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FACULTEIT INDUSTRIËLE INGENIEURSWETENSCHAPPEN
master in de industriële wetenschappen: nucleaire technologie

Masterproef

Analysis of calibration, accuracy and uncertainty of activity meters in nuclear medicine

Promotor :
Prof. dr. Brigitte RENIERS
Prof. dr. Wouter SCHROEYERS

Promotor :
Prof. dr. KRISTOF BAETE

Michiel Vromans

Scriptie ingediend tot het behalen van de graad van master in de industriële wetenschappen: nucleaire technologie

Gezamenlijke opleiding Universiteit Hasselt en KU Leuven

KU LEUVEN | universiteit hasselt

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Abbreviations

NIST	National Institute of Instruments
SCK	Studiecentrum voor Kernfysica
FANC	Federal Agency for Nuclear Control
SPECT	Single-photon emission computed tomography
PET	Positron emission tomography
FDG	Fluodeoxyglucose
IAEA	International Atomic Energy Agency
HV	High voltage
CF	Calibration factor
NEMA	National Electrical Manufacturers Association
Bq	Becquerel
pA	Picoampere
DPM	Disintegrations per minute
CPM	Counts per minute
ml	Millilitre
g	Gram
FWHM	Full width half maximum

Abstract (Dutch)

In de nucleaire geneeskunde worden radiofarmaca voor de toediening gemeten in een activiteitsmeter. De gebruikte calibratiefactor is aanbevolen door de producent en werd bepaald voor standaard 5 ml NIST ampoules. In de klinische routine worden echter andere geometrieën gebruikt waardoor de meting vaak afwijkend is. Deze afwijkingen zijn vnl. te wijten aan 3 factoren: volume, positie en container type. Het doel van deze thesis is de concrete bepaling van de invloeden en het bepalen van correctiefactoren voor ^{18}F, ^{99m}Tc, ^{123}I en ^{111}In door middel van experimenten. Bijkomend evalueert deze thesis de mogelijkheid tot traceren van de activiteit aan een secundaire standaard.

De invloed van de positie werd bepaald door de isosensitiviteit op te meten. Die van de container door het meten van de activiteitsconcentratie van een stockoplossing in vaak gebruikte recipiënten. De invloed van het volume werd bepaald door een geconcentreerde oplossing te meten en te verdunnen. Als interne referentie wordt een gamma counter geïntroduceerd die gerefereerd werd aan de Fidelis ionisatiekamer van het SCK. De bepaling van de activiteit met de activiteitsmeter is zo traceerbaar naar een secundaire standaard. Om de accuraatheid van de gamma counter te garanderen wordt een kwaliteitscontrole programma aanbevolen.

Het FANC stelt in een besluit dat de meting maximaal 5% afwijkt van de activiteit mag bedragen. De experimenten tonen aan dat er een correctie nodig is voor de positie en het type container.

Abstract (English)

Radiopharmaceuticals used in diagnostics or therapy in the nuclear medicine are measured in activity meters before administration. The settings used are recommended by manufacturers and were determined for standard 5 ml NIST ampoule. In the clinical routine, however, other geometries are used during the measurement causing frequent deviations. These deviations are mainly due to 3 factors: volume, position and recipient. This thesis deals with the concrete determination of these influences and the determination of correction factors for ^{18}F, ^{99m}Tc, ^{123}I and ^{111}In through experiments. Additionally, this thesis evaluates the possibility to trace the measured activity to a secondary standard.

The influence of the position is estimated by measuring the isosensitivity, the influence of the container by measuring the activity concentration of a stock in commonly used recipients and the volume dependence is determined through the dilution of a concentrated solution. As internal reference, the gamma counter is introduced who is traced to the Fidelis ionization chamber of the SCK. The measuring of the activity using the activity meters is therefore traceable to the secondary standard via the gamma counter. To ensure the accuracy of the gamma counter a quality control program is introduced.

The FANC maintain in their standard that the deviation in the measurement of activity is maximum 5%. The experiments show that a correction is needed for position and container type.

