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Top-Down and Bottom-Up Biofabrication of Biomimetic Cartilage Scaffolds for Regenerative Applications

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INTRODUCTION & AIM

Articular cartilage (AC) is a highly specialized, load-bearing tissue whose extracellular matrix (ECM) composition and zonal organization are essential for its exceptional biomechanical performance. However, due to its avascular and aneural nature, AC possesses very limited intrinsic repair capacity, making functional regeneration a longstanding clinical challenge, e.g. for more than 600 million people worldwide suffering from Osteoarthitis. Although current biomaterials and scaffold-based strategies can reproduce aspects of gross architecture and mechanical properties, they often fail to replicate the anisotropic collagen type II organization and biochemical complexity required for durable joint function [1].

AIM: Creation of a cartilage model that aims to mimic the **native hierarchical structure** of **articular cartilage** in all **three layers**, especially in regard to the **orientation** and **alignment** of **collagen type II fibres in an arch-like manner**

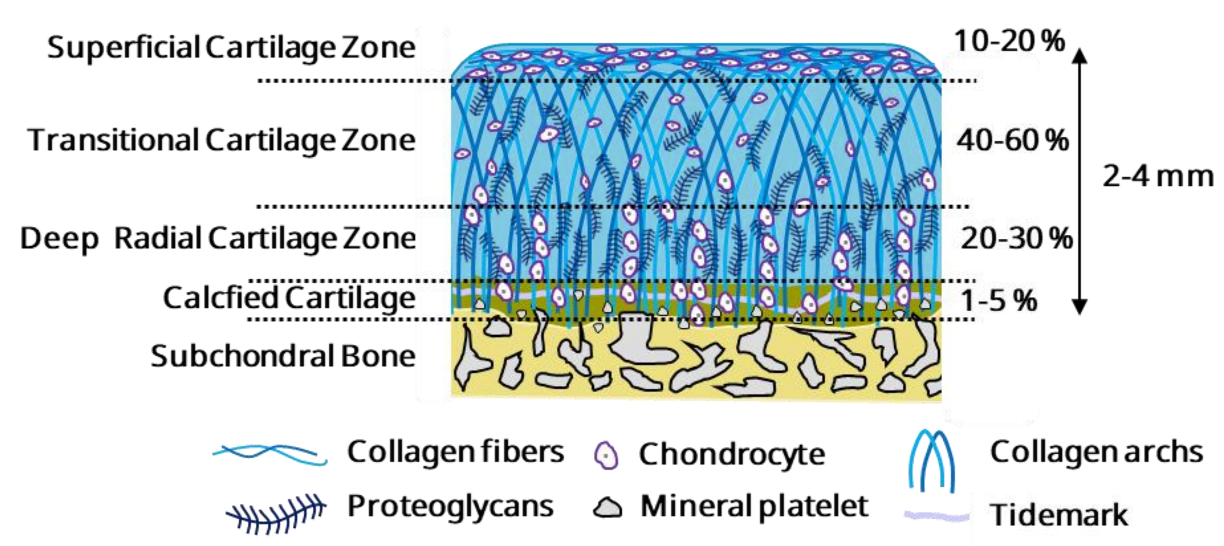
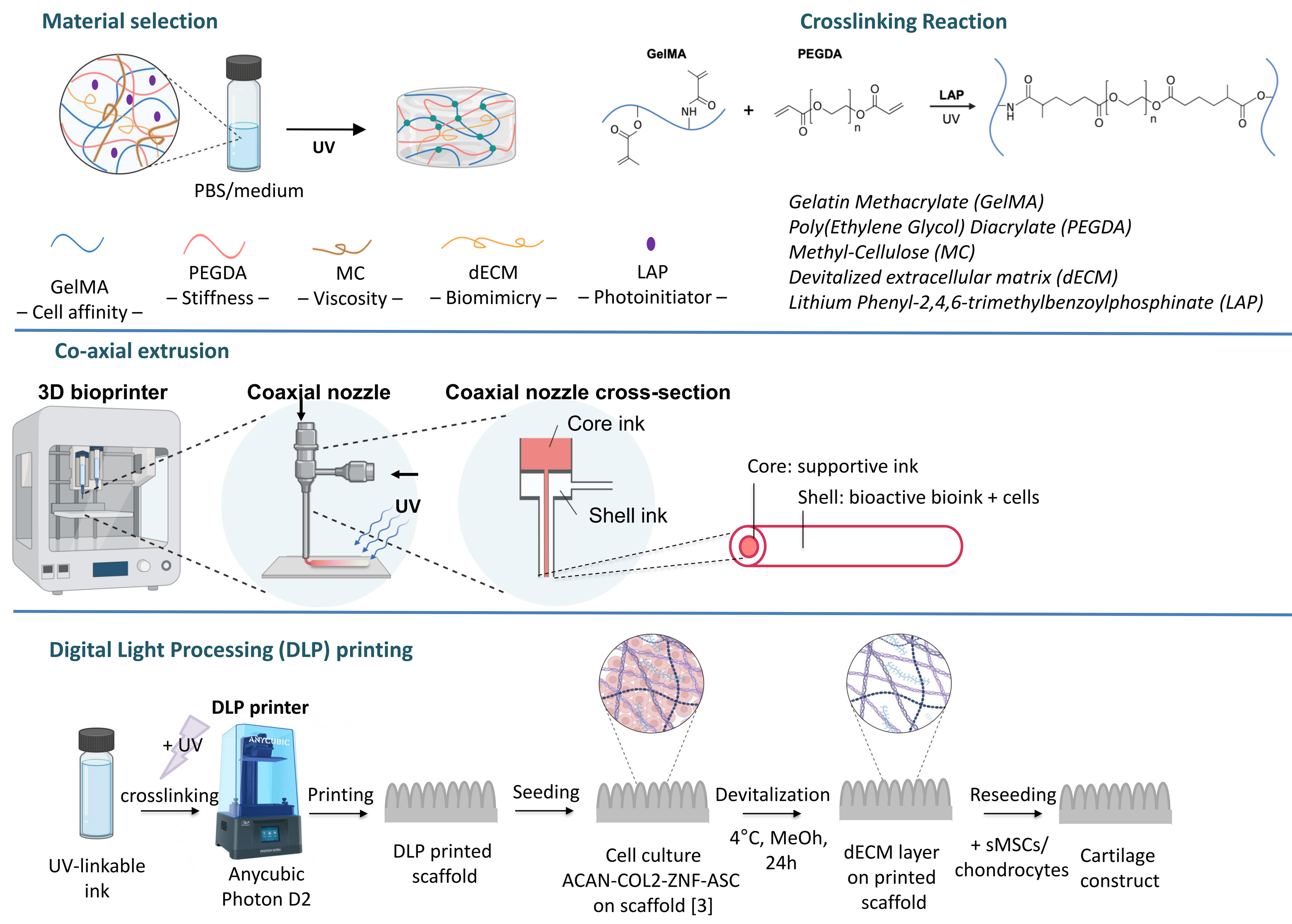


