Supply of At-211 for investigator-initiated clinical test of targeted alpha therapy at the University of Osaka hospital

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Targeted alpha therapy (TAT) using radioisotopes emitting several alpha particles during the radioactive decay chain is one of the most effective treatment methods for refractory cancer such as metastatic cancer and invasive cancer. Especially TAT has a great advantage of dose concentration in a cancer cell, resulting from the large energy loss and short range of the alpha particles[1]. The energy and range of the alpha particles emitted from radionuclides such as At-211, Ac-225 and Ra-223 are around 7 MeV and 50 μm, respectively. Targeting medicine labeled with the alpha emitter is intravenously injected, selectively delivered to tumor tissues, and spontaneously accumulated in cancer cells. The cancer cell intaking the targeting medicine is severely damaged due to DNA double strand break caused by the energy loss of the emitted alpha particle or chemical reaction with free radicals generated by alpha-induced ionization.

Astatine is a radioactive halogen element without any stable natural nuclei. At-211 has a half-life of 7.2 hours, much shorter than Ac-225($T_{1/2}$=10.0 days) and Ra-223 ($T_{1/2}$=11.4 days). The mean energy of two alpha particles emitted from At-211 in a sequential decay chain is 6.8 MeV which is sufficient to kill a cancer cell. At-211 is directly produced by the nuclear reaction of ^{209}Bi(^{4}He,2n)^{211}At using a 28.5 MeV $^{4}He^{2+}$ ion accelerated by the RCNP AVF cyclotron[2]. The beam energy was decreased to 28 MeV by the energy loss in a Havar foil used as a diaphragm between a beamline section and target space. The energy of $^{4}He^{2+}$ ions should be tuned to 29 MeV or less to avoid production of At-210 which decays to a toxic element of Po-210.

The target chamber for At-211 production is located at the end of F-course in M Experimental Room. A thin bismuth target with a thickness of 15 - 20 mg/cm^2, formed on the surface of an aluminum backing plate with cooling water behind the plate, was set at an angle of 15 degrees on a target basement as shown in Fig. 1. A helium gas is additionally blown on the surface of the bismuth target to cool down the target heated by a beam power loss. A 28.5 MeV $^{4}He^{2+}$ ion beam was focused on the target with a beam

spot size of around 10 mm in diameter. The beam was scanned on the target by a wobbling magnet system to spread beam loss power widely. We started supplying 600 MBq At-211 for investigator-initiated clinical test of TAT using [At-211]-PSMA-5 labeled with At-211 for Castration-resistant prostate cancer at the University of Osaka hospital in June 2024. Enough At-211 for treatment was produced by almost half a day irradiation with a beam current of more than 6 electric-μA. The At-211 production beam time was regularly scheduled once a month. The annual beam time for At-211 production at the RCNP cyclotron facility reached to 840 hours in 2024.

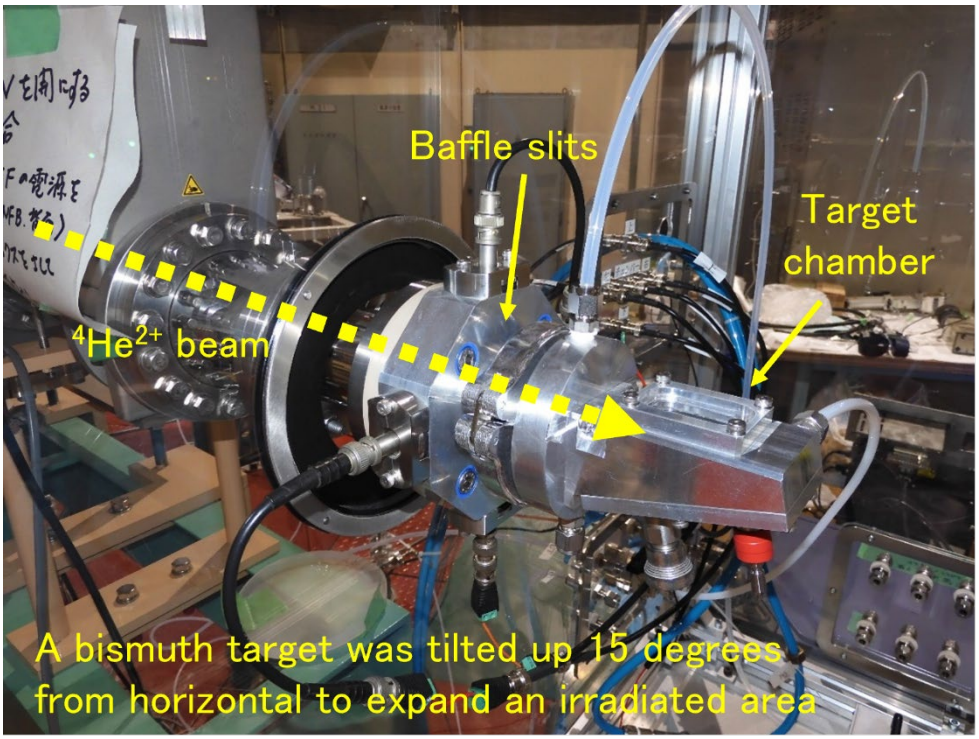

Figure 1: Target chamber for production of At-211 located at the end of F-course beamline.

References

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