Multiphoton ablation as a tool to create repeatable true 3D architectures for breast tissue engineering[1]

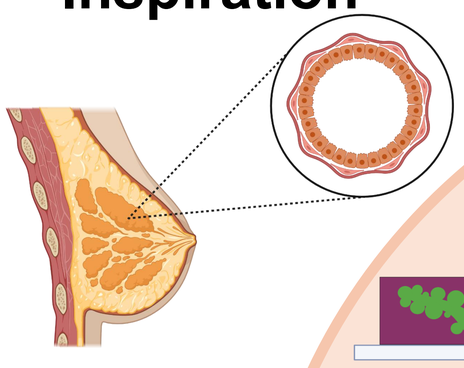
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Introduction

- *Curvature is important for epithelial cells.*
- *Current methods are limited in geometrical control, repeatability and surface control.*
- *MPA does not have these limitations, but it is slow and limited to small features.*

Scale up Multiphoton Ablation (MPA)

Inspiration



Methods

tissue engineering + biofabrication

ETH zürich

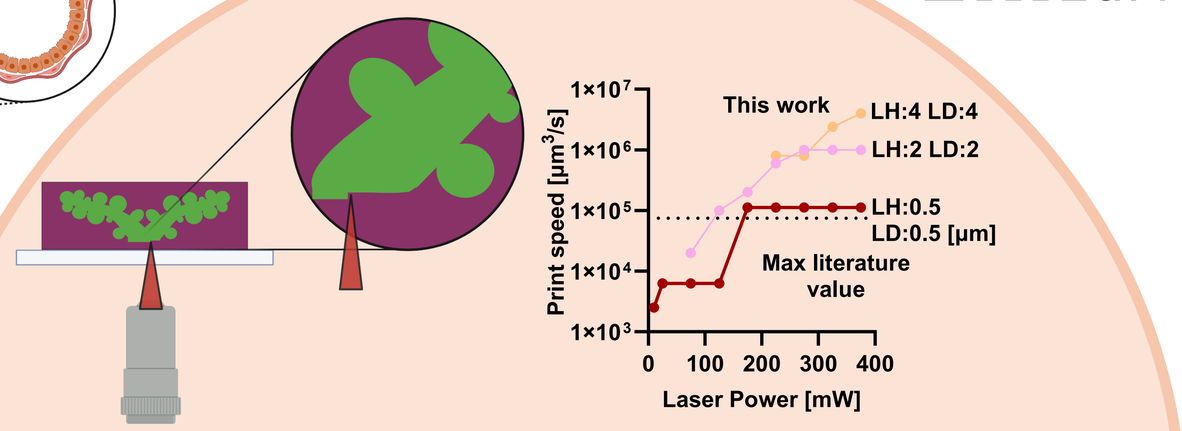


Figure 1: Right: Multiphoton ablation with an IR femtosecond(fs) laser adapted to larger duct and alveoli like features relevant to epithelial tissue engineering in hydrogels using 2PP sensitizer P2CK. Left: Print speed as a function of laser power for 0.5, 2 (1mM P2CK) and 4µm (2mM) layer height (LH) and line distance (LD) for GelMA

- *We use multiphoton ablation (MPA) to locally degrade GelMA-based (5wt%) hydrogels using a focused laser beam to mimic alveolar and duct-like shapes.*
- *Add sensitizer P2CK (0.5mM-2mM) to increase print speed.*
- *Increase layer height (LH) and line distance (LD to improve ablation quality and increase print speed further (down to minutes).*

High resolution + precise geometrical control



Figure 2: Design (top) and ablated structure (bottom) of ETH Zürich Logo (left, 20µm) and complex duct and alveolar geometry (right, 50µm) in GelMA

Adaptivity to hydrogels

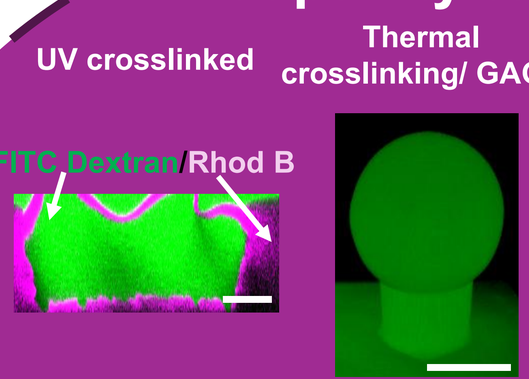


Figure 3: 200 µm cylinder ablated in PEGDA 700 (left, 50µm) and duct and alveolar geometry ablated in dECM from bovine udders + HepMA (right, 50µm)

- *Thermal crosslinks more easily disrupted compared to chemically crosslinked bonds.*
- *Glycosaminoglycans (GAG)-based hydrogels are effective for rapid MPA and can be combined with decellurized Extracellular matrix (dECM).*
- *Faster print speed leads to better ablation.*[1]

