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Microfluidic Synthesis of Uniform Embolic Microspheres

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Extended Abstract

Embolization therapy is a nonsurgical, minimally invasive procedure that involves the selective occlusion of blood vessels by purposely introducing embolic agents. It has become a major branch of modern interventional therapy, its applications fundamental in treating a wide variety of conditions affecting different organs of the human body including tumors, hemorrhages and vascular anomalies. To obtain good clinical outcomes and minimize complications, embolic particles uniform in shape and size are essential. To date, the functional outcomes of existing embolic particles have not been satisfactory due to the inadequacies of conventional fabrication approaches in engineering their shape, size and microstructures.

We develop an approach for precise fabrication of embolic microparticles that are uniform in shape and size. The key is to replace the "top-down" bulk process used in conventional approaches with a "bottom-up" microfluidic process of polymer cross-linking. The approach uses a glass capillary microfluidic device to generate micro droplets containing the particle material, exploiting the capability offered by microfluidics to precisely handle small fluid volumes and accurately control formation of droplets. Cross-linker solution is used for droplet solidification, and is injected into each individual droplet at formation to ensure solidification at individual droplet level. These methods allow control over the formation of individual particles and enable the generation of highly uniform particles overall. The spherical shape of the microfluidic capillary channels used, together with the thermodynamic principle of minimum interfacial energy, allow the formation of perfectly spherical droplets and particles whose size is invariable along all directions (geometrical isotropy). The shape and size of the fabricated particles, therefore, are not variable from particle to particle or from direction to direction in individual particles.

Our aim is to define the potential of this promising approach against the important targets of accurately controlling particle morphology and correlating processing parameters and particle morphology reliably. We develop and characterize the approach for fabricating uniform embolic microparticles with three well-established, biocompatible materials: polyvinyl alcohol (PVA), gelatin, and sodium alginate. Main results include: (1) an effective microfluidic approach for a direct on-chip precision fabrication of uniform embolic microspheres (the polydispersity index of fabricated particles, defined as the standard deviation of the particle diameter divided by the mean diameter, is less than 2%), (2) reliable correlation between processing parameters and particle morphology, (3) detailed features of three kinds of uniform embolic particles using polyvinyl alcohol, gelatin, and sodium alginate. The work might change the way embolic particles are fabricated for effective target embolization, as well as approaches for precise fabrication and development of high-quality microparticles. The findings also pave the way for further progress in the creation of embolic particles by design, and in tailoring their morphology to suit a desired customized embolization. In addition, the findings offer revolutionary embolic particles which will help set new standards for control, precision and ease of use in the treatment of many conditions and diseases such as uterine fibroids and liver cancers.