Near-Infrared Fluorescent Polymeric Micelles for The Sentinel Lymph Node Imaging of Breast Cancer

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Keywords: Near Infrared Fluorescence, Surgical Navigation, Polymeric Micelle, Nanoparticles

The gold standard of sentinel lymph node for breast cancer surgery is based on the use of lymphoscintigraphy and blue-dye injection. Owing to high cost of radionuclide imaging and the short retention time of blue dye, near Infrared (NIR) fluorescent imaging receives high attention.[1] However, the random diffusion with body fluid and poor photo-stability are the main drawbacks for NIR dyes. To overcome the drawbacks, nano-sized NIR nanoparticles (NPs) are considered better solution.[2] In the present study, we have prepared NPs loading with newly synthesized NIR dye. The self-assembled poly (ethylene glycol)-*block*-poly(ε-caprolactone) micelles (PEG-PCL) having average hydrodynamic particle size of 62.7 ± 0.6 nm are found to be suitable for Interstitial/lymphatic fenestration. The *in vitro* releasing test showed that less than 10 % of NIR dyes were released from NPs in 48 hours post fabrication of NPs in phosphate buffered solution. In addition, the particle size of the NPs remained stable for at least 14 days.

It has been reported that the anti-PEG antibodies exist in the healthy people. That leads to reduced therapeutic efficacy and adverse immune response when PEGylated drugs are administered in patients. This study evaluated whether the PEGylated NPs consisting of PEG-PCL copolymer and fluorescent dye can affect the fluorescent imaging in the mice with pre-existing anti-PEG antibodies (IgG and IgM) in serum. To that purpose, we have induced anti-PEG antibodies in mice by intramuscular injection of PEG. The ELISA was used to detect the serum antibodies of mice. Then, an orthotopic breast cancer tumor in mice bearing anti-PEG antibodies was established. The PEGylated fluorescent NPs were subcutaneously injected around breast tumor. The IVIS Spectrum Imaging System was employed to observe the fluorescent images and intensity. As a control group, phosphate buffered solution was injected in mice. The concentrations of anti-PEG IgG and IgM in the serum of mice were determined by ELISA assay. When a PEGylated fluorescent NPs were injected in mice, the secondary immunity in mice was initiated. However, there was no difference in the fluorescent intensity of PEGylated NPs (around tumor) as compared with that of the control group (mice without anti-PEG IgG and IgM). In conclusion, this study found that the fluorescent intensity of PEGylated NPs was not affected when the mice were induced with anti-PEG antibodies.

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