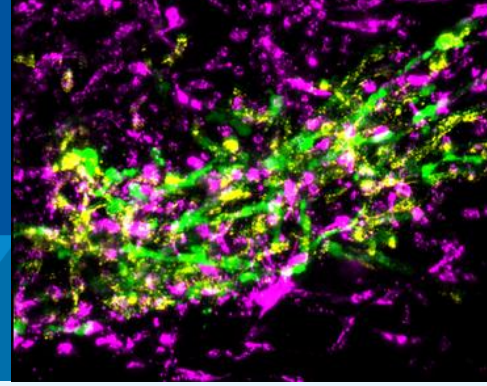
UMC Utrecht



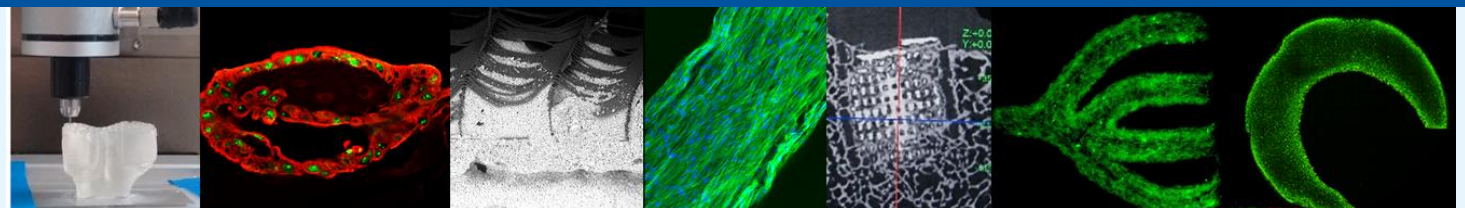


Designing Engineered Tissues from the Microscale to the Macroscale via Bioprinting

Riccardo Levato[1,2,3]

Assistant Professor, [1]Regenerative Medicine Center and [2]Dept. of Orthopaedics, University Medical Center Utrecht, [3]Dept. of Clinical Sciences, Utrecht University, The Netherlands

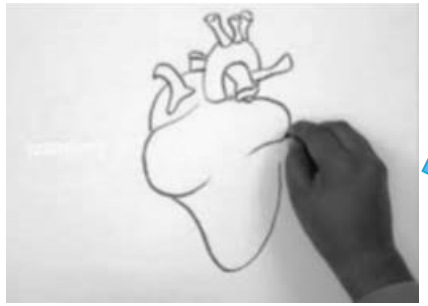
Biofabrication and tissue-mimetic biomaterials

