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Methodology for Image-driven High-resolution Additive Manufacturing Using Discretized Data Set

Henry Oliver T. Ware[a], Wenzhong Liu[b], Jianmin Hu[a],[b], Hao Zhang[b], Cheng Sun[a]*

[a]Mechanical Engineering Department, Northwestern University, Evanston, IL 60208, USA
[b]Biomedical Engineering Department, Northwestern University, Evanston, IL 60208, USA

*Corresponding author: Tel.: +1-847-467-0704. E-mail address: c-sun@northwestern.edu

Abstract

Additive manufacturing of patient-specific biomedical devices from 3D medical scans involves several steps of conversion which can introduce error into the final part. This is particularly critical to the fabrication of minute anatomical features, such as microvasculature. We show a direct conversion of the raw optical coherence tomography (OCT) volumetric data into photomasks in bitmap format, which streamlines the typical process steps used in 3D printing medical scans. OCT scans of rodent retinal microvasculature and projection microstereolithography are used to fabricate a solid vascular replica and a solid volume with hollow embedded microvessels.

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1. Introduction

In recent years, the rapid progress in the realm of 3D printing, also known as additive manufacturing, has inspired a wide range of novel applications. In contrast to the traditional subtractive manufacturing processes, 3D printing builds up sophisticated parts in a layer-by-layer fashion from geometry described in a 3D solid model. It encompasses a broad range of fabrication methods that include extrusion-based, localized melting/sintering, and light-controlled polymerization.[1] Despite their distinct difference in the underlying physical processes, they all share in common the unique geometric flexibility that is otherwise impossible for conventional subtractive manufacturing techniques.[1, 2] Furthermore, 3D printing also supports the fully computerized process flow and thus, results in a significant savings in time and the overall cost in manufacturing individualized parts and products. These unique characteristics make 3D printing particularly suited for manufacturing biomedical devices, as they often demand highly patient-specific features being tailored to fulfill the anatomic variation among individual patients, but require only singular or small batch manufacturing [2, 3]. While 3D printed biomedical devices have found broad applications in customized implants/prosthetics, microfluidic lab-on-a-chip applications, tissue scaffolding, or surgical planning/teaching [4-13], direct printing of diagnostic imaging has typically been limited to larger structures, such as bone segments, whole organ geometry, and large vasculature, as many diagnostic modalities fail to capture very fine structures such as the nerves and microvasculature [3, 8-10, 14]. The diagnostic medical imaging technologies are the key cornerstone of medical 3D printing in determining the patient-specific design parameters [6, 7, 15].

Medical imaging modalities being used in diagnostics include magnetic resonance imaging (MRI), ultrasound, and X-Ray Computed Tomography (CT), and related optical imaging modalities. Among the well-established medical

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imaging modalities (as well as most associated with direct 3D printing), MRI and CT are mostly used for imaging the whole body at hundreds of micrometers. Although special versions of the MRI and CT modalities are able to achieve sub 50 μm resolution, they still cannot resolve the fine details of the capillaries of the organ (5 - 10 μm) [16-18]. Optical Coherence Tomography (OCT) has gained much clinical attention in the ophthalmology field to diagnose eye diseases by providing the greatly improved spatial and depth resolution of 5 - 20 μm. [19-22] Besides static structural information, OCT can also image motion contrast, allowing the ability to capture blood vessels with high signal to noise ratio. Yi and Chen (separate works) showed that the visible light OCT angiography (OCTA) was capable of capturing the large vessels of rodent retina as well as the microvasculature and capillary beds [19, 20].

