RADIOCHEMISTRY AND RADIOPHARMACEUTICAL CHEMISTRY FOR MEDICINE

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Summary

Radiopharmaceutical chemistry has progressed over the last decades leading to the establishment of an independent field of modern science. Today, radiopharmaceuticals do belong to the key tools of medicine in general and nuclear medicine in particular, both in the context of diagnosis and therapy. Radiopharmacy is adding its value to fundamental biochemical and medicinal research. Parallel to the application of radiopharmaceuticals in hospitals, radiopharmaceutical chemistry demonstrates its capability to contribute to the industrial development of new drugs.

It is fascinating to realize, that radioactivities of several TBq are produced every day of those "medical" radionuclides, which are in turn transferred chemically into a variety of radiodiagnostics and radiotherapeutics. Accordingly, well educated and trained specialists in radiochemistry and radiopharmaceutical chemistry are employed and increasingly needed to cover the scientific and technical demands of modern radiopharmaceutical development and production. The IAEA, for example, is accompanying this strategy by helping to proliferate the special know-how existing in the industrial countries to all the other areas of our world.

1. Introduction

Radiopharmaceutical chemistry has progressed over the last decades leading to the establishment of an independent field of modern science. Looking back, it began with the discovery of the phenomenon of radioactivity (1903 Nobel prize to H. Becquerel, M. and P. Curie for ... *the discovery of spontaneous radioactivity ... and researches on the radiation phenomena ...*). Next, I. Curie and F. Joliot (1935 Nobel prize for ... *their synthesis of new radioactive elements ...)* utilized nuclear reactions to create artificial radionuclides. In addition to the radionuclides isolated from naturally occurring decay chains, these artificially produced, no-carrier-added (n.c.a.) radionuclides opened the window for the oncoming tracer concept: The tracer principle applied to biology adopted radionuclides and labeled compounds at a nano-molar scale for the investigation of physiological processes *in vivo* (1943 Nobel prize to G. Hevesy for his work on "*... the use of isotopes as tracers in the study of chemical processes ...*"). This pioneering application of radioactive nuclides for biochemistry and physiology provided the first insights into the dynamics of chemical and physiological reactions in living systems.

In parallel, the experimental and theoretical cognition of nuclear fission in 1938 by O. Hahn and F. Strassmann, and the theoretical explanation by L. Meitner and O.R. Frisch (1944 Nobel Prize to O. Hahn for *"... discovery of the fission of heavy elements ..."*) had a spin-off for radiopharmaceutical chemistry. The fission of uranium today provides an important resource of radionuclides applied in nuclear medicine diagnosis and therapy. The uranium fission product ^{131}I, for example, became a key radionuclide in the 1950s, when R.S. Yalow and S.A. Berson developed the approach of radioimmunoassay for quantitative *in vitro* analysis of physiological and biochemical processes (1977 Nobel prize to R.S. Yalow for *"... the development of radioimmunoassays ..."*)

The experience in hot atom chemistry, and the bridging of radiochemistry with organic chemistry, for example, further facilitated the production and use of radionuclides and labeled compounds adequate for diagnostic and therapeutic application *in vivo*. This part of the route of radiopharmaceutical chemistry was accompanied not only by sciences like mathematics, physics, and biology, but also by industry and technology, providing the necessary equipment such as detectors and tomographs, reactors and cyclotrons. In fact, radiopharmaceutical chemistry shows itself as an excellent example of modern interdisciplinarity in the today's world of science and technology. Isn't it breathtaking, that hundreds of thousands of diagnostic procedures are performed every year, with a variety of tracers labeled with ^{99m}Tc, a radioisotope of an element, absolutely non-relevant to our biological nature? Or that a naturally non-existing ^{18}F-labeled derivative of glucose is routinely used for the quantification of glucose metabolism of the human brain, the heart and of tumors?

