Special Requirements in the Development of Biokinetic Models for Radiopharmaceuticals

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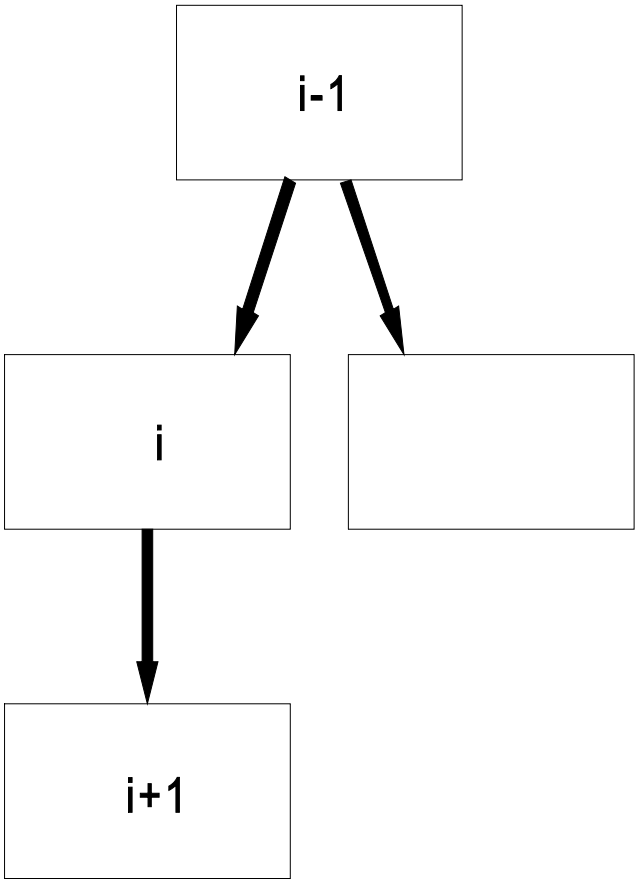
What are Biokinetic Models?

Biokinetic models

- (as well as dosimetric models) are used and needed in internal dosimetry - in the assessment of doses from incorporated radionuclides;
- describe the uptake, distribution, retention and excretion of radionuclides in the body;
- are used for the calculation of the numbers of nuclear transformations in (source) regions of the body where the radionuclide considered accumulates.

Then with dosimetric models the internal dose to target tissues can be calculated.

General Structure of Biokinetic Models



- Compartment models
- 1st order kinetics

  i.e. the retention can be described by a (biological) half-time

Biokinetic Models for Different Situations

Biokinetic models are needed for all kinds of intakes of radionuclides

- by workers
  - inhalation, ingestion and uptake via wound by workers in the occupational environment
- by members of the public
  - ingestion and inhalation by infants, children, adolescents and adults from environmental sources
- by patients
  - in diagnostic nuclear medicine
  - in nuclear medicine therapy

Why Different Biokinetic Models May Be Needed for Radiopharmaceuticals?

- Short half-lives of the radioisotopes used need better modelling
  - for blood retention,
  - for excretion pathways,
  - but to a less extent for skeleton retention.
- Diseases of patients afford consideration of changed biokinetics.
- For therapeutic administration of radiopharmaceuticals an individual dose assessment is essential considering the individual behaviour of the radiopharmaceutical.

Blood Kinetics for Radiopharmaceuticals with (very) short Half-lives

For radiopharmaceuticals remaining mainly in the circulation blood volumes of organs are used.

For very short-lived radioisotopes values of the fractional cardiac output are used, in ICRP Publication 53 for example for ^{38}K (half-life 7.6 min) in contrast to ^{42}K and ^{43}K (half-lives 12.4 h and 22.3 h, respectively) for which a distribution according to stable K has been assumed.

For ^{82}Rb (half-life 1.3 min) also a distribution according to cardiac output has ben assumed in ICRP Publication 53 which, however, overestimates the organ doses substantially because of a delayed uptake. There will be a new ICRP model based on a blood flow model resulting in an effective dose less by a factor of 3-4.

Urinary Excretion

In general also the urinary bladder voiding is modelled by 1st order kinetics which is a good approximation for most radionuclides in the environment and at workspace (difference less than 0.1% for example for ^{137}Cs).