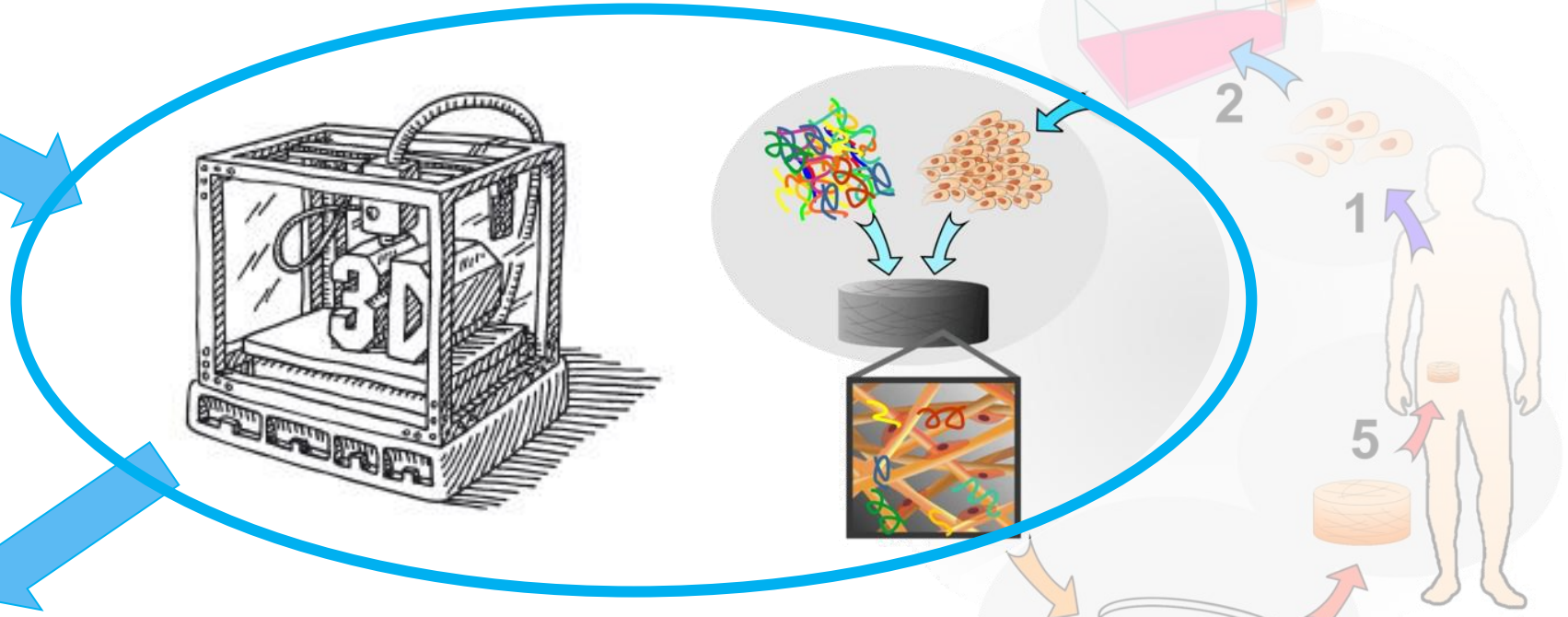


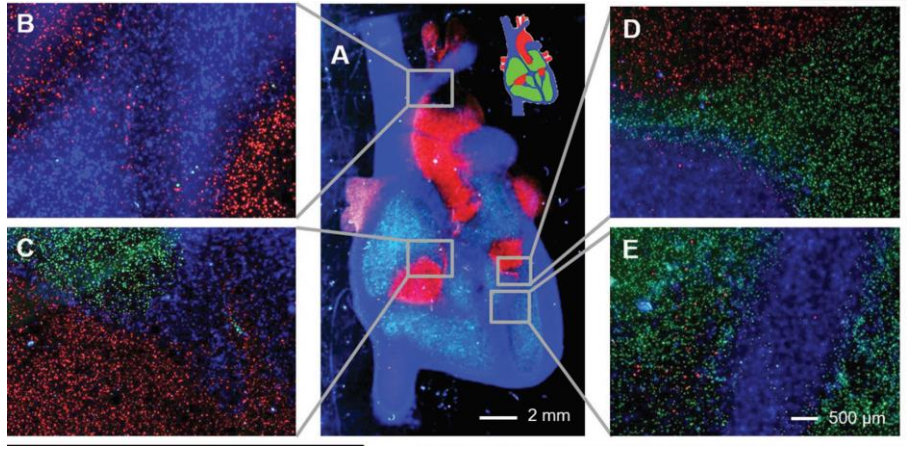
@RicLevato

r.levato-2@umcutrecht.nl

From the idea to the biological object

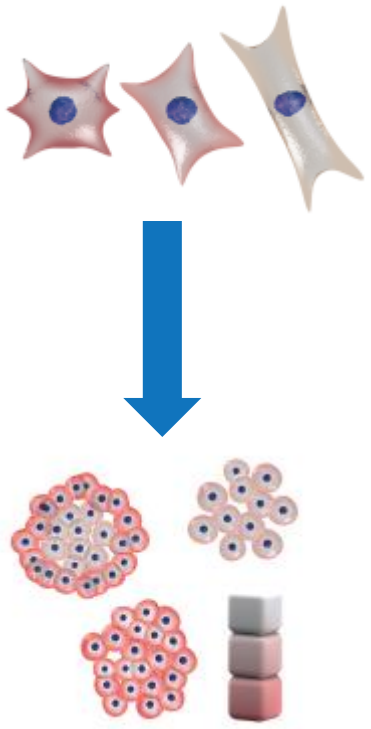






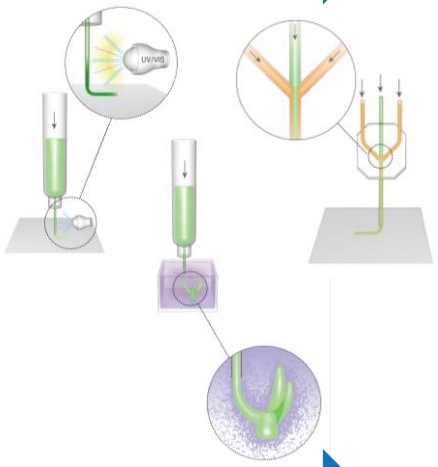
Liu et al., Adv Mater, 2016

Capturing the Shape-to-Function relationship

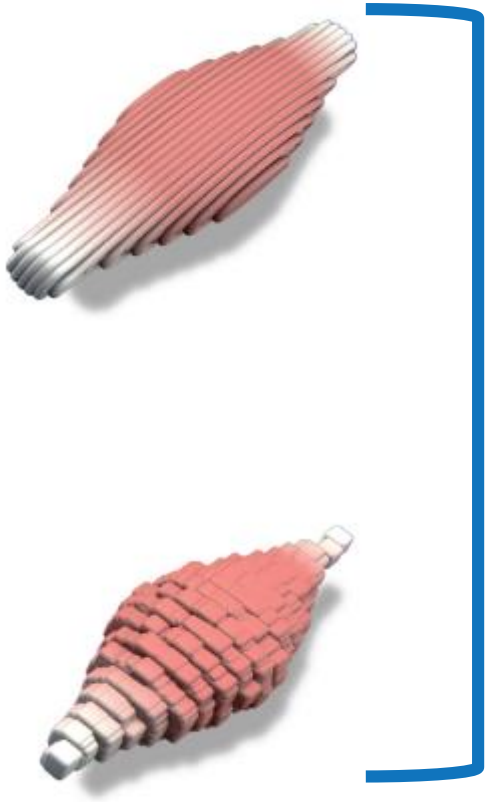


Cells and materials

Bioprinting



Technologies and design

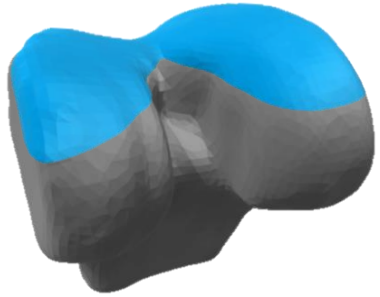


Guided maturation

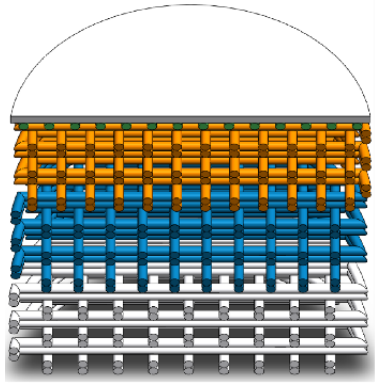
- Multi-tissue and interfaces
- Nutrient supply
- Mechanical performance
- Physiological scale (size)

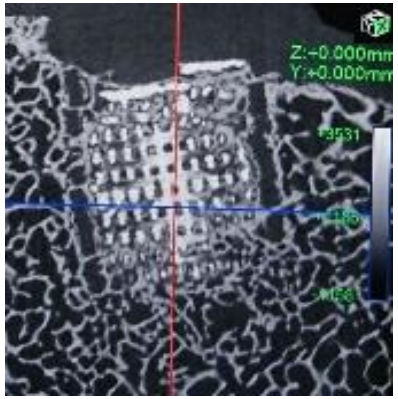
Levato&Jungst+, Adv Mater **2020**

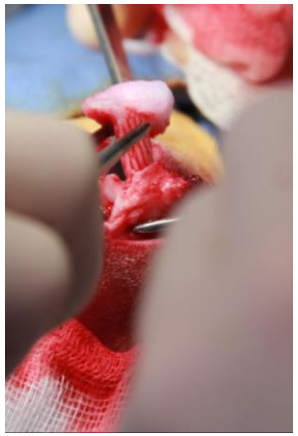
Bone, Cartilage and Joint restoration



Levato+, Acta Biomater **2017**
Lim&Abinzano+, Adv Healthc Mater **2020**

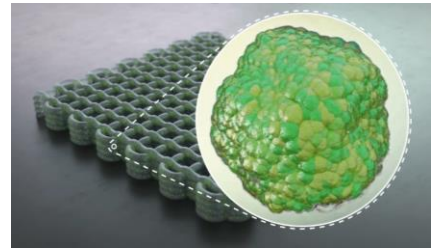






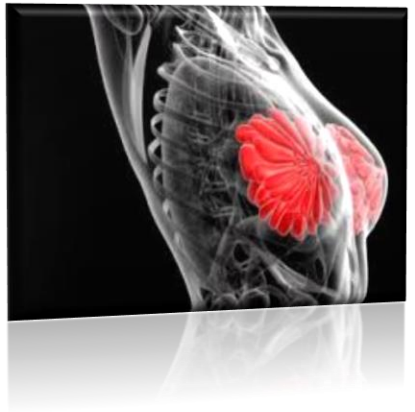
Diloksumpan+, Adv Healthc Mater **2020**
Diloksumpan+, Biofabrication **2020**

