Master of Science Thesis

Reduction of the absorbed dose to the urinary bladder from radiopharmaceuticals – an investigation of influencing parameters

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Abstract

Introduction: The main route of excretion of activity for most administered radiopharmaceuticals is via the urinary bladder and it is important to estimate the absorbed dose to the mucosal surface of the bladder wall, especially when radiopharmaceuticals are given for therapeutic purposes. The purpose of this thesis was to investigate how the absorbed dose varies with changes in the parameters, which control the volume in the bladder.

Material and Methods: A dynamic bladder model was used, which makes it possible to evaluate what would be the optimal first void time after administration, and how the dose pattern changes with the variables that control the volume in the bladder at any time. The investigated parameters were initial bladder content volume, residual bladder content volume, voiding interval, urine flow rate and time of administration. For the voiding interval and the urine flow rate data from 30 healthy volunteers were used. The volunteers wrote down time of micturition and the amount of urine under a period of at least 24 hours. The bladder model was transferred to STELLA, which is an interactive program for modelling dynamic systems over time. The radiopharmaceuticals used in this study were ^{18}F-FDG, ^{99m}Tc-MDP, ^{123}I-NaI, ^{131}I-NaI and ^{111}In-DTPA

Results: The best way of reducing the absorbed dose to the bladder wall surface is to increase the urine flow rate, and this is done by increasing the liquid consumption. The first void time is especially important after an administration with ^{18}F-FDG. Another parameter that is easy to control is the initial bladder content volume, if the patients do not urinate directly before the administration this helps to reduce the absorbed dose. The absorbed doses calculated by ICRP differ from the results in this report and the largest difference is obtained for ^{131}I-NaI. The value in this report is approximately 50% higher than that presented by ICRP.

Conclusions: The result shows that it is possible to reduce the absorbed dose to the bladder wall surface after an administration of a radiopharmaceutical. The absorbed dose calculated by ICRP to the urinary bladder from ^{123}I-NaI and ^{131}I-NaI needs to be revised.

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1 Introduction

In nuclear medicine, absorbed dose calculations to patients are an important part of the work as a medical physicist. Fortunately, the medical physicist does not need to calculate the absorbed doses to a specific patient or to a particular organ of interest since there are national and international agencies that provides advises and absorbed dose tables. For example, the International Commission on Radiological Protection (ICRP) has published data for absorbed doses to patients from more than 100 different radiopharmaceuticals (1, 2). There are also computer program available, OLINDA/EXM and MIRDOSE which helps the physicist to calculate the radiation dose.

To be able to estimate an accurate absorbed dose to a patient after administration of a radiopharmaceutical, biokinetic models have been developed over the years. These models are frequently under development.

One organ of particular interest is the urinary bladder. The main route of excretion of activity for most administered radiopharmaceuticals is via the urinary bladder (1) and it is important to estimate the absorbed dose to the mucosal surface, especially when radiopharmaceuticals are given for therapeutic purposes. For radiopharmaceuticals that are excreted rapidly and in substantial quantities, bladder dosimetry is of particular importance. This is because the superficial cells in the bladder, those who are in direct contact with the urine, have a low cell-renewal rate. Because of this long lifespan, accelerated proliferation following irradiation does not begin for months. Senescence[1] of the differentiated functional cells then reveals latent damage in the basal layer. Subsequent late effects are related to fibrosis and reduction in bladder capacity (3).

When radiation dose calculation is carried out, it is essential that the biokinetic data are as correct as possible. The bladder models that are used for standard calculations today are either an exponential type of model, or a more adapted model with the most parameters constant. The most commonly used model is the standard MIRD phantom (4) in which the bladder has a constant volume of 202.6 ml. Dynamic variation of parameters such as filling rate, initial volume, residual volume and first voiding time are not accounted for in this model. The voiding interval that is used is equally spaced over a 24-hr period.

Over the years a couple of different models have been developed to incorporate more accurate biokinetic data. A new dynamic bladder model was developed by Thomas *et al.* (5), which incorporated several of the features in the earlier models (6-8). This model makes it possible to evaluate, what would be the optimal time for the first bladder void after administration, and how the dose pattern changes with the above mention variables.

In this work the various parameters that influence the absorbed dose to the urinary bladder wall surface from radiopharmaceuticals has been investigated. The dynamic bladder model developed by Thomas *et al*. (5) has served as a base and the parameters studied has been the: first void time, initial bladder contents volume, residual bladder contents volume, voiding interval, urine flow rate (day

[1] Cellular *senescence* is the phenomenon where cells lose the ability to divide.

and night) and time of administration. For the voiding interval and the urine flow rate data were derived from 30 healthy volunteers.

2 Material and Methods

The bladder model developed by Thomas *et al*. (5) have been used in this study to calculate the absorbed dose to the inner surface of the bladder wall. This model makes it possible to estimate the absorbed doses to the bladder wall surface with dynamic variation of the parameters that controls the volume of the bladder at any time. An interactive modelling program (STELLA) was used to make the simulations. The simulation was performed for 5 different radiopharmaceuticals.

2.1 Radiopharmaceuticals

The choice of radiopharmaceuticals used in this study was ^{18}F-FDG, ^{99m}Tc-MDP, ^{123}I-NaI, ^{131}I-NaI and ^{111}In-DTPA. These substances are often used in nuclear medicine and they are of interest for this study because a majority of the administered activity is excreted through the urinary bladder. The physical properties of the radiopharmaceutical used are given in Table 2.1.

^{18}F-FDG

This is a substance that is used in conjunction with positron emission tomography (PET) mainly for tumour detection but also for myocardial perfusion studies (9) and measurement of the cerebral metabolic rate of glucose (10). ^{18}F-FDG is a glucose analog that is transported across the blood-barrier and phosphorylated, but is not metabolised further. After administration, most of the radiopharmaceutical is rapidly cleared from the circulation with a biological half-time of less than 1 min. Mainly the myocardium and the brain take up the substance. Approximately 20% of the administered ^{18}F is excreted in urine within the first 2 hr (1). The organ that receives the highest radiation dose from the use of this compound is the bladder wall.

^{18}F is a radionuclide that emits positrons. The emitted positron is slowed down by loss of energy to the surrounding matter along its path. The final interaction, positron annihilation, results in disintegration of both the positron and the electron, with the simultaneous emission of energy equivalent to their combined mass of 1.022 MeV. The emitted energy is in the form of two photons, or γ-rays, with energies of 511 keV that travels in opposite directions (11).

^{99m}Tc-MDP

When bone scintigraphy is being performed, ^{99m}Tc labelled diphosphonate is exclusively used. This group of radiopharmaceutical shows exquisite sensitivity for skeletal abnormality. The substance is absorbed onto the surface of the bone, with particular affinity for sites of new bone formation. The main uptake is in the bone, with a further uptake in kidneys, and the excretion is via the urinary tract (1, 12). In this study ^{99m}Tc-MDP was chosen to represent the diphosphonates.

^{99m}Tc decays to ^{99}Tc by isomeric transition with a half-life of 6.02 hr. The emitted energy of the primarily photon is 141 keV (89%) (11).

^{123}I-NaI and ^{131}I-NaI

Radioactive iodine (^{123}I) in the chemical form of sodium iodide is used for thyroid cancer imaging and for tumour localization.

^{123}I decays to ^{123}Te by electron capture with a half-life of 13.2 hr and emits photons with energies 127 keV (14%) and 159 keV (83%) (11).

Trace amounts of radioactive iodine (^{131}I) in the chemical form of sodium iodide are used to measure thyroid uptake. Together with blood tests, examining how much iodine is taken up by the thyroid gland helps physicians diagnose hypothyroid conditions (when the thyroid takes up too little iodine) and hyperthyroid conditions (when it takes up too much).

^{131}I is widely used for the treatment of hyperthyroidism and thyroid cancer. A therapeutic treatment with ^{131}I involves an absorbed dose to the thyroid gland that varies with the patient and is non-uniform within the tissue itself but is on the order of many tens of Grays. In addition, there is a total body dose of typically 50 to 150 mGy, which results from the isotope circulating in the blood (3).

^{131}I decays with beta decay to ^{131}Xe with a half-life of 8 days and emits both photons of 365 keV (82%) and beta particles of 192 keV (90%) (11).

The radioactive iodine that is not taken up by thyroid is rapidly eliminated through the kidneys and the bladder.

^{111}In-DTPA

Intrathecally administered indium ^{111}In-DTPA is useful for determining the flow pattern of cerebrospinal fluid (CSF). A variation from the normal pattern may reflect a pathological process. After the administration and initial distribution in the extra cellular fluid, the substance is excreted exclusively by the renal system (1).

^{111}In is an artificial radioactive isotope of indium with a half-life of 2.8 days. It decays exclusively by electron capture, emitting primarily two gamma rays with the energies 172 keV (91%) and 245 keV (94%).

Table 2.1. Physical properties of the radiopharmaceuticals used in this study.

Radiopharmaceutical	Physical half-life[A]	Decay mode[A]	Radiation energy (abundance)[A] Gamma (γ)	Beta (β)
^{18}F-FDG	110 minutes	β+	511 keV (200%)	---
^{99m}Tc-MDP	6.01 hours	IT	141 keV (89%)	---
^{123}I-NaI	13.2 hours	EC	159 keV (83%)	---
^{131}I-NaI	8.02 days	β-	365 keV (82%)	192 keV (90%)
^{111}In-DTPA	2.83 days	EC	172 keV (91%) 245 keV (94%)	---

[A] physical data from Weber *et. al* (11)

2.1.1 Physical and Biologic Parameters

Ionizing radiation can ionize materia in two different ways, either, directly or indirectly. All charged particles emitted by radionuclides are directly ionizing. They can disrupt the atomic structure of the absorber through which they pass

directly, and produce chemical and biologic damages. X-rays and gamma-rays are however also indirectly ionizing. They do not produce chemical and biologic damage themselves in a large extent, but when they are absorbed in the material through which they pass, they give up their energy and produce fast-moving charged particles. For the calculations of the absorbed dose with the new model (5) the contribution from particles and photons emitted per nuclear transition has to be divided into two separated calculations. For the non-penetrating radiation the dose rate is calculated using the mean electron particle energy emitted per nuclear transition, Δ_β. For the penetrating radiation the dose rate is calculated using the air kerma rate constant Γ_δ. To calculate the absorbed dose to soft tissue (bladder wall), the air kerma rate has to be multiplied by the ratio of the mass energy absorption coefficient of soft tissue to that of air, which can be taken as 1.11 between 2 and 0.1 MeV and drops to 1.04 at 0.02 MeV. Since the radiation-weighting factor for gamma-rays and x- rays is 1, by multiplying air kerma rate constants by a factor of 1.11, the soft tissue-equivalent dose constant Γ' can be obtained (13, 14).

Table 2.2 Physical and biologic parameters for the radiopharmaceuticals used in the bladder wall dose calculations

Radio-pharmaceuticals	Physical parameters			Biologic parameters for the bladder contents	
	Δ_β (11) (mGy · kg/ MBq · sec)	Γ' (13) (mGy · cm^2/ MBq · sec)	λ (min^{-1})	α_j (5)	λ_j (5) (min^{-1})
^{18}F-FDG	4.00×10^{-5}	4.13×10^{-4}	6.36×10^{-3}	0.19	3.85×10^{-2}
				0.06	1.24×10^{-3}
^{99m}Tc-MDP	2.59×10^{-6}	4.31×10^{-5}	1.92×10^{-3}	-0.115	5.42×10^{-2}
				0.566	1.06×10^{-2}
				0.549	5.07×10^{-4}
^{123}I-NaI	4.51×10^{-6}	1.10×10^{-4}	8.75×10^{-4}	0.729	1.90×10^{-3}
				0.271	7.41×10^{-6}
^{131}I-NaI	3.04×10^{-5}	1.60×10^{-4}	5.99×10^{-5}	0.729	1.90×10^{-3}
				0.271	7.41×10^{-6}
^{111}In-DTPA	5.56×10^{-6}	2.54×10^{-4}	1.70×10^{-4}	0.99	6.92×10^{-3}
				0.01	6.88×10^{-5}

The activity content in a source organ depends on the uptake and the retention of the radiopharmaceutical. When a radiopharmaceutical is administered the activity redistributes among the various organs in the body with preferential uptake in the particular organs dictated by radiopharmaceutical design and administration pathway. The clearance of activity in the total body can be analysed by distributing this radioactivity into several compartments. These compartment-models are used to model a complicated system of inflow and outflow of activity between organs. From these models and from whole body activity quantifications with radiation detectors e.g. scintillation cameras, the biologic rate constant λ_j for entry of the j^{th} component into the bladder, and the biologic coefficient, α_j, representing the fraction of the administered activity entering the bladder for the j^{th} component, can be derived.

