Solid Freeform Fabrication 2019: Proceedings of the 30th Annual International
Solid Freeform Fabrication Symposium – An Additive Manufacturing Conference
Reviewed Paper

Multi-Material Soft Matter Robotic Fabrication: A Proof of Concept in Patient-specific Neurosurgical Surrogates

Chih-Chiang M. Chang*, Thomas E. Angelini*, Frank J. Bova†, Scott A. Banks*

*Department of Mechanical and Aerospace Engineering, University of Florida, Gainesville, FL 32611
†Department of Neurosurgery, University of Florida, Gainesville, FL 32611

Abstract

Soft matter 3D printing provides the capability to fabricate 3D structures by depositing hydrogel inks in granular gel support material. To date, there has been little work reported using this method to fabricate complex-shaped models with multiple materials in a timely fashion. The aim of this project is to introduce recent research of multi-material soft-matter extrusion and deposition for fast freeform fabrication of 3D structures, and to present a process for automating the fabrication of patient-specific neuro-anatomic models for surgical training. A compact design of multi-material extrusion printhead is described, which is capable of fabricating 3D structures from multiple inks. This approach provides a fast and efficient way to convert a virtual volumetric model into a physical extruded hydrogel structure using the multi-material soft-matter robotic fabrication system. In addition to fabrication of neurosurgical phantoms, the capabilities we describe may be useful in broader application contexts such as general soft matter robotic fabrication, pharmaceutical testing, and extrusion-based bioprinting.

Key words

Soft matter fabrication, 3D Printing, Robotics, Additive manufacturing, Multi-Material

Introduction

Modern 3D printing technology, also known as additive manufacturing (AM), has been developed for decades, and has been rapidly improving because of advancing computer-aid design (CAD) software, decreased cost of materials and equipment, and more applications. 3D printing in manufacturing industry and consumer markets has been increasing largely because of the ability to fabricate arbitrary shapes. 3D printing has also been commonly applied in biomedical fields and modern research, for applications including scaffolds for tissue engineering, artificial human organs, and anatomical models for surgeries (a.k.a. surgical phantoms)[1–3].

In recent work a modern 3D printing technology, soft matter 3D printing (a.k.a. Direct Ink Writing), has utilized granular gel as supporting material in 3D printing for hydrogel polymer extrusion. Soft matter 3D printing provides not only the ability to fabricate models with soft-touch textures, but also provides great flexibility for fabricating complex-shaped models without huge waste of supporting materials [4].

Most of the current soft matter 3D printing systems and fused filament fabrication (FFF) systems share the standard 3D printing architecture: a material extruder and a Cartesian motion platform. The main difference between these is the printing material and material extruder. Unlike FFF, soft matter 3D printing usually uses a soft matter extruder with liquid polymer, hydrogel, living cells, etc., while FFF uses a hot-end filament extruder with plastic filament. Soft matter extruders commonly consist of a syringe pump and a blunt-tip needle, and are built as a printhead assembly of the 3D printer, such as a modern bioprinter. Most of the soft matter extruders feature low-volume syringes and small-diameter nozzles/needles for printing small objects with high precision and resolution [5–7]. There are two major limitations on this kind of syringe pump setup: one is soft matter extruder is located at the end-effector of the 3D printer, and the other is the printing volume [8]. Placing the soft matter extruder at the printhead increases the end-effector mass and inertia and affects the dynamic performance of the 3D printer, potentially resulting in unwanted vibrations or decreased accuracy or robot motion repeatability [9]. The printing volume is usually limited by the syringe size (usually 1 ml or smaller) on most bio-printers because of the need to reduce the carriage payload at the printhead for high-precision motion, and the ease of high-precision extrusion control with rigid small-bore syringes.

