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Dosimetry Prediction of 225Ac-NOTA-Trastuzumab Based on 64Cu-NOTA-Trastuzumab in Breast Cancer: Preliminary Microdose Clinical Trial

Purpose: To predict the internal dosimetry of 225Ac-1,4,7-triazacyclononane-1,4,7-triacetic acid (NOTA)-trastuzumab and 225Ac-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA)-trastuzumab in breast cancer using 64Cu-NOTA-trastuzumab, a novel PET tracer for the HER2 and 64Cu-DOTA-trastuzumab.

Methods:
Prior to injecting the radiotracer, 45 mg of cold trastuzumab was administered for 15 mins. Five patients with breast cancer were injected with 296 MBq of 64Cu-NOTA-trastuzumab. Six patients with breast cancer were injected with 370 MBq of 64Cu-DOTA-trastuzumab. PET/CT was performed 24 and 48 hours after injection. The mean standardized uptake (SUVmean) was evaluated from the blood, liver, kidney, muscle, spleen, bladder, lung, and bone. Furthermore, the radiation activity of 64Cu-NOTA-trastuzumab and 64Cu-DOTA-trastuzumab for each organ was evaluated at imaging time points and the residence time of radiotracer was calculated from the activity of each organ. The internal dosimetry for 64Cu-NOTA-trastuzumab and 64Cu-DOTA-trastuzumab was evaluated using OLINDA/EXM software with an adult female model, which was used for evaluating the internal dosimetry for 225Ac-NOTA-trastuzumab and 225Ac-DOTA-trastuzumab.

Results:
The overall values of SUVmean in each organ decreased with time on both 64Cu-NOTA-trastuzumab and 64Cu-DOTA-trastuzumab PET images. However, the bladder showed an increasing pattern of SUVmean over time. In the liver, 64Cu-NOTA-trastuzumab showed relatively lower SUV mean (24 hours; 4.64 ± 0.28, 48 hours; 4.26 ± 0.50) compared to 64Cu-DOTA-trastuzumab (24 hours; 6.66 ± 1.57, 48 hours; 7.05 ± 1.72). 64Cu-DOTA-trastuzumab showed an increasing pattern of the SUVmean in the liver over time. In the blood pool, 64Cu-NOTA-trastuzumab showed relatively higher SUV mean (24 hours; 9.32 ± 1.23, 48 hours; 7.42 ± 1.85) compared to that of 64Cu-DOTA-trastuzumab (24 hours; 7.85 ± 1.76, 48 hours; 6.25 ± 1.64). Other tissues showed similar SUVmean values on both PET images. Any adverse was not reported. The calculated effective doses for 64Cu-NOTA-trastuzumab and 64Cu-DOTA-trastuzumab were 14.3 uSv/MBq and 53.1 uSv/MBq, respectively. 64Cu-NOTA-trastuzumab showed relatively lower radiation burden (46.4 uSv/MBq) compared to that of 64Cu-DOTA-trastuzumab (254 uSv/MBq). The predicted effective doses for 225Ac-NOTA-trastuzumab and 225Ac-DOTA-trastuzumab were 2.19 mSv/MBq and 7.83 mSv/MBq, respectively. In the case of the liver, 225Ac-NOTA-trastuzumab showed lower absorbed dose (8.44 mSv/MBq) compared to that of 225Ac-DOTA-trastuzumab (47.0 mSv/MBq).

Conclusions:
In the normal liver, lower uptake of 64Cu-NOTA-trastuzumab was observed compared to 64Cu-DOTA-trastuzumab. It may be more helpful to detect metastatic lesions in the liver. Furthermore, when the 64Cu is replaced with 225Ac for treatment purpose, liver damage may be reduced when using NOTA-trastuzumab compared to when using DOTA-trastuzumab.

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