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Fabrication of Polymer Micro Needles for Transdermal Drug Delivery System using DLP based Projection Stereo-lithography

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Abstract

Fabrication of micro needles, which reduce pain during insertion and lessen tissue injury, has recently attracted great interest. Different manufacturing systems have been utilized for the advancement of micro needles such as two-photon photo polymerization, bulk lithography, droplet-borne air blowing and injection molding [1]. This paper proposes a micro fabrication process for polymer micro needles, using DLP based projection-based stereo lithography that is capable of fabricating micro-needles using biocompatible polymers. The fabrication in the experimental setup is performed with continuous movement of the platform in the vertical direction hence good surface quality is obtained. The influence of polymerization time, light intensity of DLP projector and chemical composition of the resins on the production speed and the geometrical accuracy of the micro needles have been studied. The length and the tip diameter of the micro needle are shown to be controlled through these factors. The length and tip diameter of the fabricated micro needles were observed using SEM and optical microscope and measured to be around 520 µm and 40 µm, respectively. The results indicate that polymer micro needles with appropriate geometry can be fabricated using this technique.

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Keywords: Micro Needle; DLP Projector; Micro Stereo-lithography

1. Introduction

Additive Manufacturing (AM) has been used in customized healthcare products to improve population health and quality of life. It can be used to make custom surgical implants in a solid or resorbable material [2]. AM technologies have been used for a variety of applications such as skull [3, 4], knee joint [5], elbow [6], and hip joint [7] implants.

Stereolithography is an additive manufacturing technique in which a liquid polymer resin is cured with a UV light as thin layers. As the process platform is moved across the axis of production after each layer, system forms a digitally defined 3D shape [8]. It is also possible to decrease the size of the fabricated structures to micron level as Zhang [9] made micro-channels and micro-tubes with 1.2 µm resolution and high aspect ratio of 16. Micro stereo-lithography can be used for medical purposes as Choi [10] proposed a way to fabricate human kidney scaffold with a system that is working with resolution of 2µm in x-y and 1µm in z-axis.

Micro needles are extremely small needles used to draw blood or manage drugs without entering the skin and underlying tissue as profoundly as conventional hypodermic

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needles or syringes. When it is utilized for medical purposes, rows of several hundred smaller scale needles are put onto modest patches that are then applied to the skin. The smaller scale needles make tiny holes in the furthest layer of the skin, and either draw minute amounts of blood or deliver a drug and this process sometimes called transdermal drug delivery. They cause minimal pain and trauma compared to traditional needles and is used for various medical purposes like immunizations, pain management, and blood glucose monitoring [11].

Various methods are used to fabricate micro needle devices which would be used in the health industry for different purposes. PDMS micro molds are generated and a novel vacuum-based method is used to fill the molds with various acids and polymers to form the needles in Park's research [12]. Yung [13] used micro injection molding to produce hollow high aspect ratio micro needles with 110µm tip diameter and 500 µm length. Ashraf [14] uses some cleanroom processes like deep reactive ion etching and inductively coupled plasma (ICP) etching to create silicon micro needles integrated piezo-electrically actuated device for transdermal drug delivery. Also other MEMS manufacturing methods like photo-lithography and one of the newer and effective techniques like drawing lithography [15] are used for the production of needles of different shapes and dimensions.

In this research, a mathematical model for the cure depth calculation has been used to find the optimal parameters for fabrication of various designs. Hence, a process of DLP based projection micro-stereolithography system has been developed to fabricate micro needles and also to verify the cure depth model. The positioning system has the capability of moving in nanometer level steps. The adjustment of this movement together with curing rate allows us to control layer thickness and creates a continuous production process. Therefore, needle structures are produced without observable layers.

2. Experimental Setup

An experimental setup has been designed for projection based micro stereo-lithography process (Fig.2) including a DLP projector and a high precision linear positioning system as shown in Fig. 1.

