ADDITIVE MANUFACTURING OF INORGANIC-ORGANIC HYBRID MATERIALS FOR TRANSDERMAL BIOSENSOR APPLICATIONS

Roger Narayan, North Carolina State University
rjnaraya@ncsu.edu

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Two photon polymerization offers many advantages over conventional processes for scalable mass production of medical devices, particularly those with small-scale features. First, the raw materials (e.g., inorganic-organic hybrid materials and acrylate-based polymers) used in two photon polymerization are inexpensive and are widely available. Second, two photon polymerization can be established in a conventional “dirty” manufacturing environment; no cleanroom facilities are required. Third, two photon polymerization is a straightforward and single-step process for creating complex structures with small-scale features. In previous work, two photon polymerization was shown to be able to create microneedles with a larger range of shapes and dimensions than conventional microneedle fabrication techniques [1]. For example, 500-700 micrometer tall microneedles were created out of an acrylate-based polymer that is used in Class IIa medical devices (e.g., hearing aid shells) (Figure 1 (a) and Figure 1 (b)) [1]. A hollow microneedle was used to create pores in the outermost layer of cadaveric porcine skin; a microneedle-generated pore was shown to facilitate delivery of carboxyl quantum dots to the deep epidermis and dermis layers of the cadaveric porcine skin within fifteen minutes. We have prepared several types of hollow microneedle-based biosensors using microneedles that were fabricated using either two photon polymerization or digital micromirror device-based stereolithography. In these biosensors, the sensing mechanisms are located within the bores of the microneedles. For example, we have examined incorporating carbon fiber electrodes within a hollow microneedle array, which was created using a digital micromirror device-based stereolithography instrument [2]. Studies involving trypan blue dye demonstrated that the microneedles remained intact after they punctured the outermost layer of cadaveric porcine skin. The carbon fibers were chemically modified to allow for the detection of hydrogen peroxide and ascorbic acid; the performance of the microneedle-based sensors was demonstrated using electrochemical measurements. In another study, we prepared a multiplexed microneedle-based biosensor array for simultaneous and selective amperometric detection of lactate, glucose, and pH over physiologically relevant analyte levels in complex media (Figure 1c) [3]. In another study, a solid-state ion selective electrode for potassium ions was prepared from three-dimensional porous carbon [4]. This electrode was integrated with a hollow microneedle that was created using two photon polymerization. The functionality of the ion selective electrode was demonstrated over the physiologic range of potassium and in the presence of interfering sodium ions.

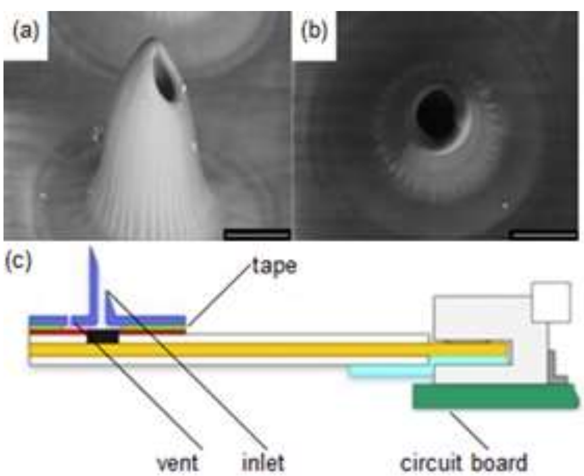

Figure 1. (a, b) Scanning electron microscopy images that were obtained from an acrylate-based polymer microneedle, which was prepared using two photon polymerization. Scale bar=100 □m. From Reference 1. (c) Schematic showing design of the multicomponent microneedle-based biosensor platform. From Reference 4.

References

[1] Gittard SD, Miller PR, Boehm RD, Ovsianikov A, Chichkov BN, Heiser J, Gordon J, Monteiro-Riviere NA, Narayan RJ. Multiphoton microscopy of transdermal quantum dot delivery using two photon polymerization-fabricated polymer microneedles. Faraday Discussions. 2011;149:171-185.
[2] Miller PR, Gittard SD, Edwards TL, Lopez DM, Xiao X, Wheeler DR, Monteiro-Riviere NA, Brozik SM, Polsky R, Narayan RJ. Integrated carbon fiber electrodes within hollow polymer microneedles for transdermal electrochemical sensing. Biomicrofluidics. 2011;5:013415.
[3] Miller PR, Skoog SA, Edwards TL, Lopez DM, Wheeler DR, Arango DC, Xiao X, Brozik SM, Wang J, Polsky R, Narayan RJ. Multiplexed microneedle-based biosensor array for characterization of metabolic acidosis. Talanta. 2012;88:739-42.
[4] Miller PR, Xiao X, Brener I, Burckel DB, Narayan R, Polsky R. Microneedle-based transdermal sensor for on-chip potentiometric determination of K^+. Advanced Healthcare Materials. 2014;3:876-881.