

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 (SUV_{mean}) 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 SUV_{mean} 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 SUV_{mean} 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 SUV_{mean} 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 SUV_{mean} 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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