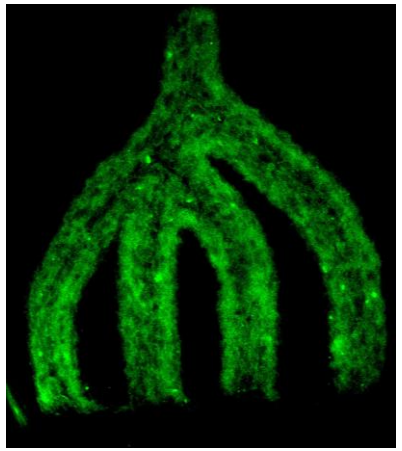
Liver organoids



Schneeberger+, Biofabrication **2016** ; Bouwmeester+, unpublished

Mammary duct

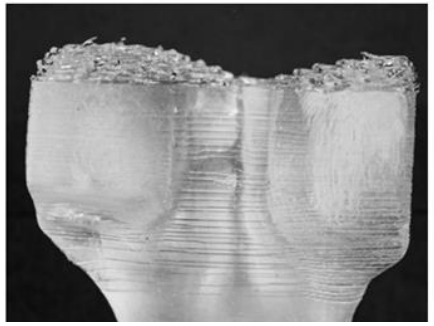


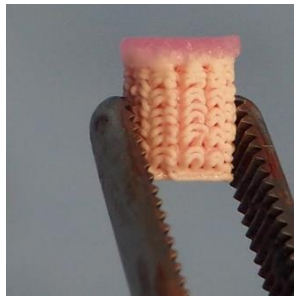


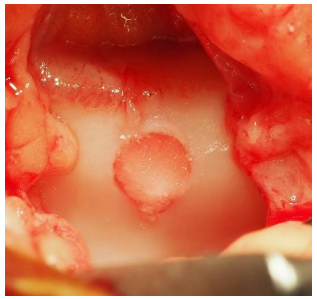
Buccholz+, unpublished

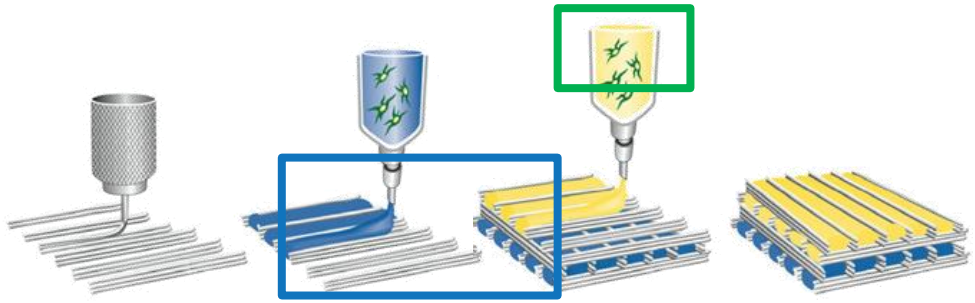
Challenges towards treating osteochondral defects

Bioprinting (UMCU)





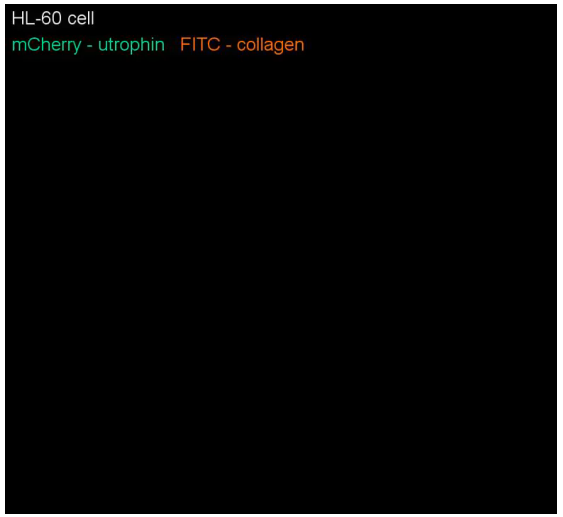




Shape
Mechanics
Biomaterials

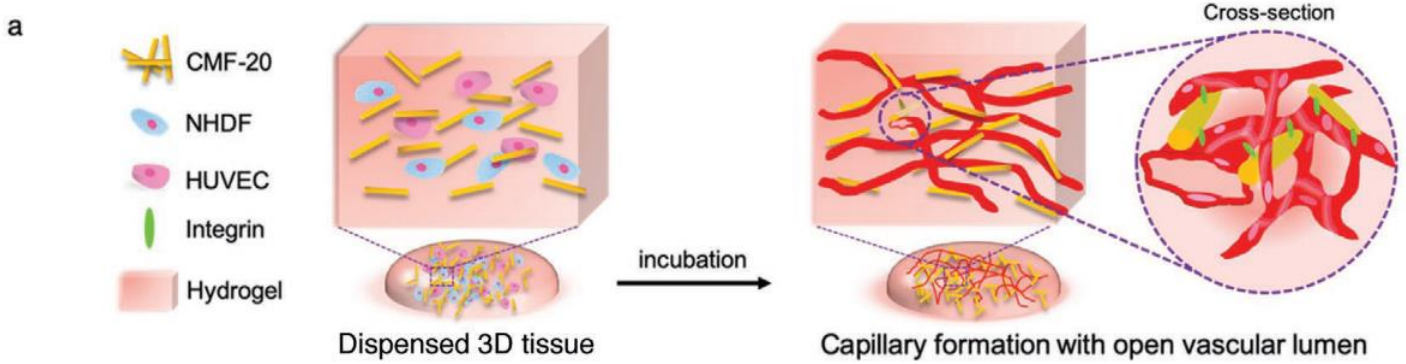
Cell-matrix interaction

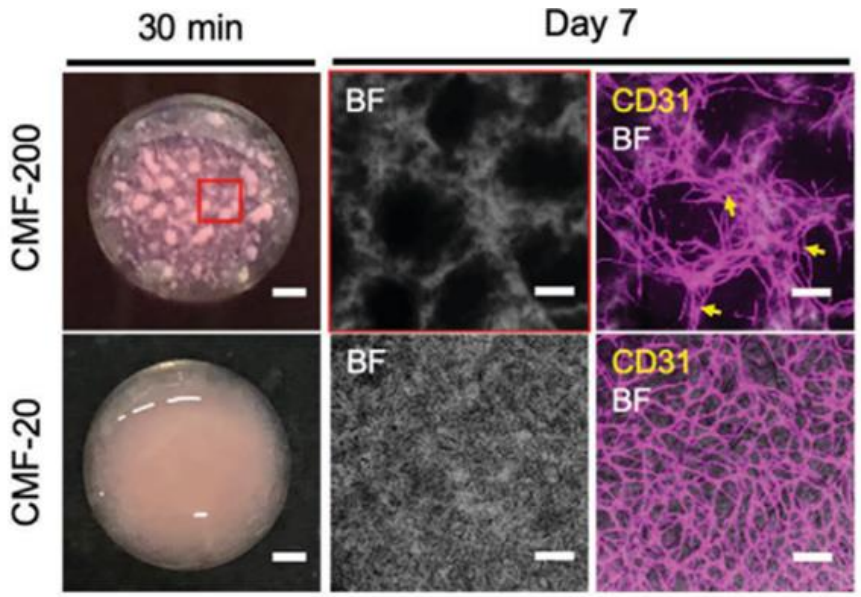
Cell Microenvironment (Osaka)