2.2 Evaluated parameters

The dynamic bladder model takes into account the variables that determine the volume of the bladder at any time, namely the urine flow rate, initial bladder contents volume, residual bladder contents volume and voiding interval. The first void time is another variable that is incorporated in the model. Thomas *et al*. (5) use a fix time of administration (9 am) but in this study the time of administration is variable. Also the time when the night time interval starts and the length of the night time interval are considered. All these parameters affect the absorbed dose to the bladder wall surface to various degrees. To determine which of these parameters that has the largest impact on the absorbed dose to the bladder wall surface one has to calculate the absorbed dose for various values of these parameters.

All of these parameters need to be established before any calculation can be carried out. For the post-void residual urine volume (PVR) an upper limit of 50 ml was used. This cut-off value is often used as an pathologic limit for the PVR (15). For the voiding interval, urine flow rate, start and length of night time interval data were collected from 30 volunteers. Healthy volunteers were asked if they would participate in the survey. A total of 22 volunteers wrote down time of micturition and the amount of urine at each micturition under a period of at least 24 h. The form that was given to the volunteers can be seen in *Appendix 2*. The measuring-cups were graded in a 10 ml-scale. From a paper by Gunnarsson. *et al*. (16) and a manuscript included in an Ph.D thesis by M Gunnarsson. (17) the micturition data from the remaining 8 volunteers were obtained. The age of the 30 volunteers ranged from 25 to 71 years, with a mean value of 42 years.

2.3 STELLA Simulations.

To calculate the absorbed dose to the bladder wall surface, the mathematical model was transferred to the simulation program STELLA (18) (version 9.0.1). STELLA is an interactive program for modelling of dynamic systems over time. There are four main components in STELLA that are used, namely:

- **Stocks**: They collect whatever flows into them.
- **Flows**: The job of flows is to fill and drain accumulations (stocks).
- **Converters**: The converter serves a utilitarian role in the software. It holds values for constants, defines external inputs to the model, calculates algebraic relationships, and serves as the repository for graphical functions. In general, it converts inputs into outputs.
- **Connectors**: As its name suggests, the job of the connector is to connect model elements.

To build the mathematical dynamic bladder model one uses the above components together with simple mathematical expressions.

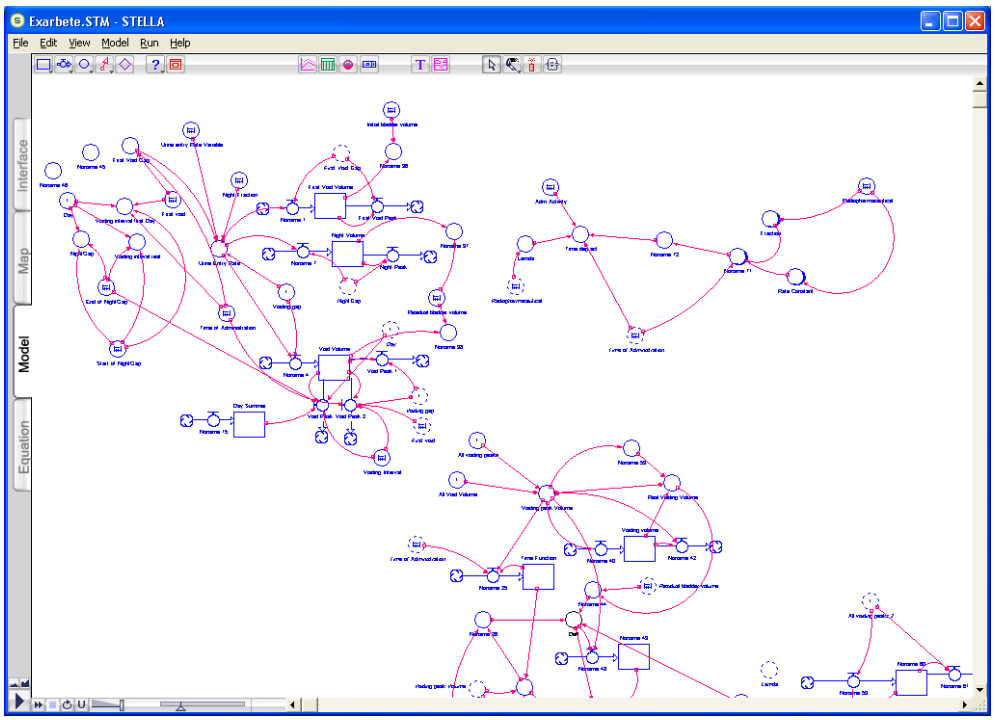

Figure 1. Schematic figure of the dynamic bladder model in STELLA.

Figure 1 shows a part of the model. For simplification in the calculations an interface can be developed and connected to the model. In this interface, as seen in Figure 2, one specifies the starting values and then start the calculation. This way of working with the model makes it easy to perform a great number of calculations for various parameters.

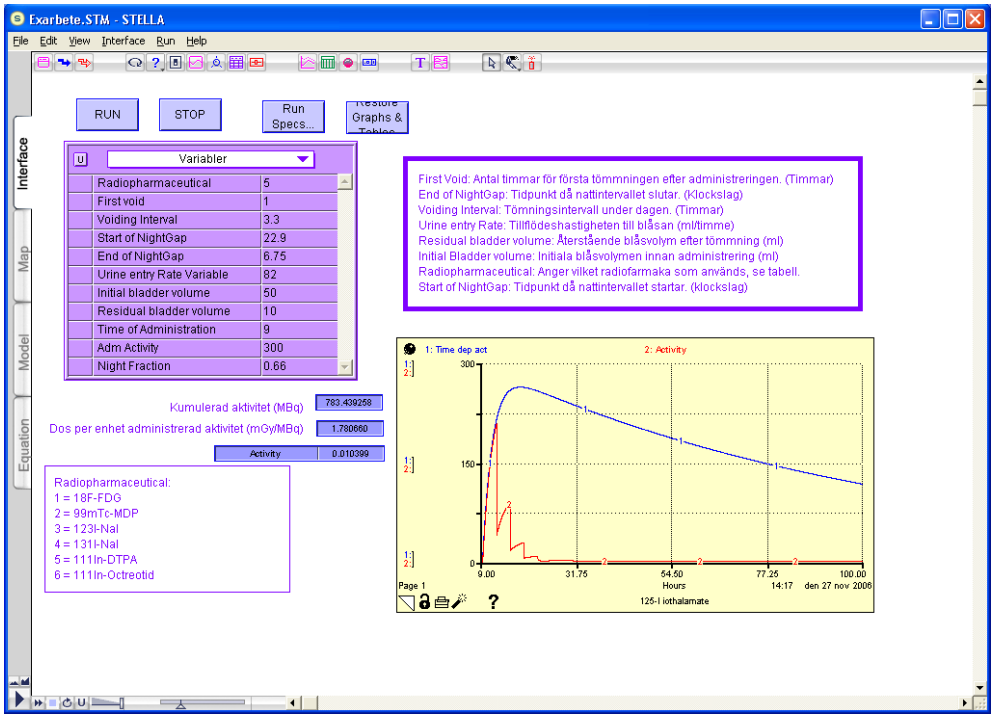

Figure 2. Graphical interface

The result of the simulation was transferred to Microsoft Excel for presentation in the form of figures.

In the bladder model by Thomas *et al*. (5), the shape of the bladder is represented by an expanding sphere, with the bladder wall represented by a spherical shell of constant volume. For large bladder volumes, see Figure 3, this is a good approximation but for small volumes, the bladder shrinks to a more irregular shape Figure 4. Both the ellipsoidal and the spherical model fail to represent the bladder in this state Figure 4. The major fraction of the total absorbed dose to the bladder wall comes from non-penetrating radiation when the bladder volume is small. This means that the absorbed dose is more or less independent of the actual shape of the bladder when the bladder volume is small as illustrated in Figure 4 (5, 8).

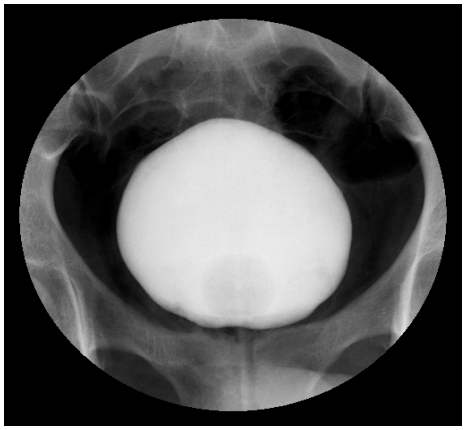

Figure 3. Spherical when volume is large

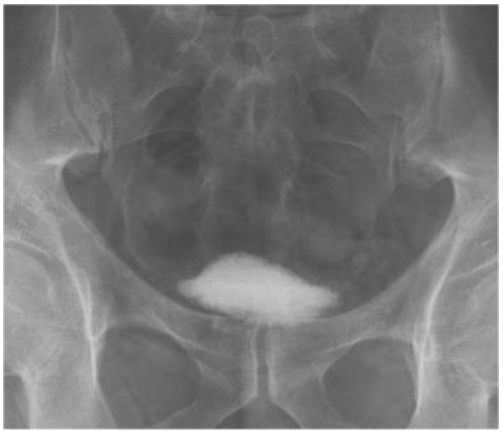

Figure 4. Irregular shape at small volumes.

The dose rate from electrons to the inner surface of the bladder wall is taken to be one half of the dose rate in an infinite medium with the same radioactive concentration as the bladder, whilst the dose rate from penetrating radiation is derived using an expression that incorporates the air kerma rate constant. A bladder radioactivity input model that is obtained from the whole-body retention curve, expressed as a sum of exponential terms, is used for the calculation of the cumulated activity in the bladder.

Figure 5 shows the model in a graphical view. All variables and constants used in the model are connected to one of the three main calculation steps, namely

- Time-dependent bladder content volume V(t)
- Time-dependent bladder content activity A(t)
- Absorbed dose per unit administered activity to the bladder wall inner surface

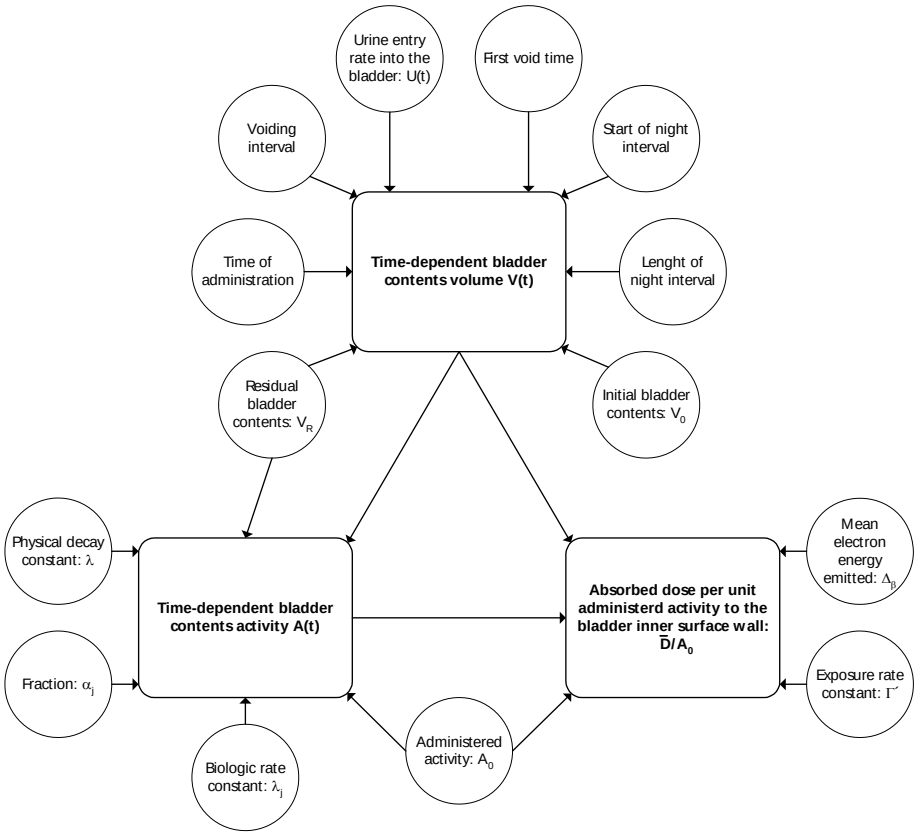

Figure 5. The dynamic bladder model represented in a graphical view.

