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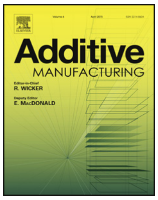

Full length article

Dual-material 3D printed metamaterials with tunable mechanical properties for patient-specific tissue-mimicking phantoms

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ABSTRACT

Patient-specific tissue-mimicking phantoms have a wide range of biomedical applications including validation of computational models and imaging techniques, medical device testing, surgery planning, medical education, doctor-patient interaction, etc. Although 3D printing technologies have demonstrated great potential in fabricating patient-specific phantoms, current 3D printed phantoms are usually only geometrically accurate. Mechanical properties of soft tissues can merely be mimicked at small strain situations, such as ultrasonic induced vibration. Under large deformation, the soft tissues and the 3D printed phantoms behave differently. The essential barrier is the inherent difference in the stress-strain curves of soft tissues and 3D printable polymers. This study investigated the feasibility of mimicking the strain-stiffening behavior of soft tissues using dual-material 3D printed metamaterials with micro-structured reinforcement embedded in soft polymeric matrix. Three types of metamaterials were designed and tested: sinusoidal wave, double helix, and interlocking chains. Even though the two base materials were strain-softening polymers, both finite element analysis and uniaxial tension tests indicated that two of those dual-material designs were able to exhibit strain-stiffening effects as a metamaterial. The effects of the design parameters on the mechanical behavior of the metamaterials were also demonstrated. The results suggested that the fabrication of patient-specific tissue-mimicking phantoms with both geometrical and mechanical accuracies is possible with dual-material 3D printed metamaterials.

1. Introduction

Tissue-mimicking phantoms have been traditionally used in the development and validation of medical imaging modalities such as ultrasound [1,2], magnetic resonance imaging (MRI) [3–6], computed tomography (CT) [7], and others [8]. With the increasing need of biomedical research, other applications of tissue-mimicking phantoms have also been demonstrated, such as the simulation of electromagnetic properties of tissues [9], mechanical properties mimicking [10], and focused ultrasound ablation [11], In these applications, phantoms were fabricated as population-averaged idealized models and the individual differences among patients were overlooked. Recent advances in computer-aided design (CAD) and 3D printing technologies have provided a rapid and low-cost method to generate patient-specific tissue-mimicking phantoms from computational models that are constructed from CT or MRI results of individuals [12]. Those patient-specific phantoms have unparalleled advantages in many biomedical applications such as computational model validation, medical device testing, surgery planning, medical education, and doctor-patient interaction.

3D printing, or additive manufacturing (AM), refers to the layer-by-layer fabrication of objects in an additive process from CAD models. It features a high ability for customization, high geometrical complexity, and cost effectiveness in some cases with low production volume, which is perfectly suited for biomedical applications like prosthetics [13], orthopedic implants [14–16], and tissue/organ printing [17–19]. Bose et al. did a comprehensive review of cases where additive manufacturing technologies were applied in bone tissue engineering [20]. In some of those cases, multiple types of materials, including ceramics and polymers, were used to tune the mechanical properties of the printed scaffolds.

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Biglino et al. demonstrated the fabrication of compliant arterial phantoms with PolyJet technology, an AM technique that deposits liquid photopolymer layer by layer through orifice jetting and then solidifies by UV exposure [21]. A rubber-like material named TangoPlus (Stratasys Ltd) was used in this study for its mechanical properties that are similar to the real tissue. Cloonan et al. did a comparative study on common tissue-mimicking materials and 3D printing materials including TangoPlus with the abdominal aortic aneurysm phantoms [12]. Their results suggested that TangoPlus was a suitable material for modeling arteries in terms of dispensability and outperformed poly (dimethylsiloxane) (PDMS) Sylgard elastomers that were commonly used in the investment casting process in terms of uniaxial tensile properties.

Although the uniaxial tensile properties of phantom materials can be close to soft tissues at small strain (<3%) range, the creep tendency, an inherent characteristic of polymers, makes them behave quite differently than the soft tissues under larger deformation. For tissue-mimicking phantoms, the strain range-of-interest is normally the working strain range of the tissue. As illustrated in Fig. 1, soft tissues typically exhibit a strain-stiffening behavior initially, which is represented by a convex stress-strain curve in the beginning. As the strain increases, the curve changes from convex to concave, which indicates yielding of the material [22]. In contrast, the stress-strain curve of a polymer material is usually concave from the beginning, indicating a strain-softening feature. Even though the initial Young's modulus of a polymeric phantom can be designed to match the Young's modulus of the real tissue, the mechanical behavior of the phantom will deviate from the real tissue at higher strain levels.