Today, radiopharmaceuticals do belong to the standard instrumentation of nuclear medicine in particular, and medicine in general, both in the context of diagnosis and therapy. Parallel to the application of radiopharmaceuticals in hospitals, radiopharmaceutical chemistry demonstrates its capability to contribute to the industrial development of new drugs. In parallel, radiopharmacy is adding its value to fundamental biochemical and medicinal research. A main focus will be on its unique contribution to brain research, probably the most exciting area of research of this new century.

This chapter starts with the radionuclides themselves, i.e. their production directly at reactors and cyclotrons or indirectly *via* radionuclide generator systems. For selected radionuclides, their individual labeling chemistry and the correspondingly labeled compounds are covered, the focus being on *in vivo* application: ^{11}C or ^{18}F as the most relevant radionuclides used for PET, and ^{99m}Tc for SPECT. The increasing significance of therapeutic applications required a specific discussion.

2. Production of Medical Radionuclides

The production of radionuclides for use in medicine, both in diagnosis and therapy, is carried out using several routes. In most cases, nuclear production facilities such as nuclear reactors as well as cyclotrons are required. Reactor-produced radionuclides are generally neutron-rich nuclides. They mostly decay by β^- emission. Cyclotron-

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produced radionuclides, on the other hand, are often neutron deficient and decay mainly by EC or β^+ emission. In parallel, nuclear reactors and cyclotrons also produce radionuclides decaying by the emission of β^- and Auger or conversion electrons and alpha particles, relevant to endoradiotherapy. Compared to direct nuclear production reaction, in a limited number of cases non-direct production routes are available using radionuclide generator systems. The following three subsections separately describe the production of radionuclides relevant to life sciences using (i) nuclear reactors, (ii) particle accelerators and (iii) generator systems.

2.1. Productions Using Nuclear Reactors

Soon after World War II the importance of the peaceful use of nuclear reactors for the production of radionuclides for biological research and clinical applications was foreseen. The Graphite Reactors at the Oak Ridge National Laboratory (ORNL) and Brookhaven National Laboratory (BNL) were the first full-scale operating reactor prototypes and were put to use immediately to investigate production of a variety of radionuclides. Carbon-14 was the first reactor-produced radionuclide for clinical use in nuclear medicine (ORNL, 1946, used at the Barnard Free Skin and Cancer Hospital in St. Louis, Missouri). In principle, there are three general reaction types available: neutron radiative capture, (n,γ); neutron capture followed by particle emission, e.g., (n,n'), (n,p) and (n,α); and fission, (n,f).

2.1.1. Neutron Radiative Capture

For direct neutron capture, the most widely used route is the (n,γ) reaction with thermal neutrons. This production route is relatively simple. Since cross sections tend to be higher than for most other reaction types, yields are generally high. The use of isotopically enriched targets can minimize production of impurities and improve yield. Despite the high cost, enriched targets are essential if the natural abundance of the target nuclide is low and significant impurities are produced. The primary disadvantage of this reaction relates to the fact that the radioactive product cannot be separated from the target. Consequently, the specific activity will be much lower than that of no-carrier-added radionuclides. The *Szilard–Chalmers process* can be utilized to improve the specific activity of (n,γ)-produced radionuclides. Due to nuclear recoil and subsequent molecular bond disruption processes, sometimes the resulting hot atom is formed in a chemical state different from that of unreacted target atoms, which allows chemical separation of the radioactive isotope formed from the stable isotope of the same element irradiated.

A more efficient approach to obtain radionuclides of high specific activity occurs as a result of a (n,γ) reaction, in which the primarily produced radionuclide decays and forms the radionuclide of interest, in generally due to β^- decay of the intermediate nucleus. A prominent example is the production of no-carrier-added ^{125}I *via* the $^{124}Xe(n,\gamma)^{125}Xe \xrightarrow{\beta^-} {}^{125}I$ process. The neutron-capture product ^{125}Xe beta decays to ^{125}I with a 16.9 h half-life. Because the final product can be chemically separated from

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the target, specific activity approaching the theoretical value for the pure radionuclide is possible.