Multiple material 3D printing has been reported with promising results in FFF [10,11], bioprinting [12–16], and soft matter 3D printing [17]. Extrusion-based material deposition is one of the most common methods for multi-material 3D printing. There are several different setups of multi-material extrusion 3D printing, such as multiple-nozzle setups, coaxial nozzle setups, and bundle-needle methods. **Multiple-nozzle** setups incorporate multiple separate printheads on a 3D printing system. Those printheads are mechanically co-registered for depositing selected inks at desired locations [12–14]. Although these systems can potentially scale up to a large number of different materials, the printing time of this technique inevitably increases as more printheads are added. Based on the nature of the multi-nozzle mechanical design, it would be difficult to achieve both fast switching among different nozzles and simultaneously depositing different inks. **Coaxial nozzle setups** were designed as an assembly of paired core-sheath needle tips, and often used to extrude multiple blended bioinks and fabricate hollow alginate filaments [16,18–20]. This setup enables multiple material extrusion for precise cell-laden structures and hollow filament fabrication, but is limited to only blending multiple materials together rather than depositing dissimilar materials separately with the same resolution. **Bundle-needle** setups have been realized by attaching multiple needles together and encasing the needles in a larger-bore needle to form a small stiff tip [21]. This design may achieve faster deposition speeds than other multi-material setups while not significantly increasing the cost of the system nor the complexity of the printhead fabrication.

To achieve the goal of multi-material soft matter 3D printing for fabricating patient-specific anatomical models in a timely manner, we require fast robotic motion of the printhead (i.e. the end effector of the 3D printing platform), using a soft matter extrusion system providing fast, accurate, and multi-material extrusion with large-volume reservoirs. A soft matter 3D printing system satisfying these requirements has not been reported previously. In this article, we report a soft matter 3D printing system with multi-material soft matter extrusion for fabricating soft-textured anatomical models, such as soft tissues, blood vessels, nerves, etc. It includes a 4-axis robotic arm, a large-volume-closed-loop-pressure-controlled hydrogel extruding system for multi-material extrusion, and a high-level controller for coordinating and synchronizing the robot and the pump. The feedback-controlled hydrogel extrusion system achieves good gel deposition with compact design on the printhead, which reduces the weight at the robot end effector, provides better dynamic performance, and provides the feasibility for use with any robotic platforms.

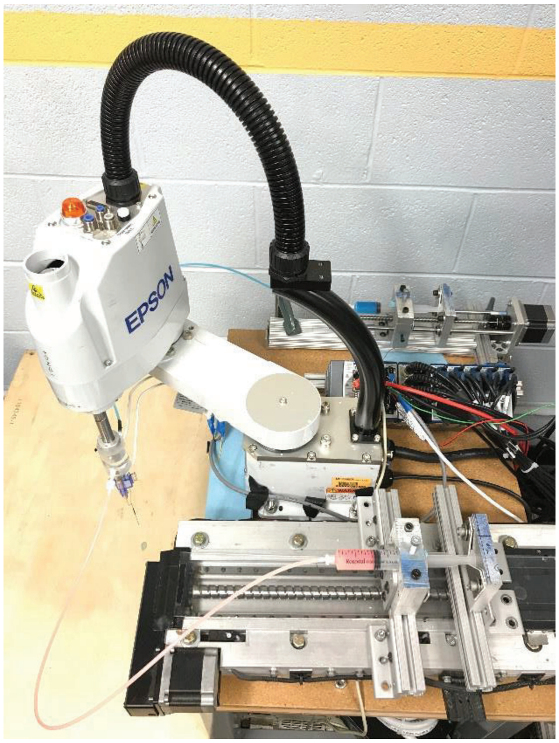

Figure 1. Robotic soft matter 3D printing system setup.

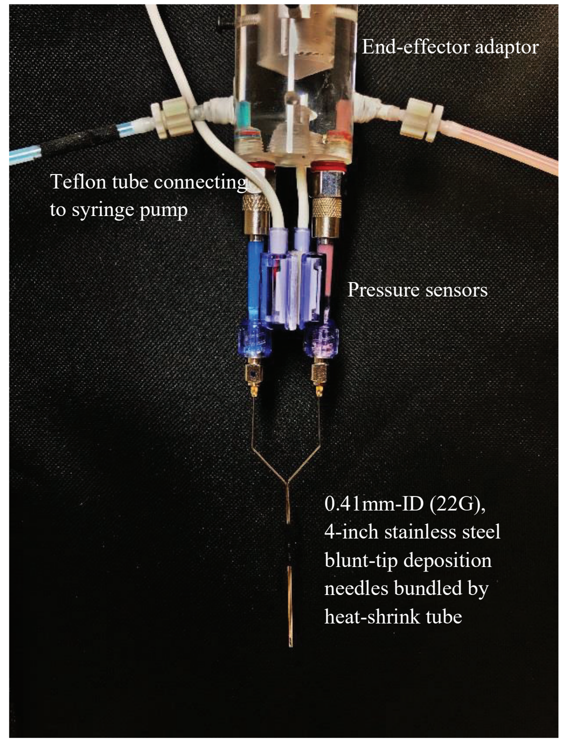

Figure 2. A dual-tip end-effector adaptor for multiple hydrogel extrusion with pressure feedback control on flowrate.