1. Time-dependent bladder-content volume V(t).

$$V(t) = \begin{cases} V_0 + \int_0^{T_1} U(t)dt : & 0 \le t < T_1 \ (1^{st} \text{ void}) \\ V_r + \int_{T_{n-1}}^{T_n} U(t)dt : & T_{n-1} \le t < T_n \end{cases} \qquad \text{Eq. 1}$$

The initial bladder content volume, V_0, is the volume of urine in the bladder at the time of administration of the radiopharmaceutical. V_r is the residual bladder content volume after each voiding. U(t) is the urine production rate at time t. T_n is the time of each micturition.

The remaining variables, time of administration, start of night time interval and length of night time interval was built in together with Eq.1 in STELLA to represent a bladder-filling scheme. In the night the urine production rate is reduced.

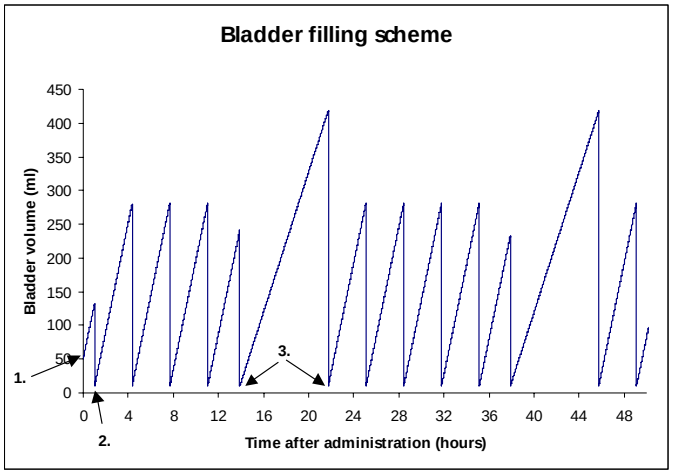

Figure 6. Bladder filling scheme. 1: Initial bladder content volume, 2: first void time, 3: start and end of night time interval

2. Time-dependent bladder content activity A(t):

If the retention of the activity in the body can be described by an m-component exponential model, the activity in the bladder at any time after administration but before any voiding, can be represented by

$$A(t)_{input} = A_0 e^{-\lambda t} \sum_{j=1}^{m} \left[\alpha_j \left(1 - e^{-\lambda_j t} \right) \right] \qquad \text{Eq. 2}$$

where A_0 is the administered activity; λ is the physical decay constant; α_j is the fraction of A_0 entering the bladder for the j^{th} component; and λ_j is the biologic rate constant for the j^{th} component. Eq.2 represent the input into the bladder from the whole body. A typical activity input $A(t)_{input}$ in the bladder for ^{99m}Tc-MDP can be seen in Figure 7.

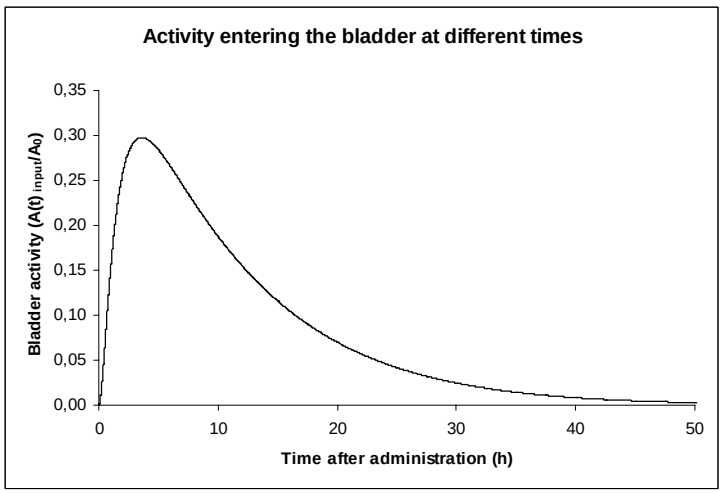

Figure 7. Activity entering the bladder at different times for ^{99m}Tc-MDP. (equation 2.) The shape of the curve depends on when the activity reaches the bladder, which is controlled by the biological parameters. The shape is also dependent on the physical decay of the radiopharmaceutical.

Equation 3 represents the activity that leaves the bladder at void time T_i.

$$A(t)_{output} = \sum_{i=1}^{n}\left[\left(1-\frac{V_r}{V(T_i)}\right)A(T_i)e^{-\lambda(t-T_i)}\right] \qquad \text{Eq. 3}$$

$V(T_i)$ is the bladder content volume at void time T_i; $A(T_i)$ is the activity in the bladder at void time T_i. $A(t)_{output}$ represents the sum of administered activity that has been previously voided. Physical decay for each term is included through the exponential function containing the physical decay constant.

When Eq.2 and Eq.3 are interconnected this will give the time-dependent bladder content activity A(t).

$$A(t) = A_0 e^{-\lambda t}\sum_{j=1}^{m}\left[\alpha_j\left(1-e^{-\lambda_j t}\right)\right] - \sum_{i=1}^{n}\left[\left(1-\frac{V_r}{V(T_i)}\right)A(T_i)e^{-\lambda(t-T_i)}\right] \qquad \text{Eq. 4}$$

input - output

The output from the bladder filling scheme module Figure 6 together with Eq.4 gives the time-dependent bladder content activity A(t). In Figure 8 this is illustrated in form of a fractional bladder activity for ^{99m}Tc-MDP.

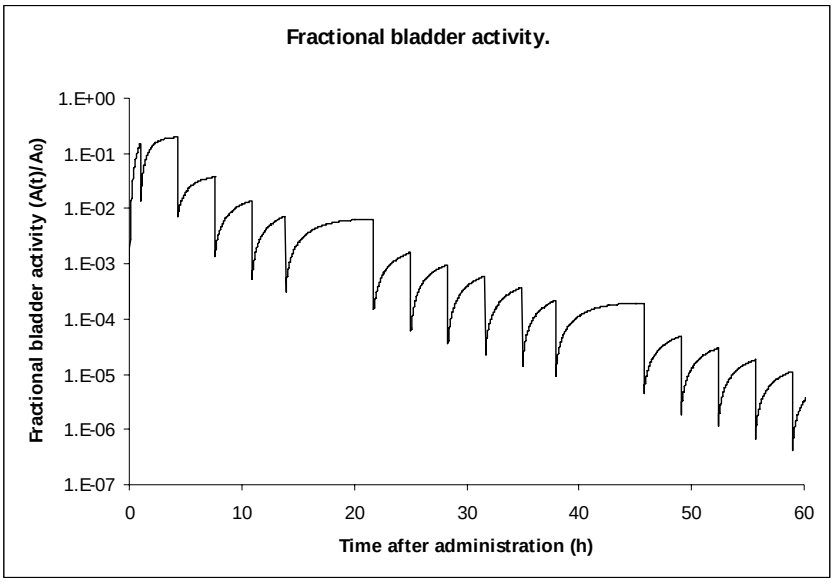

Figure 8. The fractional activity in the bladder after administration for ^{99m}Tc-MDP. (Equation 4.)

3. Absorbed dose per unit administered activity to the inner surface of the bladder wall.

The third part of the dynamic bladder model is the calculation of the absorbed dose per unit administered activity to the inner surface of the bladder wall.

$$\frac{\overline{D}}{A_0} = \left(\frac{1}{A_0}\right)\int_0^{\infty}\left[3.9\Gamma'\frac{A(t)}{V(t)^{2/3}} + \Delta_\beta\frac{A(t)}{2V(t)}\right]dt \qquad \text{Eq. 5}$$

For a full derivation of Eq.5 see appendix 1.

3 Results

For the determination of what parameters that has the largest impact on the absorbed dose to the bladder wall surface, the MIRD model by Thomas *et.al* (5) was used. The calculations in the study were applied to adults, both female and male. If calculation for another age group is desired, appropriate physiological parameters has to be used.

Data obtained from the urine collection for the 30 volunteers resulted in the values presented in Table 3.1.

Table 3.1. Parameters derived from urine collection of the 30 volunteers.

	Mean	Stdev	Max	Min
Voiding interval (min)	199	60	353	95
Night interval (min)	461	97	590	280
Start of night interval (hr:min)	22:56	---	02:00	20:16
Urine flow rate, day (ml/min)	1.37	0.58	2.94	0.65
Urine flow rate, night (ml/min)	0.91	0.42	1.75	0.36
Total volume under 1 day. (ml)	1799	647	3268	897

In the following calculations the above mean values were used. One standard deviation of the derived values was included in the calculations when the voiding interval and urine flow rate was evaluated as well as one half and twice the mean value. The voiding interval of 3.3 hours is in good agreement with the voiding interval used by ICRP, 3.5 hours for adults (1, 2). Thomas *et al*. (5) and Chen *et al.*(8) uses a voiding interval of 3 hours.

The absorbed dose per unit administered activity to the inner surface of the bladder wall was calculated for each radiopharmaceutical as a function of:

- Initial bladder content volume V_0 and first void time T_1
- Residual bladder content volume V_R and first void time T_1
- Time of administration and first void time T_1
- Urine flow rate U(t) and first void time T_1
- Voiding interval and first void time T_1

3.1 First void time

All the calculated data are presented as function of the first void time T_1. The activity that enters the bladder reaches a maximum after a specific time. This maximum in time as seen in Figure 7 depends on the physical and biologic parameters that describe the retention of the administered radiopharmaceutical. If the first void time occurs directly after the administration and before the maximum, the bladder will receive a higher absorbed dose than if the first void time occurs after the maximum. This is because a small bladder will receive a higher absorbed dose than a large bladder. This interaction between the first void time and the retention of the activity from the body is not easy to explain, Figure 9 illustrates this interaction. It is easy to se that a integration over time will result in a high absorbed dose if the first void time is 10 minutes, also that a first void time of 60 minutes would yield the lowest absorbed dose of the three examples in Figure 9.

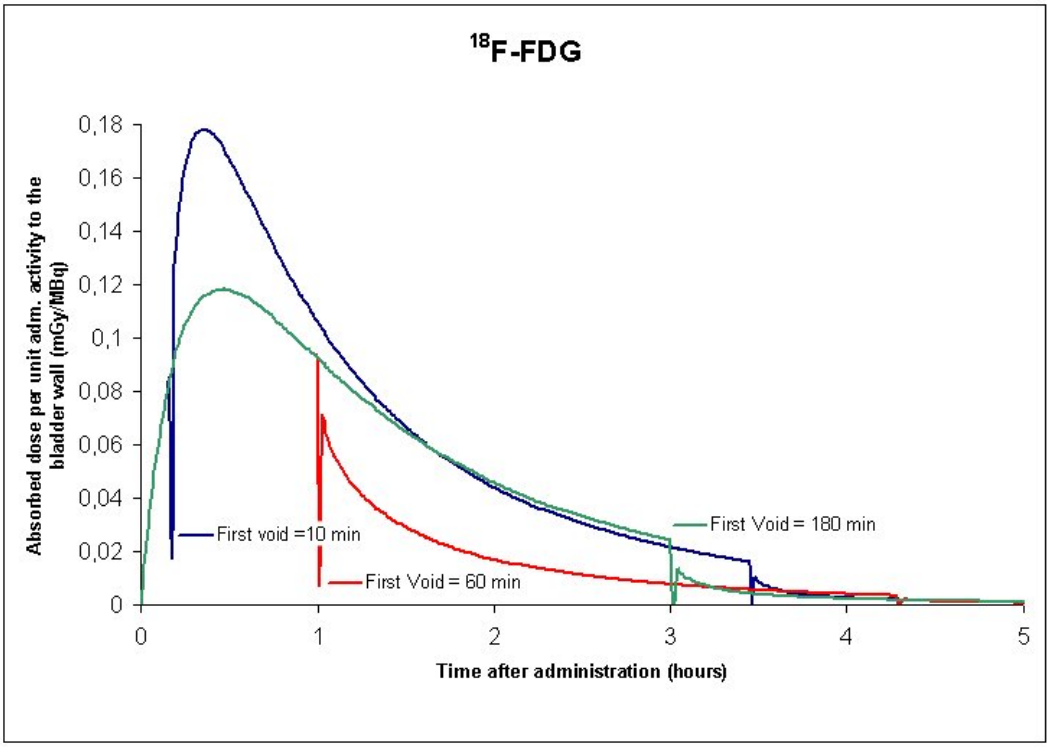

Figure 9. The absorbed dose per unit administered activity (mGy/MBq) to the bladder wall surface for various first void times.

The maximum in the retention-curve for ^{131}I-NaI is 31 hours after the administration. Because of this long time, no optimal first void time is observed for any of the calculated first void times. ^{131}I-NaI does off course also have an optimal first void time but it is longer than 4 hours.