2.1.2. Neutron Capture Followed by Particle Emission

At somewhat higher energies, neutron inelastic scattering might be used. In the case of neutron inelastic scattering, the cross section may be substantially higher than the cross section for the (n,γ) route. However, fast neutrons provide medical radionuclides in general by (n,p) reactions (e.g., ^{35}S, ^{47}Sc, ^{64}Cu, ^{67}Cu), or by indirect reactions. In terms of specific activity, the (n,p) process shares many features with the (n,γ) reaction followed by beta decay process described above, since the target and the produced radionuclide do belong to different chemical elements and are chemically separable.

The indirect mechanism appears if a particle released from an initial nuclear reaction causes a subsequent nuclear reaction in another target nucleus. The early attempts for production of ^{18}F at nuclear reactors illustrate the process: Neutron irradiation of ^{6}Li creates a triton (t: $^{3}H^{+}$) with sufficient kinetic energy to react with a neighboring ^{16}O nucleus (isotopically enriched ^{6}Li as Li_2CO_3 is used as target material) in a $^{16}O(t,n)^{18}F$ process. Again, the final radionuclide is separable from the target and shows high specific activity.

2.1.3. Neutron-induced Fission

Neutron-induced fission of ^{235}U creates fission products with high yields at mass numbers peaking around 100 and around 140 – predominantly from $Z = 30$ to 66. For radionuclide fission production, targets containing about 25 grams of highly enriched ^{235}U are irradiated. Following sophisticated chemical processing of the irradiated uranium targets (note the enormous radioactivity caused by the fission products and the large variety of chemical elements present in the target), prominent medical radionuclides such as ^{131}I, ^{99}Mo (mother of the ^{99}Mo/^{99m}Tc generator), or ^{90}Sr (mother of the ^{90}Sr / ^{90}Y generator) are produced on a large scale with high specific activity.

2.1.4. Yield

The fundamental equation to calculate the radioactivity produced in a target is described by a first order differential equation

$$\frac{\mathrm{d}N}{\mathrm{d}t} = N_{\mathrm{t}}\Phi\sigma_{\mathrm{act}} - \lambda N \qquad (1)$$

where $\mathrm{d}N/\mathrm{d}t$ is the production rate (per second), N is the number of activated atoms, and N_{t} is the total number of target atoms that are in the neutron flux Φ (number of neutrons per cm^2 per second). The cross section σ (barns; 10^{-28} m) refers to the production of the particular radioactive species. The activity of radionuclides formed at any time during or at the end of irradiation is obtained by integration of Eq. (1):

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$$A = \lambda N = N_t \Phi \sigma_{act} (1 - e^{-\lambda t}) . \quad (2)$$

2.1.5. Examples

Table 1 summarizes reactor-produced radionuclides of current interest to nuclear medicine. Modes of production and corresponding nuclear cross sections are indicated.

Among the radionuclides listed in Table 1, about 10 products may be considered as most relevant to medical applications. Their production also reflects some of the mentioned features for nuclear-reactor based production processes:

^{114m}In : produced by neutron capture (n,γ) reactions,
^{125}I : produced by neutron capture followed by β^- decay,
^{14}C, ^{3}H (t) : produced by neutron capture (n,p) reactions
^{90}Sr, ^{99}Mo, ^{131}I : produced by fission or neutron capture reactions,
^{188}W : produced by double neutron capture,
^{117m}Sn : produced by neutron inelastic scattering,
^{67}Cu : produced by fast neutron-induced reaction.