Methods and Materials

In this section, we provide a general description of the multi-material soft matter robotic fabrication platform for fabricating soft-tissue-like objects by extruding liquid polymers in granular gel. To investigate the idea of fast printhead motion and multi-material soft matter extrusion, a 4-axis SCARA industrial robot and an "off-the-end-effector" (Bowden-style) soft matter extrusion system were utilized as the platform to fabricate soft-textured models.

Hardware and Software

The new platform includes an Epson SCARA 4-axis robotic arm driven by Epson RC-700 controller, and a closed-loop-pressure-controlled hydrogel extrusion system (Figure 1). The hydrogel extrusion system consists of two custom stepper-motor-driven syringe pumps, an end-effector adaptor incorporating two pressure sensors and two blunt-tip needles, and Teflon tubes connecting the syringe pumps and the end-effector adaptor (Figure 2).

The user interface and code for high-level coordination of robot and extrusion system were implemented in LabVIEW (National Instruments, Austin, TX). We use an open-source slicing engine (Slic3r) for 3D printing tool-path planning, and for setting parameters including layer thickness and material retraction on the hydrogel extrusion system.

Soft Matter Preparation

The supporting material and printing ink for soft matter 3D printing are prepared following the methods described in Bhattacharjee et al. [4,22]. To prepare the soft carbomer granular gel medium, the support material, 0.15 % (w/w) Ashland™ 980 Carbomer is suspended in ultrapure water and 10N NaOH. For the preparation of the printing inks, 25% (w/w) Polyethylene glycol (PEG) 35000 is suspended in ultrapure water. For multi-material printing, the inks were pigmented with acrylic paints. Both were homogeneously mixed at 3500 rpm for 2 minutes in a FlackTek DAC 150 SpeedMixer before they were degassed.

Soft Matter Robotic Fabrication Process

Complex-shaped models were used to demonstrate capabilities for fabricating complex anatomy and geometries. The 3D models were either designed and created using SolidWorks (Dassault Systèmes) or segmented from medical imaging using ITK-Snap. All the 3D models were exported in the STL file format, and were processed by Slic3r or other slicing engines, and sliced into layers with 0.25 mm thickness to generate G-code instructions for 3D printing. G-code files were then post-processed by MATLAB (MathWorks, Inc.), and sent to the LabVIEW Interface for printing (Figure 3).

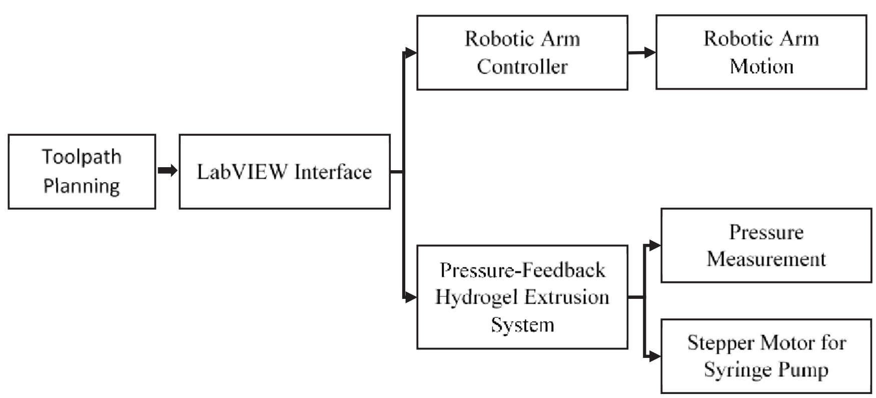

Figure 3. System process

Hydrogel printing inks were first drawn into a 20-ml disposable syringe. The syringe was then connected with the Teflon luer-lock connecting tube to the end-effector adaptor and mounted onto the stepper-motor-driven syringe pump. An open-top container to hold the printed part was filled with the carbomer granular gel supporting material, and manually placed on the build platform, which is a flat surface that is mechanically isolated from the soft matter 3D printing platform. The needle tip of the soft matter extruder was positioned at the center of the granular gel container in x and y and near the bottom of the container in z before printing.

