Abstract

Among a number of radionuclides being studied for their possible application in radionuclide therapy of cancer, considerable interest has during the last decade been focused on the α-emitting radionuclide astatine-211 (^{211}At, $t_{½}$=7.21 h). The differences in properties between ^{211}At and its halogen neighbour ^{125}I$^-$ are of great importance in the investigation of the potential use of free ^{211}At in radiation therapy of anaplastic thyroid carcinomas (ATCs) and tumours expressing the sodium/iodide symporter (NIS) and in the optimisation of radiation protection when handling ^{211}At.

The transepithelial transport and cellular uptake of free ^{211}At and ^{125}I$^-$ were studied simultaneously in an *in vitro*-reconstituted thyroid epithelium of porcine thyrocytes cultured in bicameral chambers under the influence of different substances. Neither ouabain nor perchlorate, which both almost completely abolished the transport of ^{125}I$^-$, were able to fully suppress the basolateral transport of ^{211}At, emphasizing the differences in the way in which the thyrocytes handle ^{211}At and ^{125}I$^-$, and may offer an explanation of the higher accumulation of ^{211}At than iodide in ATCs in animal models. Furthermore, the magnitude of thyroidal ^{211}At uptake and efflux was strongly dependent on the functional activity of the cells, as in the case of ^{125}I$^-$. However, ^{211}At efflux probably involves several permeating mechanisms with varying sensitivity to an anion channel blocker (DIDS), all of which are probably not shared by ^{125}I$^-$, suggesting that anion channel blockage may be useful in increasing the retention of, and hence the absorbed dose from, both ^{211}At and radioiodine in NIS-expressing tumours.

The biodistribution of ^{211}At and ^{125}I$^-$ in nude mice bearing tumours derived from human ATC cell lines was studied together with non-tumour-bearing mice. In all extra-thyroidal tissues, the activity concentration of ^{211}At was higher and the retention time longer, than that of ^{125}I$^-$. The biodistribution of ^{211}At and ^{125}I$^-$ was slightly affected by tumour growth and type of ATC cell line. The higher tumour uptake of ^{211}At in one of the tumours suggests that the potential use of ^{211}At in therapy of ATC may be tumour specific. The high uptake of ^{211}At by some normal tissues may restrict the use of ^{211}At. Therapy of ATC may be improved by the reduction of uptake in normal tissues or by increasing the cellular uptake and retention of the tumour by physiological and pharmacological means.

The absorbed dose of ^{211}At to different tissues in man was estimated based on extrapolation of biodistribution data obtained from the rat and mouse. The highest estimated absorbed doses per unit activity administered were obtained for the thyroid and stomach (based on rat and mouse data), together with the pituitary gland (rat data) and the salivary glands (mouse data), all being NIS-expressing tissues. Furthermore, the metabolism of ^{211}At was quite different from that of iodide, at least in animals, and the iodide kinetic models given by ICRP would not be valid for ^{211}At in man. The effective dose of ^{211}At to man was estimated to be 93-190 mSv/MBq, and the annual limit on intake (ALI) for intravenous injection was determined to be 0.1-0.2 MBq. However, extrapolation of biokinetic data from laboratory animals to man is complex for reasons which include the differences in rates of distribution and metabolism of the radionuclide and in the mass of an organ relative to the body mass.

Due to the unexpectedly high volatility of ^{211}At, up to 85% during one hour, and its significantly higher adsorption onto polystyrene compared with ^{125}I$^-$, it is important to ensure adequate radiation protection during the laboratory handling of free ^{211}At.

Keywords: ^{211}At, ^{125}I, Astatine, Iodine, Thyroid, Dosimetry, Volatility, Adsorption, Biokinetics, Biodistribution, Anaplastic thyroid carcinoma

ISBN 91-628-6560-9