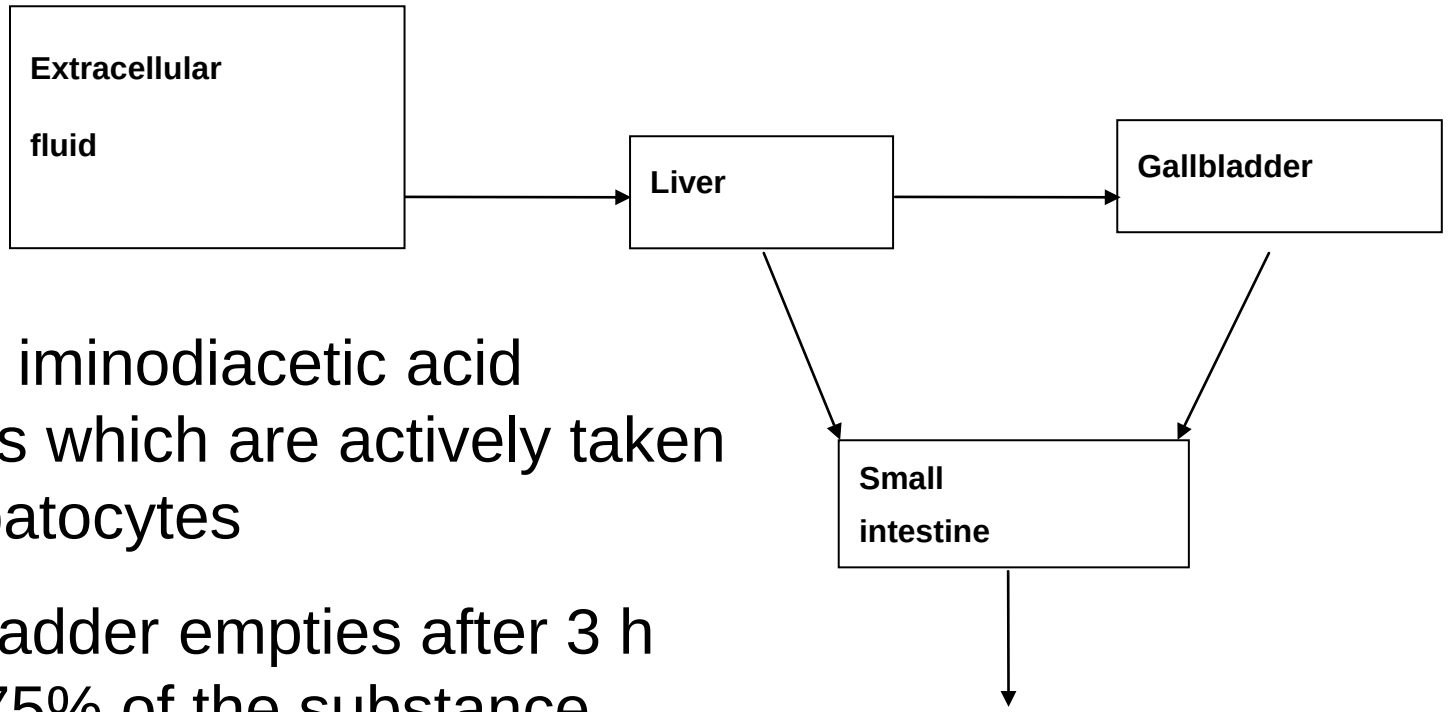
For radiopharmaceuticals

- the dose to the urinary bladder wall is often the highest organ dose;
- no 1st order kinetics in the urinary bladder contents is considered but the filling and voiding of the urinary bladder is considered for short-lived radioisotopes.

This more realistic model raises the number of the nuclear transformations in the urinary bladder contents

- by 58% for [^{18}F]FDG,
- by 48% for [^{99m}Tc]Phosphonate.

Biliary Excretion (ICRP Publications 53, 106)



mainly for iminodiacetic acid derivatives which are actively taken up by hepatocytes

the gall bladder empties after 3 h and 9 h (75% of the substance present each time) and after 24 h (rest of activity)

Skeleton Models

For the calculation of doses to bone surfaces the knowledge of the distribution on bone surfaces and in bone volume is essential.

For long-lived bone seekers models considering physiological processes like bone resorption and bone formation are needed.

For radiopharmaceuticals labelled with short-lived radionuclides in most cases consideration of retention on (cortical and trabecular) bone surfaces is sufficient.

Consideration of Patients' Diseases for Diagnostic Radiopharamceuticals

Biokinetic models are mostly models for healthy reference persons.

Diseases may change the biokinetic behaviour of radiopharmaceuticals.

Reflecting this, ICRP has developed different biokinetic models for some radiopharmaceuticals dependent on the health status of the patients

- for example in Publication 80 for [^{99m}Tc]MAG3 models
  - for normal renal function
  - for abnormal renal function
  - for acute unilateral renal blockage

  producing quite different doses to kidneys and liver.

Individual Dosimetry in Nuclear Medicine Therapy

In diagnostic nuclear medicine in general it is sufficient to know the doses to reference persons.

