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3D printed mechanically representative aortic model made of gelatin fiber reinforced silicone composite

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ABSTRACT

Additive manufacturing (AM) is a useful technology to produce artificial aortic models for the training of transcatheter aortic valve replacement (TAVR) surgery. With AM, the models can be tailored towards the individualized aortic anatomy of patients. Most of these reported models so far are manufactured using single rubber-like materials. However, such materials do not replicate the mechanical properties of natural aortic tissue, especially the stress–strain response in higher strain (>0.1) regions. This could be problematic for surgeons training for surgeries using a model which does not exhibit properties of the real aorta. To overcome this limitation, we developed a 3D-printed, mechanically representative aortic model comprising gelatin fibers and silicone. The model is promising as a realistic analog of aortic sinus for mock TAVR surgery. Computerized tomography data was analyzed beforehand using medical imaging to identify the anatomy of a specific patient's aortic sinus and the surrounding blood vessels. A novel silicone matrix composite reinforced with gelatin fibers designed in this work was tested and compared with the stress–strain response of aortic tissue. Such a model comprising both patient-specific geometries as well as realistic material properties of aortic tissue can be helpful for the development of next-generation medical phantoms.

1. Introduction

Transcatheter aortic valve replacement (TAVR) is a widely established and approved treatment for patients with severe aortic stenosis [1]. A mismatch in the TAVR implant geometries results in either a fatal rupture of the aorta or leakages. Therefore, it is vital that surgeons have a precise anatomical understanding of the aortic structure, ideally tailored for each patient, before surgery. One technique involves mock surgery on a replica of the patient's aortic anatomy [2,3]. Additive manufacturing (AM) enables such individual aortic models to be manufactured based on data collected from every patient. However, models developed from commercially available materials are expensive, do not mimic the typical J-shaped stress–strain behavior of the natural aortic tissue. Therefore, there is a need to design an affordable material with the appropriate mechanical behavior to fabricate patient-specific artificial organs. Aortic tissue is a composite material made from stiff collagen fibers embedded in a soft elastin matrix [4]. Such a structure can be mimicked by combining fibers with similar elastic moduli as naturally occurring collagen fibers embedded in a soft matrix material like silicone. In this work, with the aid of direct ink writing (DIW), a robust patient-specific aortic model was fabricated by designing gelatin fiber reinforced silicone (GFRS) composite [5] that exhibits mechanical behavior similar to natural aortic tissue.

2. Materials & methods

Firstly, patient-specific geometry was extracted from computer tomography data to initiate the manufacturing of the aortic model (Fig. S1, refer supplement). In the following steps, a silicone replica was fabricated with the help of DIW. Subsequently, gelatin fibers were produced and wrapped around the silicone model to mimic the typical stress–strain behavior of natural aortic tissue.

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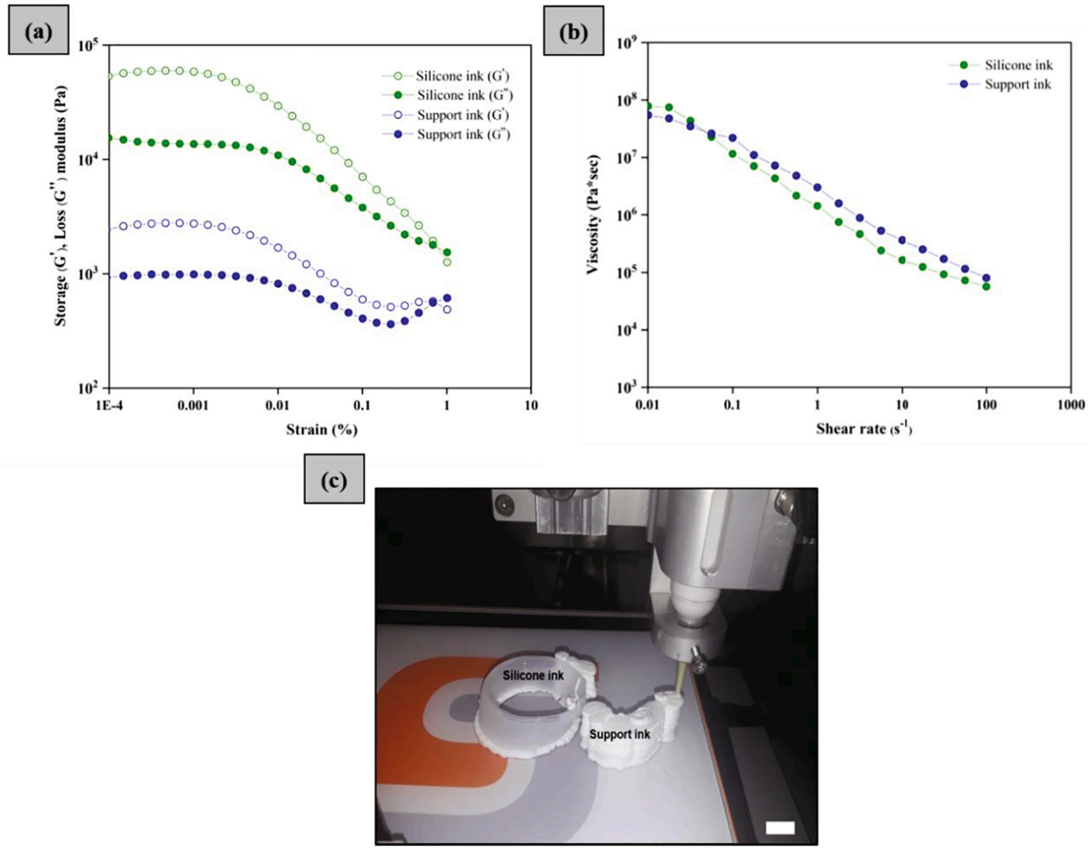

