Nils Stein*, Thore Saathoff, Sven-Thomas Antoni, and Alexander Schlaefer

Creating 3D gelatin phantoms for experimental evaluation in biomedicine

Feasibility and evaluation

Abstract: We describe and evaluate a setup to create gelatin phantoms by robotic 3D printing. Key aspects are the large workspace, reproducibility and resolution of the created phantoms. Given its soft tissue nature, the gelatin is kept fluid during inside the system and we present parameters for additive printing of homogeneous, solid objects. The results indicate that 3D printing of gelatin can be an alternative for quickly creating larger soft tissue phantoms without the need for casting a mold.

Keywords: Bioprinting; tissue mimicking materials; gelatine phantom creation; 3D-printing

DOI: 10.1515/CDBME-2015-0082

1 Introduction

Surgical procedures often involve complex interactions between the various instruments and soft tissue. This is reflected by a growing need for training systems allowing physicians to practice interventions in a realistic setting [1]. Similarly, evaluation of novel approaches for minimally invasive and robotic surgery requires reproducible setups for experimental evaluation. For example, to assess the actual accuracy achievable with methods for soft tissue needle navigation, a tissue mimicking phantom is needed [2]. While some aspects of needle tissue interaction can be simulated, the validation of the underlying models is typically performed in soft tissue phantoms [3–5]. A typical material used for phantoms is gelatin, which can be easily adjusted to reflect different mechanical and optical tissue properties, e.g., by adding scattering material. Furthermore, varying gelatin concentrations result in different visco-elastic behaviors [6]. For example, ultrasound elastography experiments may involve anisotropic phantoms with inclusions of variable stiffness or particles.

A common way to create gelatin phantoms is the use of casting molds [7]. However, this approach is rather inflexible and expensive, especially in case of single production. Moreover, more complex, non-convex shapes may not be easily extracted from the mold. Hence, we study creation of gelatin phantoms used an additive 3D printing method. Similar approaches have been considered for bio-printing, including inkjet bioprinting, laser-assisted bio-printing and 3D bioprinting [8–11]. As these devices are typically designed for cell-level applications, their workspace and build volume are small and the speed is relatively low. Moreover, commercial devices like the 3D-Bioplotter (Envisiontec) are expensive .

We propose a different approach to create larger scale gelatin phantoms using a robotic arm. Particularly, we study how to control feeding of material, robot motion, and temperature to create phantoms in comparably short time. Our results indicate that 3D printing can be used to reproducibly create phantoms of more complex shapes.

2 Material and methods

2.1 General setup

In general, our system consists of a robotic arm (UR5, Universal Robots, Denmark), a custom designed print head, a heated gelatin reservoir and a cooled base plate (Figure 1). The print head consists of a 0.55 mm nozzle connected to a double layer tube. The inner layer holds fluid gelatin while warm water is circulated through the outer layer to keep the material fluid. The tubes are connected to a gelatin reservoir with the inner container holding the gelatin embedded in a temperature controlled water filled cylinder. The inner container is made of a syringe and connected to a linear actuator driven by a stepper motor. Motor control is based on the Arduino Uno microprocessor. The base plate is actively cooled to approximately 9 °C to achieve a fast cooling and solidification of the printed gelatin. The

***Corresponding Author: Nils Stein:** Institute of Medical Technology, Hamburg University of Technology, Am Schwarzenberg-Campus 3 E, D-21071 Hamburg, Germany, E-mail: nils.stein@tuhh.de
Thore Saathoff, Sven-Thomas Antoni, Alexander Schlaefer: Institute of Medical Technology, Hamburg University of Technology, Am Schwarzenberg-Campus 3 E, D-21071 Hamburg, Germany, E-mail: thore.saathoff@tuhh.de, antoni@tuhh.de, schlaefer@tuhh.de

UR5 robotic arm has a specified repeatability of 0.1 mm and a maximum speed of 1 m/s.