3.2 Initial bladder content volume

The initial bladder content volume has an obvious effect on the absorbed dose to the bladder wall. The initial bladder content volume does not have any effect on the absorbed dose however, if the patient voids directly after the administration. This can be seen for all of the radiopharmaceuticals studied. If the first void time is prolonged the effect of the initial bladder content volume on the absorbed dose is increased. For a larger initial volume the absorbed dose is reduced because of the dilution and self-absorption in the urine. Results from the calculations of the impact of the initial bladder contents volume are given in Figure 20 to Figure 24 for the various radiopharmaceuticals. For these calculations the voiding interval were kept at 3.3 hr, the residual bladder content volume at 10 ml and the urine flow rate at 1.37/0.91 ml/min (day/night). ^{18}F-FDG is the agent that shows the largest change in the absorbed dose to the bladder wall surface as function of the initial bladder content volume. This is due to the rapid elimination of the substance from the body. The substance that shows the smallest change in absorbed dose, as a function of the initial bladder content volume, is ^{131}I-NaI were the reduction in absorbed dose is up to 20% depending on the first void time.

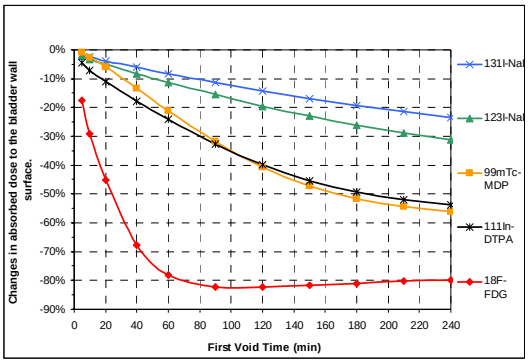

Figure 10. Changes in absorbed dose to the bladder wall surface when initial bladder content volume V_0 is increased from 10 ml to 500 ml.

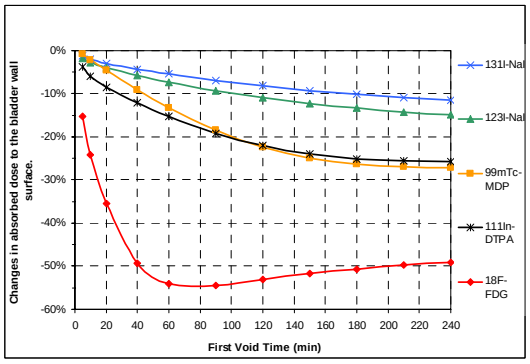

Figure 11. Changes in absorbed dose to the bladder wall surface when initial bladder content volume V_0 is increased from 10 ml to 100 ml.

As can be seen in Figure 10, the reduction of the absorbed dose to the bladder wall from the various radiopharmaceuticals, due to the increased initial bladder content volume from 10 ml to 500 ml, is obvious. However, it should be mentioned that the upper limit of 500 ml is not a typical initial bladder content volume. If the first voiding interval occurs at 240 min, and the initial bladder content volume is 500 ml, the total volume of urine in the first micturition would be 828 ml. If the initial bladder content volume is 100 ml instead, the reduction of the absorbed doses is illustrated in Figure 11. The agent that gives the highest absorbed dose to the bladder wall surface is ^{131}I-NaI. For this agent the reduction of the radiation dose is between 5-10 % and even higher if the initial bladder content volume is larger than 100 ml. ^{18}F-FDG shows the largest reduction in dose, up to 55%, Figure 11. This indicates that the patients that are administered with ^{18}F-FDG should not urinate directly before the administration of the activity, if the intention is to minimize the absorbed dose to the urinary bladder.

3.3 Residual bladder content volume

The residual bladder content volume is a parameter that cannot be affected deliberately by the patient. The residual bladder content volume is considered to increase with age as a consequence of age-related changes in the lower urinary tract (19). An increased residual bladder content volume tends to increase the absorbed dose to the bladder wall surface for all of the radiopharmaceuticals in this study if the first void time is later than 20 min after the administration of the substance as can be seen in Figure 12. For ^{18}F-FDG and ^{99m}Tc-MDP, a decrease in absorbed dose is obtained if the first void time is earlier than 20 min.

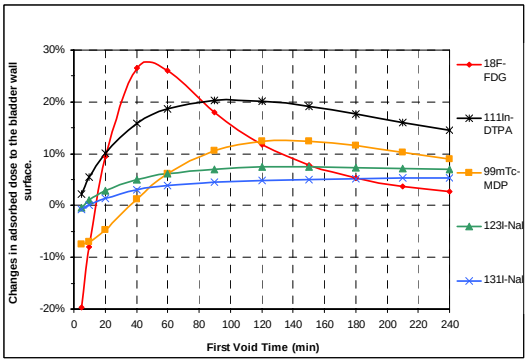

Figure 12 Changes in the absorbed dose to the bladder wall surface if the residual bladder content volume is increased from 10 ml to 50 ml.

For ^{111}In-DTPA, the increase of absorbed dose to the bladder wall is up to 20%. If the residual volume is higher, an even higher absorbed dose is obtained. For patients with a large post-void volume, catheterization could be an option to

reduce the absorbed dose to the bladder wall surface, especially when ^{18}F-FDG and ^{111}In-DTPA are used. The radiopharmaceutical that shows least dependence from the residual bladder volume is ^{131}I-NaI

The results from the calculations for the residual bladder content volume for the individual radiopharmaceuticals are shown in the *Appendix 3* (Figure 25 to Figure 29). The other variables were fixed at the following values: voiding interval 3.3 hr, initial bladder content volume 50 ml, and urine flow rate 1.37/0.91 ml/min (day/night).

3.4 Voiding interval

If the voiding interval is half the mean value (3.3 hr) i.e. 1.7 hr the reduction in absorbed dose to the bladder wall varies considerably as can be seen in Figure 13.

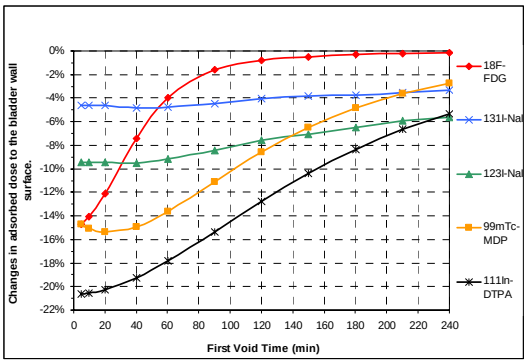

Figure 13. Changes in absorbed dose to the bladder wall surface when the voiding interval is reduced to 1.7 hr, half the mean value (3.3 hr)

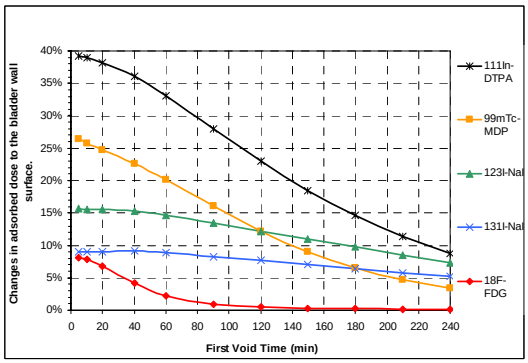

Figure 14. Changes in absorbed dose to the bladder wall surface when the voiding interval is increased to 6.6 hr, twice the normal mean (3.3 hr).

A shorter time between the micturitions reduces the time that the activity is present in the bladder, and therefore reducing the absorbed dose to the bladder wall. For all of the radiopharmaceuticals in this study, except for ^{131}I-NaI, this reduction in absorbed dose is greatest if the first void time is early, for the same reason as mentioned above. The largest reduction in absorbed dose is obtained for ^{111}In-DTPA with up to 20%, if the voiding interval is reduced to half the mean value. If the voiding interval is increased to twice the mean value an increase in the absorbed dose is obtained as can be seen in Figure 14.

3.5 Urine flow rate

In the calculations yielding the results presented in the *Appendix 3* (Figure 35 to Figure 39) the voiding interval is kept at a constant value of 3.3 hr, initial bladder content volume at 50 ml and the residual bladder content volume at 10 ml. The effect of halving and doubling the mean urine flow rate on the bladder wall surface dose is shown in Figure 15 and Figure 16.

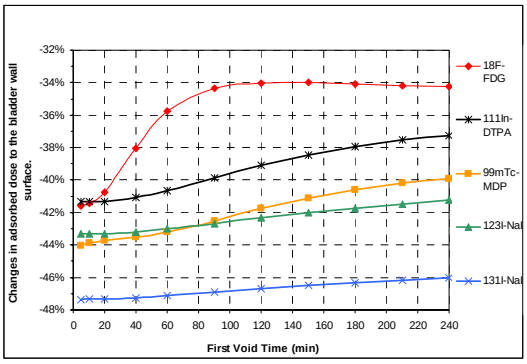

Figure 15 Changes in absorbed dose to the bladder wall surface when the urine flow rate is increased to 2.74 ml/min, twice the mean value (1.37 ml/min).

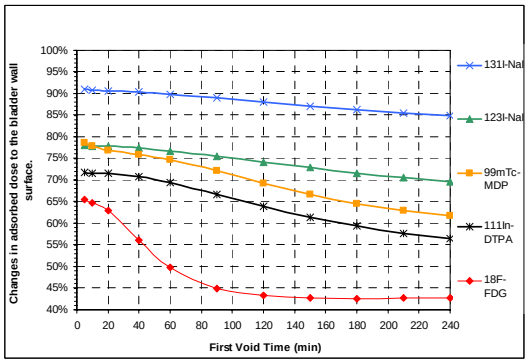

Figure 16 Changes in absorbed dose to the bladder wall surface when the urine flow rate is reduced to 0.69 ml/min, half the mean value (1.37 ml/min).

A doubling in the urine flow causes a reduction in bladder dose for all of the radiopharmaceuticals in this study. ^{131}I-NaI shows the greatest reduction with up to 47%, as shown in Figure 15. For ^{18}F-FDG the reduction is larger if the first void time is short, which also is true for the other radiopharmaceuticals but not to the same extent. If the urine flow rate is reduced to half the mean value, the increase in absorbed dose is up to 90% for ^{131}I-NaI (Figure 16). For ^{99m}Tc-MDP, ^{123}I-NaI and ^{111}In-DTPA the increase in absorbed dose is between 60-80% if the urine flow rate is reduced to half the normal value. A halving in the urine flow rate shows the same dependency with the first void time as for a doubling, but in the opposite direction. A short first void time when the urine flow rate is half the mean value tends to increase the absorbed dose.

In practice, an increase in the urine flow rate is automatically followed by a decrease in the voiding interval. If the liquid consumption is doubled, the number of micturitions is almost increased with a factor of two. The mean volume voided at each micturition is almost the same, independent of the liquid consumption (20). For a more accurate estimation of the absorbed dose, the voiding interval and the urine flow rate has to follow each other in the calculations. If the urine flow rate is doubled the voiding interval is decreased to 1.7 hr, and if the urine flow rate is half the normal, value the voiding interval is increased to 6.6 hr. These calculations are based on the normal voiding interval of 199 min and the urine flow rate of 1.37 ml/min that gives a total mean voiding volume of 273 ml.

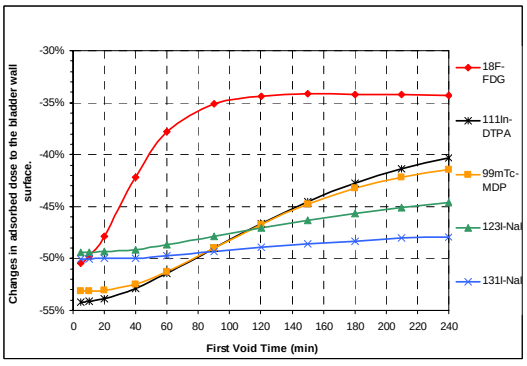

Figure 17. Changes in absorbed dose to the bladder wall surface when the urine flow rate is twice the normal and the voiding interval is decreased to 1.7 hr

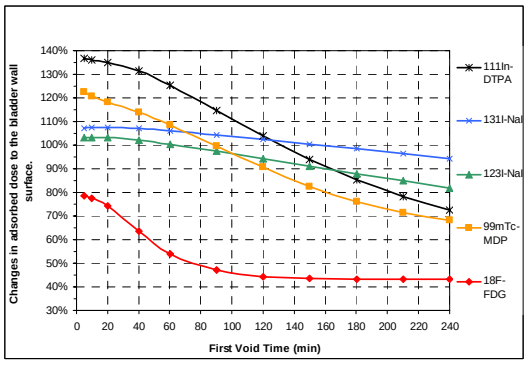

Figure 18. Changes in absorbed dose to the bladder wall surface when the urine flow rate is half the normal and the voiding interval is increased to 6.6 hr

The decrease in the absorbed dose to the bladder wall is seen in Figure 17. The major difference from the results shown in Figure 15, when the voiding interval was fixed at 3.3 hr, is the reduction of absorbed dose for ^{111}In-DTPA. This is due

to the strong relationship between the voiding interval and the absorbed dose from ^{111}In-DTPA as seen in Figure 13. If the urine flow rate is half the normal value and the first void time occurs before 1 hour after administration the increase in absorbed dose to the bladder is up to 135% for ^{111}In-DTPA. For the iodine isotopes ^{123}I and ^{131}I the increase is between 80-105% depending on the first void time. For the two radiopharmaceuticals ^{131}I-NaI and ^{111}In-DTPA that gives the highest absorbed doses to the bladder wall, additional liquid consumption is recommended to lower the absorbed dose, especially when ^{131}I-NaI is used for therapy i.e when high activity is administered to the patient.