Fig. 1. (a) Storage modulus, (G′), and loss modulus, (G//), of silicone and support inks as a function of the strain amplitude applied in an oscillatory sweep measurement (b) Inks exhibiting shear-thinning behavior visible from the decrease in viscosity with increased shear rates (c) Silicone ink and support ink were easily distinguished while printing (scale bar = 10 mm).

2.1. Rheological characterization of inks

The viscoelastic properties of the specially designed printable silicone ink and support ink were measured to ensure they satisfied rheological requirements for DIW (Table S1, refer supplement). The dynamic modulus at 20 ℃ was measured using an Anton Paar MCR501 rheometer with a cone-plate geometry. Oscillatory amplitude sweeps at 1 Hz were performed within strain values ranging from 0.0001% to 1%. Steady-state flow curves were also obtained at shear rates varying between 0.01 s^{-1} and 100 s^{-1} (Fig. 1(a), (b), (c)).

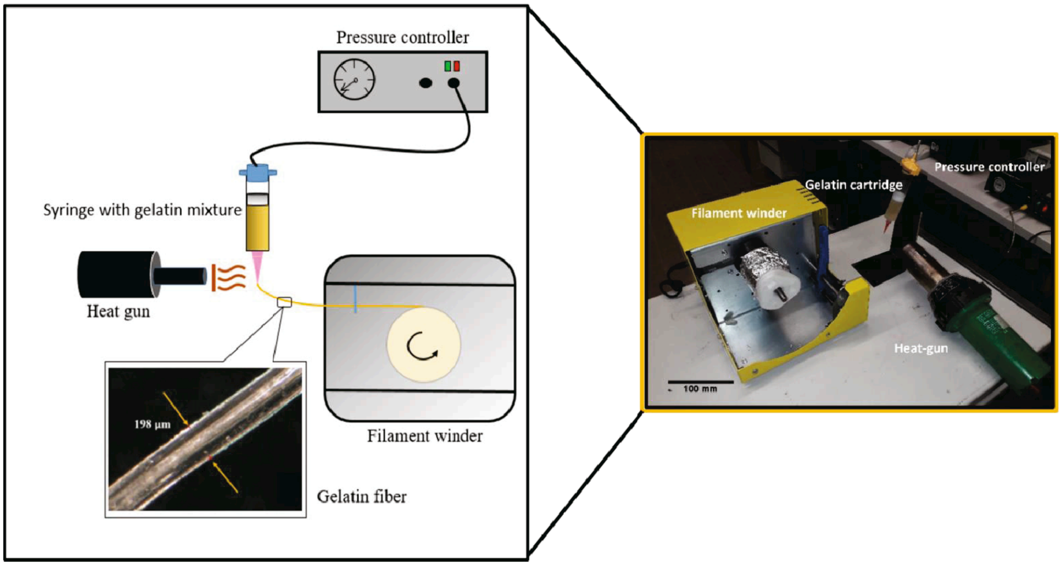

Fig. 2. Customized laboratory setup developed for gelatin fiber production consisting of filament winder, a cartridge containing gelatin solution, a heating gun, and pressure controller; inset: light optical microscopy image of gelatin fiber after drying process.

