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RADIOPHARMACEUTICALS

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In Radiopharmaceuticals (RI pharmaceuticals), a noticeable trend observed in recent years is over the technical development on the synthesis of radiopharmaceuticals labeled with positron emitting radionuclides, C-11, N-13, O-15, F-18, as well as with single photon emitting radiometallic nuclides, Tc-99m, In-111. Moreover, the great potentiality for an increased use of I-123 and of generator produced radiometallic nuclides Ga-68, Cu-62 is becoming a subject of interest.

Although, diagnostic study is now been carried out with $15O_2$, $13NH_3$, 18F-FDG, C-11 methylation as a reaction to introduce the positron radionuclide, or in other word, as a labeling reagent in organic radiopharmaceutical synthesis, is now also an active field of work in various leading research center. The labeling of receptor binding molecules is a good representative of successful use of the methodology and it has become the topic of current interest. As regard to the single photon metallic radionuclides, great changes are taking place centered particularly on Tc-99m; from the development of technetium radiopharmaceuticals based on classical technetium chemistry to new drug-designed radiopharmaceuticals holding a desired biological or biochemical activity. Recent achievement of radiometallic labeled monoclonal antibodies is a good example of the approach.

On the other hand, considerations as for the use of I-123 or of those positron RI depend on the physical properties or if the radioiodination is recalled, on the achievement of appropriate synthetic method. Concurrently, as for the labeling with single photon radiometallic nuclides, research on the synthesis of various ligand is now under progress.

In the coming future of radiopharmaceuticals, the character of each labeled compound will play a determining factor. Thus, as for the positron RI, the great possibility and diversification of chemical structures and as for the radiometallic nuclides its ready availability for routine diagnosis will constitute decisive arguments; most probably I-123 holding an intermediate position may undergo a rising progress. However, instead of being satisfy with the interesting biokinetic data gathered with the positron labeled compound, more meaningful research centered on its use as diagnostic agent should be carried out. Moreover, those data can be used with good advantages for building up new radiopharmaceuticals, either of I-123 or radiometallic nuclides of higher availability for routine clinical diagnosis. Thus, a concurrent effort to correlate those results with the easy available radionuclides, I-123 or radiometallic nuclides are desirable.

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ANALYSIS MODEL AND QUANTITATION IN EMISSION TOMOGRAPHY. I.Kanno. Research Institute for Brain & Blood Vessels-Akita, Akita.

The emission tomography provides an in vivo quantitative distribution of a radioisotope tracer with sufficiently fine spatial and temporal dimensions. In order to describe behaviors of the radiotracer a spatial and temporal distribution of it in the target organ and a temporal distribution of it in the arterial blood are measured. Using these data mathematic description solves a 'physiological' black box. Movements of tracer from arterial plasma pool to extravascular space are mainly controlled by physics process, i.e. diffusion, permeation and transportation, then tracer will be trapped or fixed in the tissue mainly by biochemical process, i.e. metabolism, binding and dissociation. These processes can usually be dealed with a compartment model. However, once we try to describe the physiological behavior as accurate as possible, we should have debts of too many compartments to solve uniquely. Thus, it is always important that the model is forced to be simplified in mathematical description. Most of the generalized compartment models are mainly discussed here. Firstly two compartments are considered. From the mass conservation, a temporal change of the tracer in the tissue compartment equals difference between input and output rates,

$$dC_2/dt = k_1 \cdot C_1 - k_2 \cdot C_2 - mu \cdot C_2 \qquad (1)$$

where Ci is concentration of tracer in the compartment i, ki is rate constant between the compartments, and mu is physical decay coefficient. This differential equation describes model. This model typically used in blood flow measurement. If tracer is diffusible tracer, the solution of Equation (1) will be a well known Kety-Schmidt equation. If tracer is microsphere, flow is given by a microsphere model. Secondly three compartments are considered. Similar differential equations are described between the compartments,

$$\begin{aligned} dC_2/dt &= k_1 \cdot C_1 - k_2 \cdot C_2 - k_3 \cdot C_2 + k_4 \cdot C_3 \\ dC_3/dt &= k_3 \cdot C_2 - k_4 \cdot C_3 \end{aligned} \qquad (2)$$

where C_1, C_2 and C_3 are decay corrected concentration of the tracer or its metabolite. In general, if $k_4=0$, the solution is a well known Sokoloff model. In case that k_4 is non-zero, Huang model is applied. This model has been widely adapted in various tracer analysis in the positron emission tomography.

In case of tumor, however, the hypothesis that requires instantaneous equilibrium in Equation (1) or (2), is not always correct. Then, a finite diffusion model which considers a diffusion speed from the capillary into the tissue, has been proposed recently.