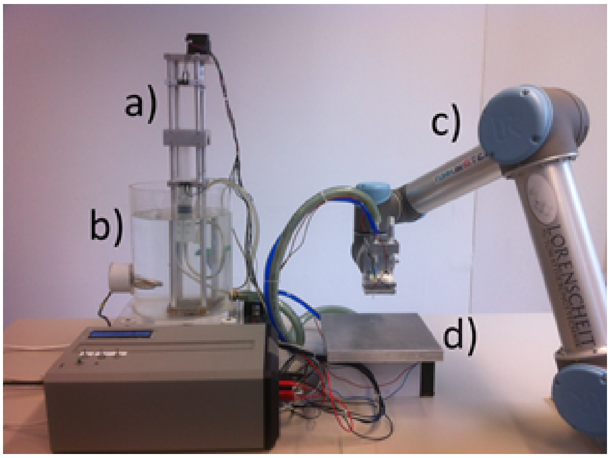

Figure 1: System components: a) extruder with plugged syringe, b) heated water cylinder, c) robotic arm with mounted print head, d) cooled base plate.

2.2 Material handling

Printing gelatin depends on its viscosity, which in turn depends on concentration and temperature [9]. We considered these two parameters and studied gelatin samples with a concentration of 2.5 %, 3.3 %, 5 % and 10 % at temperatures ranging from 15 to 35 °C to determine their melting and their gelling points.

2.3 Control parameters

To achieve even layer thickness, material flow $V^{'}(s)$ and robot movements need be coordinated. Considering a rectangular line profile and the parameters width w, layer height h, robot velocity v, and extruder speed $s$we get

$$V^{'}(s) = w \cdot h \cdot v$$

The flow rate denotes the extruded volume per second and can be calculated as

$$V^{'}(s) = \left(\frac{d}{2}\right)^2 \cdot \pi \cdot s \cdot \frac{h}{N}$$

with d the inner nozzle diameter, h pitch of the threaded rod, and N the number of steps per turn.

2.4 Printing procedure

We consider shapes given as triangulated surface models, e.g., in the STL format [12]. The models are converted into slices along the z-axis, and the resulting G-code is then interpreted to control the robot motion. In our current setup, we keep speed and flow rate constant. To allow for continuous robot motion, print patterns like the one illustrated in Figure 2 are used, with the orientation of the lines changes by 90 degrees for every layer.

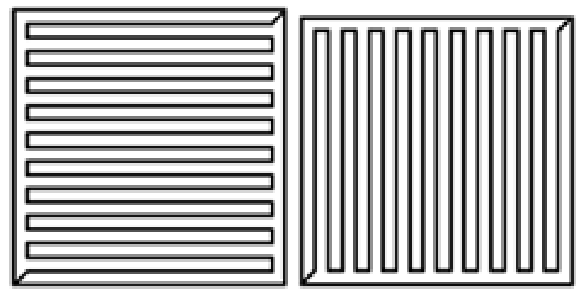

Figure 2: Print pattern to fill a square area by parallel lines. For solid phantoms, the orientation of the pattern is rotated for every layer.

3 Results

3.1 Material characteristics

Figure 3 shows results of experiments studying the melting and gelling temperatures. The phase changes successively from solidified (5) over alternating gel strengths (1-4) to completely liquid (0). The curves show a hysteresis with an offset of 5-8 °C between melting and gelling point. For printing this means that the material first has to be melted before the temperature can be decreased by about 5 °C without solidification.

Figure 4 illustrates the importance of temperature adjustment, as the surface tension leads to drop formation and, thus, to poor printout quality, when the viscosity decreases too much. Here, the robot velocity increases from 5 mm/s (outer lines) up to 50 mm/s (inner lines) by steps of 5 mm/s, while the flow rate remains at 8.25 mm/s. However, at well adjusted temperatures, we obtain sharp, continuous lines. A further improvement is recognizable by the addition of small amounts of surfactants.