Radionuclide	$T_{1/2}$	**Production**	**Reaction cross section σ^a (barns)**
^{64}Cu	12.7 h	^{63}Cu(n,γ)	4.50±0.02
^{67}Cu	2.6 d	^{67}Zn(n,p)	(1.07±0.11)×10^{-3}
^{90}Y	64.0 h	^{90}Sr(β^-, 28.79 a)	N/A
		^{89}Y(n,γ)	1.28±0.02
		^{90}Zr(n,p)	0.175·10^{-3} [f]
^{99}Mo	66 h	^{235}U(n,f) (6.07%)	582.6±1.1
		^{98}Mo(n,γ)	0.13±0.06
^{103}Pd	17.0 d	^{102}Pd(n,γ)	3.4±0.3
^{114m}In	49.5 h	^{113}In(n,γ)	8.1±0.8
^{117m}Sn	14.0 d	^{116}Sn(n,γ)	(5.8±1.2)·10^{-3}
		^{117}Sn(n,n')	(2.22±0.16)·10^{-1} [e]
^{125}I	59.4 d	^{124}Xe(n,γ)^{125}Xe (β^-, 16.9 h)	165±20
^{131}I	8.0 d	^{235}U(n,f) (2.89%)	582.6±1.1
		^{130}Te(n,γ)^{131g}Te (β^-, 25.0 min)	0.27±0.06
^{153}Sm	46.3 h	^{152}Sm(n,γ)	206±6
^{166}Ho	26.8 h	^{165}Ho(n,γ)	61.2±1.1
		^{164}Dy(n,γ)^{165}Dy (β^-, 2.33 h)	(2.65±0.10)·10^{3}

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		$^{165}Dy(n,\gamma)^{166}Dy$ (β^-, 81.5 h)	$(3.6\pm0.3)\cdot10^3$
^{169}Yb	32.0 d	$^{168}Yb(n,\gamma)$	$(2.3\pm0.17)\cdot10^3$
^{177}Lu	6.7 d	$^{176}Lu(n,\gamma)$	$(2.09\pm0.07)\cdot10^3$
		$^{176}Yb(n,\gamma)^{177}Yb$ (β^-, 1.9 h)	2.85
^{186}Re	3.7 d	$^{185}Re(n,\gamma)$	112±2
^{188}Re	17.0 h	$^{187}Re(n,\gamma)$	76.4±1.0
^{188}W	69.8 d	$^{186}W(n,\gamma)^{187}W$ (β^-, 23.72 h)	36.48 [e]
		$^{187}W(n,\gamma)$	14.5 [e]
^{191m}Ir	4.9 s	$^{190}Os(n,\gamma)^{191}Os$ (β^-, 15.4 d)	13.1±0.3
^{194}Ir	19.3 h	$^{192}Os(n,\gamma)^{193}Os$ (β^-, 30.11 h)	2.0±0.1
		$^{193}Os(n,\gamma)^{194}Os$ (β^-, 6.0 a)	38±10
^{195m}Pt	4.0 d	$^{194}Pt(n,\gamma)$	$(4.2\pm0.8)\cdot10^{-2}$
		$^{195}Pt(n,n')$	$(2.87\pm0.20)\cdot10^{-1}$ [e]
^{199}Au	75.3 d	$^{198}Pt(n,\gamma)^{199}Pt$ (β^-, 31 min)	3.66±0.19
		$^{197}Au(n,\gamma)^{198}Au$	98.7±0.1
		$^{198}Au(n,\gamma)$	$(2.51\pm0.04)\cdot10^4$

Table 1: Reactor-produced radionuclides of current interest to nuclear medicine (after Mirzadeh et al., 2003). ([a] thermal neutron; [e] epithermal neutrons; [f] fast neutron)

As ^{99m}Tc is the main radionuclide used in medical imaging, details are given for the nuclear-reactor based production of its mother radionuclide molybdenum-99:

There are two predominant strategies to produce large-scale activities of ^{99}Mo, namely *via* fission of ^{235}U and *via* neutron capture by a ^{99}Mo target. Other reactions for the production of ^{99}Mo such as $^{100}Mo(\gamma,n)^{99}Mo$, $^{96}Zr(\alpha,n)^{99}Mo$, and $^{102}Ru(n,\alpha)^{99}Mo$ are less important.

