Non-invasive real-time imaging of pre-formulated lipid nanoparticles in the living-body using positron emission tomography

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Background: Positron emission tomography (PET) is a non-invasive imaging technology, which enables the determination of biodistribution and topical accumulation of labeled compounds. Lipid nanoparticles are useful in drug delivery system (DDS) including anti-cancer drugs, anti-biotics, and nucleic acids for gene therapy. However, there has been no appropriate method to label pre-formulated DDS-drugs by positron emitters. We have developed an immediate labeling method for lipid nanoparticles and applied it to determine the trafficking of liposomal drugs.

Methods: Positron-labeled probe for lipid nanoparticles was originally designed and synthesized. Positron labeling of liposomes with [^{18}F]probe were conducted by a novel solid phase transition method. Real-time analysis of liposomal trafficking was performed by a planar positron imaging system (PPIS, Hamamatsu Photonics, Hamamatsu, Japan) or a small animal PET system (Clairvivo, Shimadzu, Kyoto, Japan) in mice and rats with or without brain ischemia.

Results: Real-time imaging experiments by PPIS revealed the whole body distribution of liposomal drugs in mice and rats. Precise distribution of the liposomal drugs in the brain under ischemia was examined by the small animal PET. While the blood flow was almost absent in the ischemic region observed by [^{15}O]H_2O imaging, the distribution of liposomal drugs in the ischemic region was gradually increased during 60 min dynamic imaging.

Conclusion: The new methodology for positron labeling enabled us a real time observation of flow pattern, deposition and excretion (i.e. pharmacokinetic properties) of lipid nanoparticles in the whole body or in a particular organ under physiologic or ischemic conditions.