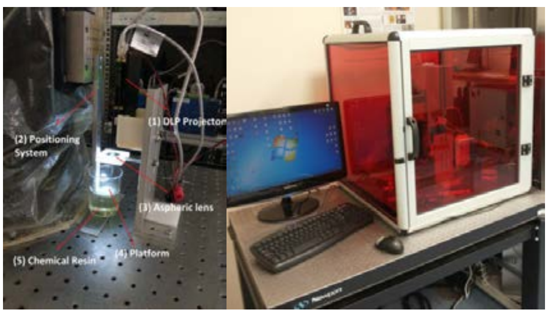

Fig. 1. (a) Working principle of the system (b) Overview of the PSLA system

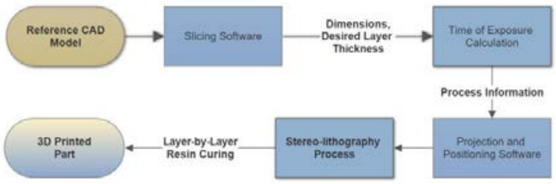

Fig. 2. Stereo-lithography process flow.

An optical lens is used to converge the light rays of the projected image on the platform. It decreases the chromatic and spherical aberrations and increases the layer image exposure quality on the fabrication platform. A PC system is used for the continuous control and positioning and projection devices during the process. An outer housing is designed, which blocks the outer lights in a specific wavelength interval, therefore minimizes the environmental effects as showed in Fig. 1(b). In this setup, process parameters such as light intensity, vertical speed of the platform and exposure time are used to fabricate micro structures. The optimal parameters are also taken into consideration for micro needle fabrication based on our previous study [16].

3. Cure Depth Model

3.1. Characterization of the Resin

In order to find cure depth of the resin under specific light intensity, the Beer-Lambert law has been used. The relation between the depth of cure (Cd) and the exposure on the resin surface (E) is given by Equation 1 as:

$$C_d = D_p \ln{(E/E_c)} \quad (1)$$

Depth of penetration (D_p) and critical energy (E_c) values depends upon the resin chemistry and in order to identify these values an experimental approach has been conducted as described in Limaye et al. [17]. Figure 3 shows the working curve of the resin used in this study.

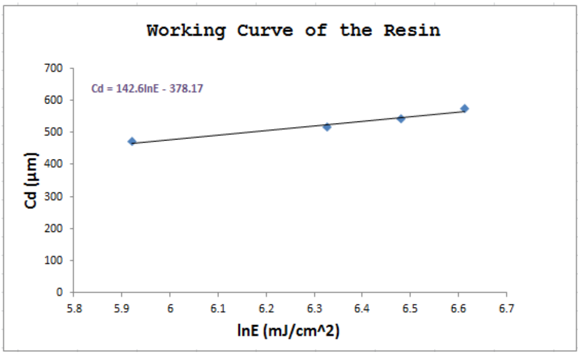

Fig. 3 The working curve of the resin

The slope of the graph shown in Figure 3 gives the value of the D_p , while the x-intercept value is equal to ln (E_c).

3.2. Exposure Time Calculation

In order to set the process parameters, time of exposure (TOE) for a single layer is calculated according to the irradiation amount on the surface and total number of layers as shown in Equation 2.

$$T\,OE = \left(e^{C_d/D_p}\right) * E_c/I \quad (2)$$

TOE value for a single layer was used to produce micro needles. The total number of layers is defined as 1128 on slicing software using layer height 0.01mm. Exposure time has been calculated as 2 seconds for each layer. The layer thickness is defined by the speed of the stage on z-axis, which is 1.1µm/sec hence the layer thickness is 2.2µm.

4. Micro Needle Designs

Three basic needle designs has been considered in fabrication trials as shown in Figure 4. The conical and pyramidal base design has been used as basic shapes for trial purposes [18]. A hollow shape as described in [19] was also used to test the capabilities of the system to produce more complex micro needle structures.

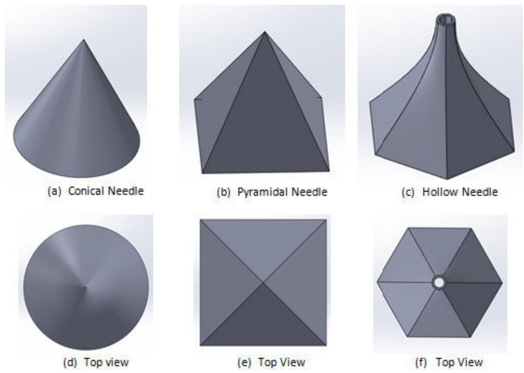

Fig 4. Micro needle CAD Models.