Hydrogel Extrusion System for Single- and Multi-Material Extrusion

To achieve fast dynamic response and low vibration at the end effector of robotic platform, an "off-the-end-effector" (Bowden-style) [23] soft matter extrusion system is used. In order to compensate for the mechanical compliance of the Teflon connecting tube and viscous hydrogel, and to get high-quality soft matter 3D printing, closed-loop control of hydrogel extrusion pressure was implemented to provide consistent extrusion rate and eliminate general 3D printing issues, such as leaking nozzle/needle, stringing, and oozing [24]. Flow rate is proportional to the tip pressure measurement [25]:

$$Q = \frac{\Delta P \, \pi r^4}{8 \mu L} \quad \text{(Eq. 1)}$$

where Q is the volumetric flow rate (mm^3/s), ΔP is the pressure difference between the two ends of the needle (psig), r is the needle radius (mm), μ is the dynamic viscosity (centipoise (cP) = millipascal seconds (mPa·S)), and L is the length of the needle (mm).

A PID controller (Figure 4.) was employed as a highly responsive and stable pressure controller. The proportional, derivative and integral gains are tuned for particular setup (needle diameter, syringe size, hydrogel viscosity, length of the Teflon connecting tube, motor performance, etc.) for optimal performance. For characterizing the performance of the soft matter extrusion system, a well-characterized setup in Table 1 is used.

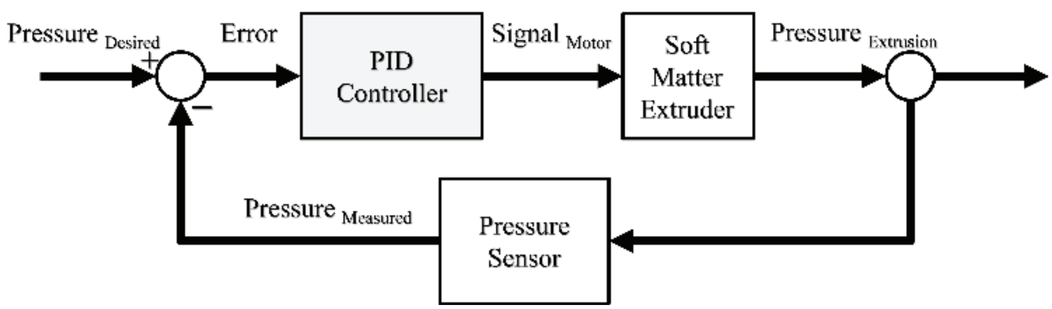

Figure 4. Block diagram representation of the closed-loop control of pressure feedback soft matter extrusion

Needle	Single-material: 2-inch blunt-tip needle with 0.5-mm-ID (inner diameter) Multi-material: 4-inch blunt-tip needles with 0.41-mm-ID (inner diameter)
Syringe	20 ml disposable syringe
Connecting tube	2 feet
Hydrogel viscosity	~200 CP
Motor holding torque	22.6 N-cm / 32 oz-in
Lead screw	Diameter: 8mm, Lead: 2mm

Table 1. Parameters for system setup

To achieve both single- and multi-material extrusion, we designed a new end-effector adaptor, which allows to connect with two syringe pumps and two pressure sensors. Two needles were bent and bundled with heat-shrink tube, and were attached to two pressure sensors (Figure 2). Hydrogel inks are extruded through the two needles by closed-loop pressure control.

