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Letter to the Editor

Different radionuclides in DOTA-EB-TATE effect different uptake in somatostatin receptor positive HEK293 cells

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Tian et al. developed a trifunctional ligand with an albumin binding component (Evans blue) which features a longer circulation half-life as compared to an unmodified DOTA-conjugate. It has been shown in a preclinical model that the prolonged circulation improved the accumulation of this tracer in somatostatin receptor (SSTR) positive tumors (1). In this study, bioimaging was performed by Y-86-DOTA-EB-TATE and positron emission tomography as substitute for Y-90-DOTA-EB-TATE for therapy. Dosimetric calculations revealed an increase of the tumor dose by a factor of 4 compared to the biodistribution without an albumin binding functionality.

Similarly, Bandara et al. showed in a preclinical study that, in comparison to Lu-177-DOTATATE, Lu-177-DOTA-EB-TATE resulted in an increased tumor uptake over time, no unexpected accumulation and efficient tumor control, despite similar activities (2).

Chen et al. applied Lu-177-DOTA-EB-TATE in humans and derived an increase in the tumor dose by a factor of 8 while kidney and bone marrow dose increased by a factor 3.2 and 18, respectively (3).

We investigated the labeling and the in vitro binding characteristics of Ga-68-, Cu-64-, Lu-177- and Y-90-DOTA-EB-TATE in SSTR-positive HEK293-$sstr_2$ cells (4) in comparison to unmodified DOTA-TATE-conjugates. The cells were plated in six well plates 24 h before adding the radiolabeled DOTA-EB-TATE and DOTA-TATE conjugates (200 kBq). Experiments were performed in 1 mL of standard cell culture medium at 37°C for 60 and 120 minutes. At each time point, the cells were washed with PBS and lysed with 0.3 M NaOH. The uptake was determined in triplicate for each radionuclide and each time point and was expressed as a percentage of the total activity associated with one million cells. The labeling procedure was similar for all preparations and the yields were more than 95%. We found for DOTA-EB-TATE that after one hour the cellular uptake was 9.1±0.69, 2.0±0.12, 4.9±0.26 and 4.6±0.21% and increased at two hours to 15.6±0.51, 4.3±0.18, 9.0±0.71 and 8.1±0.12%, respectively. In comparison, the bi-functional probes without the albumin binding unit revealed a one hour uptake of 23.7±1.47, 4.3±, 8.7±0.90 and 7.2±1.09% which increased at two hours to 27.3±1.66, 5.5±0.36, 12.6±1.71 and 10.2±0.18%, respectively.

These data demonstrate that the modified radiotracer featured a lower initial uptake compared to the unmodified one, regardless which isotope was used. However, the incremental gain of the uptake within the second hour was comparable between both radiotracers. This demonstrates that the radioisotope strongly influences the uptake of the SSTR-ligand. The highest diagnostic performance is expected from the radiopharmaceutical with the highest uptake, namely Ga-68-DOTATATE.

As a consequence of the different uptake, only different isotopes of the same element (like Y-86/Y-90 or Cu-64/Cu-67) can be used for assessment of biokinetic data, while theranostic “pairs” of isotopes (like In-111/Lu-177) are not appropriate. No solely diagnostic isotope of lutetium is known. Therefore, the use of a low amount of radioactivity for qualitative and quantitative (e.g. dosimetry) imaging is an elegant approach that allows a subsequent therapeutic application (3).

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No potential conflicts of interest relevant to this article exist.

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