Changes in the urine flow rate are likely to change the biological turnover - an increase of the urine flow rate or additional hydration can speed up the elimination from the body whilst a reduction in urine flow will slow down elimination of the radiopharmaceutical from the body (21). This change in total body clearance, due to change in the urine flow rate, could have an impact on the absorbed dose to the urinary bladder. The calculations performed in this study do not take these changes in the rate of whole-body clearance, into account.

3.6 Time of administration

The time of administration of the radiopharmaceutical has a moderate effect on the absorbed dose to the bladder wall surface. If the administration occurs at 3 pm instead of 9 am the increase in absorbed dose is up to 10% as illustrated in Figure 19. This increase of absorbed dose is due to the shortened time between the administration and the first night interval. The two substances that show the largest increase in absorbed dose are ^{123}I-NaI and ^{131}I-NaI.

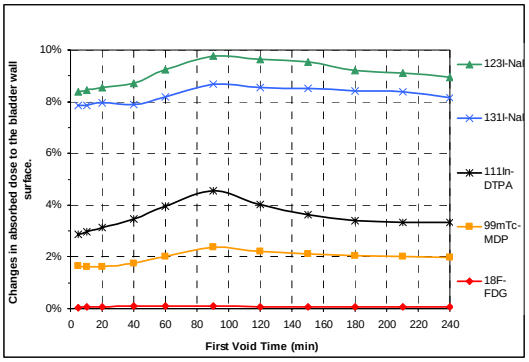

Figure 19 Changes in absorbed dose to the bladder wall surface when the time of administration occurs at 3 PM instead of 9 AM.

The extraordinary relationship that is seen in Figure 19 is due to the reduction of the voiding interval that is closest to the night interval.

3.7 Optimal first void time

To obtain the first void time that yields the minimum absorbed dose to the bladder wall surface, a mean value of the absorbed dose as function of first void time was calculated from the results presented in Figure 20 to Figure 44 for each radiopharmaceutical. The optimal first void times after the administration for the various radiopharmaceuticals are given in Table 3.2

Table 3.2. The first void time after the administration that provides the minimal absorbed dose

Radiopharmaceutical	Optimal first void time (min)
^{18}F-FDG	60
^{99m}Tc-MDP	150
^{123}I-NaI	180
^{131}I-NaI	---
^{111}In-DTPA	150

The first void time that provides the minimum absorbed dose for ^{131}I-NaI was not possible to obtain, since the absorbed dose does not vary with time, i.e there is no minimum, as shown in Figure 48. This indicates that the actual dose minimum may occur at a longer initial voiding time than 240 minutes.

3.8 Absorbed doses

Estimated mean absorbed doses per unit administered activity to the bladder wall surface are given in Table 3.3. These results are compared with the bladder wall doses calculated by ICRP (1, 2). The time of first voiding is chosen so that the minimum dose is obtained.

Table 3.3. Estimated absorbed doses per unit administered activity to the surface of the bladder wall for various radiopharmaceuticals. The results are compared with data from ICRP (1, 2)

Radiopharmaceutical	This report			ICRP
	First void[A] (min)	Abs. dose (mGy/MBq)	Stdev (mGy/MBq)	Abs. dose (mGy/MBq)
^{18}F-FDG	60	1.3E-01[B]	5.0E-02	1.6E-01
^{99m}Tc-MDP	150	3.7E-02 [B]	9.0E-03	4.8E-02
^{123}I-NaI	180	9.7E-02 [B]	2.0E-02	6.9E-02
^{131}I-NaI	---	6.9E-01[C]	1.5E-01	4.6E-01
^{111}In-DTPA	150	3.2E-01 [B]	7.4E-02	2.5E-01

[A] represent the initial first void time that provides minimum absorbed dose
[B] represents the minimum absorbed doses calculated as mean values, Figure 45 to Figure 49
[C] is the mean value of the absorbed dose over all first void times Figure 48

The contribution from penetrating and non-penetrating radiation to the absorbed dose can be seen in Table 3.4.

Table 3.4. Contribution to the absorbed dose from penetrating and non-penetrating radiation. First void time = 60 minutes, initial bladder volume:50 ml.

Radiopharmaceutical	Abs. dose (mGy/MBq)	Penetrating radiation (mGy/MBq)	Non-penetrating radiation (mGy/MBq)
^{18}F-FDG	1.5E-01	3.9E-02	1.1E-01
^{99m}Tc-MDP	4.5E-02	1.7E-02	2.8E-02
^{123}I-NaI	1.0E-01	4.9E-02	5.2E-02
^{131}I-NaI	6.8E-01	1.2E-01	5.6E-01
^{111}In-DTPA	3.5E-01	2.2E-01	1.3E-01

3.9 Uncertainties

The choice of using STELLA for calculation of the absorbed dose to the bladder wall with the above described model introduced some inaccuracies in the result. In STELLA, one can choose the time interval DT (the time between calculations), but it is not possible to have a long calculation-time and a short DT. Because of this feature the calculated absorbed doses to the bladder wall surface, differs slightly (1-2%) compared with the results from Thomas *et al.* (5), especially when radionuclides with long physical half-life are used.

In the calculation of the dose rate from penetrating radiation (Eq.5) an approximation is made that the geometrical factor g_c is equal to $4\pi R$ (see Appendix 1). This approximation produces an inaccuracy between 2-10% in the absorbed dose. The calculated absorbed doses presented in this report are 2-10% higher than if this approximation wouldn't have been done.

The soft tissue-equivalent dose constant Γ' calculated by Thomas *et al*. (5) differs from the soft tissue-equivalent dose constant used in this study. Thomas *et al* does not specify how these values are calculated nor is there any references. The calculated Γ' in this study compared with the calculated Γ' from Thomas *et al*. (5) differs up to 30%. For ^{18}F the same Γ' is obtained, for ^{99m}Tc the difference is 30%, which results in a discrepancy of 12% in the absorbed dose to the bladder wall surface. For ^{123}I, there is a difference of 6% in Γ' which gives a discrepancy of 3% in the absorbed dose. ^{131}I has a difference of 0.6% in Γ' that gives a discrepancy if 1% in the absorbed dose. For ^{111}In the difference in Γ' is 10%, which gives a discrepancy in absorbed dose of 6%.

4 Discussion

If one asks a medical physicist the question: How can you lower the absorbed dose to the urinary bladder wall, after an administration of a radiopharmaceutical to a patient, most physicists would answer: I recommend the patient to drink additional water and urinate more frequently.
But if you instead ask the question: Should the bladder be full or empty at the time of administration, and at what time should the patient urinate for the first time after the administration, to minimize the absorbed dose, the physicist would probably hesitate since the answer is not that simple.

The answer depends on the type of radiopharmaceutical administered. For a substance that is rapidly excreted from the body, such as ^{18}F-FDG, the initial bladder content volume and the first void time, are parameters that have a great effect on the absorbed dose to the bladder wall surface. Additional hydration does of course lower the absorbed dose, but not at much as the initial bladder content volume. If a patient administered with ^{18}F-FDG, has a full bladder at the time of administration but urinate directly after the administration, the effect of lowering the absorbed dose is gone. Thus, the relationship between the initial bladder content volume and the first void time are strong. Another parameter that affects the absorbed dose to the bladder wall from ^{18}F-FDG, is the residual bladder content volume. A large residual bladder content volume increases the absorbed dose compared with a smaller volume. This increase in absorbed dose has its maximum at the optimal first void time for ^{18}F-FDG. So if a patient with a large residual bladder content volume who is administered with ^{18}F-FDG, is well hydrated, the lowering of the absorbed dose to the bladder wall surface, could be smaller than expected, if the first void occurs at the optimal first void time after administration. For this reason, urinary catheterisation could be an option or lowering the first void time. For ^{131}I-NaI and ^{123}I-NaI, a change in the residual bladder content volume does not change the absorbed dose to any substantial extent.

^{111}In-DTPA is the radiopharmaceutical in this study that shows the strongest relationship between the voiding interval and the absorbed dose to the bladder wall surface. This is due to the fast absorbed dose build-up time, 60% of the radiation dose administered to the bladder wall is delivered in the first 3.5 hours, 80% within 5 hours and 99% within 15 hours. Because of this fast build-up time a change in the voiding interval under these 15 hours results in a large change in absorbed dose to the bladder wall surface. ^{99m}Tc-MDP is also a radio-pharmaceutical with a fast absorbed dose build-up time. As seen in Figure 13 and Figure 14 ^{99m}Tc-MDP is the substance that shows the second largest change in absorbed dose due to a change in voiding interval. ^{131}I-NaI has a very long absorbed dose build-up time and a change in the voiding interval does not have an appreciable effect on the absorbed dose to the bladder wall surface.

A change in the urine flow rate is followed by a large change in the absorbed dose to the bladder wall surface for all of the radiopharmaceuticals. A higher urine flow rate has the effect of filling the bladder in a shorter time, and therefore the concentration of the activity in the bladder is lowered which affect the absorbed dose. ^{131}I-NaI shows the largest change in absorbed dose due to a change in the urine flow rate. As mentioned before, a change in the urine flow rate is automatically followed by a change in the voiding interval. If this is taken into

account as illustrated in Figure 17 the decrease in absorbed dose for the radiopharmaceuticals when the urine flow rate is doubled is between 40-55%. For ^{18}F-FDG that does not have such a strong relationship between the urine flow rate and the absorbed dose the decrease begins at 50% and falls to 35% as function of the first void time. If the urine flow rate is half the normal value as seen in Figure 18 the increase in absorbed dose is very large, between 40-140% as function of first void time and type of radiopharmaceutical. This shows how important it is that the patients are well hydrated.

Additional hydration is likely to change the whole-body clearance of a radiopharmaceutical. Darte and Tenvall (22) report that additional hydration improved the rate of clearance from the body when the patient was administered with ^{131}I-MIBG. For ^{18}F-FDG, there is also results reported (23) that hydration of patients lead to more FDG reaching the bladder. How much this change in clearance affect the absorbed dose to the bladder wall surface is difficult to estimate without appropriate fractions and biological half-lives. This change in whole-body clearance has another side effect if it exists, in therapy with ^{131}I-NaI the patients are told to drink additional water, this could have the effect that the thyroid does not take up sufficiently amounts of ^{131}I.

The time at which the administration occurs does not seem to change the absorbed dose to a large extent for any of the radiopharmaceuticals e.g. if the administration occurs at 3 pm instead of 9 am.

All of the radiopharmaceuticals in this study except ^{131}I-NaI have an optimal first void time. For a radiopharmaceutical that is rapidly excreted from the body this optimal first void time has a large effect on the absorbed dose to the bladder surface wall. For ^{18}F-FDG this time is between 40 and 60 minutes after the administration as seen in Figure 45. If the first void occurs directly after the administration instead at the optimal time for ^{18}F-FDG an increase in absorbed dose up to 115% is possible.

As seen in Table 3.3 the absorbed doses calculated in this report differs from the absorbed doses calculated by ICRP (1, 2). For ^{18}F-FDG and ^{99m}Tc-MDP the absorbed doses calculated by ICRP are higher than the absorbed doses calculated in this report. For the three remaining radiopharmaceuticals the absorbed doses calculated by ICRP are underestimated. This result, especially when ^{131}I-NaI is administered is also reported by Thomas *et al.* (5) and Bolster *et al*. (21).

The voiding interval mean:(3.3 hr) derived from the volunteers in the survey is in good agreement with voiding interval used by ICRP (1, 2). The urine flow rate (1.37 ml/min) and the daily urine volume (1799 ml) are higher than reported in literature. The Geigy Scientific Tables (24) report a mean daily urine volume for men of 1360 ml and for women of 1130 ml. The reason for this large difference in total urine volume could be different way of living. If some of the volunteers were doing workout at the time for the survey this has an impact on the water consumption.

