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In Vivo MR Imaging of Tissue Engineered Human Mesenchymal Stem Cells Transplanted to the Mouse- Preliminary study

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목적 : Current progresses in harmony with stem cell biology and tissue engineering techniques have extremely contributed to the clinical applications. Transplantation of cells into patients will require techniques that can monitor their tissue biodistribution noninvasively. For this purpose, firstly, human bone marrow-derived mesenchymal stem cells (hMSCs) were labeled with superparamagnetic iron oxide (Feridex®). The gelatin sponge containing Feridex-labeled hMSCs was implanted into a nude mouse subcutaneously, followed by monitored noninvasively with MR imaging. In this preliminary study, we would like to present an approach to not only monitor the implanted tissue-engineered product, but to visualize the behavior of magnetically labeled cells within and around the tissue engineered product in the host animal.

대상 및 방법 : hMSC cultured until 90% confluence of the surface area of the culture flask. The culture of hMSCs was done in a DMEM (Invitrogen Corp., Carlsbad, CA, USA) supplemented with 10% FBS, 100 U/ml penicillin, and 0.1 mg/ml streptomycin at 37℃under 5% CO2. hMSCs were allowed to grow until 90% confluence of the surface area of the culture flask before further experiment.

Preparation of Feridex-PLL complex and cell labeling:
Superparamagnetic iron oxide (Feridex IV; Berlex Laboratories, Inc., Wayne, NJ) was used labeling agent and Poly-L-lysine (PLL; Sigma, St. Louis, MO) was used for transfection agent. Feridex (50 μg/mL) was put into a centrifuge tube containing media and then PLL (1 μg/mL) was added to the solution. Then, the solution was allowed to mix for 1 hr at 4℃. After mixing, old cell culture media was discarded and replaced with Feridex-PLL complex solution, and then hMSCs were treated with complex solution at 37℃ under 5% CO2 for 18-24 hr.

Implantation of gelatin sponge in vivo:
After 6-day culture in vitro, a gelatin sponge (3 mm × 3 mm ×3 mm) containing cells was implanted subcutaneously at the proximal thigh to a six-week-old BALB/C-nude mouse. Three and 4 weeks after the implantation, mice were imaged by 1.5 T clinical magnet with 47mm micro surface coil.

결과 : Histological study and MTT assay showed that cell labeling with MR contrast agent did not give harm in the cell viability. Also, Feridex-labeled hMSCs showed significant decrease in T2 signal intensity, even within the gelatin sponge in vitro. Lastly, there was in accordance with in vivo MR imaging and histological study.

결론 : MR imaging played significant roles not only in visualizing the tissue engineered implant, but in monitoring the biodistribution of implanted cells in vivo, which illustrates the potential of new approach proposed here for in vivo monitoring of implanted cell-based tissue engineered product.