Results

Single Material Printing

Ultimately, the aim for our soft matter fabrication system is creation of neurosurgical surrogates or any vascular-mimetic structures with soft-tissue-like materials. Therefore, a variety of hollow objects were printed to demonstrate this capability (Figure 5). We show a variety of test objects fabricated using PEG hydrogel, which include a CAD model of double-helical tubes, a CAD-generated blood-vessel model, a segmented blood-vessel model, and CAD models for UF letters. These models were printed using a 0.5-mm blunt-tip needle with a layer of 0.25mm, using settings chosen to balance build rate and build quality. Each structure was printed individually in a timespan ranging from several minutes to half an hour, depending on model size, complexity, and the continuity of printing paths. Table 2 provides a summary of statistics of these models including their volumes and average volumetric print rate. Objects where continuous paths predominate result in 4x faster volumetric build rates (Table 2).

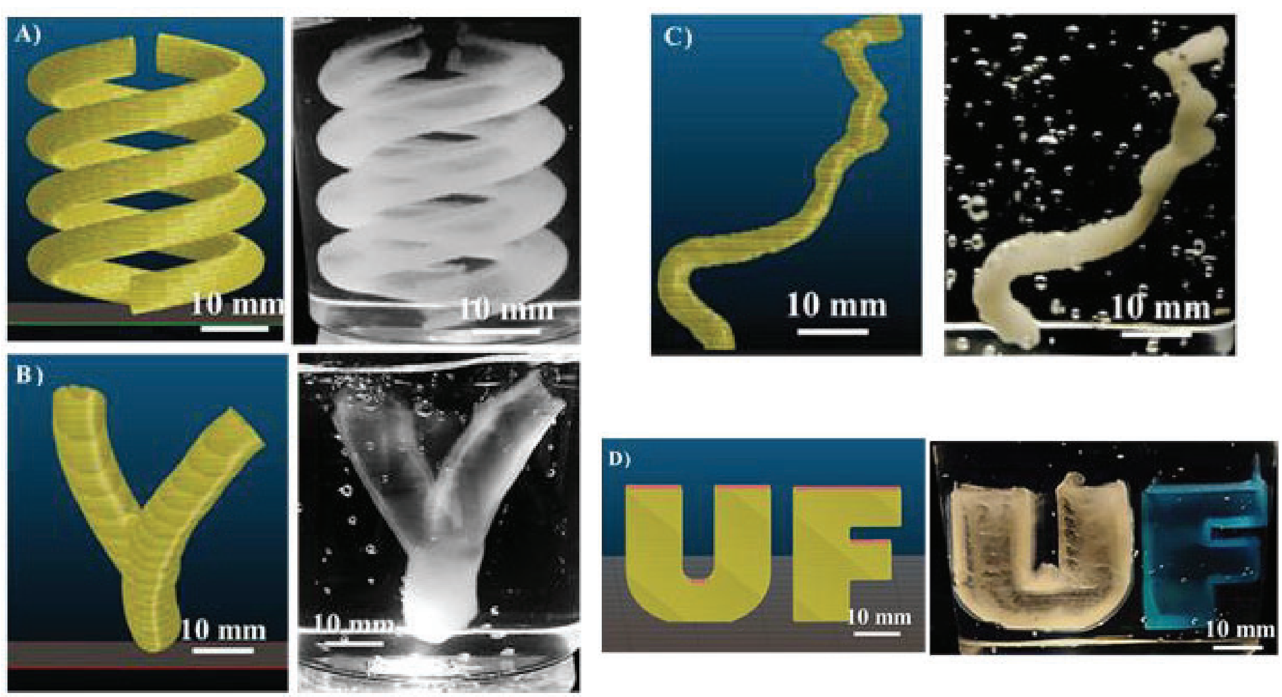

Figure 5. Printing results for single-material printing: (A) dual helix, (B) bifurcating vessel, (C) life - like blood vessel, (D) UF letters

Part	Volume (mm3)	Layer resolution (mm)	Print time (s)	Average build rate (cm^3/hr)
(CAD) Helix	951.35	0.25	1800	1.9
(CAD) Blood vessel	167.86	0.25	270	2.24
(CAD) Alphabets	491.27	0.25	450	3.93
Segmented Blood vessel	414.61	0.25	210	7.11

Table 2. Summary of printing results (single-material)

Multiple Material Printing

After establishing the single-material soft matter fabrication process, we subsequently expanded the soft matter extrusion system to multiple materials to further demonstrate the potential of the pressure-feedback extrusion on soft matter fabrication. This technique will potentially make soft matter fabrication possible for printing neurosurgical surrogates and improving current biofabrication processes. Unlike the single-material soft matter extrusion, an on-off switching between the materials is required for multi-material soft matter extrusion. Switching between materials can be completed within a few seconds by pressure-feedback control on the soft matter extrusion flowrate.