While OCTA can capture the fine details of the patients' anatomical features such as microvascular structures, direct 3D printing of the corresponding biomedical structures or devices will require not only the matching fabrication precision but more importantly the high-throughput to ensure the building up of the fine features toward the final 3D structures can be accomplished in a timely manner [14]. However, traditional 3D printing methods, such as Fused Deposition Modeling (FDM), Selective Laser Sintering (SLS), and conventional stereolithography process (μSL), utilize a point-by-point scanning of the material are inherently time consuming [23]. Fabrication time scales approximately to $\left(\frac{\text{dimension}}{feature\ size}\right)^3$ [24]. Although the μSL process that utilizes the focused laser beam has the ultra-high precision up to 100 nm, the fabrication time can take hours, which is highly undesirable for practical application.[25] In addressing this issue, Projection microstereolithography (PμSL) was developed to eliminate the point-by-point scanning process by employing a dynamic mask to polymerize a full 2D layer in a single exposure [2, 9, 26]. The fabrication time of PμSL scales approximately to$\left(\frac{dimension}{feature\ size}\right)$, which results in a significant time saving in high-resolution 3D printing [2, 24]. PμSL lateral resolution is dependent on the pixel size of the dynamic mask, which can be reduced to single-digit micrometer level [24].

Motivated by these unique capabilities, we report in this paper a method for image-driven high-resolution 3D printing of biological structure via synergetic integration of OCTA and PμSL. While CAD models are commonly used in representing the designed geometry in 3D, the acquired 3D image using OCT are in the form of discrete voxels as the result of the raster scanning process. Thus, converting the discrete image into the CAD model is not only time consuming, but often may introduce unnecessary artifact during the conversion. On the other hand, in the PμSL process, 3D models are presented as the stacks of 2D bitmap images, which are also in the form of discrete array of pixels [7, 27]. Thus, a streamlined process flow can be established by directly bridging the 3D image and 3D printing process via discrete images and bypass the use of 3D CAD model. It can be further adopted to develop an automated process flow for direct fabrication of biomedical devices containing patient-specific features. In this work, we will demonstrate that combination of high resolution diagnostic imaging of OCT and high resolution fabrication of PμSL can be used to directly fabricate replicas of microscale-vasculature of the retina.

2. Materials and Methods

2.1 OCT Imaging of Retinal Vasculature:

Spectral domain-OCT (SD-OCT) is the standard for current ophthalmic imaging practice. With broadband illumination and spectral detection, micrometer level axial resolution and millimeter depth penetration are achieved in SD-OCT. One illumination by SD-OCT at a single location refers to A-line scan, which gives the depth information at the illumination point. Raster scanning of multiple A-lines along one direction generates B-Scan, which is the cross-sectional imaging. Raster scanning of multiple B-scans along one direction generates 3D imaging. Recent advance in SD-OCT enables angiography imaging. In OCT angiography (OCTA), repeatable B-line were performed at single B-line location, the moving red blood cells will de-correlate the detected signals between these adjacent B-line, and the difference between sequential B-line captures the retinal/choroidal vascular bed.

As shown in Figure 1a, we employed a broadband SLED for illumination (center wavelength: 840 nm; bandwidth: 95 nm; IPSDW0825C-0314, Inphenix), and a 50×50 fiber coupler (OZ optics) for interferometry. Interference signals between the sample and reference arm were collected by a homemade spectrometer, comprising a blazed grating (Wasatch, 1200 lines/mm), a focal lens (Thorlabs, focal length =150 mm) and a line-camera (Basler, 2048 pixels, 140 KHz highest sampling rate, 50 KHz in our current experiment). Theoretical lateral and axial resolutions of the system were approximately 5.6 μm and 3.2 μm, respectively and imaging depth approximately 1200 μm. Because of the aberration of the eye, the practical resolution will be less than theoretical ones. OCTA was performed on a rodent prepared via the method described in [21].

Briefly, we repeated 5 B-scan imaging at every location, with 400 A-lines in each B-scan and 512 discrete B-scan positions in total to produce a volumetric retinal map (2 mm by 2 mm). To visualize vasculature, we first analyzed OCTA data[28] by evenly dividing the 95-nm bandwidth into 4 non-overlapping sub-bands and reconstructing corresponding B-scan images from each sub-band. Then, within each sub-band, we took the complex signal differences between sequential B-scans at the same location to generate vasculature imaging.[19, 21, 29] Results from four sub-bands were averaged to enhance the signal to noise ratio (SNR). Finally, this process was repeated across 512 discrete B-scan locations to produce the angiography map.