Efficacy of nuclear medicine therapy with $^{67}CuCl_2$ in mice bearing LS180 colon cancer

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Nuclear medicine is one of the effective methods for early diagnosis and therapy of cancer, and various radioisotopes (RI) have been used. Among them, radioactive Cu is expected to be a promising RI with diagnostic and therapeutic properties. Radioactive Cu includes ^{60}Cu, ^{61}Cu, ^{62}Cu, and ^{64}Cu, which are effective for PET diagnosis, and ^{67}Cu, which can be applied for treatment. ^{67}Cu is a therapeutic radionuclide that emits β-particles of energy 0.392 to 0.577 MeV with a half-life of 61.8 h. Although the β-particle energy of ^{67}Cu is low, it is expected to be effective in treating small cancers.[1] RIs that have high-energy β-particles, such as ^{90}Y, show a good therapeutic effect, but they also have a large effect on surrounding tissues, and the injected dose is limited by exposure to other organs.[2] ^{67}Cu has a low-energy β-particles and can be administered in large doses, leading to effective and efficient treatment.[3] Another advantage of ^{67}Cu is the ability to calculate exposure doses accurately. Injected doses of radiopharmaceuticals used in nuclear medicine therapy are calculated from the exposure doses. ^{67}Cu-labeled drugs can accurately calculate the exposure doses with ^{64}Cu-labeled ones, contributing to safe and effective personalized medicine.

Various studies have been conducted on cancer diagnosis and therapy using radioactive Cu-labeled drugs, and in recent years, the possibility of PET diagnosis using $^{64}CuCl_2$ has been demonstrated. Copper transporter protein 1 (CTR1) is overexpressed in various cancers, suggesting that ^{64}Cu accumulates in cancer via CTR1.[4] Based on these studies, the tumor accumulation of $^{67}CuCl_2$ was also evaluated, and it was found to have the same pharmacokinetics as $^{64}CuCl_2$.[5] In this study, we investigated the therapeutic effect of $^{67}CuCl_2$ on tumor-bearing mice to clarify the potential of cancer therapy using $^{67}CuCl_2$.

Tumor-bearing mice were prepared by implantation of LS180 tumor cells (5×10^6 cells) in 0.1 mL PBS into the flanks of nude mice (BALB/c-nu/nu, male). Biodistribution experiments were performed by intravenously administering $^{67}CuCl_2$. The mice were killed at 1, 24 and 48 h after administration, and tissues of interest were excised and weighed before their radioactivity was measured. LS180 tumors were grown in BALB/c mice in the same way for therapeutic studies. Mice were administered with 17.0–23.2 MBq of $^{67}CuCl_2$ intravenously. Saline-treated mice were used as a control. Mice were weighed and tumor diameters were recorded regularly. The diameters of tumorswere measured with a caliper, and tumor volumes were determined using the formula: (longer diameter) $\times$ (shorter diameter)^2/2. This study was performed in accordance with the recommendations by the Guide for the Care and Use of Laboratory Animals of the Suzuka University of Medical Science.

$^{67}CuCl_2$ showed high accumulation in the tumor, 6.50 ± 2.34, 6.85 ± 1.83, and 5375 ± 1.26% ID/g at 1, 24, and 48 h after administration, as shown in a previous study. Tumor size reduction was observed in all mice treated with $^{67}CuCl_2$ (Fig. 1). However, but relatively significant weight loss was also observed in them (Fig. 2). Therefore, ^{67}Cu is a promising RI for

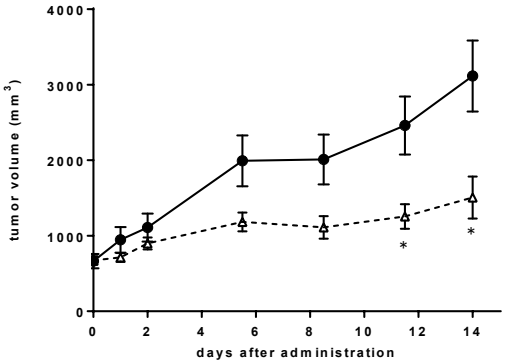

Fig. 1. Therapeutic studies of $^{67}CuCl_2$ in LS180 tumor-bearing mice. (•; saline ($n = 7$), △; $^{67}CuCl_2$ ($n = 4$). *, $p < 0.05$ (2-way ANOVA followed by sidack-test).

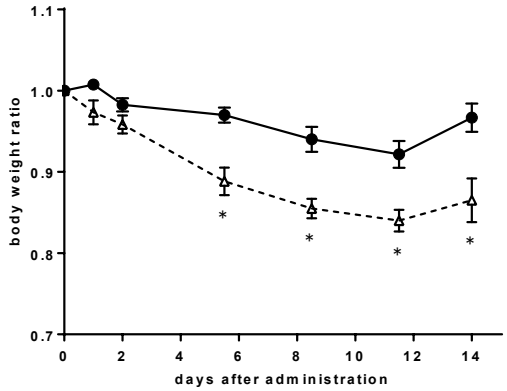

Fig. 2. Changes in body weight of mice after saline or $^{67}CuCl_2$ administration. (•; saline ($n = 7$), △; $^{67}CuCl_2$ ($n = 4$). *, $p < 0.05$ (2-way ANOVA followed by sidack-test).

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the treatment of cancer, but the use of ^{67}Cu-labeled drugs that selectively accumulate in cancer cells are thought to be more suitable for cancer therapy.

References

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