In nuclear medicine therapy it is essential to know the individual doses of the patients to assure

- a sufficient dose to the target tissue and
- tolerable doses to other (healthy) organs and tissues.

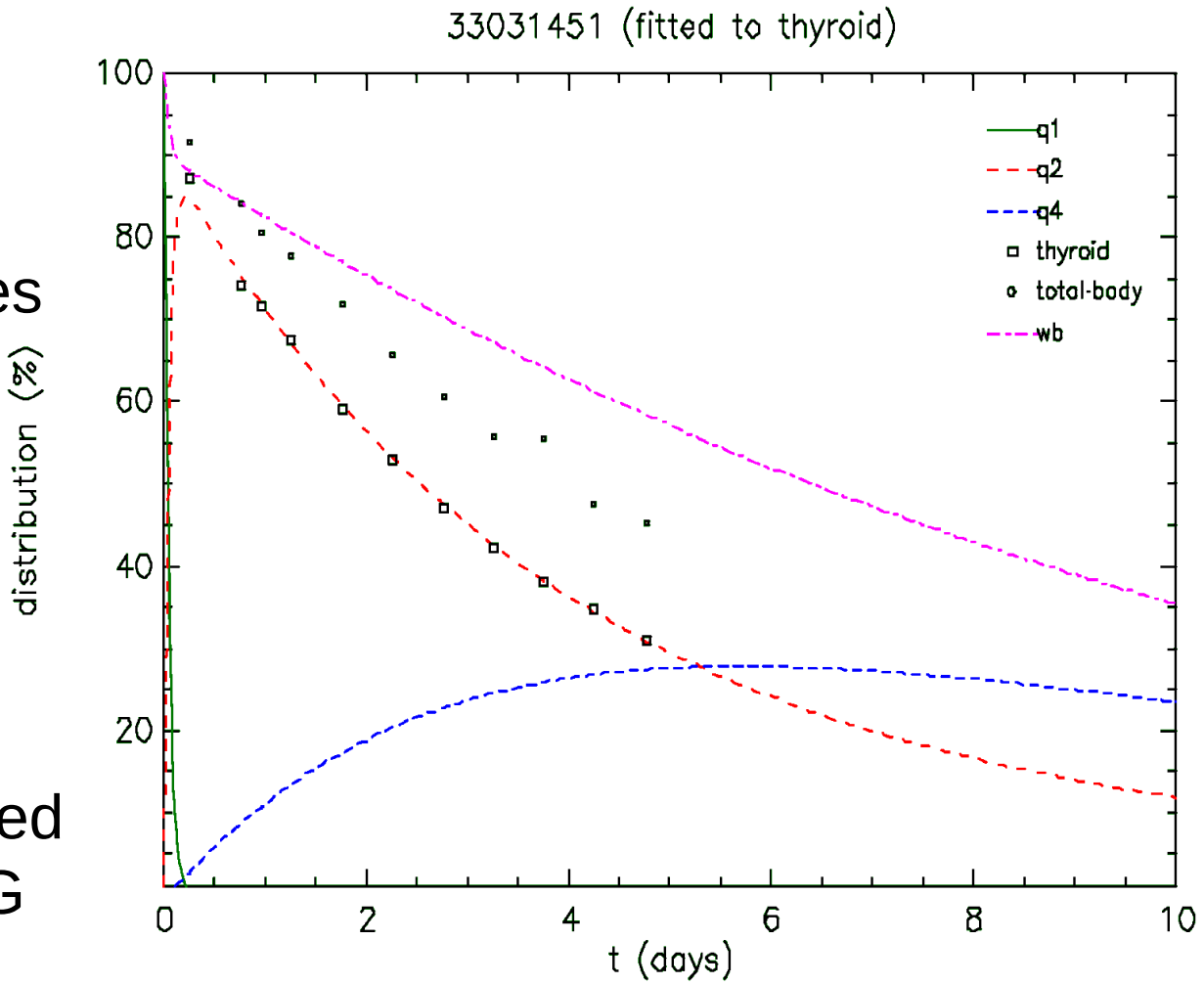
For this standard methods are being developed (NukDos in Germany, MetroMRT in Europe).

Non-Thyroid Doses in Radioiodine Therapy

important for example for the assessment of fetal (uterus) doses

for an individual dosimetry also total body measurements are necessary

this will be analysed by EURADOS WG 7.2



according to Wolfgang Eschner, University of Cologne

Conclusion

The development of biokinetic models must consider
- which physiological processes are important for the specific situation and must be considered in more detail;
- which tissue doses are of interest.

Important issues for radiopharmaceutical dosimetry are
- the short half-lives of the used radioisotopes;
- the potential need for individual dosimetry.