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Increased uptake of At-211 in thyroid gland by the preparation with ascorbic acid for targeted alpha therapy of thyroid cancer

Objectives: Astatine-211 (²¹¹At) is an alpha-emitting radionuclide suitable for targeted alpha therapy. Because At is a heavier homolog of iodine, astatide ion (At^-) is expected to be applied to the treatment of thyroid cancer. In this study, ²¹¹At was treated by ascorbic acid (AA) as reducing agent to prepare At^-. We aimed to evaluate the uptake change in the thyroid after the preparation of ²¹¹At solutions with AA and demonstrate the treatment effect in the differentiated thyroid cancer xenograft mice.

Method: Astatine-211 was produced in the ²⁰⁹Bi(α, 2n) reaction and supplied through Short-lived RI Supply Platform. Produced ²¹¹At was then separated from the target materials by a dry distillation method and dissolved in pure water. The aliquot of ²¹¹At solution was mixed with 1% AA solution to prepare At^-. The radiochemical yield was checked by radio-TLC. The crude ²¹¹At solution or ²¹¹At with AA solution was administered to normal rats (n=3 for both solution) through tail vein under isoflurane anesthesia. In vivo imaging of ²¹¹At in the normal rats was then carried out using a gamma camera at 0.5, 3, 6 and 24 hrs after administration. The ²¹¹At solution with AA was also administered to mice with implanted K1 cells (human papillary thyroid carcinoma) expressing sodium iodide symporter (NIS). Mice were divided into 4 groups according to the injected dose [1 MBq (n=6), 0.4 MBq (n=6), 0.1 MBq (n=6), control (n=6)]. Distribution of ²¹¹At administered in the mice was investigated at 3 and 24 hrs after administration by the gamma camera.

Results: The radiochemical yield of At^- checked by radio-TLC increased from approximately 20% to 90% after treatment of the crude ²¹¹At solution with AA. In vivo imaging of ²¹¹At in the normal rats showed high uptakes in the thyroid, the stomach, and the bladder. Uptake of At with AA in thyroid gland was 2–3 times higher compared to crude ²¹¹At solution. In the xenograft mice, there was a stable accumulation in the thyroid tumor at 3 and 24 hrs post administration (23 ± 11 %ID and 13 ± 7 %ID, respectively). Tumor growth was immediately inhibited after administration of ²¹¹At in a dose-dependent manner. Suppression of tumor growth was maintained until 17, 31, and 41 days after administration of ²¹¹At in 0.1, 0.4, and 1 MBq groups, respectively.

Conclusion: Uptake of ²¹¹At can be enhanced in the normal thyroid by increasing the radiochemical purity of At^-. The administered ²¹¹At showed good treatment effect in thyroid cancer xenograft, suggesting that ²¹¹At solution with AA is promising for the targeted alpha therapy for the thyroid cancer.

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