The model used in this report does only calculate the absorbed dose to the inner surface of the bladder wall and not the absorbed dose the whole bladder wall. The absorbed doses calculated in this report would have been lower if the total bladder wall has been the investigated organ. Thomas *et al*. (5) solves this by calculating

the electron depth doses separately by using the percentile distance parameter. Future work could be to make a model based on the dynamic bladder model developed by Thomas *et al*. (5) that calculates the absorbed dose to the whole bladder wall.

5 Conclusions

The result shows that it is possible to reduce the absorbed dose to the bladder wall surface after an administration of a radiopharmaceutical. The best way of reducing the absorbed dose is to increase the urine flow rate, and this is done my increasing the water consumption. The first void time is especially important after an administration with ^{18}F-FDG. Another parameter that is easy to control is the initial bladder content volume, if the patients do not urinate directly before the administration this helps to reduce the absorbed dose.

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Appendix 1

At a point x within a volume V that's containing a uniform distribution of radioactivity, the dose rate from the penetrating radiation is

$$\dot{D}_{p,x} = C\rho\Gamma'\int_V \frac{e^{-\mu r}}{r^2}dV \qquad \text{Eq. 6}$$

$D_{p,x}$ is the dose rate [mGy/s] at point x; C is the concentration [MBq/g]; ρ is the density of the medium in [g/cm^3]; Γ´ is the air kerma rate constant converted to dose in tissue in [(mGy·cm^2)/(MBq·s)]; μ is the effective linear absorption coefficient in [cm^{-1}].

The integral term in Eq.5 is called the geometrical factor g_x [cm]. This term can be simplified by making the approximation that μR << 1. At the center of a sphere of radius R the geometrical factor g_c can be determined at follows

$$g_c = \int_0^R \frac{e^{-\mu r}}{r^2} 4\pi r^2 dr = \frac{4\pi}{\mu}\left(1 - e^{-\mu R}\right) \qquad \text{Eq. 7}$$

If we assuming that μR << 1 this will give us

$$g_c = 4\pi R \qquad \text{Eq. 8}$$

For a point at the surface of a sphere the geometrical factor g_s is ½ of that at the center of the same sphere.

$$g_s = 2\pi R \qquad \text{Eq. 9}$$

If one assumes that the tissue density is 1 g/cm^3 and that the activity concentration is

$$C(t) = \frac{A(t)}{V(t)} \qquad \text{Eq. 10}$$

and the radius R(t) is given by

$$R(t) = \left[\frac{3 \cdot V(t)}{4\pi}\right]^{1/3} \qquad \text{Eq. 11}$$

The penetrating dose rate at the surface of a sphere can then be represented by

$$\dot{D}_{p,s}(t) = \Gamma' \cdot A(t) \cdot \left[\frac{6 \cdot \pi^2}{V(t)^2}\right]^{1/3} \qquad \text{Eq. 12}$$

The dose rate from non-penetrating radiation at a point within a medium of reasonable size is

$$\dot{D}_{np} = 2.13 \cdot \frac{\overline{E}_{\beta} \cdot C}{\rho} \qquad \text{Eq. 13}$$

$\overline{E}_{\beta}$ is the average energy of beta or beta-like radiation per disintegration in [MeV]. If the radionuclide emits more than one type of non-penetrating radiation, the term $\overline{E}_{\beta}$ must be calculated as the sum of each type of non-penetrating radiation on the basis of the relative abundance of each type. The mean electron particle energy emitted per nuclear transition (formerly equilibrium dose constant) is

$$\Delta_{\beta} = 2.13 \cdot \sum_{i} n_i \cdot \overline{E}_{\beta i} \qquad \text{Eq. 14}$$

Equation 14 can be rewritten as

$$\dot{D}_{np} = \frac{\Delta_{\beta} \cdot C}{\rho} \qquad \text{Eq. 15}$$

The dose rate at the surface of a sphere is ½ of that within the medium, so this gives us

$$\dot{D}_{np,s} = \frac{\Delta_{\beta} \cdot C}{2\rho} \qquad \text{Eq. 16}$$

Using Eq.10, the non-penetrating dose rate at the surface of a sphere is

$$\dot{D}_{np,s}(t) = \frac{\Delta_{\beta} \cdot A(t)}{2 \cdot V(t)} \qquad \text{Eq. 17}$$

If the range of the non-penetrating radiation is small compared with the physical dimensions of the medium, eq.17 holds for geometrical configurations other then spheres.

The total dose rate to the inner surface of the bladder wall is given by Eq.12 and Eq.17. An integration over time gives the total absorbed dose to the bladder wall.

$$D = \int_0^{\infty} \left[\frac{\left(6\pi^2\right)^{1/3} \cdot \Gamma' \cdot A(t)}{V(t)^{2/3}} + \frac{\Delta_{\beta} \cdot A(t)}{2V(t)} \right] dt \qquad \text{Eq. 18}$$

Absorbed dose per unit administered activity to the bladder wall is

$$\frac{\overline{D}}{A_0} = \left(\frac{1}{A_0} \right) \int_0^{\infty} \left[3.9\Gamma' \frac{A(t)}{V(t)^{2/3}} + \Delta_{\beta} \frac{A(t)}{2V(t)} \right] dt \qquad \text{Eq. 19}$$

Appendix 2

En annorlunda undersökning…

Vid behandling och undersökningar då man använder radionuklider så är det viktigt att man vet vilken stråldos som ges till patienten. Ett utsatt organ är urinblåsan eftersom så gott som all aktivitet som inte stannar kvar i kroppen, eller som sönderfaller, kommer att samlas i blåsan. Beroende på hur ofta man tömmer blåsan efter en administrering av ett preparat innehållandes en radionuklid så kommer stråldosen till urinblåsan att variera. Eftersom det inte går att mäta hur stor stråldos urinblåsan får så använder man sig av olika modeller för att beräkna stråldosen. De data som ligger till grund för beräkningarna med avseende på tömningsintervall m.m. är ca 20 år gamla.

Därför skall jag med mitt examensarbete verifiera om dessa data är hållbara även idag. Genom att låta en stor grupp individer notera tidpunkten och mäta volymen urin när de tömmer blåsan, hoppas jag att med mitt arbete kunna förbättra modellen.

Med Din hjälp kommer mitt examensarbete att kunna verifiera om modellen är hållbar eller om det behövs göras förändringar i den.

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e-mail: morgan.schonbeck@gmail.com

☐ *Man*
☐ *Kvinna*
☐ *Ålder*

Gör så här: Kissa i den bifogade mätbägaren och anteckna mängden (ml) vid varje tillfälle och även tidpunkten. Skulle du missa något tillfälle så är det viktigt att du gör en notering om detta.

	1	2	3	4	5	6	7	8
Tid								
Volym (ml)								

	9	10	11	12	13	14	15	16
Tid								
Volym (ml)								

	17	18	19	20	21	22	23	24
Tid								
Volym (ml)								

Kommentarer: (Fortsätt på baksidan om utrymmet inte räcker till)

Appendix 3
Initial bladder content volume, V_0

Figure 20 to Figure 24 present the relationship between the initial bladder content volume and the absorbed dose to the bladder wall surface as function of first void time, obtained in this study. In the calculations the voiding interval are kept at 3.3 hr, the residual bladder content volume at 10 ml and the urine flow rate at 1.37/0.90 ml/min (day/night).

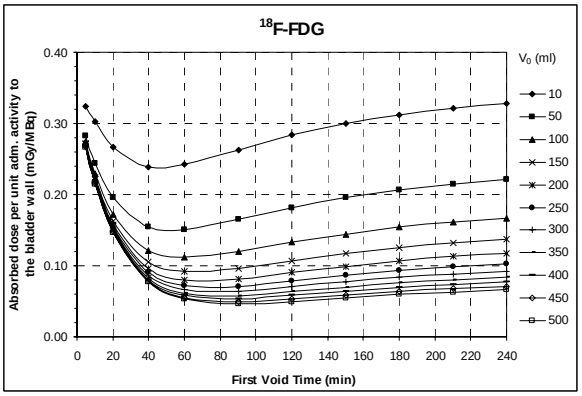

Figure 20. Absorbed dose per unit administered activity to the bladder wall from ^{18}F-FDG for various initial bladder content volumes. Voiding interval = 3.3hr, V_r=10 ml and U(t)=1.37/0.90 ml/min (day/night)

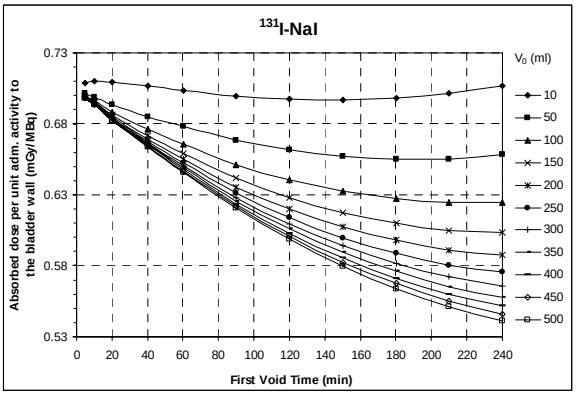

Figure 23. Absorbed dose per unit administered activity to the bladder wall from ^{131}I-NaI for various initial bladder content volumes. Voiding interval = 3.3hr, V_r=10 ml and U(t)=1.37/0.90 ml/min (day/night)

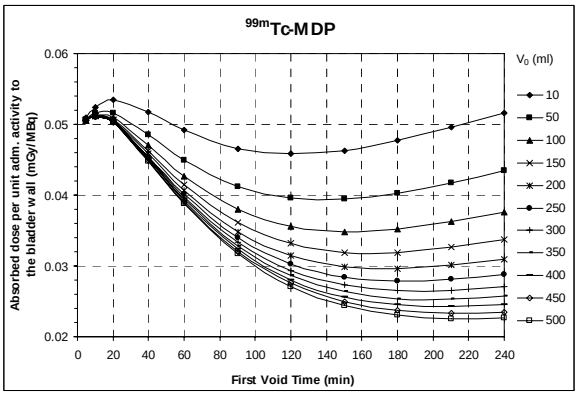

Figure 21. Absorbed dose per unit administered activity to the bladder wall from ^{99im}Tc-MDP for various initial bladder content volumes. Voiding interval = 3.3hr, V_r=10 ml and U(t)=1.37/0.90 ml/min (day/night)

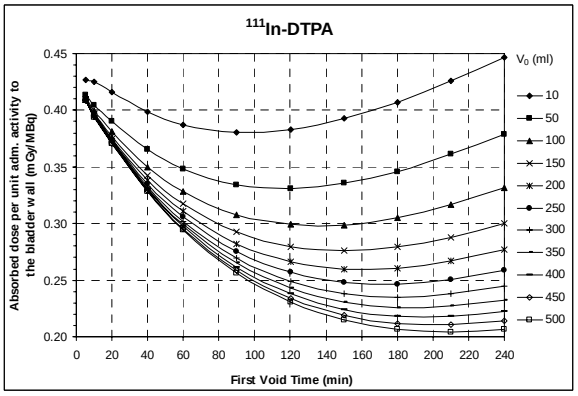

Figure 24. Absorbed dose per unit administered activity to the bladder wall from ^{111}In-DTPA for various initial bladder content volumes. Voiding interval = 3.3hr, V_r=10 ml and U(t)=1.37/0.90 ml/min (day/night)

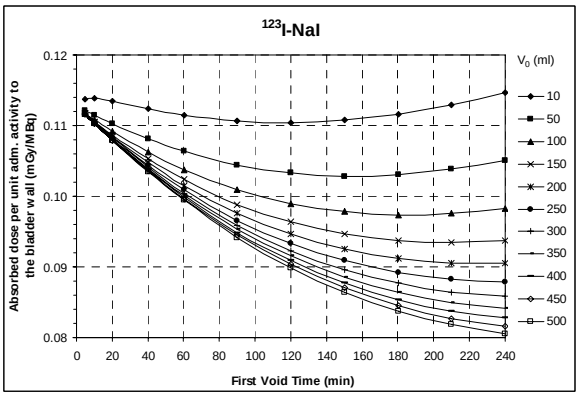

Figure 22. Absorbed dose per unit administered activity to the bladder wall from ^{123}I-NaI for various initial bladder content volumes. Voiding interval = 3.3hr, V_r=10 ml and U(t)=1.37/0.90 ml/min (day/night)

Residual bladder content volume, V_R

Figure 25 to Figure 29 present the relationship between the residual bladder content volume and the absorbed dose to the bladder wall surface as function of first void time, obtained in this study. In the calculations the voiding interval are kept at 3.3 hr, the initial bladder content volume at 10ml and the urine flow rate at 1.37/0.90 ml/min (day/night).

