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Geometrically Optimized 3D Printed Mini-Devices for Oral Drug Delivery

Lukas Vaut[1], Kristian E. Jensen[1], Alina J. Andersen[1], Guido Tosello[2], Anja Boisen[1]

[1]Department of Micro- and Nanotechnology, Technical University of Denmark, Denmark

[2]Department of Mechanical Engineering, Technical University of Denmark, Denmark

Introduction: Polymeric microcontainers featuring sizes around 300µm have recently been proposed as a new carrier platform for oral drug delivery. While fabricated with the use of high-throughput fabrication techniques (UV photolithography, hot embossing), the freedom for geometrical design proves to be limited. The shape of the microcontainers is considered to be an important factor for the performance of the carrier system with regards to mucoadhesion and orientation of adhesion. Therefore, the presented research aims at manufacturing the microcontainer in advantageous geometries exhibiting better mucoadhesive properties.

Methods: Computational tools designed for topology optimization of heat conduction gives branching designs and we thus use these tools to generate a strong geometric contrast between the top and bottom of the microcontainers. The microcontainers are then fabricated with the use of a Digital Micromirror Device (DMD)-based micro-Stereolithography 3D printing system (30µm voxel size) in the shape of a small chip with seven microcontainers (diameter: 1400µm) placed on it. The chip is consequently used for analysis of mucoadhesion, carried out using a texture analyzer. This is done by first applying force to push the sample into real porcine intestinal tissue and subsequent release, and thereby the instrument measures the force needed for the separation of sample and tissue.

Results: The computational topology optimization of the microcontainers converted the basic microcontainer design (Fig.1 A1) into a design possessing "hairy" extrusions pointing out from the microcontainer edge (Fig.1 A2). The successfully printed samples (Fig.1 B1, B2) were used for the determination of the mucoadhesive force employing texture analyzer experiments (Fig.1 C). Consequently, the comparison of the average peak force clearly shows a significantly ($p = 0.0022$) higher value for the optimized "hairy" samples towards the non-optimized samples (Fig.1 D).

Conclusion: The obtained results suggest that the geometrical optimization of microcontainers can lead to an improved mucoadhesion and therefore, potentially to a generally improvement of the performance as an oral drug delivery system.

Learning Objectives:

1. Explain why 3D printing was chosen as fabrication method for this work.
2. Discuss how geometrical optimization of the mini-devices might lead to an overall improvement of the performance as a drug carrier system.
3. Identify the major difference in the design approach of this drug delivery system in comparison to others like e.g. nanoparticles, liposomes etc.

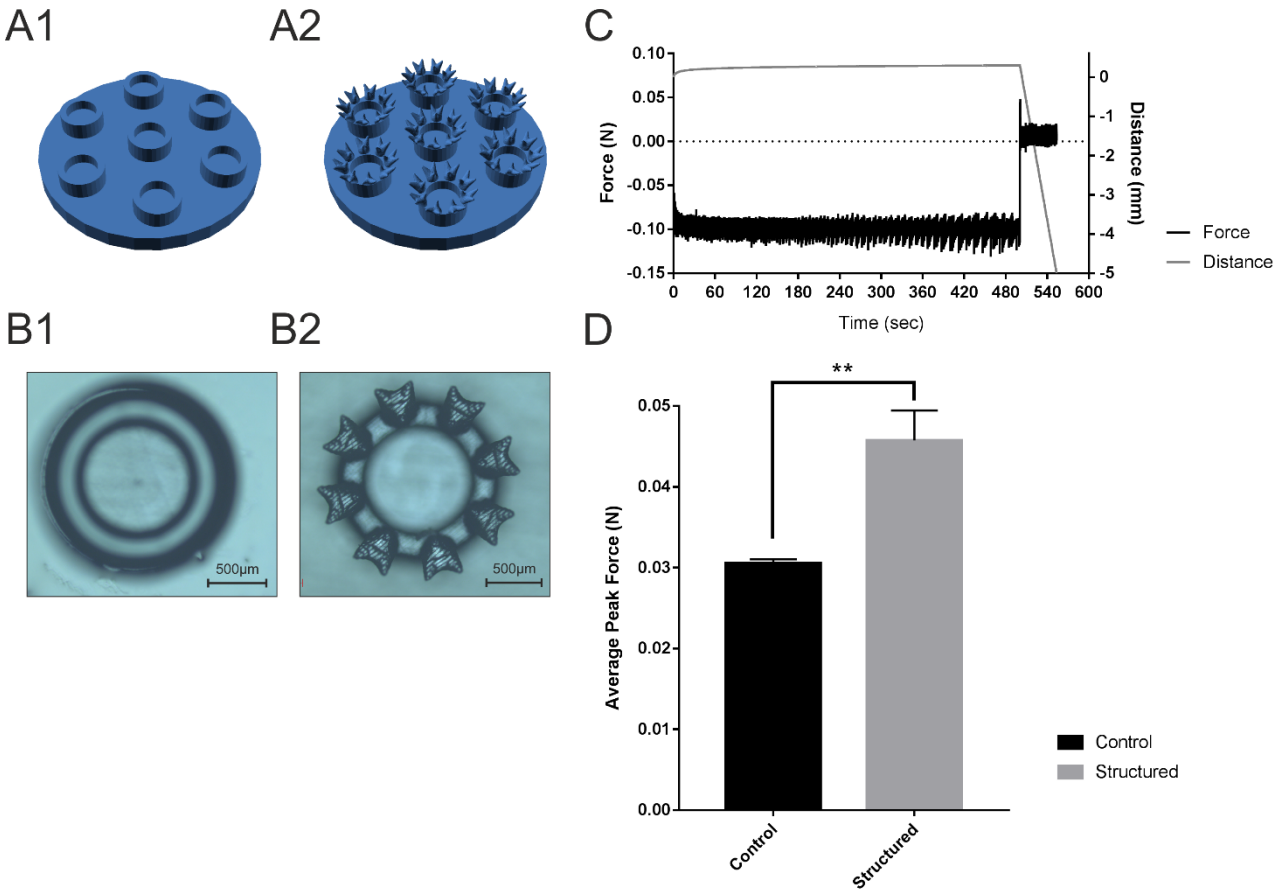

Figure 1 Experimental determination of mucoadhesive properties of topology optimized and non-optimized 3D printed mini-devices (microcontainers) for oral drug delivery. (A1) CAD-drawing of non-optimized sample. (A2) CAD-drawing of topology optimized sample. (B1) Light-microscope image of a single non-optimized microcontainer. (B2) Light-microscope image of a single topology optimized microcontainer. (C) Typical plot of a force measurement of a topology optimized sample using a texture analyzer instrument and porcine intestinal tissue. (D) Comparison of the average peak force of non-optimized samples (Control) and topology optimized samples (Structured) (n=3, **: p=0.0022).