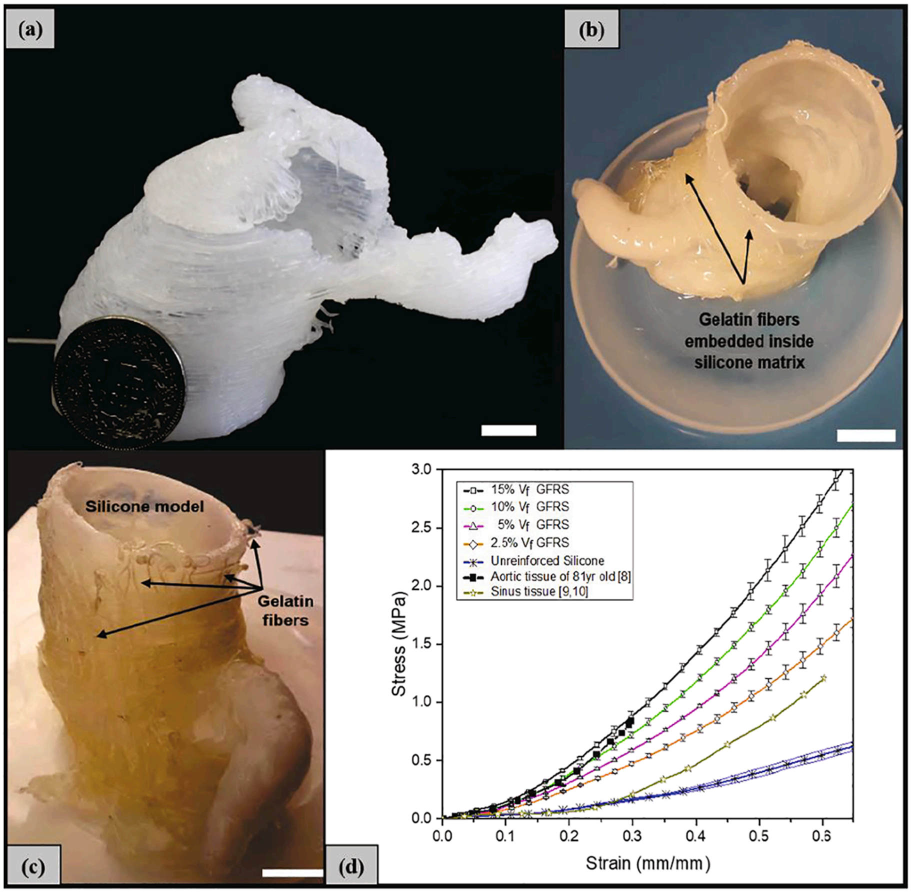

Fig. 3. (a) 3D printed aortic model of silicone (scale bar = 10 mm) (b) GFRS aortic model after postprocessing (scale bar = 10 mm) (c) Printed silicon model reinforced with gelatin fibers (scale bar = 10 mm) (d) Tensile tests results of the materials in this works plotted alongside other reported values [8–10] at high strain region (V_f = volume fraction of fibers).

2.2. *Direct ink writing of silicone model*

An aortic sinus was fabricated using a 3D Discovery printer (regenHU Ltd, Villaz-Saint-Pierre, Switzerland). Cylindrical extrusion nozzles (H. Sigrist & Partner AG, Matzingen, Switzerland) with an inner diameter of 0.84 mm were used for the silicone ink. Similar nozzles with an inner diameter of 1.60 mm were used to print support ink. The extrusion rate was optimized to match an optimum printing velocity. The aortic sinus and corresponding blood vessels were printed with a controlled dispensing unit using an eco-PEN300 (Preeflow, Töging am Inn, Germany) attached to the printer. Printing velocities ranging from 4 to 10 mm s^{-1} and printing pressures in the range 0.1–0.6 MPa were used. After every two layers, a curing step of 60 s was performed using a 300 W-230 V infrared lamp (RS PRO, Corby, UK) (Fig. S2, refer supplement). The support structure Nivea cream was washed out with water after printing.