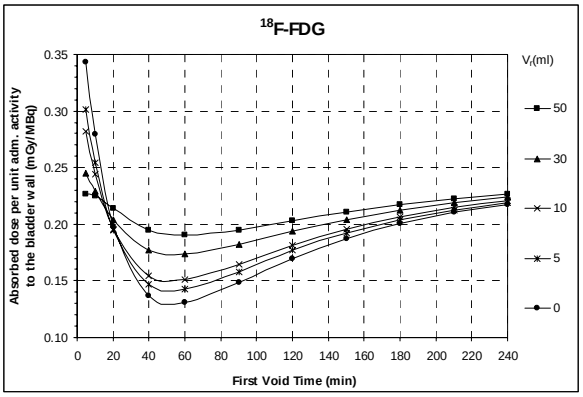

Figure 25. Absorbed dose per unit administered activity to the bladder wall from ^{18}F-FDG. Voiding interval = 3.3hr, V_0=50 ml and U(t)=1.37/0.90 ml/min (day/night)

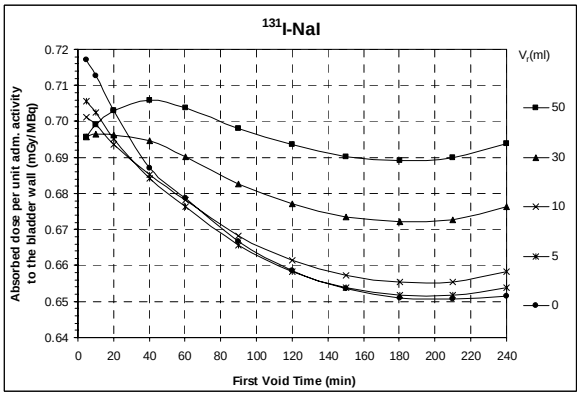

Figure 28. Absorbed dose per unit administered activity to the bladder wall from ^{131}I-NaI. Voiding interval = 3.3hr, V_0=50 ml and U(t)=1.37/0.90 ml/min (day/night)

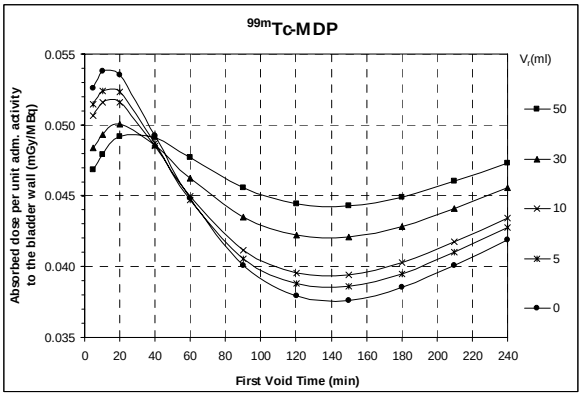

Figure 26. Absorbed dose per unit administered activity to the bladder wall from ^{99m}Tc-MDP. Voiding interval = 3.3hr, V_0=50 ml and U(t)=1.37/0.90 ml/min (day/night)

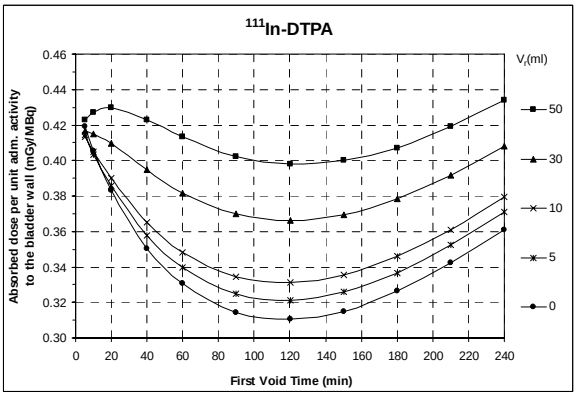

Figure 29. Absorbed dose per unit administered activity to the bladder wall from ^{111}In-DTPA. Voiding interval = 3.3hr, V_0=50 ml and U(t)=1.37/0.90 ml/min (day/night)

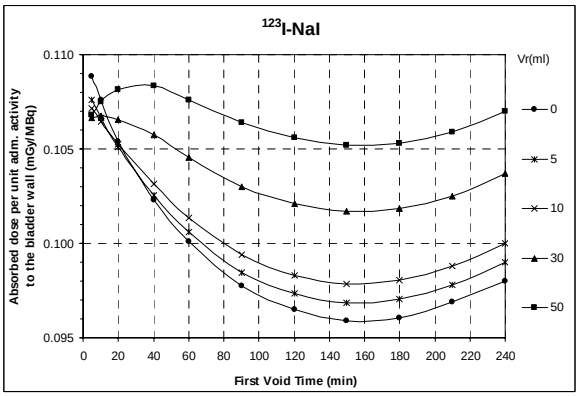

Figure 27. Absorbed dose per unit administered activity to the bladder wall from ^{123}I-NaI. Voiding interval = 3.3hr, V_0=50 ml and U(t)=1.37/0.90 ml/min (day/night)

Voiding interval

Figure 30 to Figure 34 present the relationship between the voiding interval and the absorbed dose to the bladder wall surface as function of first void time, obtained in this study. In the calculations the initial bladder content volume are kept at 50ml, the residual bladder content volume at 10 ml and the urine flow rate at 1.37/0.90 ml/min (day/night).

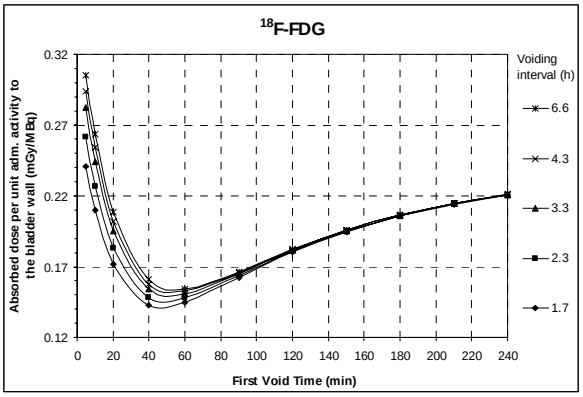

Figure 30. Absorbed dose per unit administered activity to the bladder wall from ^{18}F-FDG. V_r= 10 ml, V_0=50 ml and U(t)=1.37/0.90 ml/min (day/night)

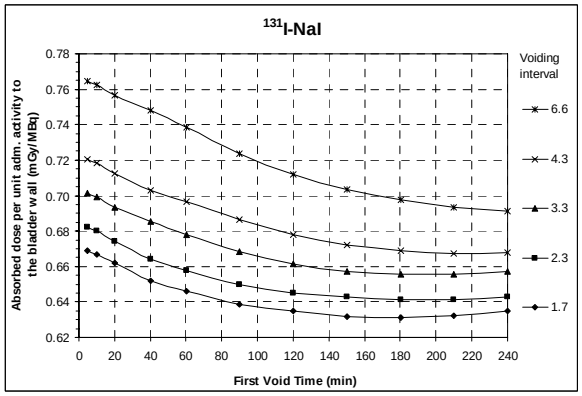

Figure 33. Absorbed dose per unit administered activity to the bladder wall from ^{131}I-NaI. V_r= 10 ml, V_0=50 ml and U(t)=1.37/0.90 ml/min (day/night)

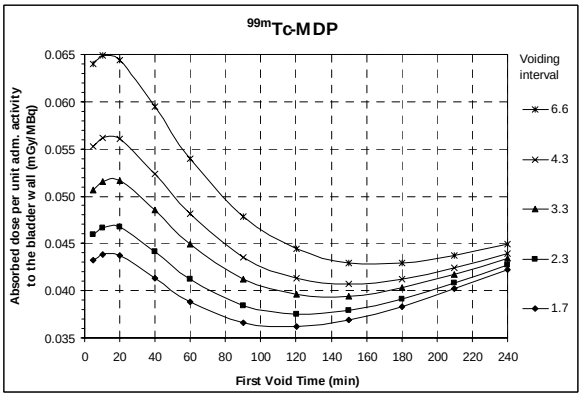

Figure 31. Absorbed dose per unit administered activity to the bladder wall from ^{99m}Tc-MDP. V_r= 10 ml, V_0=50 ml and U(t)=1.37/0.90 ml/min (day/night)

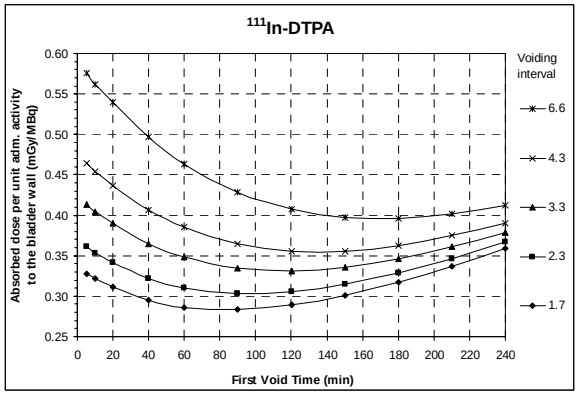

Figure 34. Absorbed dose per unit administered activity to the bladder wall from ^{111}In-DTPA. V_r= 10 ml, V_0=50 ml and U(t)=1.37/0.90 ml/min (day/night)

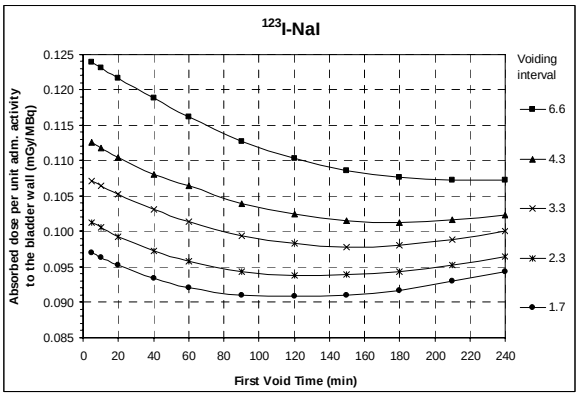

Figure 32. Absorbed dose per unit administered activity to the bladder wall from ^{123}I-NaI. V_r= 10 ml, V_0=50 ml and U(t)=1.37/0.90 ml/min (day/night)

Urine flow rate, U(t)

Figure 35 to Figure 39 present the relationship between the urine flow rate and the absorbed dose to the bladder wall surface as function of first void time, obtained in this study. In the calculations the initial bladder content volume are kept at 50ml, the residual bladder content volume at 10 ml and the voiding interval at 3.3 hr.

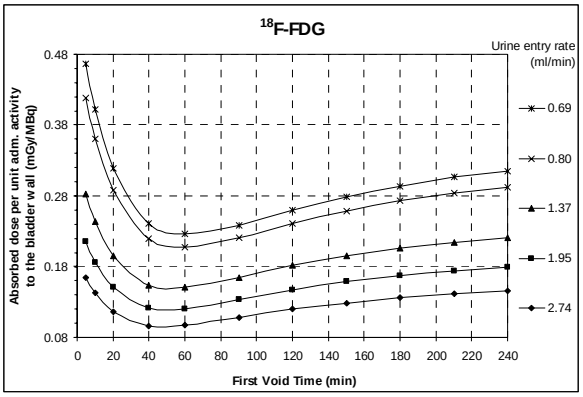

Figure 35. Absorbed dose per unit administered activity to the bladder wall from ^{18}F-FDG. Voiding interval = 3.3hr, V_0=50 ml and V_r=10ml.

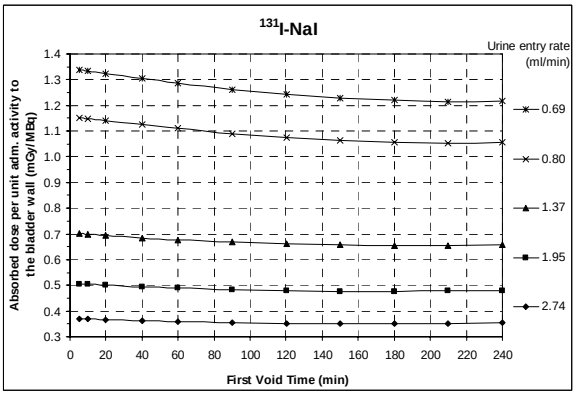

Figure 38. Absorbed dose per unit administered activity to the bladder wall from ^{131}I-NaI. Voiding interval = 3.3hr, V_0=50 ml and V_r=10ml.

