Magnetic Stem Cell Labeling Using Focused Ultrasound

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Introduction: Magnetosonoporation (MSP) is an instant, safe and efficient magnetic cell labeling technique for non-invasive MRI stem cell tracking in vivo (1,2). However, the MSP device described previously was an "open" system that might cause contamination on stem cells, and not convenient for clinical applications as well. In this study, we designed a "closed" cell labeling system by using focused ultrasound, and validated the feasibility of this device for magnetic stem cell labeling.

Materials and methods: The new MSP cell labeling apparatus was designed and implemented as shown in Figure 1. For clinical use, we assumed that fresh stem cells had been collected in a sterilized polystyrene tube with a Dual-position snap cap, mixed with a MR contrast agent, and then placed above the focused ultrasonic transducer by immersing the tube in the water. This design enabled MSP labeling by focused ultrasound in a "closed", clinically-used tube to reduce the contamination possibility. To validate the feasibility of this device for magnetic cell labeling, we firstly evaluated the cell viabilities at different power intensities of focused ultrasound without MR contrast agents. First, the cells were harvested and suspended in phosphate-buffered saline at a density of approximately 1×10^6 cells/mL. Then, the cells were treated in triplicate with a 1.05-MHz ultrasound wave of various intensities from 0 to 12 Watts, 20% duty circle, and 3-min exposure time. Cell viability was detected by trypan blue assay. The maximal power with a high cell viability (>95%) was selected for the next step of MSP cell labeling with Feridex (Berlex Imaging, Wayne, NY), a FDA-approved MR contrast agent, at a concentration of 2 mg Fe/mL. At last, the success of MSP cell labeling with focused ultrasound was confirmed by Prussion blue staining.

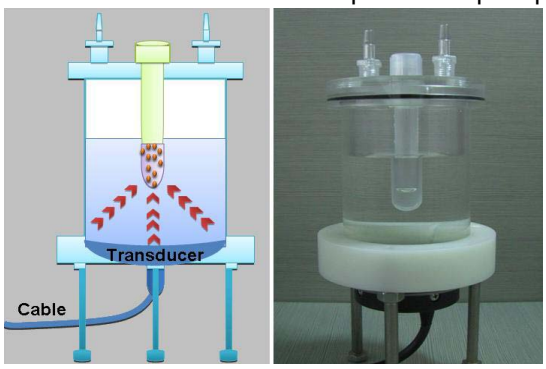

Figure 1. **(Left)** Design of a focused ultrasound MSP apparatus for convenient clinical applications; **(Right)** Photograph of the MSP device.

Results and Discussion: Figure 2 presented the cell viabilities after focused ultrasound treatment without Feridex, which demonstrated that more than 96% cell viability could be achieved at the power intensity from 0 to 8 Watts. The Prussion blue staining showed the successful MSP cell labeling using this device. Other evaluations on intracellular uptake of iron, cell differentiation and migration capabilities, the optimization of this technique/device, and the following *in vivo* study will be warranted in the near future.

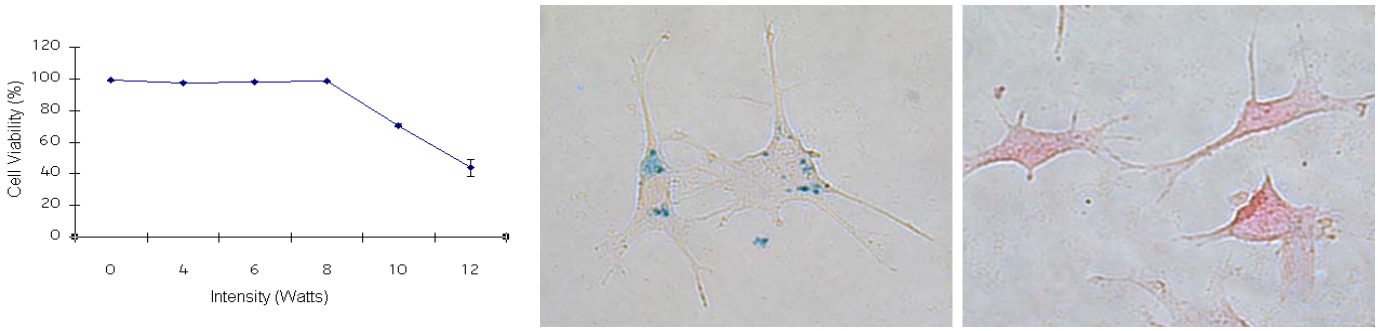

Figure 2. (left) Cell viability after focused ultrasound treatment at power intensity from 0-12 watts, 20% duty cycles and 3 minutes, which demonstrated that more than 96% of cell viability could be achieved from 0-8 W power intensities. **(Middle and Right)** Prussion blue staining showed the successful MSP cell labeling (blue dots) using this newly designed device while few cells were labeled with Feridex in the control group.

Conclusion: This study initially validated the feasibility of this new MSP apparatus using focused ultrasound. Design and application of the "closed" MSP cell labeling system will be beneficial to reduce cell contamination potential and convenient for future clinical applications.

Reference:

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2. Qiu B, Walczak P, Ruiz-Cabello J, Bulte J, Yang X. ISMRM 2007, May 19-25, Berlin, Germany.