Contribution ID: **19** Type: **not specified**

Synthesis and evaluation of 64Cu (225Ac)-labeled rituximab for CD20 expression

Objectives: Chimeric monoclonal antibody rituximab, which selectively binds to CD20 surface antigen on B lymphocytes, has become a standard treatment for non-Hodgkin's lymphoma. This study aims to synthesize 64Cu-DOTA-rituximab and evaluate its potential for targeted alpha therapy by in vitro, in vivo studies, and evaluation of the dosimetry of 225Ac-DOTA-rituximab.
Methods: DOTA-rituximab immunoconjugate was prepared by incubation of rituximab with DOTA-NHS-ester in 1:5, 1:10, and 1:20 ratios. DOTA-rituximab conjugate was incubated with dried 64CuCl2 in acetate buffer (pH 5-6), and radiolabeling yield was confirmed by ITLC. For stability test, 64Cu-DOTA-rituximab was incubated in serum or phosphate buffered saline for 48 hours, and %dissociation was analyzed by ITLC. Cell binding assay of 64Cu-DOTA-rituximab was performed using Daudi human lymphoma cell line, and specific binding was determined by comparing non-specific binding with total binding. Binding affinity was presented as %injected dose (%ID). Biodistribution was carried out using BALB/c mouse at 1, 2, 6, 24, and 48 h post-injection, and the data is expressed as %ID/g. Residence time were computed via time activity curves of the acquired biodistribution 5 time series data. In order to calculate 225Ac S-value was simulated by Monte Carlo simulations using mice CT images. The organ absorbed dose for 225Ac-labeled DOTA-rituximab was estimated by Monte Carlo simulated 225Ac S-value.
Results: MALDI-TOF indicated that 1.3, 2.6, and 5.5 molecules of DOTA were conjugated to rituximab from 1:5, 1:10, and 1:20 conjugation ratio, respectively. Radiolabeling efficiency was higher than 98%, and 64Cu-DOTA-rituximab was used directly without purification. In vitro analysis of the stability showed that no significant dissociation of radioactivity from the complex was observed until 48 h. 64Cu-DOTA-rituximab showed significant specific binding to Daudi cells upon 3-h incubation having 19.8-24.5 %ID. It was shown that the lower the number of DOTA conjugated to rituximab, the higher the binding affinity to CD20. Biodistribution in BALB/c mouse (n=4) indicated that 64Cu-DOTA-rituximab has prolonged blood circulation up to 48 h, and heart, liver, lungs, spleen, and kidneys had high uptake at early time point. The estimated 64Cu-DOTA-rituximab absorbed dose in liver, lung, spleen, and kidney were 0.099, 0.028, 0.079, and 0.14 mSv/MBq, respectively. The estimated 225Ac-DOTA-rituximab absorbed dose in liver, lungs, spleen, and kidneys were 18.1, 5.54, 1.57, and 29.5 mSv/MBq, respectively. The RBE5 of kidney was 0.33 SvRBE5/MBq.
Conclusions: DOTA-rituximab was successfully synthesized and in vitro and showed high binding affinity to CD20-expressing cells. DOTA-rituximab will be successfully applied to targeted alpha therapy by labeling with 225Ac.

Email Address

ck190@kirams.re.kr

Presentation Type

Poster

Primary author: Dr KANG, Choong Mo (Korea Institute of Radiological & Medical Sciences)

Co-authors: Dr LEE, Chul-Hee (Korea Institute of Radiological & Medical Sciences); Dr LIM, Ilhan (Korea Institute of Radiological & Medical Sciences); Dr PARK, Ji-Ae (Korea Institute of Radiological & Medical Sciences); Dr KIM, Kwang Il (Korea Institute of Radiological & Medical Sciences); Dr LEE, Kyo Chul (Korea Institute of Radiological & Medical Sciences); Dr LIM, Sang Moo (Korea Institute of Radiological & Medical Sciences); Dr WOO, Sang-Keun (Korea Institute of Radiological & Medical Sciences); Dr JANG, Su Jin (Korea Institute of Radiological & Medical Sciences); Dr LEE, Yong Jin (Korea Institute of Radiological & Medical Sciences)

Presenter: Dr KANG, Choong Mo (Korea Institute of Radiological & Medical Sciences)

Track Classification: Dosimetry & Instrumentation