2.3. *Gelatin fiber production*

Gelatin (Dr. Oetker Ltd., Bielefeld, Germany) was mixed with propan-2-ol (Fluka Analytical, Munich, Germany) and de-ionized water in a mass ratio gelatin: de-ionized water: propan-2-ol of *1:4:5*. The mixture was magnetically stirred in a water bath at 60 °C for 30 min. The resulting mixture consisted of two phases: one yellow semi-solid (used for fiber making) and a transparent supernatant liquid (discarded). The yellow semi-solid was transferred into a 10 mL plastic cartridge. A custom-built setup (Fig. 2), was developed to extrude thin gelatin fibers.

2.4. *Post-processing treatment*

The produced gelatin fibers were dispensed manually on the fabricated silicone model (Fig. S3, refer supplement). A dip-coating process was used later to cover the gelatin fibers with an outer layer of silicone by dipping the fiber-equipped silicone model inside the silicone ink.

2.5. *Mechanical characterization*

A Zwick Roell Z005, tensile testing machine with 5 kN load-cell was used to perform tensile tests on the GFRS composite at a cross-head speed of 500 mm min^{-1}. All tests were carried out according to ASTM D412. Dog-bone-shaped specimens made from either pure silicone or a silicone matrix reinforced with 2.5 vol%, 5 vol%, 10 vol%, and 15 vol% gelatin fibers wound at 45° to the tensile axis were prepared (Fig. S4, refer supplement). The volume fraction of fibers in specimens was analyzed from micrographs of the specimen taken across the cross-section (Fig. S5, refer supplement). Digital image correlation (Correlated solutions-VIC-3D, USA) was used to measure local strain and deformation during the tensile tests.

3. Results and discussion

Previous studies suggested that the J-shape stress–strain behavior of aortic tissue is associated with collagen fibers' orientation and volume fractions inside the soft elastin [6]. After analyzing these structural aspects of the aortic tissue, a robust mechanism of producing stiff gelatin fibers was developed, which could then be embedded in the 3D printed soft silicone model (Fig. 3(a),(b),(c)). Since collagen fibers are known to stiffen in diseased aortic tissue, it is reasonable to assume that the deposited gelatin fibers are representative of real diseased tissue, similar to that which will be present in many patients suffering from aortic stenosis [4,7]. To achieve the desired mechanical behavior of diseased aortic tissue, GFRS composite with different fiber volume fractions were tested and compared with the behaviors of real human aortic tissues (Fig. 3(d)). We found from experimental results that such structures could be tuned with increasing volume fraction of gelatin fibers up to 15% to achieve the desired stiffness. Although GFRS composite with a volume fraction of 2.5% (the smallest value tested in this study) was stiffer than real sinus tissue, the stress–strain curve of GFRS composite followed a more appropriate J-shaped pattern than the stress–strain response of unreinforced silicone.

GFRS composite with volume fraction between 10 and 15% could replicate the mechanical behavior of 81-year-old human aortic tissue. Testing biological materials in a biaxially usually makes them behave stiffer. GFRS in a biaxial orientation with a fiber orientation of +/- 45° could behave stiffer, compared to uniaxial direction. This fact should be examined efficiently in the future. Moreover, it could also be possible to mimic the regional mechanical anisotropy by carefully tuning the orientation of gelatin fibers in the silicone matrix. The technology for integrating long continuous gelatin fibers inside silicone models from 3D printing was not implemented in this work. Researchers recently discovered integrating continuous carbon fibers using 3D printing [11]. Similar methodologies can be envisioned in the future for direct integration of gelatin fibers inside silicone matrix.

4. Conclusion

A mechanically representative 3D printed aortic model was successfully manufactured using unidirectional gelatin fiber reinforced silicone composite. The necessary J-shaped stress–strain response of aortic tissue was mimicked with gelatin fibers deposited in various volume fractions inside the printed silicone model. The accurate fiber dispensing on silicone could be improved in the future, which would make the model an efficient surgical training tool in TAVR, as different structures in the aorta would be seen more easily and behave more realistically.

CRediT authorship contribution statement

Sudhanshu Kuthe: Conceptualization, Methodology, Software, Investigation, Writing – original draft, Formal analysis, Validation. **Arthur Schlothauer:** Conceptualization, Methodology, Writing – review & editing, Visualization. **Sampada Bodkhe:** Conceptualization, Methodology, Writing – review & editing, Visualization. **Christopher Hulme:** Writing – review & editing, Visualization, Supervision, Resources, Project administration. **Paolo Ermanni:** Writing – review & editing, Supervision, Project administration, Resources.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.matlet.2022.132396.

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