Chapter 1

Introduction

Nuclear medicine is the department where radiopharmaceuticals are used to diagnose or treat patients with cancer. The activity that will be administered to the patient is measured in activity meters or radionuclide calibrators before the administration. This master's thesis studies the impact of the geometry on the accuracy of the activity meter. In certain situations, the use of geometries that differ from the geometries used to calibrate the activity meter can have an impact on the apparent activity measured in the activity meter. This is due the interaction of the radiation with the materials. This thesis has the goal to make a quantitative determination of the deviation of the measurement of available isotopes in commonly used recipients due to a change of container, position or volume. The solution to reduce the deviation can be an alteration of the calibration factors or the use of a specific recipient in a certain geometry for that isotope. The experiments executed are the analysis of calibration factors for isotopes in different geometries. This is done for activity meters used in the hospital which are made by 2 manufacturers: Comecer and Capintec. The influence of the recipients is already indicated in several experiments and manufacturers are recommending calibration factors for specific geometries. The need for the determination of corrections comes from 3 reasons: the new regulatory standards, the technological evolution in diagnostics and raising opportunities to use radionuclide therapy. When the apparent activity in the activity meter is e.g. 10% overestimated then the treatment will not reach the desired effect. For this and similar other reasons, the goal of this thesis is the determination of correction factors for the used geometries. To have an internal reference and to make the apparent activity traceable to a secondary standard, the gamma counter is introduced. This master's thesis will evaluate the possibility to use the gamma counter as internal reference and will recommend additional procedures to maintain the reliability of the gamma counter.

1.1 Situation

In the nuclear medicine department at UZ Leuven, radiopharmaceuticals are used in several applications, e.g. SPECT, PET and treatment of cancer. In diagnostic applications, gamma ray emitting isotopes are used as a tracer. The tracer is coupled with a chemical compound to analyse specific physiological processes, for example ^{18}F is combined with glucose analogue to form FDG which is used to visualize glucose uptake. The isotope is administered to the patient before the scan is made. The scan measures the emitted photons and from the position of the photons during the scan a reconstruction can be computed for the concentration of the tracer in

the body. Based on the concentration a diagnosis can be made and with this a treatment plan. In the treatment of cancer the use of nuclear medicine is an upcoming opportunity. To treat a tumour, a high radioactive drug can be administered to the patient. The radiation emitted from the drug will destroy the malignant cells. By choosing the radiopharmaceutical carefully the isotope will affect the desired cells without affecting healthy tissue. In contrary to radiotherapy, the treatment is done in vivo. Therefore, the choice of the isotope and activity is determined by the pathway inside the body and physical half-life of the isotope.
The department uses different activity meters and gamma counters to measure the activity of samples. Because the technological evolution in other medical devices, the possibility to quantify the activity in the patient becomes real. By measuring the delivered activity accurately, the concentration in the patient can be determined more precise which allows the physician to plan the treatment more precisely which results in more effective treatments.

1.2 Problem

The measurement of the activity before the radiopharmaceutical is injected in the patient is done with activity meters. The activity meter consists of an ionization chamber where ionizing radiation generates current, which is measured by the electro meter. The current is converted in to units of activity by applying an appropriate calibration factor. To ensure that the appropriate activity is injected it is important that the calibration factor is accurately determined and optimized so that the exposure of the patients is the minimum required to achieve the intended diagnostic objective [1]. The measurement of activity can be influenced by several factors associated with the radiopharmaceutical or the activity meter. This indicates that the calibration factor for a specific isotope should be different when, for example, the container differs. To measure the stability and accuracy of the activity meter and the calibration factor, several quality control and quality assurance programs are described by the manufacturers. These procedures are executed and confirm the performance of the activity meter. The problem that the hospital is facing is that the commonly used recipients vary from the standard geometries and thus will cause erroneous results independent of the performance of the activity meter. Following to this problem the calibration factors should be checked and potentially be recalculated for the geometries used in the clinical situations.

1.3 Goals

The goal of this paper is to analyse the calibration factors of the activity meters and determine the accuracy, reproducibility and uncertainty of the measurements done with the activity meter in different geometries. The main parts of the paper are the characterisation of the activity meters used in UZ Leuven and the deviation of the response in different geometries. The calibration factors are analysed for the available isotopes, in the most commonly used recipients. A second goal is the formation of a reference chain which is a cross-calibration of the activity meters to the gamma counter. Using this approach, a general procedure for quality control and quality assurance for the gamma counter is recommended. With this procedure the measurement must have a maximum deviation of 5 percent for each isotope, independent from the recipient.