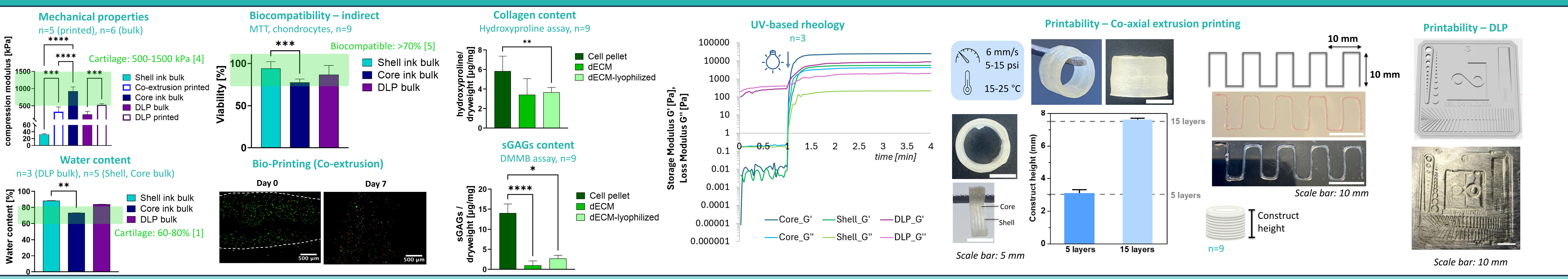
Fig.1 Hierarchical structure of cartilage with characteristic arch-like arrangement of collagen type II fibers [2, unpublished]

