

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

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

**Method:** Astatine-211 was produced in the  $^{209}\text{Bi}(\alpha, 2n)$  reaction and supplied through Short-lived RI Supply Platform. Produced  $^{211}\text{At}$  was then separated from the target materials by a dry distillation method and dissolved in pure water. The aliquot of  $^{211}\text{At}$  solution was mixed with 1% AA solution to prepare  $\text{At}^-$ . The radiochemical yield was checked by radio-TLC. The crude  $^{211}\text{At}$  solution or  $^{211}\text{At}$  with AA solution was administered to normal rats ( $n=3$  for both solution) through tail vein under isoflurane anesthesia. In vivo imaging of  $^{211}\text{At}$  in the normal rats was then carried out using a gamma camera at 0.5, 3, 6 and 24 hrs after administration. The  $^{211}\text{At}$  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  $^{211}\text{At}$  administered in the mice was investigated at 3 and 24 hrs after administration by the gamma camera.

**Results:** The radiochemical yield of  $\text{At}^-$  checked by radio-TLC increased from approximately 20% to 90% after treatment of the crude  $^{211}\text{At}$  solution with AA. In vivo imaging of  $^{211}\text{At}$  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  $^{211}\text{At}$  solution. In the xenograft mice, there was a stable accumulation in the thyroid tumor at 3 and 24 hrs post administration ( $23 \pm 11\% \text{ID}$  and  $13 \pm 7\% \text{ID}$ , respectively). Tumor growth was immediately inhibited after administration of  $^{211}\text{At}$  in a dose-dependent manner. Suppression of tumor growth was maintained until 17, 31, and 41 days after administration of  $^{211}\text{At}$  in 0.1, 0.4, and 1 MBq groups, respectively.

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

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### Presentation Type

Contributed Oral

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