Chapter 2

Activity meter

Nuclear medicine is a branch where radiation physics meet molecular biology. Its practise is in the simplest description: the application of a radioactive isotope to diagnose or treat patients. The basic safety standard presented by IAEA dictates that the dosismetry of patients is performed and documented. The dose to the patient can be related to the activity administered. it is therefore required to measure the activity before administration. [2] The activity meter is the global most commonly encountered detector to assay the activity of solutions that will be administered to patients and will be examined in this thesis. [3] Another commonly used name for the device is the dose or radionuclide calibrator. The name activity meter is more appropriate, hence this master's thesis will use that instead of dose or radionuclide calibrator. The activity meter normally consists of an ionisation chamber, a stabilised high voltage supply (HV supply) and an electro meter with processing electronics. The activity meter is schematically represented in figure 2.1.

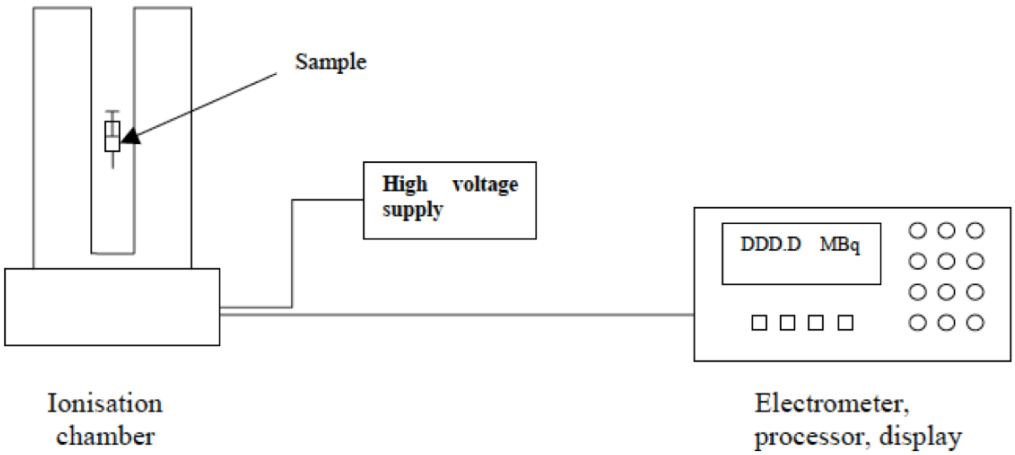


Figure 2.1: schemetic representation of an activity meter [4]

The overall principle is the same for activity meters produced by different manufacturers. Small differences are real and will be mentioned where needed but these will not be examined as it is not the scope of the paper. The experiments in this thesis are executed on the activity meters:

- Capintec CRC-15R
- Capintec CRC-35R

- Capintec CRC-55t
- Veenstra VIC-202

2.1 Ionisation chamber

The ionization chamber is the measuring instrument of the activity meter. The chamber has a well-type configuration to achieve maximum geometric efficiency in combination with practical use . This means that to assay the activity, the radioactive sample is placed into the cavity of the ionization chamber, as can be seen on figure 2.2.

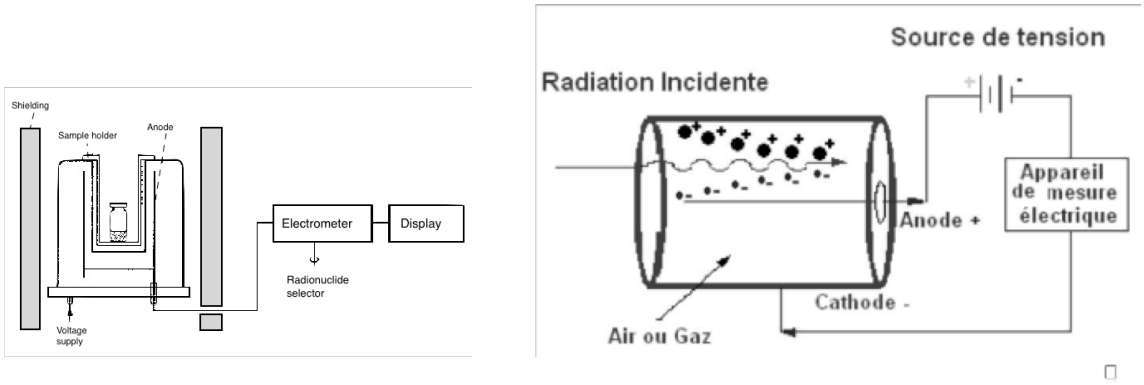


Figure 2.2: The ionisation chamber and the working principle [5]