METHODS



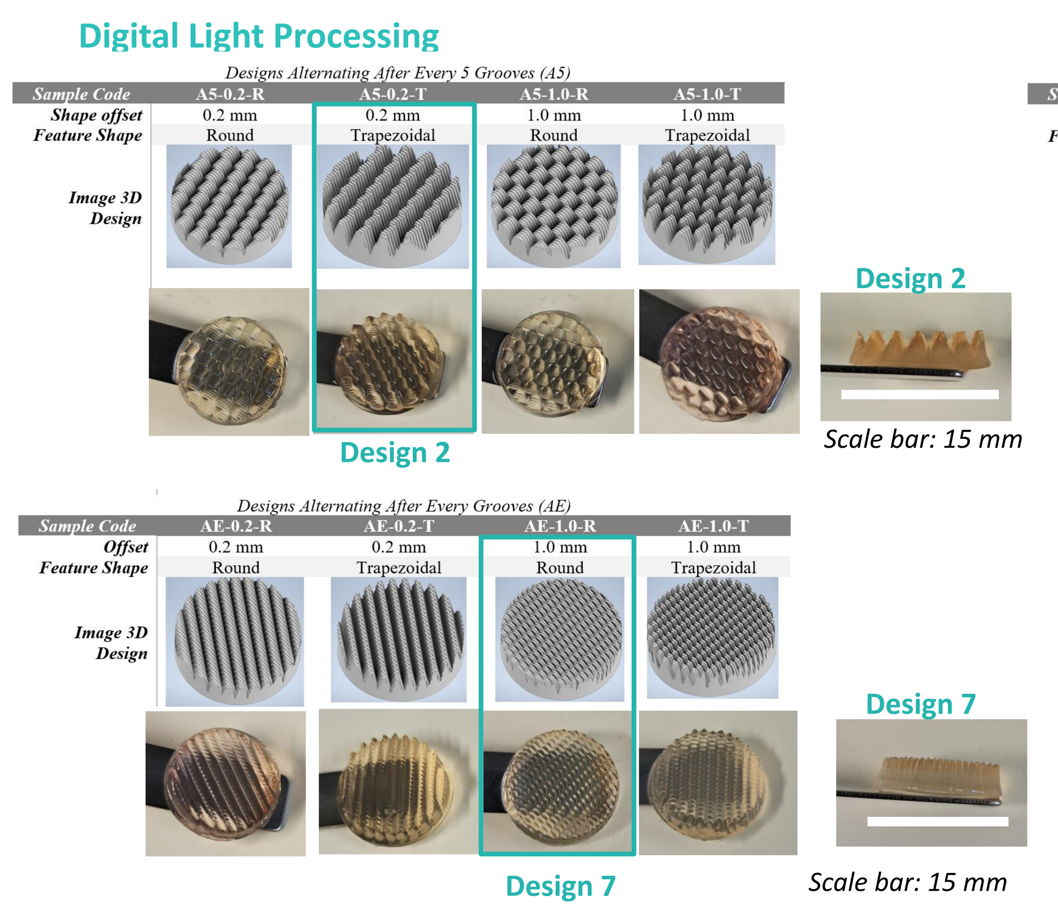
RESULTS & DISCUSSION

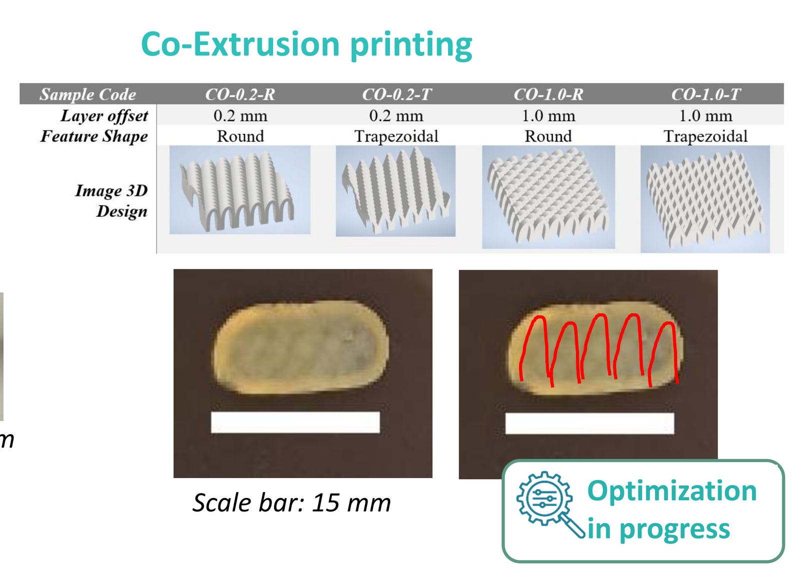
Material characterization



- Similar properties to native cartilage
- Stability over 3 weeks @ 37°C
- Biocompatible (indirect and direct cytotoxcity test acc. to ISO 10993)
- Bio-Printing with high cell viability after printing
- High content of ECM components
- Retention of collagen
- Fast crosslinking after irradiation
- Temperature-related crosslinking ~ 11°C
- Good printability using co-extrusion system
- High shape fidelity
- High shape fidelity and resolution with DLP printing technique

