外　人　講　演　I

SHORT-LIVED RADIONUCLIDES AND RADIOPHARMACEUTICALS FOR TUMOR LOCALIZATION

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Efforts to find potential tumor specific radiopharmaceuticals have generally relied on the affinity of metals for neoplasms and have concentrated on systematic approaches. Difficulties which persist are the selection of a tumor model which is extrapolatable to human disease, and the availability of an arsenal of radionuclides of varying physical properties (half life and decay mode) which can be applied for diagnosis or therapy. The cyclotron chemistry and radiopharmaceutical status of selected short-lived cyclotron-produced radionuclides which have been studied as simple inorganic species or incorporated into labeled compounds will be summarized.

Lead-203 (52.1 h, 279 keV) was produced by the ^{203}Tl (d, 2n) ^{203}Pb nuclear reaction at 22.7 MeV on Tl metal. The ^{203}Pb was separated by an extraction procedure with a radionuclidic purity of $>99.99\%$. It typically contained 10 μg of Pb and 3–24 μg of Tl. Tris-hydroxymethyl-aminomethane was chosen as a complexing agent for ^{203}Pb because of the known physiological characteristics of the ligand. Pb (tris)$_2$ has a log K_f of 5.22 in water. The radiopharmaceutical preparation contained $0.08–0.24 \times 10^{-4}$ moles tris/ml and was administered at pH 6.8 to 7.2. The time course of Pb (tris)$_2$ in the major organs and tumor following the i.v. or i.p. administration was determined in normal mice and mice bearing sarcoma-1, sarcoma-180, Adenocarcinoma of breast, Ependymoma, and in Syrian Golden hamsters bearing either skin or ocular Greene melanoma. Tumor uptake was generally 1 to 4.5%/g. Significant tumor/nontumor ratios were found in the ocular melanoma model, and the concentration in the lens was minimal. The tumor eye to control eye ratio was 26 at 24 hrs. Mice bearing the Ependymoma gave a tumor/brain ratio of 10 between 3 and 120 hrs. The pharmacodynamics of ^{203}Pb-tris-(^{14}C-hydroxymethyl), ^{203}Pb-tris-(^{14}C) were determined in mice bearing sarcoma-1 ascites tumors. Tris-(^{14}C) cleared the blood with a 2 component half time of 0.25 and 6 hrs, and did not preferentially localize in any tissue. With the double labeled tris, the ^{14}C and ^{203}Pb both rapidly cleared the blood during the first hour, but were then relatively constant. The ^{203}Pb activity in the tumor increased during the first 3 hrs to 2%/g; whereas the ^{14}C activity, while initially higher, plateaued to a value identical to the ^{203}Pb. In muscle the ^{203}Pb activity was relatively constant (0.46–0.24%/g), whereas the ^{14}C activity decreased by 50% during the first 5 hrs. It appears that the ligand or a complex involving the Pb (tris)$_2$ is involved in the delivery of

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the ^{203}Pb to the tumor cells. Comparative data for 8 other conventional radiopharmaceuticals have been determined in the Green melanoma model. The affinity of ^{203}Pb (tris)$_2$ for melanoma appears to be as clinically promising as other compounds presently being evaluated for ocular scintigraphy, namely quinoline analogs such as (iodine-123)-4-(3-dimethylaminopropylamino)-7-iodoquinoline. However, the iodinated quinoline appears to be melanin specific which offers some advantage in the dianosis of ocular melanoma. The animal data suggest that an initial evaluation of ^{203}Pb (tris)$_2$ in patients is warranted.

Radiopharmaceuticals labeled with short-lived positron emitting radionuclides may prove useful if used in conjunction with a positron emission tomograph to locate, size and stage the remission of tumors. However, there are no successful examples to date. A promising radionuclide is potassium-38 (7.62 m, β^+). The ^{40}Ar (p, 3n) ^{38}K reaction with Ep=32$\rightarrow$29.8 MeV was used to conveniently produce ionic ^{38}K in $>$99.99% radionuclidic purity. Following an irradiation to 85% of saturation, the argon gas was vented, 3 ml of sterile water for injection was introduced into the Ni target to wash the ^{38}K through a Dowex 1-X8 anion exchange resin attached to a Millipore filter, and into a syringe for injection. Mice bearing amelanotic B-16 melanoma displayed on uptake of 2.3 ± 0.1%/g at 7 min post-i.v. administration.

This research was performed at Brookhaven National Laboratory under contract with the U.S. Department of Energy and supported by its Division of Basic Energy Sciences.

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