The chamber is typically filled with pressurized argon to maximize intrinsic detection efficiency. [3] The pressure of the gas in the ion chamber differs for each manufacturer. The Veenstra activity meters have a pressure of 14 bar [6] and the Capintec meters have 12 bar [7]. The principle of measuring activity is shown in figure 2.2. The radiation enters the chamber and ionizes the gas. The ions and electrons are attracted to respectively the cathode and anode because of the voltage supplied by the HV supply. The electrons are collected by the anode causing an electrical current in the circuit.
The measured charge reflects the total ionizations produced by interactions of all photons emitted by the radiopharmaceutical. It takes approximately 15,8 eV to ionize Argon [8], the magnitude is therefore proportional to the energy deposited in the chamber. Isotopes emitting high energy photons cause more ionizations per transformation than isotopes emitting low energy photons. The ionization chamber has no energy discrimination capability, thus to transform the amount of energy to the activity, the emitted particles must be known.

2.2 Electro meter and processing electronics

The current generated in the ionization chamber ranges from 10's of femtoamperes to microamperes. This current is sent to the electrometer and the processing electronics. The electrometer is capable of making accurate measurement over this dynamic range. The processing electronics automatically convert the measured current into an activity. This conversion is different for each isotope and is accomplished through the use of isotope specific calibration factors, which are entered by the user. Via the interface the user can select the isotope

in a list or can set the calibration factor manually. The conversion is relatively straight forward when the energy of the photons is known and the geometry is identical for each assessment. Errors are caused when the geometry changes and when the energy emitted becomes complex, e.g. when beta emitters are measured or when a radio-isotope with low energy photons are emitted and the influence of the X-rays becomes significant. [9] Here is a first difference between the manufacturers, the current in the activity meters designed by Comecer are biased. This means that the current will never be zero. In the Capintec activity meters, the current is not biased and the readout can therefore be zero of even negative when the current is lower than the calibrated value for zero activity. [6]

2.3 Calibration

To measure the activity, the dependence on the energy of the photons must be eliminated which is done with the isotope specific calibration factor (CF). This is the ratio of the electric current induced and the activity of the sample in the chamber. The CF is dependent on the emitted particles and their energy of the isotope and the interaction with the container. Manufacturers have determined CFs for isotopes used in clinical routines. Commonly, the method used for determining the CF is using a fit of ionization chamber response versus the calibration factor created by measuring 2 isotopes, one emitting high energy (^{60}Co) and one emitting low energy radiation (^{57}Co).
The CF's for isotopes that are not common are interpolated values and not confirmed by experiment. Next to the interpolation the determination is only done for the standard geometry, a standard NIST 5 ml ampoule with 5 ml of solution. The use of different containers result in a difference in attenuation, scatter and position. Using the recommended CFs can cause possible erroneous determination of the activity. Therefore, it is recommended to determine the calibration factor experimentally for the used geometry. [10]
Zimmerman et al. (1999) describe 2 methods to determine the calibration factor for isotopes in an activity meter: the dialling-in method and the calibration curve method. The dialling-in method is used when the activity of the source is well-known or when the activity can be accurately determined with liquid scintillation counting. The correct calibration factor can then be found by turning the dial with the source in the chamber until the correct activity is displayed. When it is undesirable or infeasible to determine the true activity before the dose calibration measurement. It is possible to take the dose calibrator data prior to the measurement. The reason for this may be: very high specific activity requiring multiple dilutions, extremely short half-life and large number of samples. In this case, the calibration curve method must be used. First, a calibration curve is developed of apparent activity versus calibration factor for a source gravimetrically related to the one that will be measured. The protocol involves varying the dial setting with the radioactive source of interest in place and recording the readout activity value and time of measurement. After decay-correcting to the reference time, one can form the ratio:

$$R = \frac{V_S/m_S}{A_{stand}/m_{stand}}$$

where V_S and A_{stand} are the activity readout and the calibrated activity and m_S and m_{stand} are the sample masses for the dose calibrator source and the standardized samples. The correct CF for the isotope in that particular counting geometry can then be determined from a fit of the

resulting curve of R versus CF in the form:

$$R^{-1} = a.(\text{CF}) + b$$

The experimental calibration factor for the source can be determined by solving this equation for R =1. [11] The determination of calibration factors is also described in the manuals of the activity meters. For each manufacturing the determination is done differently. The determination of a calibration factor in the Comecer activity meter that is not in the isotope list is done with a calibrated source and the formula given in the manual:

$$1009 - \frac{K_{sc}.V_s}{V_{Tc}}.773 = \text{CF}$$

Where V_s is the actual activity of the source, V_{Tc} is the readout with the "^{99m}Tc" setting (Calibration factor: 236), K_{sc} is the scaling and CF is the indicated calibration factor. When the indicated calibration factor is greater than 999 or negative, a suitable scale factor should be chosen. The actual factor should be determined with the calibration source. [6]
For the Capintec devices the calibration factors are calculated in a different way. The calculation is based on the response and sensitivity of the chamber to the radioisotope for which the setting number must be calculated. The manual of the Capintec activity meter contains a sensitivity curve, this curve is shown in fig. 2.3. The graph depicts the sensitivity of the ionization chamber as a function of photon energy up to 1.9 MeV. Above an energy of 200 keV the ionization are mainly caused by Compton scattering photons. In the low-energy region of the sensitivity curve is a peak due to the increase in photo-electric effect and absorption by materials between the radioactive substance and the chamber. The relation of the detector response and the sensitivity is the following:

$$R_i = I_i.S_i$$

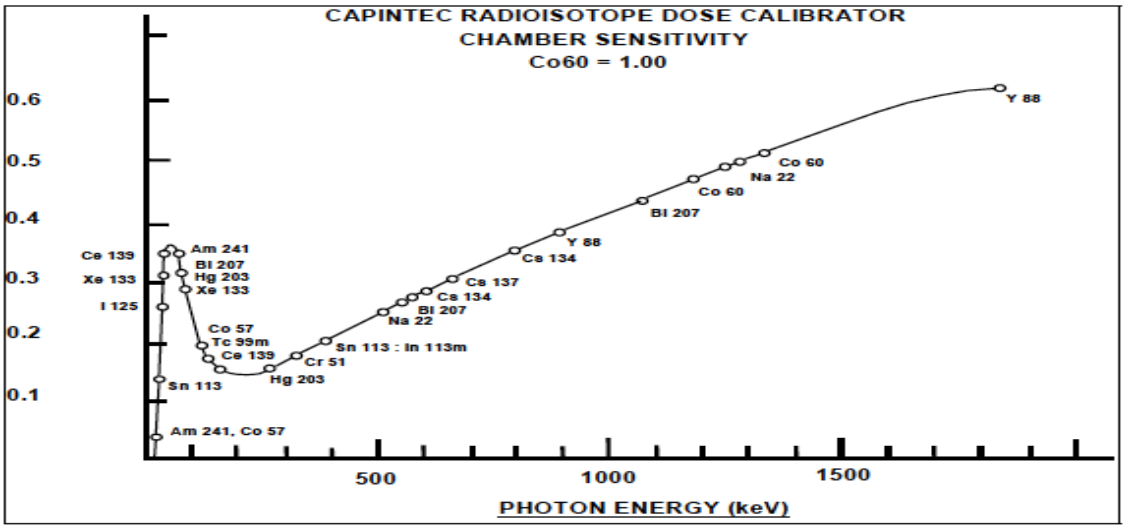


Figure 2.3: Sensitivity curve of Capintec CRC-55t [7]

Where R_i is the detector response to photons with energy E_i and I_i and S_i are respectively the intensity and the sensitivity of the photon with an energy E_i. The sensitivity for a photon of energy E_i is defined as:

$$S_i = \frac{\text{response to } 3,7 * 10^{10} \text{ photons of } E_i}{\text{response to } 3,7 * 10^{10} \text{ photons of } ^{60}\text{Co}}$$