Scaffold design + selection

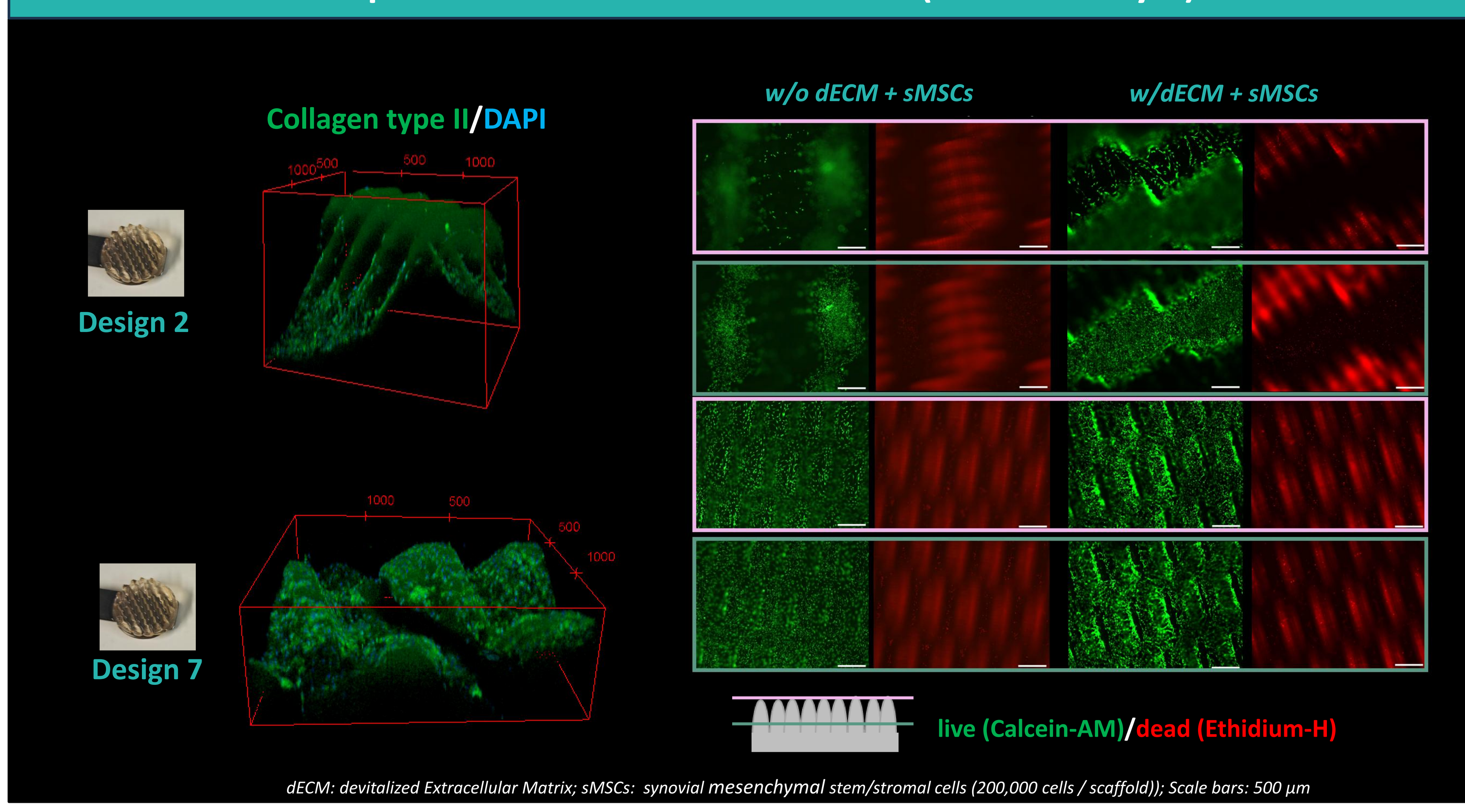




Advantages Co-extrusion:
- Multi-material, multi-functional scaffold
- Fast printing with lower resolution (needle diameter of 1.07mm)

Advantages DLP:
- High shape fidelity (xyz resolution: ~50 µm)
- Mass production possible (<30min printing for 8+ samples)

DLP printed Scaffold + dECM + Cells (sMSCs – Day 3)



dECM: devitalized Extracellular Matrix; sMSCs: synovial mesenchymal stem/stromal cells (200,000 cells / scaffold)); Scale bars: 500 µm

CONCLUSIONS & FUTURE WORK

Thorough characterization demonstrated high print fidelity, suitable mechanical properties, and improved support for synovial mesenchymal stem/stromal cells (sMSCs) viability and function. Further characterization is planned, to confirm the enhanced potential of replicating the complex chondral architecture and phenotype (real time-quantitative PCR, immunofluorescence staining and histological analysis).

By integrating top-down (DLP) and bottom-up (coaxial extrusion printing) fabrication with engineered dECM, this approach advances the development of biomimetic scaffolds that more closely recapitulate the hierarchical organization of native AC, offering a promising translational pathway for functional cartilage regeneration.

Future work also includes the integration in microfluidic systems, to better recapitulate the dynamic environment found *in vivo*.

REFERENCES ACKNOWLEDGMENTS

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