5. Manufacturing

5.1. System Parameters

In this study, the irradiance amount on the platform has been measured to calculate the exposure time for curing a single layer. The irradiance at light intensity 274mA has been measured via power meter device as 6,21 $mW/(cm^2)$. Using this irradiance value, the exposure time for single layer has been determined as shown in Equation 2. The speed of the vertical movement has been determined using time of exposure (TOE) and cure depth from Equation 1 and 2. These parameters have been applied to produce micro needles. The exposure time of a micro needle patch has been calculated according to the height of the needle patch as well as the total no of layers that has been received after slicing it. The Flashpoint software has been used to slice the STL file of the needle patch design and the layer height is set as 0.01 during slicing.

5.2. Measurements

Dimensional and geometrical measurements of the manufactured micro needles have been done for 3 different structures. Measurements are done by SEM, laser and optical microscope. The SEM images of conical, pyramidal and hollow needles are shown in Figure 5. The diameter of the tip has been found using SEM which is around 40µm. Also, the 3D view of these needles can be seen in Fig. 6.

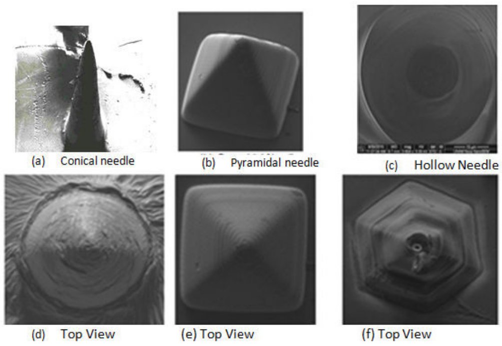

Fig. 5. SEM images of conical, pyramidal and hollow micro needles.

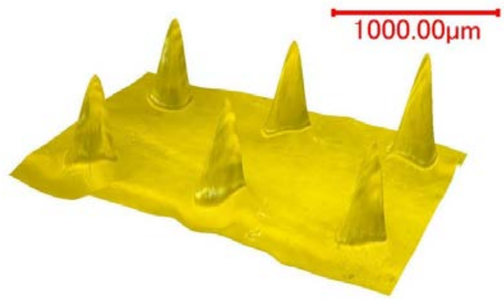

Fig. 6. 3D view of micro needle using optical microscope.

The measurements showed that parameters defined by the cure depth modeling resulted in good fabrication of conical and pyramidal needles structures. However, for the hollow needle structures, the results show some irregularities on the top side of the needle. The possible reason for this irregularity is believed to relate to image projection and light distribution on the platform. Image accuracy on the production platform and chemical reaction of polymerization based on resin curing with light, are the main issues that affects the production capabilities of the system. These should be controlled carefully for minimizing the geometrical errors and dimensional differentiations with the original CAD design of the micro needles. Similar errors are also observed among simple geometry needles as shown in Figure 7. Projected layer reflection on the resin surface could be improved with the use of a more dedicated optical lens system containing more than a single lens. As the light rays could be converged more, the micro hollow structures can be produced more accurately.

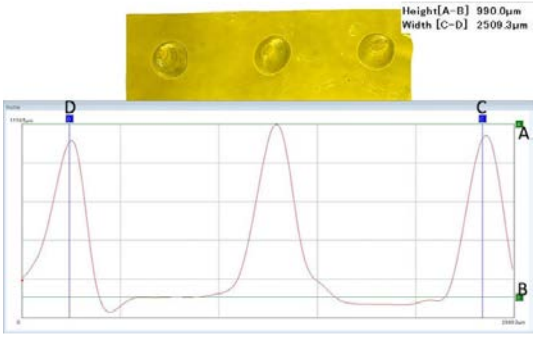

Fig 7. Height differences between single needles.

Biocompatibility and biodegradability are two important aspects of the micro needle production. Additive manufacturing of devices that will be used in medical field is mostly considered within the necessities of the compatibility of material with the body. The polymer resin used in this research (Poly-ethylene glycol diacrylate (PEGDA)) takes the 98% percent volume of the resin is widely used in biological applications. Physical insertion testing of fabricated micro needles has been left as future work.

6. Conclusion

In this study, our motivation is to show that production of micro needle patches is feasible using the DLP projection based micro-stereo lithography process. A cure depth model has been used to fabricate various micro needle designs. Our initial results show that the solid micro needles can be successfully produced.

Various MEMS and injection-molding processes are commonly used to produce micro needle structures. Stereo lithography method is shown to be a viable process for prototyping and fabrication of micro needles.

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