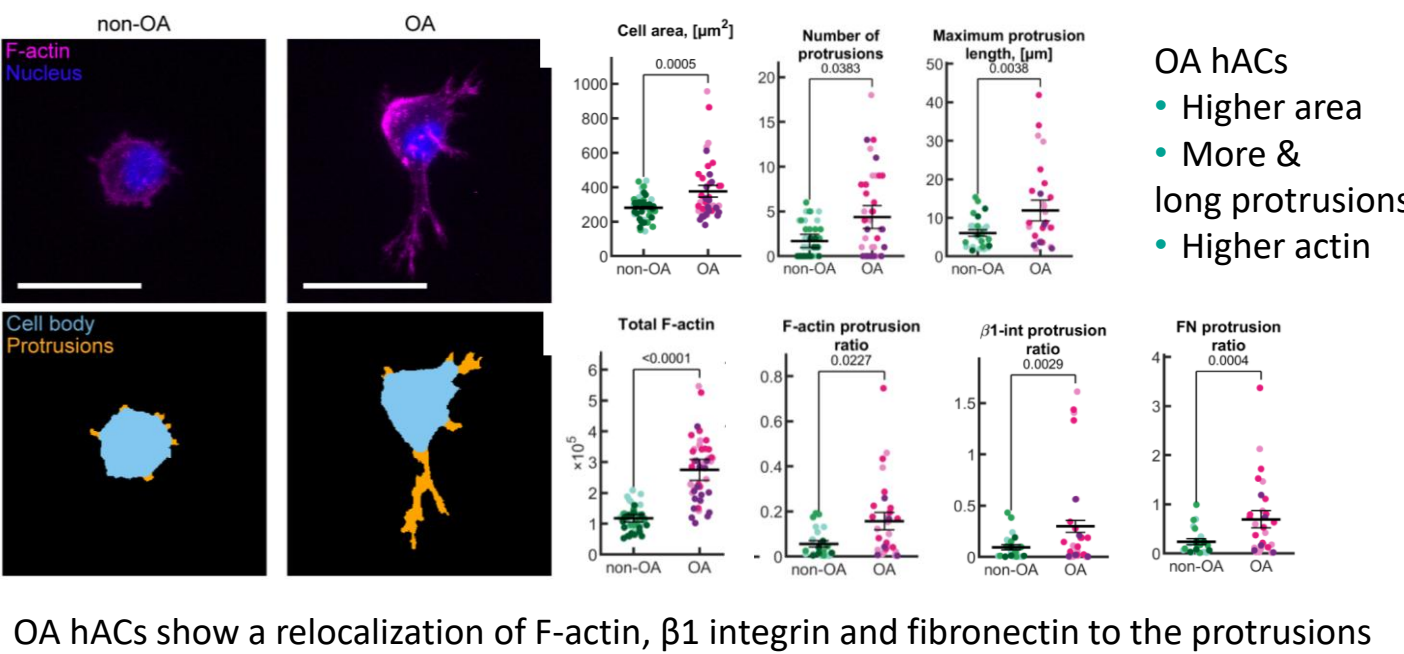


RESULTS

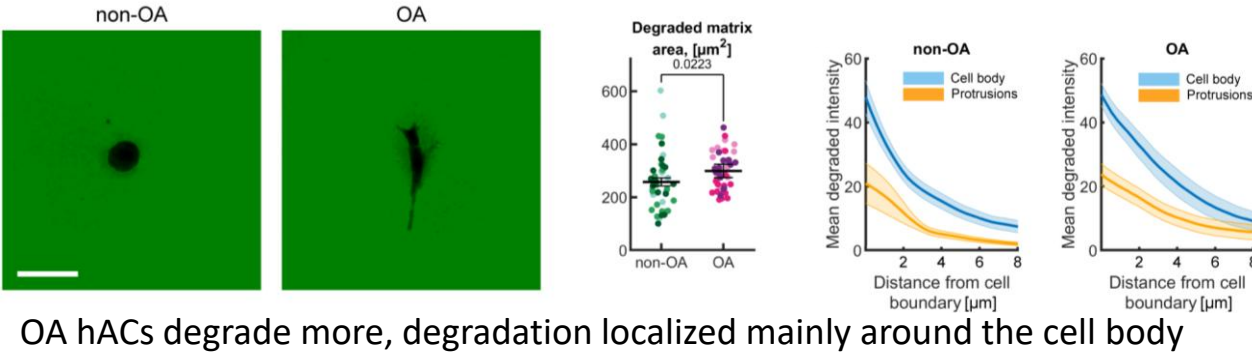
OA chondrocytes demonstrate enhanced force generation in 3D degradable hydrogels