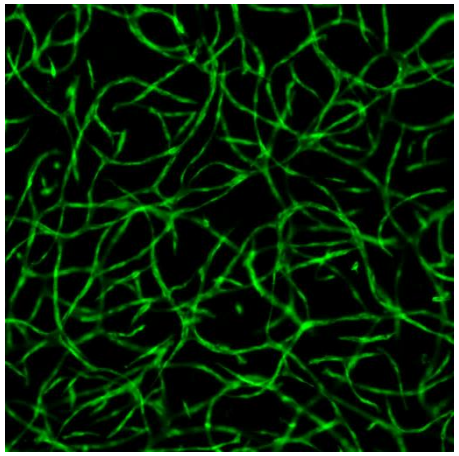
How can we modulate the microenvironment to promote bone vascularization?

Collagen Microfibers (CMF) to regulate cell behavior at the microscale

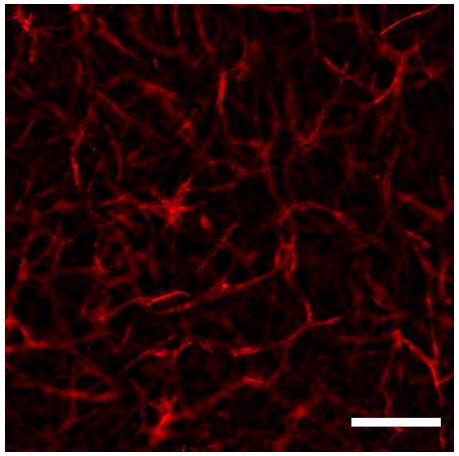




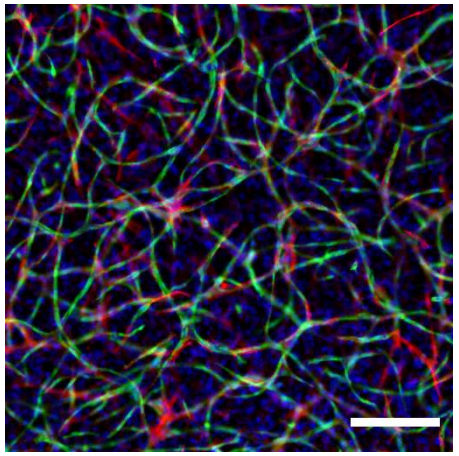
Endothelial cells (blood vessels)



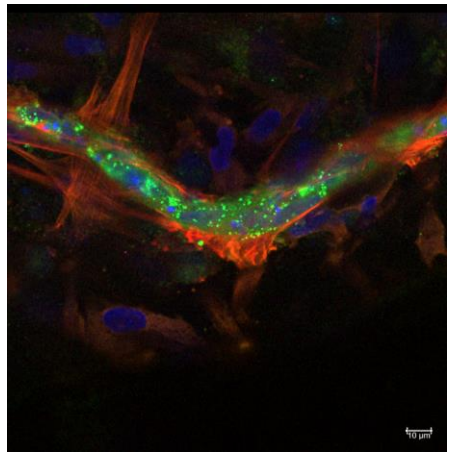
Pericytes (support blood vessels)



Combined



Combined, zoomed in



Utrecht-Osaka collaboration and staff exchanges (2019)

June -> First visit to Osaka (RL)

July -> Prof. Matsusaki Lectures at the RMCU and at the Utrecht Summer School

Sept-Oct -> Margo Terpstra performs secondment in Osaka (learning cell coating and microfiber preparation techniques)

Nov-Dec -> Jinyu Li performs secondment in Utrecht (bioprinting of microfibers and angiogenesis)