The setup was applied to 3D-printing of cuboids using a line width and layer height of 0.5 mm and 0.8 mm, respectively. The robot velocity was 20.6 mm/s. Moreover, different robots velocities were evaluated to test printing

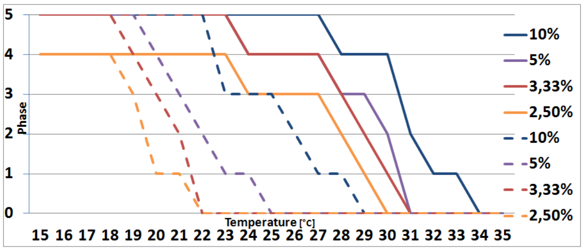

Figure 3: Variation of gelatin samples of different concentrations while heating resp. cooling, evaluated in successive steps from solidified (5) to liquid (0), continuous lines: melting, interrupted lines: gelling.

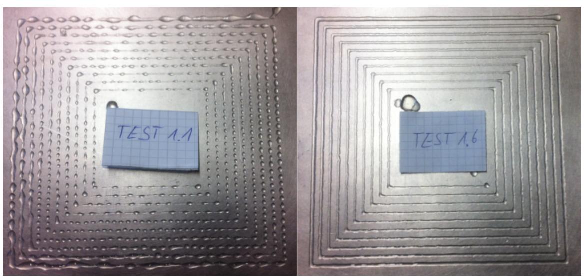

Figure 4: Left: poor print quality due to surface tension and drop formation, right: good print quality characterized by continuous lines.

with different resolution with a layer height and line width between 0.5 and 1.0 mm. Figure 5 shows 3D-printed solid cuboids with 0.5 and 1.0 mm resolution, respectively. The line pattern is visible but there are no air inclusions or material overlaps.

3.2 Repeatability and resolution

To assess the repeatability of the printing, a cuboid with target dimensions 21.5 mm x 21.5 mm x 20 mm was printed 5 times. Table 1 summarizes measurements.

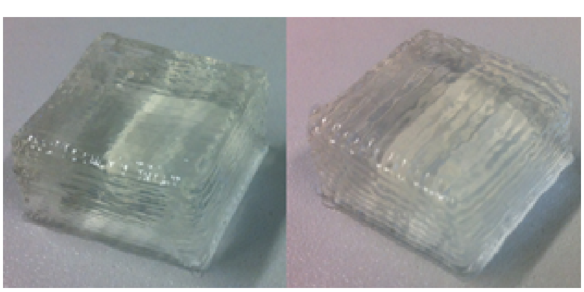

Figure 5: 3D-printed cuboids, illustrating the homogenous material distribution. Left: phantom with 0.5 mm line width. Right: phantom with 1.0 mm line width.

Table 1: Evaluation of repeatability.

Print no.	Evaluated quantities		
	Length [mm]	*Height [mm]*	*Weight [g]*
1	22	18.5	9.45
2	22	19	9.47
3	22	19	9.72
4	22	19	9.43
5	22	19	9.64

Measurement using an optical coherence tomography (OCT) system to image gelatine printouts with titanium-oxide applied in between layers illustrate that the desired layer height of 0.5 mm is closely matched (Figure 6).

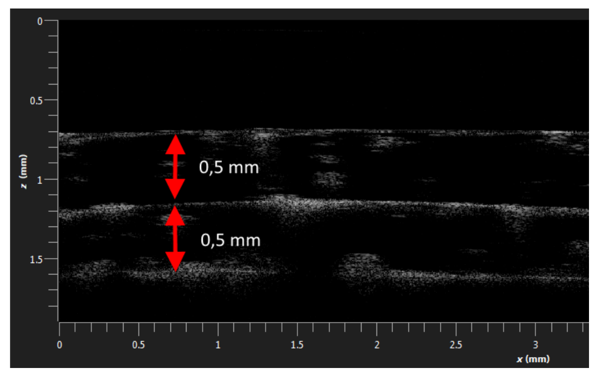

Figure 6: OCT plot, highlighting titanium-oxide in between layers, confirming a layer thickness of 0.8 mm.

3.3 Printing of complex phantoms

Also phantoms with much higher grade of complexity, designed by CAD-software, are creatable. The generated code can be either copied and executed at the Panel or sequentially transmitted via network for real-time control. Figure 7 shows the upper part of a prostate model as STL-model (left) and in comparison as created phantom (right) with a resolution of 0.5 mm.