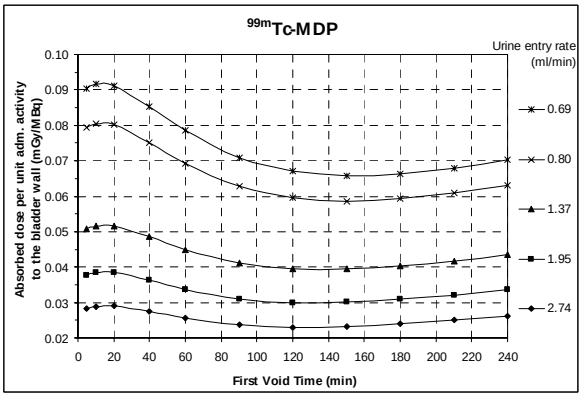

Figure 36. Absorbed dose per unit administered activity to the bladder wall from ^{99m}Tc-MDP. Voiding interval = 3.3hr, V_0=50 ml and V_r=10ml.

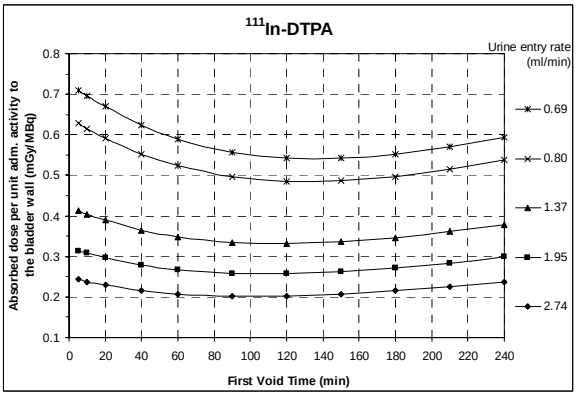

Figure 39. Absorbed dose per unit administered activity to the bladder wall from ^{111}In-DTPA. Voiding interval = 3.3hr, V_0=50 ml and V_r=10ml.

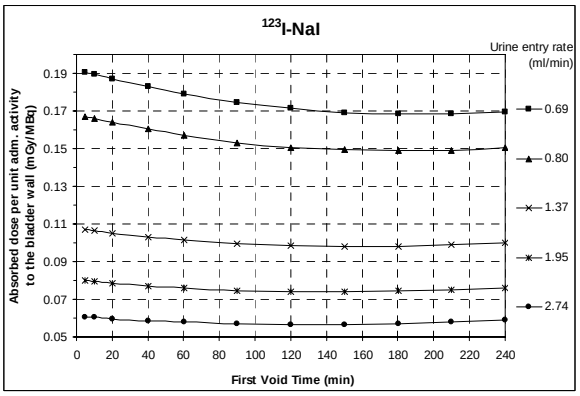

Figure 37. Absorbed dose per unit administered activity to the bladder wall from ^{123}I-NaI. Voiding interval = 3.3hr, V_0=50 ml and V_r=10ml.

Time of administration

Figure 40 to Figure 44 present the relationship between the time of administration and the absorbed dose to the bladder wall surface as function of first void time, obtained in this study. In the calculations the initial bladder content volume are kept at 50ml, the residual bladder content volume at 10 ml, the urine flow rate at 1.37/0.90 ml/min (day/night) and the voiding interval at 3.3 hr.

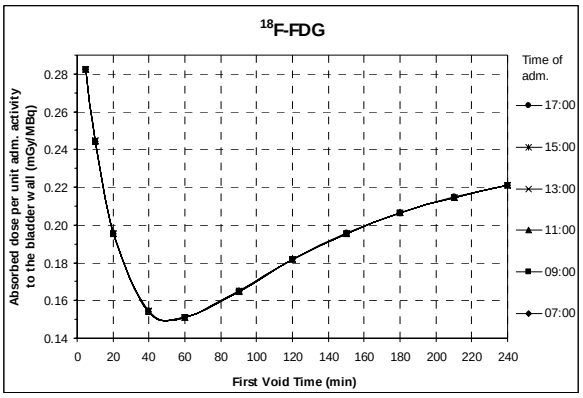

Figure 40. Absorbed dose per unit administered activity to the bladder wall from ^{18}F-FDG. Voiding interval = 3.3hr, V_0=50 ml, V_r=10ml and U(t)=1.37/0.90 ml/min (day/night)

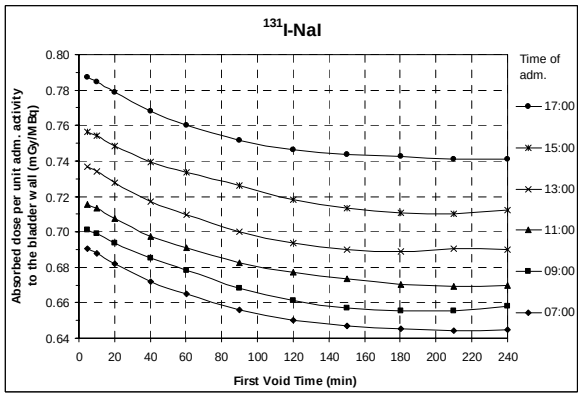

Figure 43. Absorbed dose per unit administered activity to the bladder wall from ^{131}I-NaI. Voiding interval = 3.3hr, V_0=50 ml, V_r=10ml and U(t)=1.37/0.90 ml/min (day/night)

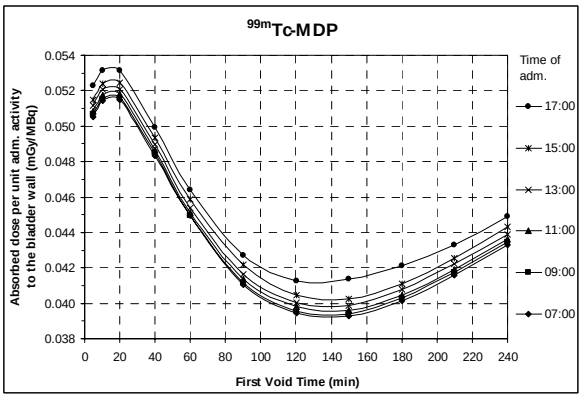

Figure 41. Absorbed dose per unit administered activity to the bladder wall from ^{99m}Tc-MDP. Voiding interval = 3.3hr, V_0=50 ml, V_r=10ml and U(t)=1.37/0.90 ml/min (day/night)

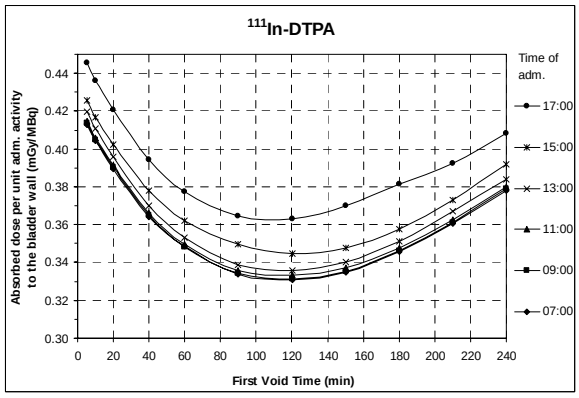

Figure 44. Absorbed dose per unit administered activity to the bladder wall from ^{111}In-DTPA. Voiding interval = 3.3hr, V_0=50 ml, V_r=10ml and U(t)=1.37/0.90 ml/min (day/night)

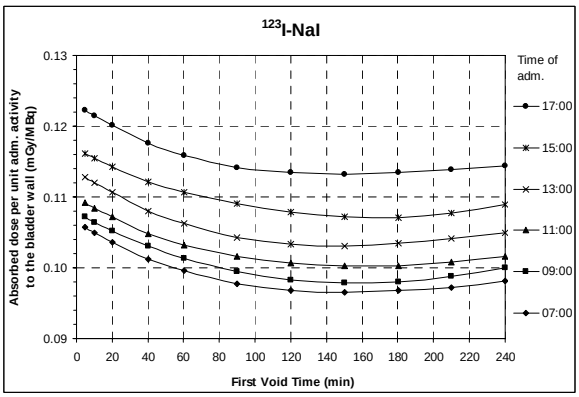

Figure 42. Absorbed dose per unit administered activity to the bladder wall from ^{123}I-NaI. Voiding interval = 3.3hr, V_0=50 ml, V_r=10ml and U(t)=1.37/0.90 ml/min (day/night)

Mean absorbed dose as function of first void time

Figure 45 to Figure 49 present the mean absorbed dose to the bladder wall surface as function of first void time, obtained in this study. The mean absorbed doses are obtained by taking the mean values of all the calculated absorbed doses from Figure 20 to Figure 44 for respectively radiopharmaceutical. One standard deviation is included in the figures.

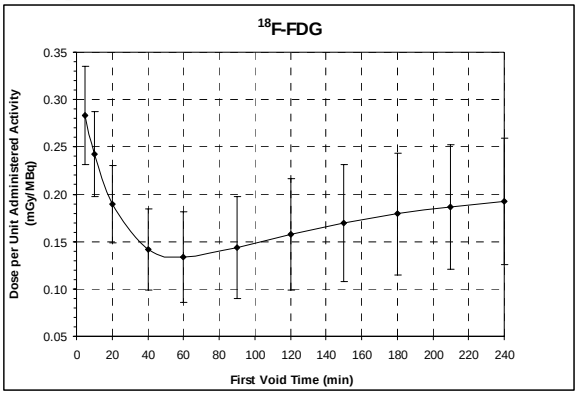

Figure 45. Mean absorbed dose per unit administered activity to the bladder wall from ^{18}F-FDG.

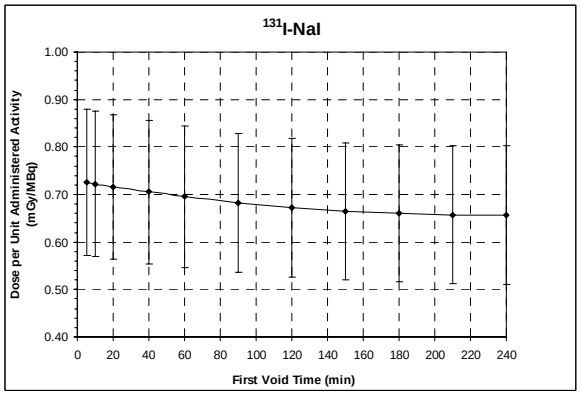

Figure 48. Mean absorbed dose per unit administered activity to the bladder wall from ^{131}I-NaI.

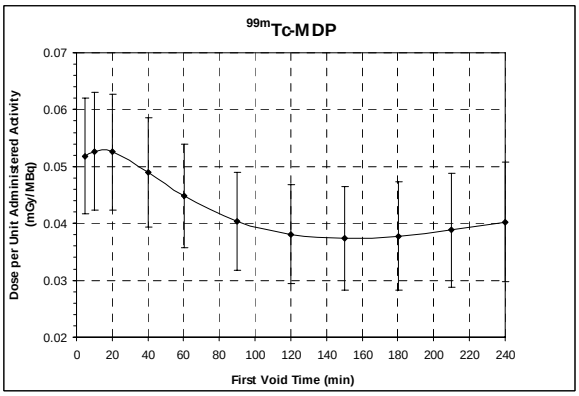

Figure 46. Mean absorbed dose per unit administered activity to the bladder wall from ^{99m}Tc-MDP.

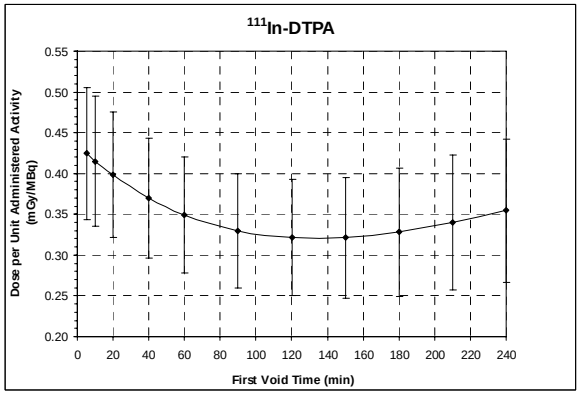

Figure 49. Mean absorbed dose per unit administered activity to the bladder wall from ^{111}In-DTPA.

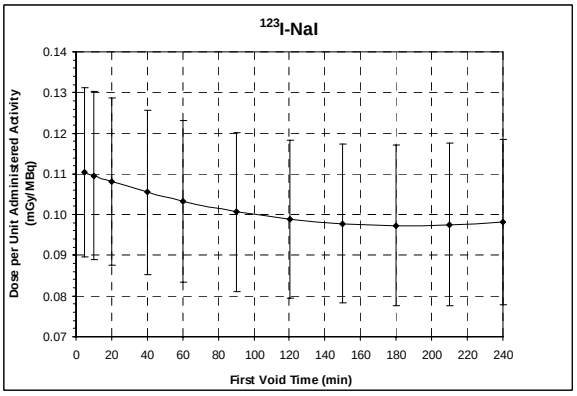

Figure 47. Mean absorbed dose per unit administered activity to the bladder wall from ^{123}I-NaI.