

Study on Tumor Affinity of ^{99m}Tc -labeled Radiopharmaceuticals
The Comprehensive Investigation of Various ^{99m}Tc -labeled Radiopharmaceuticals for
Tumor Affinity in Contrast to Biologic Behaviour of ^{67}Ga -Citrate

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Biologic characteristics of various ^{99m}Tc -labeled radiopharmaceuticals have been comprehensively investigated to get a promising indicator for tumor imaging in contrast to biologic behaviour of ^{67}Ga -citrate in Ehrlich's tumorbearing mice. In this paper were included the following eleven preparations: ^{99m}Tc -HSA (human serum albumin), $^{99m}\text{TcO}_4$ (pertechnetate), ^{99m}Tc -TSL (trasyolol), ^{99m}Tc -EHDP (diphosphonate), ^{99m}Tc -DMSA (dimercaprosuccinic acid), ^{99m}Tc -DSDP (diethyl stilbestrol diphosphate), ^{99m}Tc -LASP (L-asparaginase), ^{99m}Tc -BLM (bieomycin), ^{99m}Tc -UK (urokinase), ^{99m}Tc -Man (mannitol), ^{99m}Tc -Con A (concanavaline A). Each one has been comprehensively investigated about the following principal biologic characteristics: 1) an absolute concentration in tumor tissue (expressed as a percent

administered dose per gm. of tissue weight), 2) a concentration ratio of tumor tissue to organ, 3) the clearance from blood and skeletal muscle tissue, 4) the relative superiority index (RSI) calculated from the comparison with biologic characteristics of ^{67}Ga -citrate.

It could be concluded from this preliminary investigation that ^{99m}Tc -labeled radiopharmaceuticals such as ^{99m}Tc -Man and ^{99m}Tc -BLM which possess the biologic characteristics with the faster blood disappearance and without the accumulation to specific organs may be more preferable and practical for tumor imaging, considering the short physical half life of technetium-99m and the hazardous radiation to patients due to the considerable extensive administration.

On a Current Progress of Labelling Method with F-18

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In developing a clinical application of cyclotron produced short-life radio nucleides, it is important to establish the labelling methods with their nuclides. We studied improvement of specific activity, shortening of preparation time, radiation safety and convenient handling in labelling of various fluoro-compounds.

The nuclear reaction, (A) $^{20}\text{Ne}(d, \alpha)^{18}\text{F}$, (B) $^{20}\text{Ne}(^3\text{He}, \alpha n)^{18}\text{F}$, produced anhydrous, carrier-free ^{18}F and the reaction (C) $^{16}\text{O}(\alpha, pn)^{18}\text{F}$, produced ^{18}F in water. The reaction (A) is most adapted for labelling synthesis.

Isotopic exchange was used to incorporate ^{18}F into fluorinating agent or precursor of fluoro-compounds. Anhydrous, carrier-free ^{18}F was eluted semi-automatically with AgF , diazonium salts or

BF_3 -ether complex in some anhydrous organic solvents. ^{18}F in water was also used for organic synthesis, by effective trapping with quartz sand and drying up.

^{18}F -benzoic acid (1), ^{18}F -hippuric acid (2), ^{18}F -phenylalanine (3) and ^{18}F -tryptophan (4) were synthesized by Schiemann decomposition of their diazonium fluoroborates. 2- and 6- ^{18}F -purine derivatives (5) were prepared by halogen exchange of AgF with chloro-derivatives. 3-acetoxy-5-hydroxy-6-fluorocholestane- ^{18}F (6) was given by the reaction of BF_3 -ether with its epoxide. Amino acids were obtained as salt-free solution by Amberlite IR-4B or Porapak Q column chromatography. Moreover it was succeeded in preparation of bioactive, L-form of 5-F-tryptophan by enzyme reaction.

The specific activity of these ^{18}F -compounds was high enough to apply to clinical use. The compound (1) and (2) were synthesized as kidney scanning

agent, and (3) and (4) as pancreas scanning agent, (5) as tumor affinity agent, (6) as adrenal gland scanning agent.

Fundamental Studies on Production and Quality of ^{201}Tl

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Thallium(I)-201, having good biological and physical properties as a myocardial imaging agent, is now an object of interest in nuclear medical field in Japan.

With the intention of routine production of ^{201}Tl for medical use, we have investigated the nuclear reaction, chemical processing and testing method. Natural mercury and thallium were tried first as target material in expectation of possible ^{201}Tl producing nuclear reactions; ^{202}Hg (p, 2n) ^{201}Tl and ^{203}Tl (p, 3n) $^{201}\text{Pb} \xrightarrow{\text{EC}} ^{201}\text{Tl}$. Thus the target were bombarded with proton accelerated to 26 MeV with the cyclotron of model CS-30 (Tcc). When mercury was used as target material, number of (p, xn) reactions seemed to occur to produce non-separable radionuclidic impurities such as ^{200}Tl and there were some problems and difficulties related to target material treating and chemical processing. On the other hand, thallium target, by bombardment with 26 MeV proton, gave the intended ^{201}Pb in a satisfactory yield and then radionuclidic and chemical purities of final

product (^{201}Tl , daughter of ^{201}Pb) were expected to be good after chemical separation. Thus the thallium target system was examined further, using ^{203}Tl -enriched target material. After bombardment, by solvent extraction method, ^{201}Pb was separated from ^{203}Tl target material which would be recovered for the next bombardment. Thallium-201, which has been born from ^{201}Pb was re-extracted from ^{201}Pb - ^{201}Tl mixture about 30 hrs after first separation when its radioactivity reached maximum. Separated ^{201}Tl was purified by passing through an ion exchange column to obtain the pure monovalent ^{201}Tl . And the final product was examined by paper chromatography in n-BuOH saturated with 1 N HCl. And it was proved to be consist of exclusively monovalent ^{201}Tl and to contain no radiochemical impurities. No more than 2 ppm of Tl and Cu were detected by chemical test and average radionuclidic purity of recent 10 lots at calibration time was $99.76 \pm 0.03\%$ with $0.24 \pm 0.03\%$ of ^{202}Tl .

The Production of ^{13}N Labelled Ammonia

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The nitrogen-13 labelled ammonia, which is useful for the liver function studies, has been produced using a remote control system at NIRS medical cyclotron facility.

When a sterilized water was irradiated with 10 uA protons (15 MeV) for 20 minutes, over 90% of radio-activity was determined as NO_2^- NO_3^- and 3% of that was the ammonia in the irradiated water with the impurities as ^{18}F which was produced by the $^{18}\text{O}(\text{p}, \text{n})^{18}\text{F}$ and ^{48}V (from titanium target cell).

These ^{13}N labelled nitrogen oxides were reduced to ^{13}N labelled ammonia by the action of Devarda's alloy and sodium hydroxide. Finally, the reduced $^{13}\text{NH}_3$ was distilled into the 5 ml of 1% NH_4Cl solution which is useful for the study of liver function by the administration from a large intestine. The 80 mCi/5 ml of the final product has been obtained with 99.7% of radiochemical purity.

All of these procedures were operated remotely from the outside of the hot-cell using the specially designed control system.