Imaging and biodistribution of Her2/neu expression in non-small cell lung cancer with ^{64}Cu labeled trastuzumab PET

Pramila Paudyal

Pramila Paudyal, Bishnuhari Paudyal, Noboru Oriuchi, Yashuhiko Iida, Hirofumi Hanaoka, Hiroki Yoshioka, Keigo Endo

Diagnostic Radiology and Nuclear Medicine, Gunma University Graduate school of Medicine, Japan

Non-small cell lung carcinoma (NSCLC) overexpress Her2/neu gene in approximately 59% of the cases. Trastuzumab, a humanized monoclonal antibody interferes with Her2 signaling and is approved for the treatment of Her2/neu overexpressing breast cancer. However, its therapeutic use in Her2/neu overexpressing NSCLC remains obscure. The present study aimed to determine the in vivo positron emission tomography (PET) imaging of Her2/neu expression in NSCLC with ^{64}Cu labeled trastuzumab. Trastuzumab was conjugated to the bifunctional chelator 1, 4, 7, 10-tetraazacyclododecane-1, 4, 7, 10-tetracetic acid (DOTA) and was radiolabeled with ^{64}Cu. Molecular specificity of DOTA-trastuzumab was determined in NSCLC cell lines with Her2/neu overexpression (NCI-H2170) and negative expression (NCI-H520). Imaging of Her2/neu expression was performed in NCI-H2170 tumor bearing mouse with ^{64}Cu-DOTA-trastuzumab PET. In vitro studies revealed specific binding of DOTA-trastuzumab in the Her2/neu positive NCI-H2170 cells while no binding was seen in Her2/neu negative NCI-H520 cell line. Biodistribution and PET studies revealed significantly high accumulation of ^{64}Cu-DOTA-trastuzumab in the Her2/neu overexpressing NCI-H2170 tumor at 24 h and 48 h post injection (21.37±1.39 and 23.23±5.12% injection dose/gram, respectively). Estimated radiation dosimetry based on the extrapolation of the animal data revealed that the liver receives highest radiation absorbed dose (2.20mGy/MBq). The success of ^{64}Cu-DOTA-trastuzumab brought an insight to PET imaging of Her2/neu gene expression in NSCLC suggesting its potential for clinical translation to stratify patients that might be benefited from trastuzumab based therapy.

Figure 3