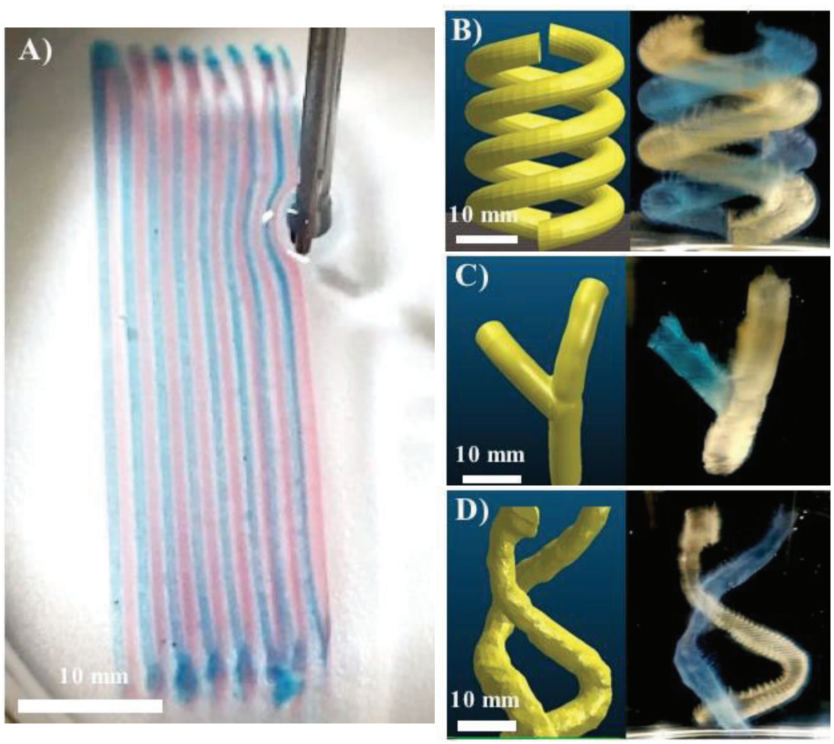

Figure 6. Printing examples with two materials, showing the CAD model and the printed part: (A) 2-material sheet, (B) dual helix, (C) bifurcating vessel, (D) life-like blood vessel.

Part	Volume (mm3)	Layer resolution (mm)	Print time (s)	Average build rate (cm^3/hr)	Versus single-material
(CAD) Helix	951.35	0.25	2100	1.63	1.9
(CAD) Blood vessel	167.86	0.25	1500	0.72	2.24
Segmented Blood vessels	674.41	0.25	1800	1.35	7.11

Table 3. Summary of printing results (multi-material)

To demonstrate the ability to print multi-material structures, we used similar CAD models for single-material printing, but modified them for multi-material printing: a two-material sheet-like 2D structure, a CAD model of double-helical tubes, a CAD-generated blood-vessel model, and a segmented blood-vessel model. It should be noted that this study on the multi-material setup has been conducted using only one material, that is PEG, colored with different paints. It simplifies the control on the extrusion rate, and also the rheological properties between the ink and supporting gel. These multi-material prints show build times 2x-7x longer than the single-material prints of the same physical objects (Table 3).

Discussion

This study was designed to investigate the capability of the multi-material soft matter 3D printing system for directly fabricating complex-shaped soft-tissue-like models with single and multiple materials in a timely manner. We found the use of this new platform, which consists of a SCARA robot arm and a pressure-controlled hydrogel extrusion system, enhanced the current capability for hydrogels extrusion and printing soft-textured objects with multiple materials. By implementing fast robotic motion and pressure-controlled soft matter extrusion, complex-shaped 3D geometries can be printed in less than an hour. This system is by far the first system that has the capability for fast printing nozzle motion and pressure-feedback-controlled hydrogel extrusion comparing to conventional extrusion-based 3D printing platforms for soft matter 3D printing [26]. To get optimal hydrogel extrusion, further investigations on modeling and experiments on the relation between extrusion pressure, nozzle moving speed, and filament diameter is needed [27,28]. Nonetheless, these results suggest the new soft matter robotic fabrication system has a great potential for fast fabricating patient-specific anatomical models in the near future.