A roadmap to large, clinically relevant bioprinted tissues

Physiologically relevant scale

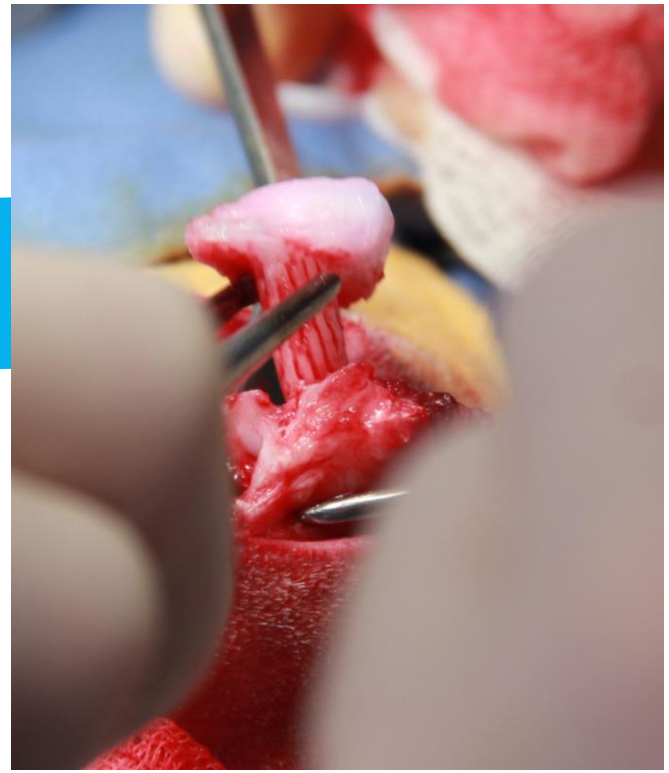
Complex anatomy

Integration of multiple tissues

Functional cell printing

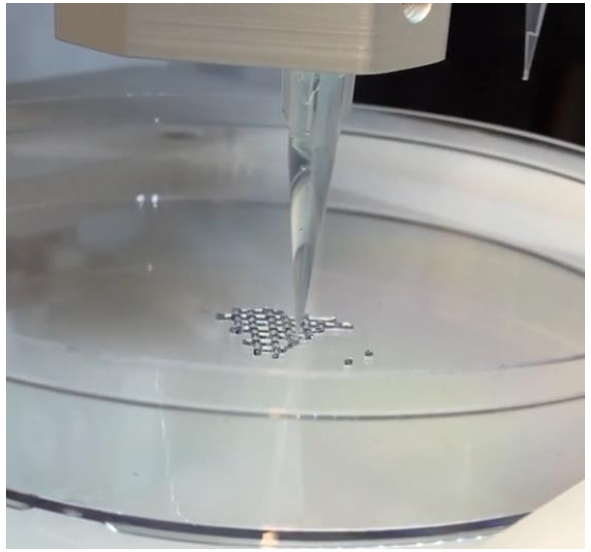
Mechanical performance

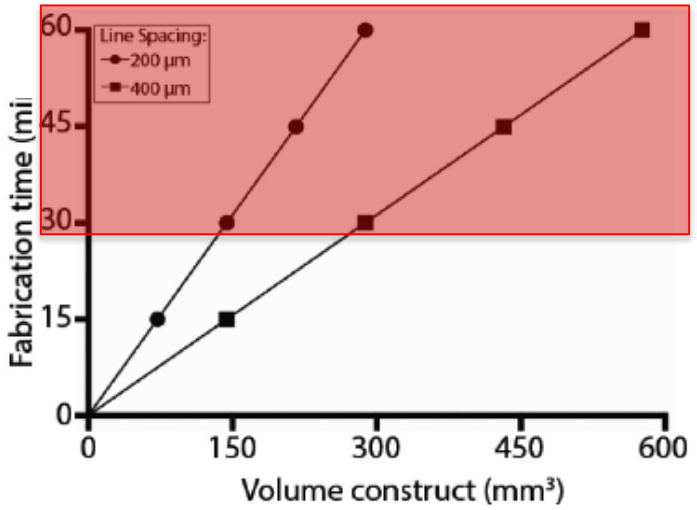
Nutrient supply

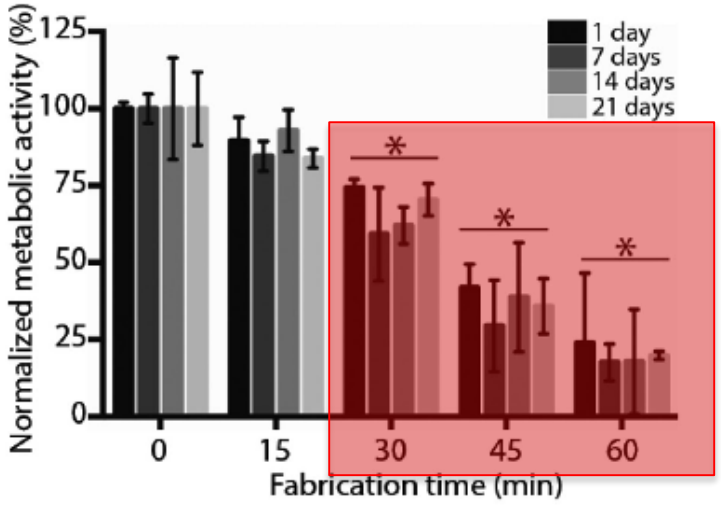


Layer-by-layer manufacturing: rapid prototyping, but how rapid?

Extrusion-based

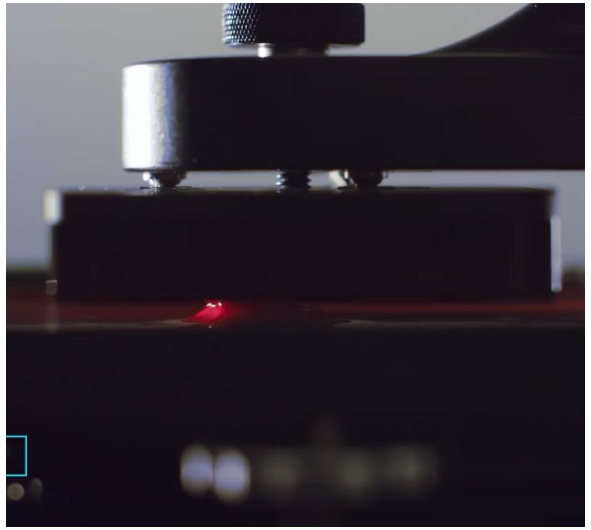






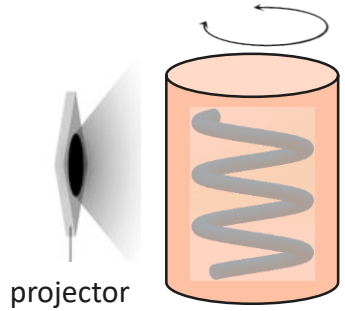
De Ruijter+, *Adv Healthc Mater* **2018**