For fission reactions, typical targets consists of 45% enriched ^{235}U in the form of U/Al alloy. The typical yield of fission-produced ^{99}Mo is on the order of 148-370 GBq (4-10 Ci) per g of ^{235}U irradiated for 50-200 h in a neutron flux of 1.5×10^{14} n cm^{-2} s^{-1}. For each Ci of ^{99}Mo, $3.7\cdot10^3$ GBq (100 Ci) of other fission products are produced. Following sophisticated radiochemical processing, the radioisotopic purity is 99.9999% and the chemical purity is 99.99%. Fission-produced ^{99}Mo in most cases has a specific activity of ~ $2.6\cdot10^3$ GBq mg^{-1} (~ 70 Ci mg^{-1}). Maximum achievable specific activities are $2.66\cdot10^4$ GBq mg^{-1} ($7.2\cdot10^1$ Ci mg^{-1}) for t_{irr} = 7 d at $\phi = 7\cdot10^{13}$ n cm^{-2} s^{-1}. $^{99}Mo/^{99m}Tc$ generators require a specific activity of 37-74 GBq mg^{-1} (1 - 2 Ci mg^{-1}).

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In comparison, production of ^{99}Mo *via* neutron capture by ^{99}Mo does not require difficult and expensive radiochemical separation. The key problem, on the other hand, is the specific activity of neutron capture-produced ^{99}Mo, which even in the case of highest available neutron flux (Oak Ridge National Laboratory High Flux Isotope Reactor hydraulic tube) is approximately 1.9-3.7 GBq mg^{-1} (50-100 mCi mg^{-1}), a factor of 10-20 times lower than required for the traditional single-stage generator system.

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Bibliography

Alberto R., Abram U. (2003). *^{99m}Tc: Labeling Chemistry and Labeled Compounds*, in A. Vértes, S. Nagy, Z. Klencsár, F. Rösch (eds.), *Handbook of Nuclear Chemistry* – Vol. 4, pp 211-256, Kluwer Academic Publishers (Springer), Dodrecht. [A review of Tc coordination chemistry, research and development of ^{99m}Tc-based radiopharmaceuticals].

Browne E., Firestone R.B. (1986). *Table of Radioactive Isotopes* (V.S. Shirley, editor) Wiley, New York. [Comprehensive summary of nuclear decay data of most radionuclides]

Eisenhut M., Mier M. (2003). *Radioiodination Chemistry and Radioiodinated Compounds*, in A. Vértes, S. Nagy, Z. Klencsár, F. Rösch (eds.), *Handbook of Nuclear Chemistry* – Vol. 4, pp 257-278, 2003, Kluwer Academic Publishers (Springer), Dodrecht. [A review of research and development with ^{123}I-labeled compounds].

Fowler J.S., Ido T. (2002). Initial and subsequent approach for the synthesis of ^{18}FDG. *Semin. Nucl. Med.* **32**, 6 [Review on design and synthesis of radiolabeled deoxyglucose derivatives for molecular imaging]

Gambhir S.S. (2002). Molecular imaging of cancer with positron emission tomography. *Nature Rev. Cancer* **2**, 683 [A review on the principles of PET radiopharmaceuticals for molecular imaging of tumors]

Halldin C., Gulyas B., Langer O., Farde L. (2001). Brain radioligands - state of the art and new trends. *Q. J. Nucl. Med.* **45**, 139 [A review on the principles of radiopharmaceuticals for molecular imaging of the brain]

Hamacher K., Coenen H.H., Stöcklin G. (1986). Efficient stereospecific synthesis of no-carrier-added 2-[^{18}F]-fluoro-2-deoxy-D-glucose using aminopolyether supported nucleophilic substitution. *J. Nucl. Med.* **27**, 235 [State-of-the-art synthesis of [^{18}F]FDG].

