Effect of tumor size on the accumulation of ^{67}Cu-labeled compounds targeting the somatostatin receptor in tumor

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Nuclear medicine therapy, in which a radiopharmaceutical is administered into patients for treatment, is an effective medical treatment that can target cancer cells spread throughout the body, and is attracting attention as an effective treatment that places less burden on patients. Recently, four radionuclides are used in Japan: ^{131}I, ^{90}Y, and ^{177}Lu, which are β-particle emitting nuclides, and ^{223}Ra, which is an α-particle emitting nuclide. ^{90}Y yields a high energy β-particle of 2.28 MeV and shows a good therapeutic effect, but it also has a significant impact on surrounding tissues, and the injected dose is limited by exposure to other organs.[1] There are several radionuclides expected to be used for nuclear medicine therapy. For example, ^{67}Cu has a low energy β-particle of 0.392 MeV and may have only a weak therapeutic effect, but it can be administered in large doses. Therefore, depending on the properties of cancer tissues, it effective and efficient treatment may be realized. In fact, the effectiveness of nuclear medicine therapy is affected by properties such as the size of the target cancer tissue, radiation quality, and energy, *etc.*, suggesting that a most efficient radiation energy may exist for each target.[2] In other words, although the range of therapeutic effect is limited due to low energy, it is considered that sufficient effects can be obtained even with a low energy β-particle if the tumor is small to some extent, leading to effective and efficient treatment.[3] We previously demonstrated that ^{67}Cu-ToDBTTATE, which is targeted at the somatostatin receptor, constricted tumor growth in mice model bearing AR42J rat pancreatic tumor cells. This effect was observed in tumors of various sizes less than 800 mm^3, but some tumor growth was observed in the group with size less than 200 mm^3.[4] It may be because the days after cell implantation were short and targeted somatostatin receptor was not well expressed.

In this study, we prepared model mice with tumors of various sizes and investigated the difference in the accumulation of ^{67}C-ToDBTTATE between the small and large sized tumors.

Tumor-bearing mice were prepared by implantation of AR42J tumor cells (5×10^6 cells), in 0.1 mL phosphate-buffered saline, into the flanks of nude mice (BALB/c-nu/nu, male). After the tumors grew to various sizes, biodistribution experiments were performed by intravenous administration of ^{67}Cu-ToDBTTATE from mice tail vein. The mice were discarded 48 hours after administration. Tissues of interest were extracted and weighed after which their radioactivity was measured. Results are presented as a percentage of the injected dose per gram of tissue weight. This study was performed in accordance with the recommendations by the Guide for the Care and Use of Laboratory Animals of Suzuka University of Medical Science.

Mice were divided into two groups based on the tumor size, and the weight of tumor was 0.48 ± 0.31 g in the small group and 2.16 ± 0.96 g in the large group. As a result, no difference in the accumulation of ^{67}Cu-ToDBTTATE on tumors between the small and large groups was observed in this study (Fig. 1). These data indicate that the observed tumor growth in the group less than 200 mm^3 is not due to decreased accumulation of ^{67}Cu-ToDBTTATE in tumors. Another cause of tumor growth may exist in the group with size less than 200 mm^3. However, this study may not have been able to obtain a statistically significant difference due to the small number of cases. We must examine the accumulation studies of ^{67}Cu-ToDBTTATE in tumors between the small and large groups using larger sample sizes.

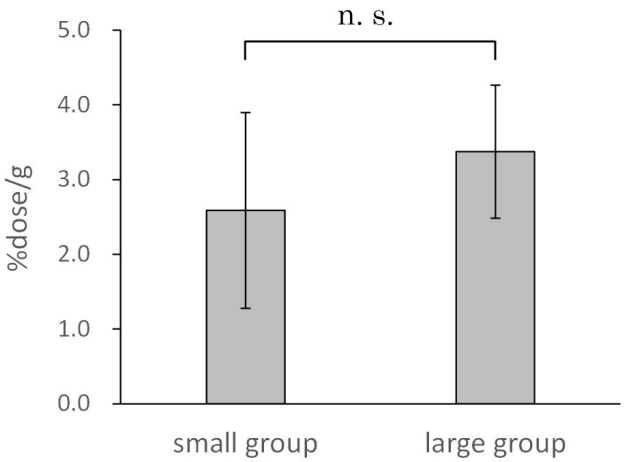

Fig. 1. Differences in the tumor accumulation of ^{67}Cu-ToDBTTATE between the small ($n = 4$) and large ($n = 4$) sized tumor groups (Student's t-test).

References
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