DLP

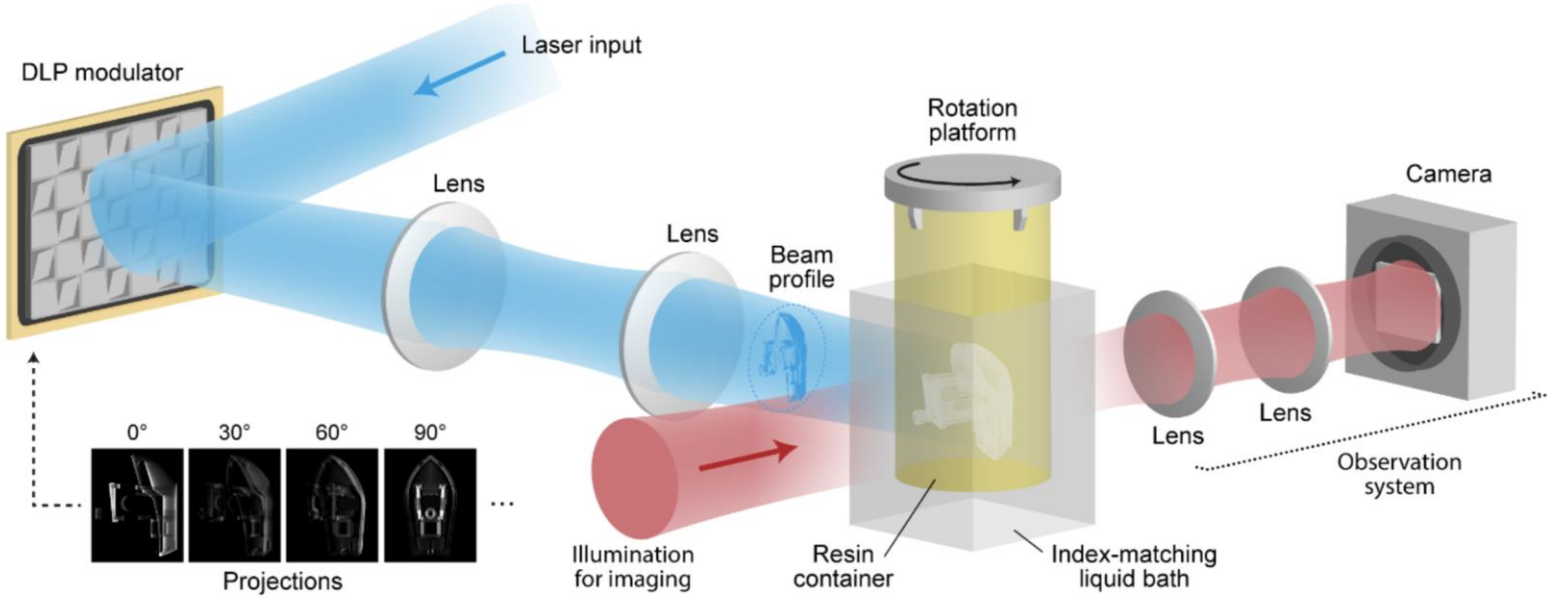


Volumetric Bioprinting

Volume-in-Volume

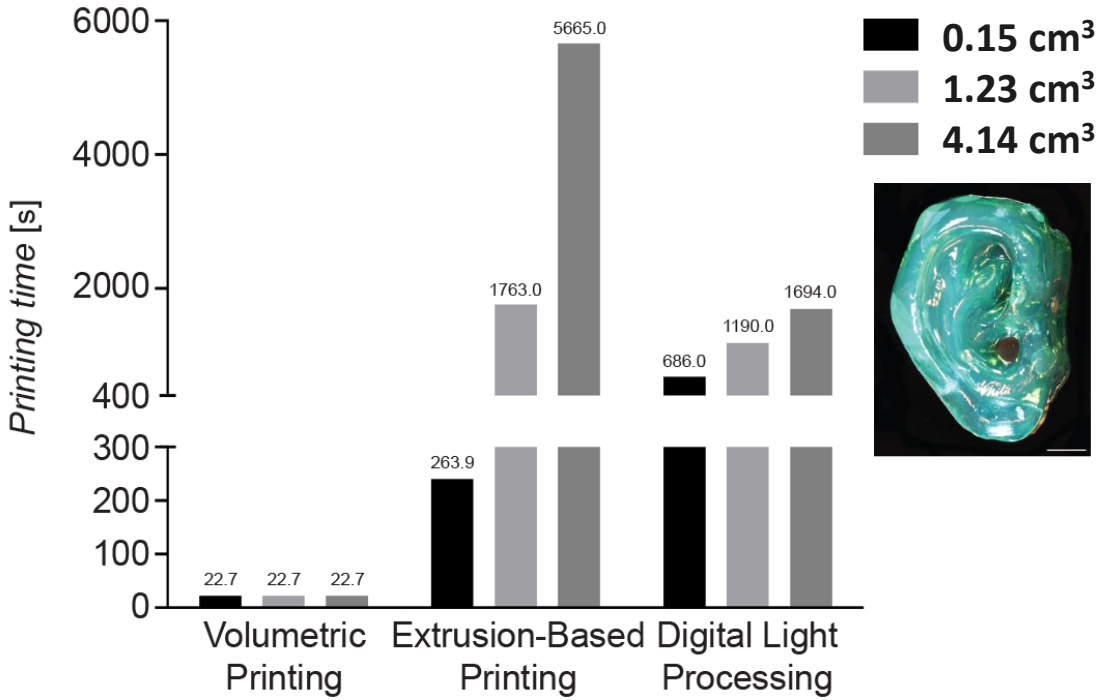


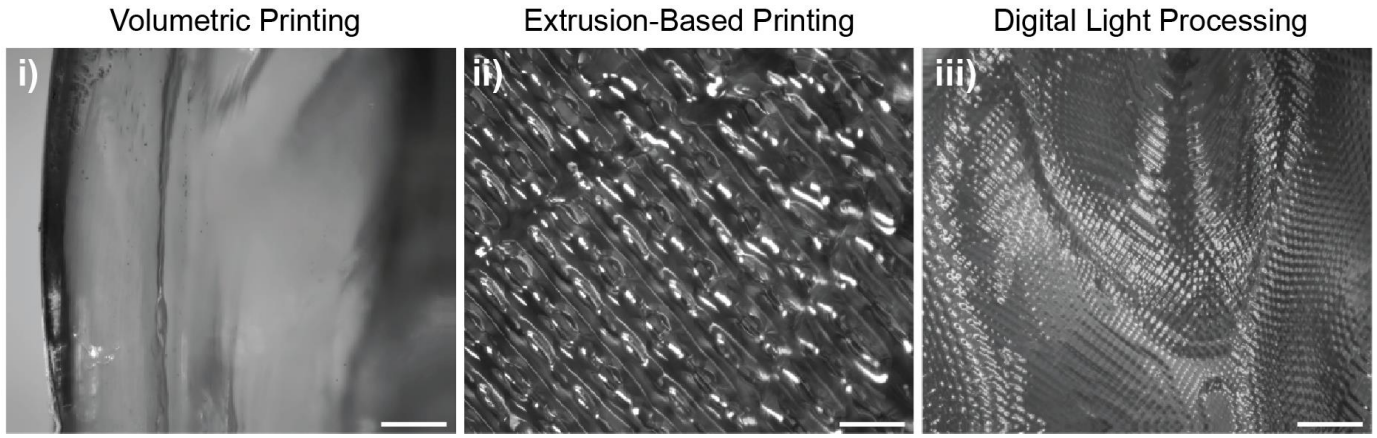
From 2.5D-layers to 3D field-based manufacturing