Based on the single-material printing results in Table 2, the segmented blood vessel model (Figure 5C) has the highest average printing rate, and the helix model (Figure 5A) has the lowest. Although the alphabet model (Figure 5D) has only a slightly larger volume than the segmented blood vessel model, it took more than twice the printing time. This shows that the printing time does not totally depend on the volume of the model, but also depends on path complexity and path discontinuities of the model. Further refinements will address the relation between the model geometric complexity and the printing rate.

For multi-material printing results in Table 3, it shows that it takes longer to print models with multiple materials compared to using only one material. The main reason is because longer needles were used for making the bundled extrusion tip. According to Hagen-Poiseuille's equation (Eq. 1), higher pressure is required for achieving the same flowrate using longer needles. Practically, this requires longer times for priming and retracting the printing ink for switching between the two materials. To shorten the time for multi-material printing, further investigation is needed on path planning strategies that require less switching between materials.

Conclusions

In summary, we have demonstrated a new multi-material soft matter extrusion system for printing soft-tissue-like models with two materials using polymer hydrogels. This system will serve as an example of how soft matter fabrication may be improved from single to multiple materials. To achieve the true potential of quickly fabricating large volume objects with soft-tissue-like materials, it will be necessary to develop an advanced large-volume hydrogel dispensing system, improved toolpath planning algorithms, and further evaluate the coupling between the dynamics of fast robotic motion and hydrogel extrusion. Nevertheless, the capability to fabricate soft-textured and complex-shaped objects in 5–40 minutes allows us to conceptualize the ideas for fast fabrication of patient-specific anatomical models.

Acknowledgments

The authors extend thanks to University of Florida Opportunity Seed Fund and the McJunkin Family Charitable Foundation for supporting this project.

References

1. Rengier, F.; Mehndiratta, A.; Von Tengg-Kobligk, H.; Zechmann, C.M.; Unterhinninghofen, R.; Kauczor, H.U.; Giesel, F.L. 3D printing based on imaging data: Review of medical applications. *Int. J. Comput. Assist. Radiol. Surg.* **2010**, *5*, 335–341.
2. Kurenov, S.N.; Ionita, C.N.; Sammons, D.; Demmy, T.L. Three-dimensional printing to facilitate anatomic study, device development, simulation, and planning in thoracic surgery. *J. Thorac. Cardiovasc. Surg.* **2015**, *149*, 973–979.e1.
3. Klein, G.T.; Lu, Y.; Wang, M.Y. 3D printing and neurosurgery--ready for prime time? *World Neurosurg.* **2013**, *80*, 233–5.
4. Bhattacharjee, T.; Zehnder, S.M.; Rowe, K.G.; Jain, S.; Nixon, R.M.; Sawyer, W.G.; Angelini, T.E. Writing in the granular gel medium. *Sci. Adv.* **2015**, *1*, e1500655.
5. Truby, R.L.; Lewis, J.A. Printing soft matter in three dimensions. *Nature* **2016**, *540*, 371–378.
6. Mandrycky, C.; Wang, Z.; Kim, K.; Kim, D.H. 3D bioprinting for engineering complex tissues. *Biotechnol. Adv.* **2016**, *34*, 422–434.
7. Hinton, T.J.; Jallerat, Q.; N., P.R.; Park, H.J.; Grodzicki, M.S.; Shue, H.-J.; Ramadan, H.M.; Hudson, A.R.; Feinberg, A.W. Three-dimensional printing of complex biological structures by freeform reversible embedding of suspended ... Three-dimensional printing of complex biological structures by freeform reversible embedding of suspended hydrogels. **2015**.