Kung H.F., Kung M.P., Choi S.R. (2003) Radiopharmaceuticals for single-photon emission computed tomography brain imaging. *Semin. Nucl. Med.* **33**, 2 [A review on the fundamentals and application of radiopharmaceuticals for SPECT imaging]

Kibourn M.R. (1990) *Fluorine-18 labeling of radiopharmaceuticals*. Nuclear Science Series., NAS-NS-3203 (Washington DC: National Academy Press). [A review on the fundamentals of ^{18}F-labelled radiopharmaceuticals]

Langer O., Halldin C. (2002). PET and SPET tracers for mapping the cardiac nervous system. *Eur. J. Nucl. Med*. **29**, 416 [A review on the principles of radiopharmaceuticals for molecular imaging of the heart]

Lundquist H., Tolmachev V. (2002). Targeting peptides and positron emission tomography. *Biopolymers* **66**, 381 [A review on the fundamentals and application of radiolabeled peptides for PET imaging]

Mäcke H.R., Good S. (2003). *Radiometals (non-Tc, non-Re) and Bifunctional Labeling Chemistry*, in A. Vértes, S. Nagy, Z. Klencsár, F. Rösch (eds.), *Handbook of Nuclear Chemistry* – Vol. 4, pp 279-314, Kluwer Academic Publishers (Springer), Dodrecht. [A review of radiometal coordination chemistry, research and development of radiometal-based radiopharmaceuticals].

MacCarthy K.E. (2000). Recent advances in the design and synthesis of carbon-14 labelled pharmaceuticals from small molecule precursors, *Current Pharmaceutical Design* **6**, 1057-1083 [Review on design and synthesis of carbon-14 labelled pharmaceuticals]

Mirzadeh S., Mausner L.F., Garland M.A. (2003). *Reactor-Produced Medical Radionuclides*, in A. Vértes, S. Nagy, Z. Klencsár, F. Rösch (eds.), *Handbook of Nuclear Chemistry* – Vol. 4, pp 1-46, Kluwer Academic Publishers (Springer), Dodrecht. [A review of theory and practice of radionuclide production at nuclear reactors].

Qaim S.M. (2003). *Cyclotron Production of Medical Radionuclides*, in A. Vértes, S. Nagy, Z. Klencsár, F. Rösch (eds.), *Handbook of Nuclear Chemistry* – Vol. 4, pp 47-80, Kluwer Academic Publishers (Springer), Dodrecht. [A review of theory and practice of radionuclide production at particle accelerators].

Rösch F., Knapp F.F. (2003). *Radionuclide Generators*, in A. Vértes, S. Nagy, Z. Klencsár, F. Rösch (eds.), *Handbook of Nuclear Chemistry* – Vol. 4, pp 81-118, Kluwer Academic Publishers (Springer), Dodrecht. [A recent review of the developments of radionuclide generators].

Rösch F., Forssell-Aronsson E. (2004). *Radio-lanthanides in Nuclear Medicine*. in *Metal Ions and Their Complexes in Medication* (2004) Vol. 42. p. 77-108, A. Sigel, H. Sigel, Eds. M. Dekker, Inc., New York & Basel. [Review on design and synthesis of radiolanthanide-based radiopharmaceuticals].

Saljoughian M., Williams P.G. (2000). Recent developments in tritium incorporation for radiotracer studies, *Current Pharmaceutical Design* **6**, 1029-1056 [Review on design and synthesis of tritium labeled pharmaceuticals]

Saljoughian M. (2002). Synthetic tritium labelling: reagents and methodologies, *Synthesis* **13**, 1781-1800 [Review on design and synthesis of tritium-labeled pharmaceuticals].