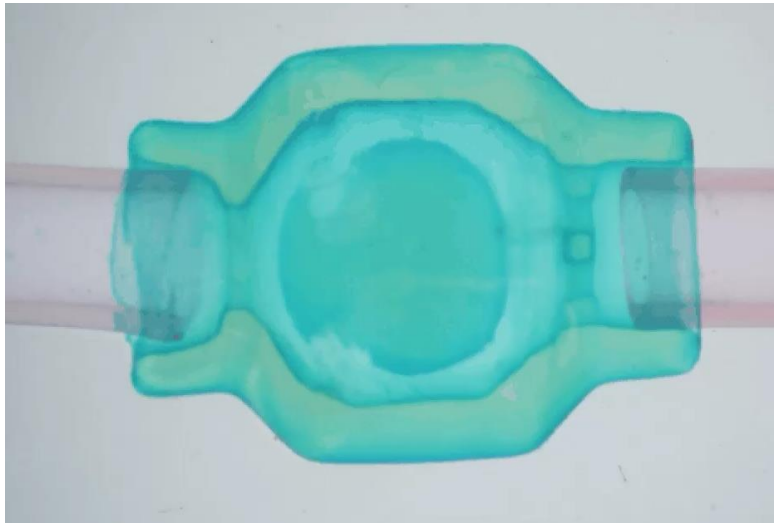


Bernal+, Adv Mater 2019 ; Loterie+, Nat Commun 2020

Improved printing time, surface finishing and free-form fabrication







Smooth surface features

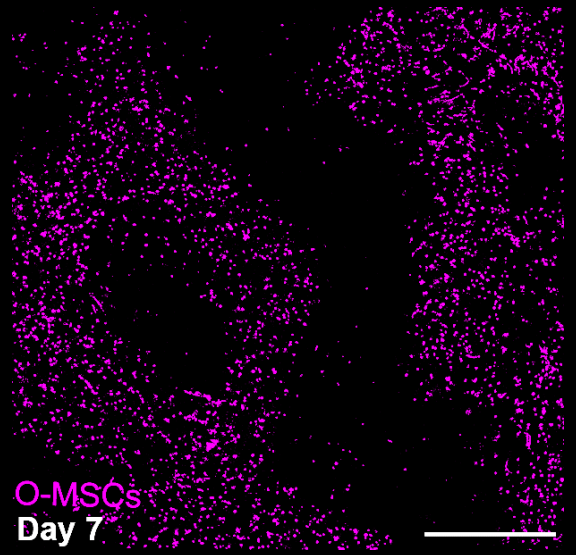
5.71 ± 2.31% volume variation compared to STL