Since creep is an intrinsic property of polymeric materials, single-material polymer 3D printing is fundamentally not capable of generating phantoms that are mechanically accurate in the strain range-of-interest. Recent advances in 3D printed metamaterials provides new insight to this challenge. Metamaterials were first introduced as novel electromagnetic (EM) materials and their characteristic structural length is one or more orders smaller than the EM wavelengths [23], [24]. Since then, the concept of metamaterials has been extended to include any materials whose effective properties are delivered by its structure rather than the bulk behavior of the base materials that composed it [25]. In other words, the geometry, size, orientation and arrangement of the unit cells of metamaterials grant them the desired properties. In context of tissue-mimicking phantom, the key value of the "metamaterial" concept is the idea of constructing artificial models of tissue with heterogeneous microstructures that, although difficult to do conventionally, can be easily rendered by 3D printing. With multi-material 3D printing technologies, the feasibility of designing the mechanical properties of metamaterials has been proven [26]. Similarly, if a micro-structured material is embedded into a soft polymer, the mechanical properties of the combined material should be tunable by adjusting the structural parameters. With this principle, we designed and fabricated metamaterials with three microstructures. Finite element analysis (FEA) was used to predict their mechanical behaviors under tensile loadings. The simulation results were compared with experimental testing results. The relationships between structural parameters and mechanical properties were also investigated.

2. Materials and methods

2.1. Design of metamaterial samples

The passive biomechanical properties of human soft tissues were determined by the microstructure of the tissues and extracellular matrix (ECM) at the cellular level and how those structures organize and interact at higher levels. For instance, the nonlinear behavior of human vessels comes from the wavy collagen fibers in the proteoglycans, which is a major component of the ECM, being straightened under tensile loading [27], [28]. We imitated this observation by embedding wavy stiff structures into soft polymeric matrix. Ideally, those stiff structures will straighten up during elongation and compensate for the creep of the matrix polymer. Three types of metamaterial samples were designed using SolidWorks (Dassault Systems SOLIDWORKS Corp.): those containing sinusoidal wave (SW) fibers, double helix (DH) fibers, and interlocking chains (IC), respectively. The CAD models and pictures of printed samples are demonstrated in Fig. 2. The SW design has often been used as an assumption for theoretical analysis or numerical simulation of natural wavy fibrous systems. The wavelength, λ, and amplitude, A, of the sinusoidal wave could serve as design parameters for property tuning. The DH design resembles the microstructure of filament actin (F-actin) strands. The tuning parameters for the double helix design are the radius of the helix, r_h, and the pitch, h. The IC design was an attempt at achieving nonlinearity by non-continuous fiber structure, even though there is no such structural design observed in ECM. Its tuning parameters include distance between two links, d, and chain width, w. All samples shared one tuning parameter, which is the radius of fibers, r_f. Each sample model was assembled from a soft matrix part file and a stiff reinforcing microstructure. Dimensions of all samples were 30 mm in length and 4 mm in width to accommodate dimension requirements of uniaxial tensile tests. The thickness of all samples were 2 mm and each repetitive stiff structure inside the samples were 2 mm apart along the width direction.

Table 1
Samples fabricated for tensile tests.

Sample ID	Sample Type	Design Parameters (mm)
SW1	Sinusoidal Wave	$\lambda = 10, A = 0.6, r_f = 0.3$
DH1	Double Helix	$r_h = 0.6, h = 5, r_f = 0.2$
IC1	Interlocking Chain	$d = 5, w = 1, r_f = 0.15$

Table 1 summarizes the design parameters of the samples prepared for mechanical testing. For each parameter setting, three replicates were fabricated.

2.2. Materials, equipment, and testing protocols

The metamaterial samples were fabricated on a Connex350® 3D printer (Stratasys Ltd). The layer thickness of printed part is 30 μm, and the in-plane accuracy is 0.1 mm. The base materials used for stiff fiber and elastic matrix are VeroBlackPlus® (RGD875) and TangoPlus® (FullCure 930), respectively. These two materials represent the two extremes of printable materials with VeroBlackPlus being the stiffest and TangoPlus the most elastic. The Connex350 can also mix those two base materials at a certain ratio and print them simultaneously to form digital materials that have mechanical properties between the base materials. In the present study, only the base materials were used to prepare the samples, but it should be noted that the material choice may also serve as a tuning factor.

Uniaxial tensile tests were conducted using Q800 Dynamic Mechanical Analysis (DMA) (TA Instruments) under controlled strain mode at room temperature for all samples except those made of pure VeroBlackPlus, which were tested using RSA III DMA (TA Instruments) due to the large Young's modulus. The strain rate was set to a small value of 1%/min to achieve a quasi-static process. The maximum strain was set to 8% because the interface between VeroBlackPlus and TangoPlus starts to break down around a strain level of 9% in our previous experience. Testing data was analyzed using TA Universal Analysis software.