Sokoloff L., Reivich M., Kennedy C., Des Rosiers M.H., Patlak C.S., Pettigrew K.D., Sakurada O., Shinohar, M. (1977). The [^{14}C]deoxyglucose method for the measurement of local cerebral glucose utilization: theory, procedure, and normal values in the conscious and anesthetized albino rat. *J. Neurochem*. **28**, 897; and Reivich M, Kuhl D, Wolf A, Greenberg J, Phelps M, Ido T, Casella V, Fowler J, Hoffman E, Alavi A, Som P, Sokoloff L. (1979) The [^{18}F]fluorodeoxyglucose method for the measurement of local cerebral glucose utilization in man. *Circ Res*. **44**, 127. [Original papers on the in vitro and in vivo imaging of local glucose consumption rate via radiolabeled deoxyglucose derivatives].

Spencer R.P. (1978). *Therapy in Nuclear Medicine*, Grune and Stratton, New York. [Review on the fundamentals and application of radionuclides and radiotherapeuticals].

Spencer R.P., Sievers R.H., Friedman A.M. (1987). *Radionuclides in Therapy*, Boca Raton, FL:CRC Press. [Review on the fundamentals and application of radionuclides and radiotherapeuticals].

Stöcklin G. (1992). Tracers for metabolic imaging of brain and heart *Eur. J. Nucl. Med*. **19**, 527 [A review on the chemical and biochemical fundamentals and application of radiopharmaceuticals for PET imaging of brain and heart].

Stöcklin G. (1995). *Fluorine-18 Compounds*, in *Principles of Nuclear Medicine*, edited by H.N. Wagner, Jr, Z. Szabó, J.W. Buchanan (Philadelphia: W.B. Saunders Co.), 178-193 [A review on the fundamentals and application of ^{18}F-labelled radiopharmaceuticals for PET imaging].

UNESCO – EOLSS SAMPLE CHAPTERS

Stöcklin G., Pike V.W. (editors) (1993). *Radiopharmaceuticals for positron emission tomography*. P.H. Cox (series ed.): *Development in Nuclear Medicine*, Vol **24** (Dordrecht: Kluwer Academic Publishers). [A review on the fundamentals and application of radiopharmaceuticals for PET imaging].

Wagner H.N., Szabo Z., Buchanan J.W. (1995). *Principles of Nuclear Medicine*. W.B. Saunders Company, Philadelphia, second edition. [One of the excellent textbooks on the principles of nuclear medicine].

Wester H.-J. (2003). *Radionuclide Therapy*, in A. Vértes, S. Nagy, Z. Klencsár, F. Rösch (eds.), *Handbook of Nuclear Chemistry* – Vol. 4, pp 315-348, 2003, Kluwer Academic Publishers (Springer), Dodrecht. [A recent review on the fundamentals and radiopharmaceutical chemistry of fluorine-18].

www.rencyric@cyric.tohoku.ac.jp [A catalogue of references to ^{11}C-labeled compounds available on the Internet].

Zalutsky M.R. (2003). *Radionuclide Therapy*, in A. Vértes, S. Nagy, Z. Klencsár, F. Rösch (eds.), *Handbook of Nuclear Chemistry* – Vol. 4, pp 315-348, 2003, Kluwer Academic Publishers (Springer), Dodrecht. [A review on the fundamentals and radiopharmaceutical chemistry of endoradiotherapy].

Biographical Sketch

Frank Rösch is professor at Mainz University. He received a PhD degree in Nuclear Chemistry from Dresden Technical University. His general research interests are focused on fundamental radiochemistry and nuclear chemistry in terms of production and efficient separation of radionuclides, and the physico-chemical analyses of element speciation using radioanalytical methods. Over the last 10 years, his research has turned to the impact of radiochemistry on life sciences, in particular using *in vivo* molecular imaging technologies used in fundamental research as well as in diagnoses of diseases in humans. He is involved in a wide range of radiochemical and radiopharmaceutical national and European projects on the radiopharmaceutical chemistry of mainly metallic radionuclides and fluorine-18 labeled radiopharmaceuticals.

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