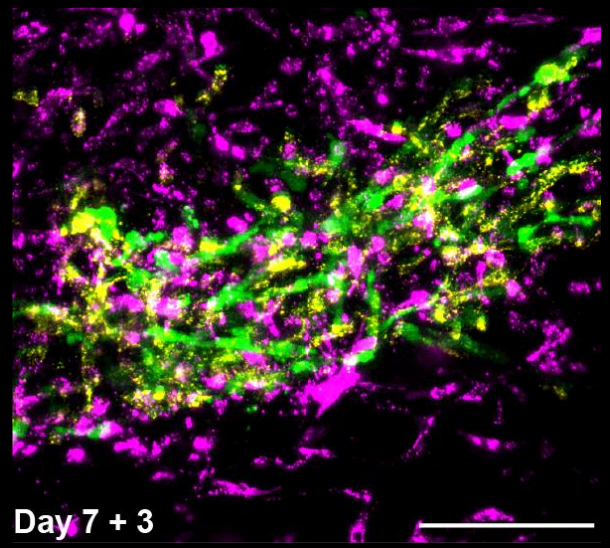
Pefusable channels = 200 µm

Positive features = 80 to 140 µm

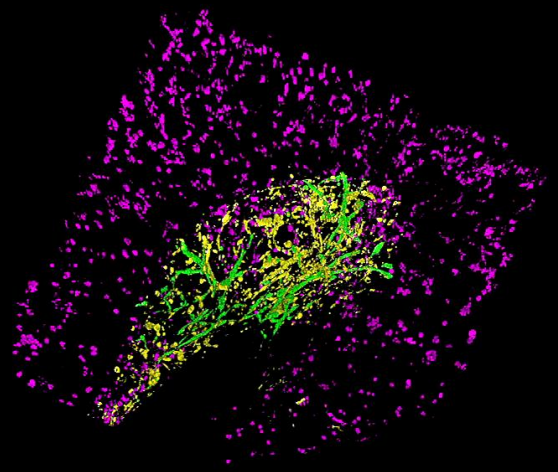
Bernal+, Adv Mater 2019

Complex architectures: anatomical trabecular bone

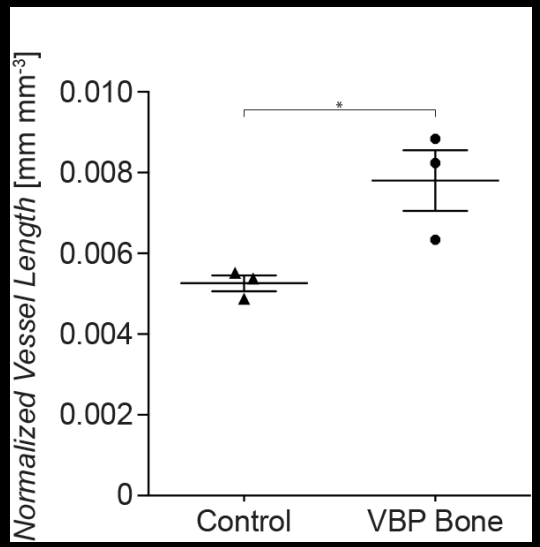


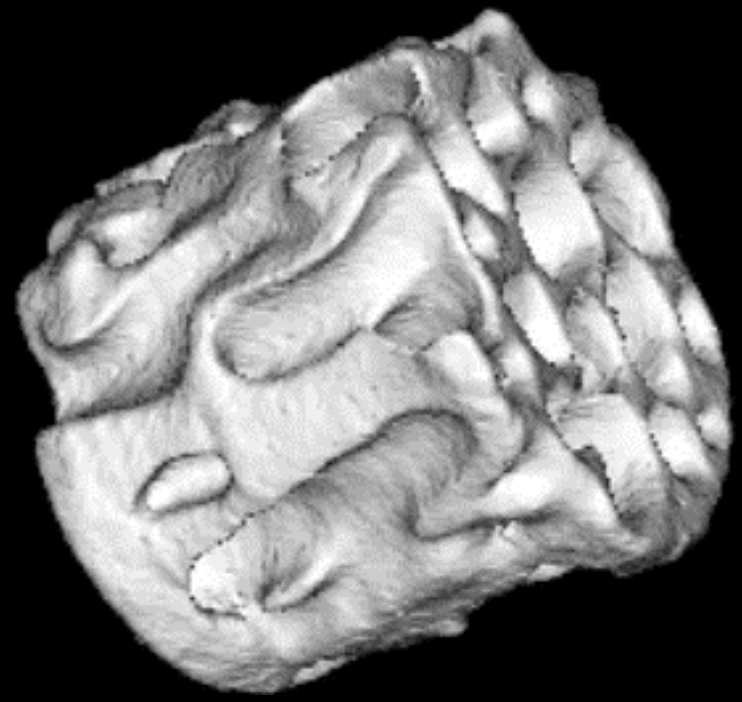


Osteo-MSC Endothelial cells Pericytes



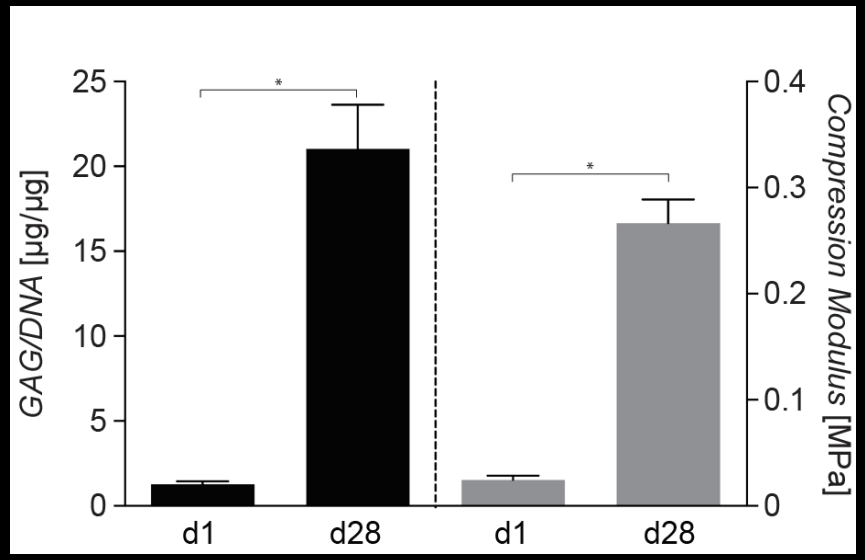
Bernal+, *Adv Mater* 2019

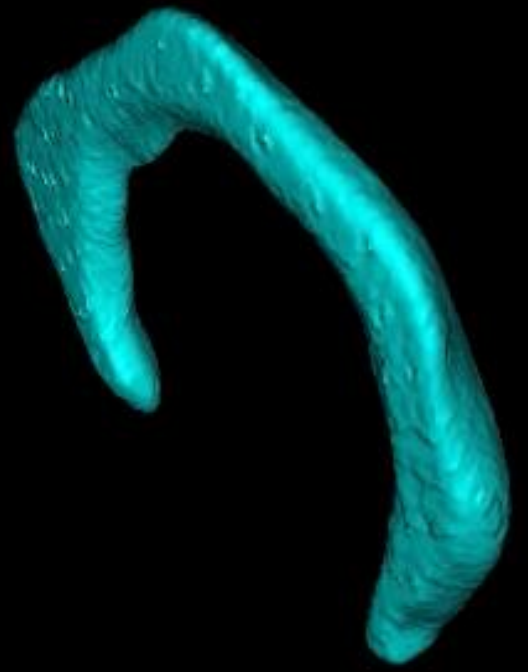


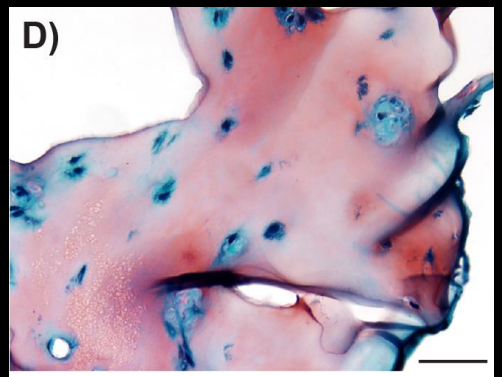


Printing time = 12.5 s
Size = 11 x 10 mm

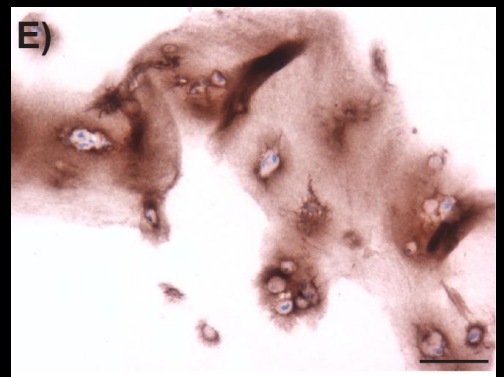
Long term cell functionality of bioprinted progenitor cells



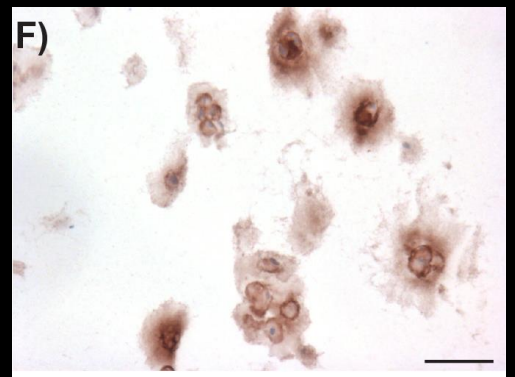




Glycosaminoglycans



Collagen Type I



Collagen Type II

Bernal+, *Adv Mater* 2019

Combining strengths…a little step forwad each time

Functional cell printing

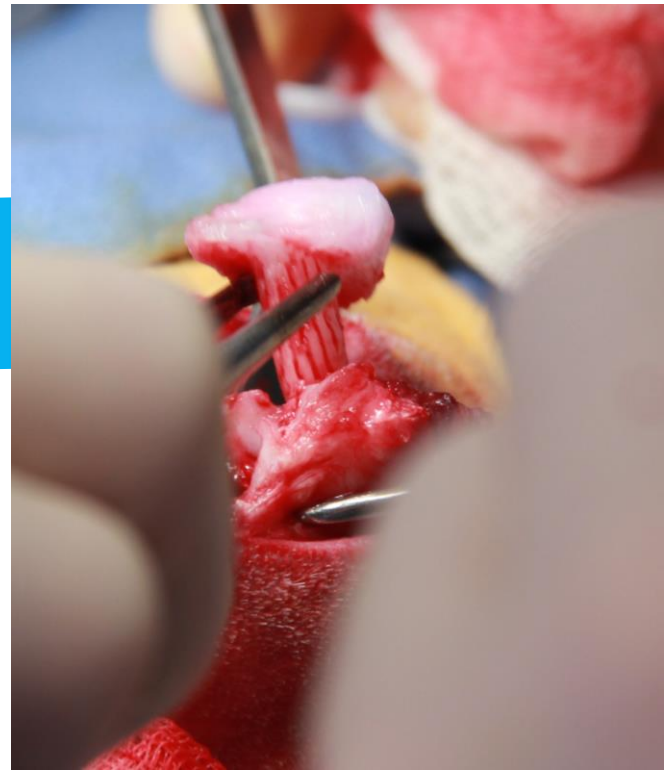
Mechanical performance

Integration of multiple tissues

Complex anatomy

Nutrient supply

Physiologically relevant scale



Thanks for your attention

RMCU Orthopaedics

Biofabrication in translational medicine

Jos Malda
Riccardo Levato
Paulina Nuñez Bernal
Florencia Abinzano
Sammy Florczak
Iris Otto
Margo Terpstra
Anneloes Mensinga
Irina Mancini
Paweena Diloksumpan
Mattie van Rijen
Margot Rikkers
Miguel Castilho
Yang Li
Susanna Piluso
Inge Dokter
Mylene de Ruijter
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Khoon Lim

Hubrecht Institute

Hans Clevers
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Swansea University

Ilyas Khan

Netherlands Organisation for Scientific Research

DutchArthritisSociety ReumaNederland

European INNOVATION Council

HORIZON 2020

MEFISTO Driving meniscus health forward

AO Foundation

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