4 Conclusion

Printing of soft materials is a challenging, as the success in creating solid objects depends on several parameters. Our results show that gelatin phantom creation by robotic arm based 3D-printing is feasible. Flexibly shaped phantoms can be created with variable resolution and flow rate, i.e.,

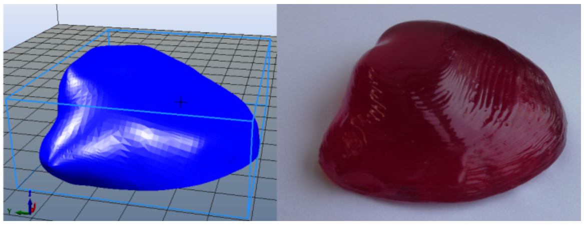

Figure 7: Phantom creation from STL-file. Left: visualized STL-model. Right: printed phantom with 0.5 mm resolution.

different speed. While not yet comparable to fused deposition modelling of solid filament, the printing results in reproducible solid and homogeneous objects. Advantages include the large workspace and the direct printout, which allows for rapid creation of individual phantoms. In contrast to casting the soft tissue phantoms could be quickly created from medical image data, facilitating the study of actual shapes, e.g., in surgical training and for evaluation of minimal invasive technology.

Author's Statement

Conflict of interest: Authors state no conflict of interest. Material and Methods: Informed consent: Informed consent is not applicable. Ethical approval: The conducted research is not related to either human or animals use.

References

[1] J. Adermann, N. Geißler, L. E. Bernal, S. Kotzsch, W. Korb, "Development and validation of an artificial wetlab training system for the lumbar discectomy," *Eur Spine J*, 23(9):1978-83, 2014

[2] C. Otte, G. Hüttmann, G. Kovcs, A. Schlaefer, "Phantom validation of optical soft tissue navigatin for Brachytherapy," MICCAI workshop on Image-Guidance and Multimodal Dose Planning in Radiation Therapy, 2012

[3] M. Abayazid, R. J. Roesthuis, R. Reilink, S. Misra, "Integrating Deflection Models and Image Feedback for Real-Time Flexible Needle Steering," *IEEE Transactions on Robotics*, 29(2):542-553, 2013

[4] J. op den Buijs, H. H. G. Hansen, R. G. P. Lopata, C. L. de Korte, S. Misra, "Predicting Target Displacements Using Ultrasound Elastography and Finite Element Modeling," *IEEE Transactions on Biomedical Engineering*, 58(11):3143-3155, 2011

[5] M. Kavitha, M. R. Reddy, S. Suresh, "Modelling, Design and Development of Tissue mimicking phantoms for Ultrasound Elastography," IEEE EMBS Conference on Biomedical Engineering and Science, Langkawi, 2012

[6] R. Schrieber, H. Gareis, "Gelatine Handbook: Theory and Industrial Practice," WILEY-VCH Verlag GmbH & Co. KGaA, 2007.

[7] B. Wang, B. Stender, T. Long, Z. Zhang, A. Schlaefer, "An approach to validate ultrasound surface segmentation of the heart," *Biomed Tech (Berl)*, 2013.

[8] B. Duran, L. A. Hockaday, K. H. Kang, J. T. Butcher, "3D Bioprinting of Heterogeneous Aortic Valve Conduits with Alginate/Gelatin Hydrogels," *Journal of Biomedical Materials Research*, Vol. 101A, 5:1255-1264, 2013

[9] B. Guillotin, F. Guillemot, "Cell Patterning technologies for Organotypic Tissue Fabrication," *Trends Biotechnol*, 29:183-190, 2011

[10] V. Mironov, N. Reis, B. Derby, "Bioprinting: A Beginning," *Tissue Eng*, 12:631-634, 2006

[11] A. Sirinterlikci, L. Walk, "Bioprinting, Science or Fiction?," *Medical Manufacturing*, 51-53, 2014

[12] P. Fastermann, "3D-Druck/Rapid Prototyping," Springer Vieweg, 2012.