Surface properties

Softening

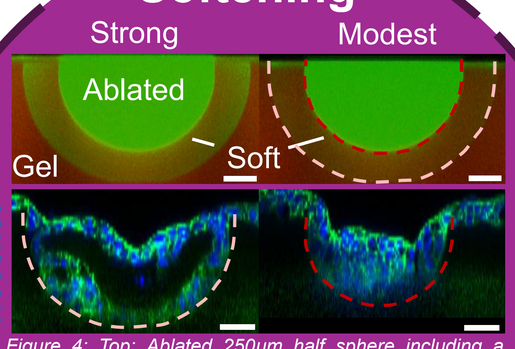


Figure 4: Top: Ablated 250µm half sphere including a strongly softened layer (left, 50mm/s) and a weakly softened layer (right, 250mm/s). Bottom: MCF10a cells on half spheres with softened surface layers. Scale bar 50µm

- *Design soft surfaces*
- *Control softening by scanning speed*
- *Cells infiltrate matrix when softened enough*

Texturing

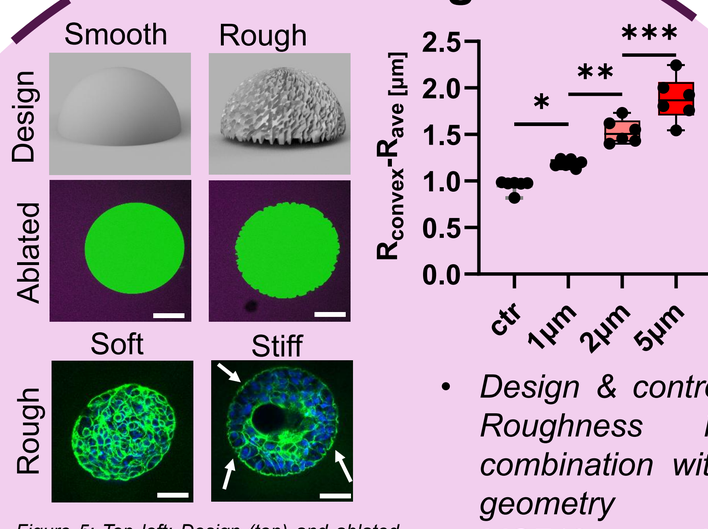


Figure 5: Top left: Design (top) and ablated half sphere (bottom) with smooth (left) or rough surface (right). Top right: control over surface roughness. Bottom: MCF10a cells on soft (left) or stiff hydrogels (right). Arrows indicate remaining roughness. Scale bar 50µm

- *Design & control Roughness in combination with geometry*
- *MCF10a cells deform soft (3.3kPa) but not stiff (6kPa) matrix*

Repeatability

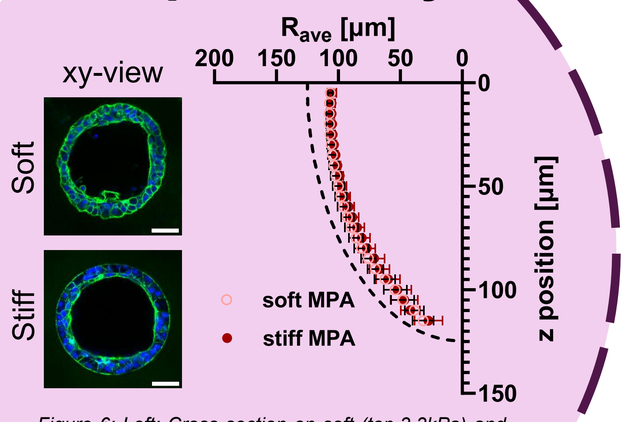


Figure 6: Left: Cross section on soft (top,3.3kPa) and stiff hydrogels (bottom, 6kPa). Scale bar 50µm. Right: Average radius of multiple wells is plotted against z position. wells=2 samples=3.

Duct+alveolar units

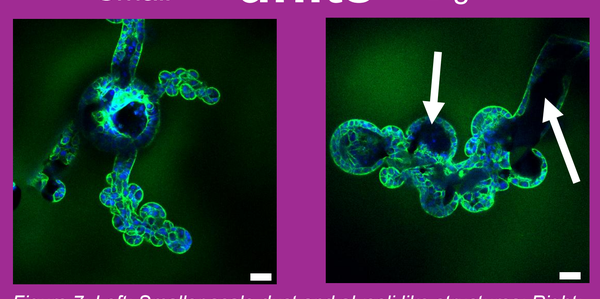


Figure 7: Left: Smaller scale duct and alveoli like structures: Right: Bigger structures. White arrows indicate lumen. Scale bar 50µm

- *MCF10a cells can be guided into more complex shapes*
- *Lumen opening in bigger structures more pronounced in duct like regions*

Outlook

- *We will study how mammary epithelial cells organize and differentiate in 3D.*
- *Influence of curvature on lactation markers*
- *Investigate the combinatory influence of geometry, surface and material properties on epithelial organization and function*

[1]: Learn more:

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