Intratumoral administration of astatine-211-labeled gold nanoparticle for alpha therapy†

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As a local radiation therapy for cancer and in addition to external irradiation with γ-rays or X-rays, the effectiveness of brachytherapy using a sealed X-ray source for prostate cancer, breast cancer, uterine cancer, head and neck cancer, and brain tumors is well known. However, the invasiveness of the procedure, extra-lesion displacement of the sealed radiation source, or adverse effects caused by the leakage of X-rays from radionuclides with a long half-life into adjacent organs are problematic issues. α-ray-emitting nuclides have a high linear energy transfer (LET) and relative biological effectiveness and are particularly toxic to proliferating cells. Because of the short range of α-ray emitters, normal tissues are minimally exposed if the radiation sources are appropriately distributed. ^{211}At is a high-energy α-ray emitter with a relatively short half-life and a high cytotoxicity for cancer cells. Its dispersion can be imaged using clinical scanners, and it can be produced in cyclotrons without the use of nuclear fuel material.

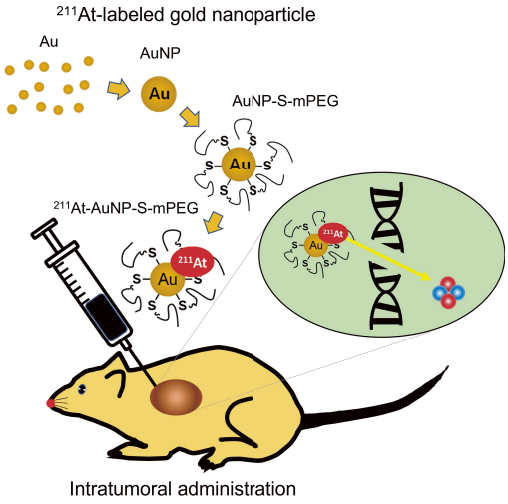

Fig. 1. ^{211}At-labeled gold nanoparticles administered intratumorally. α-ray caused DNA double-strand break and kill the malignant cells.

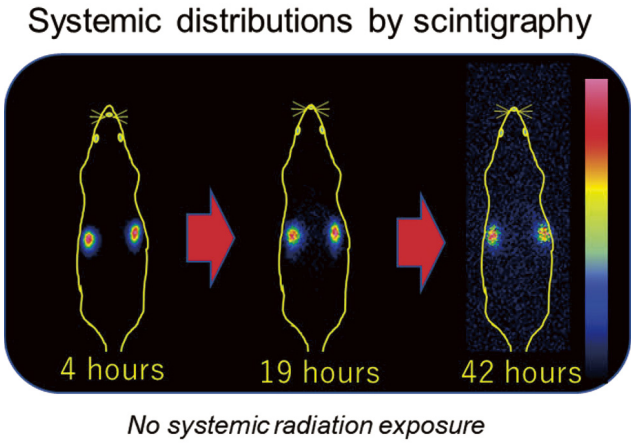

Fig. 2. The radioactivity distributions at 4, 19, and 42 hours after the administration of ^{211}At-AuNP-S-mPEG are shown. Strong radioactivity was found at the transplanted tumor sites. No systemic accumulation of radioactivity was observed in any of the organs.

The objective of this study was to propose an effective nanoseed brachytherapy with significantly reduced radiation exposure. In the present study, we investigated the systemic and intratumoral distributions and verified the antitumor effect of ^{211}At-labeled AuNP administered intratumorally (Fig. 1).

AuNP with a diameter of 5, 13, 30, or 120 nm that had been modified with poly (ethylene glycol)

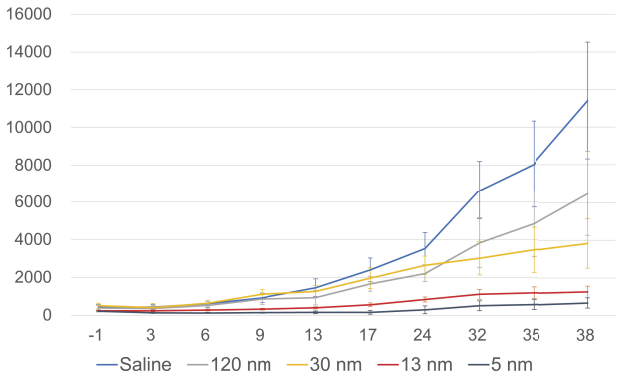

Fig. 3. Changes in the tumor volumes of the C6 glial cells after intratumoral administration (1.4±0.4 MBq/tumor for rats). The C6 gliomas treated with the 5 nm particles had the lowest growth rate, based on tumor size.

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methyl ether (mPEG) thiol and labeled with ^{211}At (^{211}At-AuNP-S-mPEG) were intratumorally administered to C6 glioma subcutaneously transplanted into rodent models. A part of ^{211}At used in this work was produced in the ^{209}Bi$(\alpha, 2n)^{211}$At reaction using the RIKEN AVF cyclotron. After intratumoral administration, ^{211}At-AuNP-S-mPEG became localized in the tumor and did not spread to systemic organs during a time period equivalent to 6 half-lives of ^{211}At (Fig. 2). Tumor growth was strongly suppressed by ^{211}At-AuNP-S-mPEG without any critical side effects. In the C6 glioma model, the strongest antitumor effect was observed in the group treated with ^{211}At-AuNP-S-mPEG with the smallest diameter of 5 nm (Fig. 3).

The intratumoral single administration of a simple nanoparticle, ^{211}At-AuNP-S-mPEG, was shown to suppress the growth of tumor tissue strongly in a particle size-dependent manner without radiation exposure to other organs caused by systemic spread of the radionuclide.