

Fabrication of PEG Hydrogel Particles for Pharmaceuticals using Electron Beam and Optical Lithography

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There is need for micro- and nanoparticles in pharmaceutical applications including, but not limited to, imaging, bioassays, and drug delivery carriers. Hydrogels have been investigated due to their unique properties and specifically the interaction with water. Poly(ethylene glycol) (PEG) based hydrogel systems are widely used due to their non-toxicity and limited immunogenic recognition. Physicochemical properties of particles (i.e., particle size, shape, surface charge, and hydrophobicity) have been known to play an imperative role in cell-material recognition. To understand the role of physicochemical properties of PEG hydrogel particles, it is necessary to develop methods to fabricate controlled particle size and shape. Here we report the use of electron beam lithography (EBL)¹ and ultra-violet optical lithography (UVL) for fabricating PEG hydrogel particles that have controlled size and shape. Geometrically uniform hydrogel particles have been fabricated in the nanometer and micrometer range.

The EBL and UVL allow fabrication of polymeric materials in highly-controlled size and shape, thus making them very suitable for pharmaceutical applications. PEG [PEG diacrylate (PEGDA)] films were spin coated on a Si wafer and patterned using a Raith 150 EBL system and by UVL with a Karl Suss MA6 optical mask aligner. For EBL, hydrogel particles were designed as disc and cubic shapes with lengths or diameters of 500 nm, 200 nm, and 50 nm, and a height of 160 nm. For UVL, hydrogel particles were designed as disc shapes with diameter from 1 μm to 2.5 μm in 0.5 μm increment and a height of 1 μm . The exposed films were developed to remove unexposed polymer. The hydrogel remaining particles were then dried in air.

Figure 1-3 show the preliminary results from patterning PEG or PEGDA films by EBL or UVL. We performed scanning electron microscopy (SEM), optical microscopy, and atomic force microscopy (AFM) to determine the size and the shape of the fabricated hydrogel particles. The results in figure 1 and 2 confirm that individual hydrogel particles can be fabricated with controlled size and shape. We performed FT-IR to determine the chemical structure of hydrogels (Figure 3). The results show the FT-IR spectra of the polymer chains produced by exposure to electron beam and UV. The PEG hydrogel spectra exhibit line broadening when compared with exposed PEG polymer. The formation of crosslinks between PEG chains in the hydrogels affects the vibration of the PEG backbone as indicated by the line broadening.

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1. V. R. Tirumala, R. Divan, L. E. Ocola and D. C. Mancini, J Vac Sci Technol B 23 (6), 3124-3128 (2005).

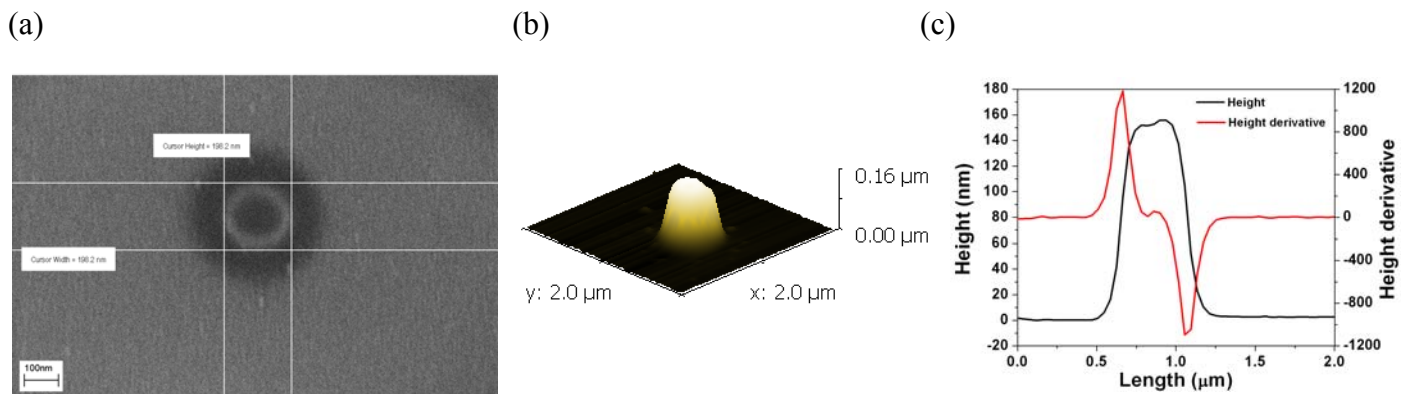


Figure 1. (a) SEM image, (b) 3-D AFM image and (c) the height and height derivative profile of 200-nm-diameter PEG hydrogel particles fabricated by EBL.

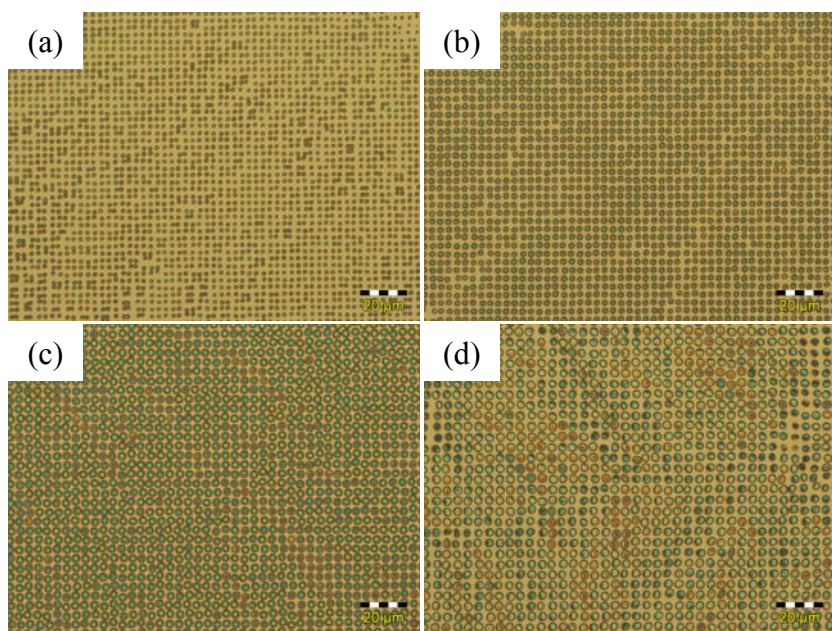


Figure 2. Optical reflection microscopy images of PEGDA hydrogel particles fabricated by UVL with diameter of (a) 1 μm, (b) 1.5 μm, (c) 2 μm, and (d) 2.5 μm.

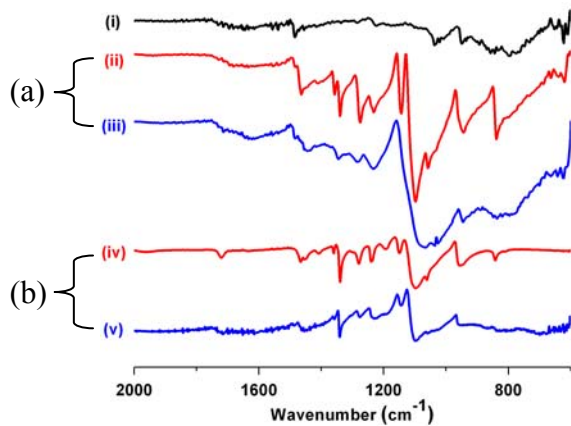


Figure 3. Representative FTIR-ATR spectra in transmission mode of (a) EBL and (b) UVL. (i) Si wafer, (ii) and (iv) PEG polymer on Si wafer, (iii) and (v) PEG hydrogels on Si wafer.