Cellular Encapsulation and MRI tracking with self-assembled RF shielded devices

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Present day cellular encapsulation therapies show great potential in treating a wide variety of diseases including diabetes, cancer, renal failure, Alzheimer's and Parkinson's disease. These therapies involve the implantation of devices loaded with cells that secrete biotherapeutic products. However, existing devices have several limitations: polymer based systems have limited mechanical and chemical stability and cannot be readily tracked in vivo; present day nanoporous biocapsules suffer from diffusion limitations due to their large encapsulation volume, and their large size prevents implantation proximal to certain therapeutic targets. To overcome these limitations, we provide proof-of-principle of a new class of devices for encapsulated cell technology— self-assembled perforated biocontainers for microencapsulation, that can be non-invasively tracked with MRI. We fabricated such encapsulation devices in large numbers using a novel self-assembling strategy characterized by high mechanical stability, controlled porosity, extreme miniaturization, high reproducibility and the possibility of integrating sensing and actuating electromechanical modules [1]. The strategy allows for implantation at the site of interest and therefore local secretion of bioactive substances. We envision incorporating biosensors on the surface of the device, and modulating surface chemistry.

Our self-assembled microencapsulation devices can be non-invasively tracked using MRI based on a strategy of RF shielding. We show cell encapsulation within the microdevices (Fig 1 a,b) and non-invasive detection of these devices with MRI (Fig. 1c). The self-assembled 3D microdevices provide a distinct MR signature resulting from RF shielding of the interior space. Simulation of the near magnetic field in the vicinity of the container was performed with finite element electromagnetic simulation package FEKO (EM Software & Systems-SA Ltd, www.feko.info/). The simulation used a linear polarized plane wave excitation at 500 MHz, and an excitation source of 1 V/m incident on the container; the simulation demonstrates that the magnetic field does not penetrate to the interior of the device (Fig. 1c), resulting in hypointensity in MR images (Fig. 1d).

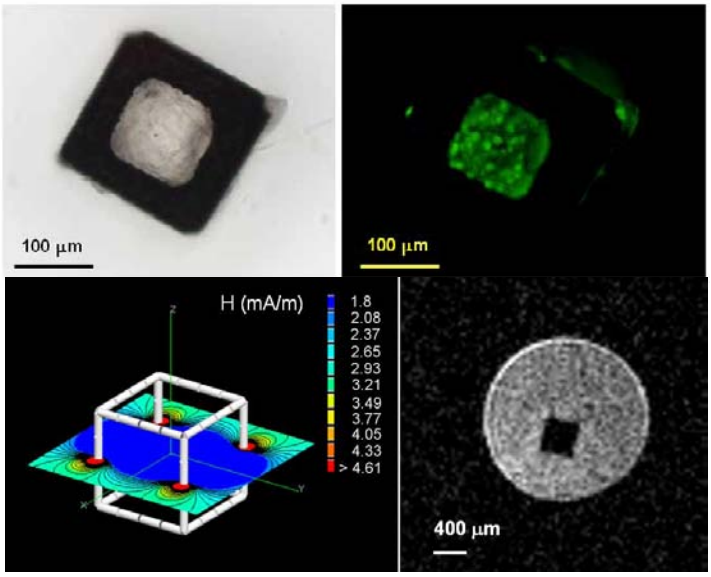

Fig. 1: **(A)** Optical microscopy image of the microdevice with cells encapsulated in an ECM gel, **(B)** corresponding fluorescence image showing cells stained with the viability stain, Calcein A-M. (c) MR image of the device showing a distinct hypointense signature. **(C)** Finite element simulation results of the near magnetic field in the region of a Cu container. The RF shielding effect caused by the container is evident. **(D)** MR images of an open faced non-magnetic Cu container showing a signature hypointensity in the shielded region.

Our current detection approach is based on negative contrast generated by RF shielding produced by the conducting material on the device. To improve in vivo MR visibility, positive contrast can be generated either by detecting the off-resonance spectral signature of the microcontainer that results from field perturbations caused by the device, or by introducing an RF resonant circuit in the device. Our fabrication strategy is compatible with MEMS and CMOS technology and can be combined with miro/nanolithography to generate micro-/nanoporous faces for immunoisolation of encapsulated cells (Fig. 2a), or to mount self-resonant RF coils (Fig. 2b) that may then be inductively coupled with an external coil. Upon self-assembly, the template shown in Fig. 2b results in 3 orthogonal Helmholtz detectors that will provide RF signal regardless of the device orientation in the body upon implantation. We are currently working on a strategy to inductively couple the devices with an external RF coil.

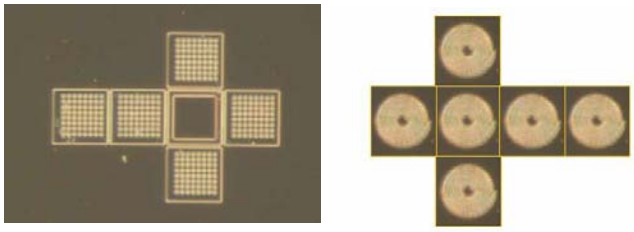

Fig 2: **(A)** 2D template of an encapsulation device with microporous faces that provide controlled porosity for immunoisolation of encapsulated cells while allowing the bi-directional diffusion of biotherapeutic products. **(B)** 2D template of the device with RF sensors on each face to provide MR signal from the encapsulated volume.

Reference: 1. B. Gimi, T. Leong, Z. Gu, M. Yang, D. Artemov, Z.M. Bhujwalla and D. H. Gracias, "Self-assembled three dimensional radio frequency (RF) shielded containers for cell encapsulation," Biomedical Microdevices, Vol. 7, Issue 4, 2005.

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