Enhanced force generation paired with a more protrusive phenotype

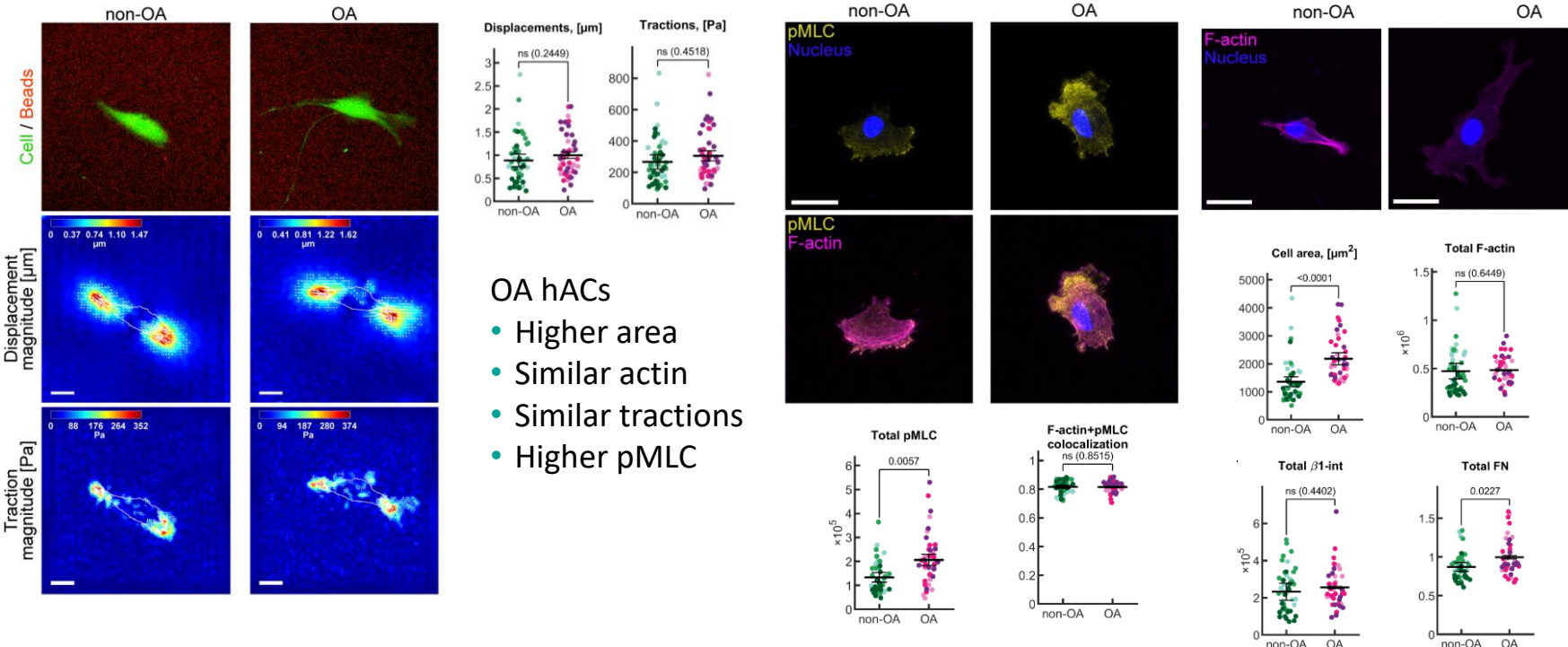


OA hACs show a relocalization of F-actin, $\beta 1$ integrin and fibronectin to the protrusions