8. Pusch, K.; Hinton, T.J.; Feinberg, A.W. Large Volume Syringe Pump Extruder for Desktop 3D Printers. *HardwareX* **2018**.
9. Hillsley, K.L.; Yurkovich, S. Vibration control of a two-link flexible robot arm. *Proceedings. 1991 IEEE Int. Conf. Robot. Autom.* **1991**, *3*, 212–216.
10. Hergel, J.; Lefebvre, S. Clean color: Improving multi-filament 3D prints. *Comput. Graph. Forum* **2014**, *33*, 469–478.
11. Sitthi-amorn, P.; Lan, J.; Wang, W. MultiFab : A Machine Vision Assisted Platform for Multi-material 3D Printing.
12. Choi, S.H.; Cai, Y.; Cheung, H.H. Reconfigurable Multi-material Layered Manufacturing. *Comput. Aided. Des. Appl.* **2015**, *12*, 439–451.
13. Khalil, S.; Nam, J.; Sun, W. Multi-nozzle deposition for construction of 3D biopolymer tissue scaffolds. *Rapid Prototyp. J.* **2005**, *11*, 9–17.
14. Ozbolat, I.T.; Chen, H.; Yu, Y. Development of "Multi-arm Bioprinter" for hybrid biofabrication of tissue engineering constructs. *Robot. Comput. Integr. Manuf.* **2014**, *30*, 295–304.
15. Merceron, T.K.; Burt, M.; Seol, Y.J.; Kang, H.W.; Lee, S.J.; Yoo, J.J.; Atala, A. A 3D bioprinted complex structure for engineering the muscle-tendon unit. *Biofabrication* **2015**, *7*.
16. Zhang, Y.; Yu, Y.; Ozbolat, I.T. Direct Bioprinting of Vessel-Like Tubular Microfluidic Channels. *J. Nanotechnol. Eng. Med.* **2013**, *4*, 020902.
17. Ryan, J.R.; Chen, T.; Nakaji, P.; Frakes, D.H.; Gonzalez, L.F. Ventriculostomy Simulation Using Patient-Specific Ventricular Anatomy, 3D Printing, and Hydrogel Casting. *World Neurosurg.* **2015**, *84*, 1333–1339.
18. Zhou, Y.; Fragasso, A.; Liu, W.; Zhong, Z.; Jin, X.; Khademhosseini, A.; Maggio, L.; Hu, N.; Miri, A.K.; Zhang, Y.S. Coaxial extrusion bioprinting of 3D microfibrous constructs with cell-favorable gelatin methacryloyl microenvironments. *Biofabrication* **2017**, *10*, 024102.
19. Gao, Q.; He, Y.; Fu, J. zhong; Liu, A.; Ma, L. Coaxial nozzle-assisted 3D bioprinting with built-in microchannels for nutrients delivery. *Biomaterials* **2015**, *61*, 203–215.
20. Zhang, Y.; Yu, Y.; Chen, H.; Ozbolat, I.T. Characterization of printable cellular micro-fluidic channels for tissue engineering. *Biofabrication* **2013**, *5*.
21. Rocca, M.; Fragasso, A.; Liu, W.; Heinrich, M.A.; Zhang, Y.S. Embedded Multimaterial Extrusion Bioprinting. *SLAS Technol.* **2018**, *23*, 154–163.
22. Schodowski, E.G.; O'Bryan, C.S.; Angelini, T.E. *Interfacial Instabilities in soft matter 3D Printing*; 2017;
23. Griffey, J. Chapter 2: The Types of 3-D Printing. *Libr. Technol. Rep.* **2014**, *50*, 8–12.
24. Mcdonald, K.T. Leaky Syringe. **2014**, *08544*, 1–4.
25. Vo, A.; Doumit, M.; Rockwell, G. The Biomechanics and Optimization of the Needle-Syringe System for Injecting Triamcinolone Acetonide into Keloids. *J. Med. Eng.* **2016**, *2016*, 1–8.
26. Chameettachal, S.; Yeleswarapu, S.; Sasikumar, S.; Shukla, P.; Hibare, P.; Bera, A.K.; Sai, S.; Bojedla, R.; Pati, F. 3D Bioprinting : Recent Trends and Challenges REVIEW. *J. Indian Inst. Sci.* **2019**, *xxx*, 1–29.
27. Krishnamoorthy, S.; Zhang, Z. Biofabrication of three-dimensional cellular structures based on gelatin methacrylate – alginate interpenetrating network hydrogel. **2019**.
28. Suntornnond, R.; Yong, E.; Tan, S.; An, J.; Chua, C.K. A Mathematical Model on the

Resolution of Extrusion Bioprinting for the Development of New Bioinks. **2016**.