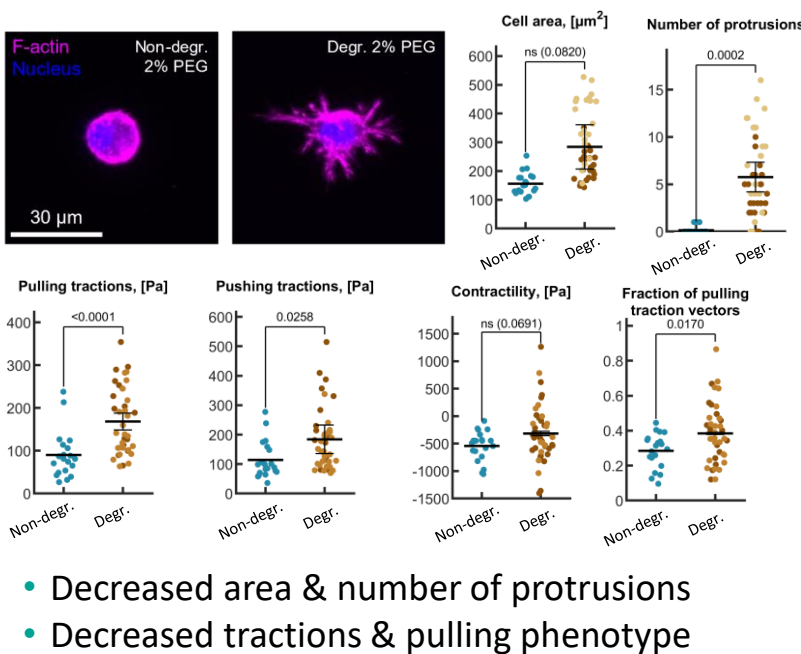


OA hACs degrade more, degradation localized mainly around the cell body

No enhanced force generation on 2D PAA hydrogels despite increased pMLC

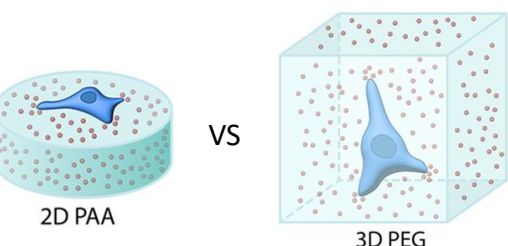


3D non degradable hydrogel system inhibits protrusion formation & decreases force generation for OA chondrocytes

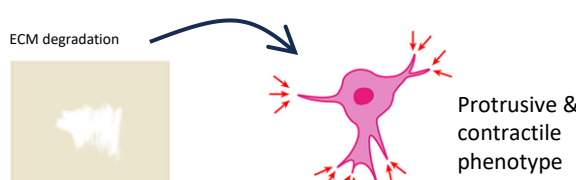


CONCLUSION

3D degradable hydrogel systems show enhanced contractility & protrusive phenotype of OA chondrocytes



Choosing the right in vitro model is crucial for studying OA mechanobiology



Our work builds upon idea that intrinsic contractility is linked to matrix degradation → Mechanochemical feedback loop

ACKNOWLEDGEMENTS

The author would like to thank KU Leuven internal funding (IDN/20/019 Project-4-earlyOA, iBOF/21/083 C), FWO project G0C2422N, FWO-ERANET (Neuron) G0L1522N and FWO postdoc fellowship JBF (1259223N) for providing financial support to this project.



nele.vaes@kuleuven.be
hans.vanoosterwyck@kuleuven.be