When the sensitivity is not available for the radioisotope, the response is expressed relative to that of a standard reference material (SRM), e.g. ^{60}Co, as shown in the following formula:

$$R_A = \frac{\frac{V_S}{A_S}}{\frac{V_{^{60}\mathrm{Co}}}{A_{^{60}\mathrm{Co}}}}$$

V_S and $V_{^{60}\mathrm{Co}}$ are the apparent activity measured by the activity meter and A_S and $A_{^{60}\mathrm{Co}}$ are the true activity of the sample and the ^{60}Co reference source. The relationship between the response of the detector and the gain setting is given by:

$$G_A = \frac{1}{R_A}$$

The calibration setting number is linearly related to the chamber response. The calibration for all the calibrators is done with certified ^{60}Co and ^{57}Co standard source. The calibration numbers for ^{60}Co and ^{57}Co are respectively 990 and 112. The calibration setting can be calculated with these values, using:

$$N_A = (R_A - (1 - \frac{R_{^{60}\mathrm{Co}} - R_{^{57}\mathrm{Co}}}{N_{^{60}\mathrm{Co}} - N_{^{57}\mathrm{Co}}})).\frac{N_{^{60}\mathrm{Co}} - N_{^{57}\mathrm{Co}}}{R_{^{60}\mathrm{Co}} - R_{^{57}\mathrm{Co}}}$$

Where N_A is the calibration factor. The values for ^{60}Co and ^{57}Co are known: $N_{^{60}\mathrm{Co}} = 990$, $N_{^{57}\mathrm{Co}} = 112$, $R_{^{60}\mathrm{Co}} = 1{,}000$, $R_{^{57}\mathrm{Co}} = 0{,}189$. The value of R_A is read from the sensitivity curve or measured using the SRM. The formula can then be simplified to:

$$N_A = 1076.(R_A - 0,080)$$

According to the manual, the agreement between the calculated and the observed responses is always within 3%, with the remark that sample configuration influences the accuracy of the chamber response calculation for a radioisotope. [7] This is contradicted in a study executed by Cessna et al. (2008) The determination of the isotope calibration factor of ^{18}F for a Capintec activity meter shows an error of 13 percent when using the factor recommended by the manufacturer. This error is seen in both geometries, the vial and the syringe. [12]. In another article, Zimmerman and Cessna [11] investigated the difference between an experimental calibration factor and the calibration factors recommended by Capintec. They found that most of the recommended settings overestimated the activity. They also observed a variation in the calibration factor due to differences in the container. [11] It can be said that the formula described in the manual is thus a simplification that neglects different influences which causes major errors. It's the scope of this thesis to estimate these errors and recommend correction factors.

2.4 Regulatory standards

In this section, the legislation applicated by the FANC concerning the activity meter is discussed together with the recommendations from other institutes as NEMA and IAEA. The directive of the FANC is implemented to assure the quality of activity meters within the context of radioprotection of the patient and the applicator. The directive gives criteria of acceptability in several tests for compliance. The criteria that are concerned in this thesis are given in art. 9 to 12. The criteria demand that the compliance for constancy is tested daily by measuring reference

sources, the deviation of the measured activity must belower than 5 %, plus the tolerance of the source the maximum deviation is lower than 10%. Additionally, it is also required to measure the source in the setting of the most used radio-isotope. The ratio between the activity measured with the most used calibration factor (^{99m}Tc) and the activity in the setting of the source is within a deviation of lower than 5%. The verification of the energy response is required to be executed at least once a month. The source is measured with the calibration factor of all the radio-isotopes used. The deviation of the ratio measured activity using a calibration factor over the measured activity using the calibration factor of the isotope is a maximum of 5% between the measured ratio and the initial ratio. The directive requires that the reproducibility is tested and that the standard deviation is at most 2%. [13] The AAPM report no. 181 recommend the same maximum deviation of 5% for the constancy and the accuracy but recommend that when the activity meter is used as secondary standard or reference activity meter that the deviation is at most 2%. For the reproducibility, the measurements are recommended to be within 1% of the average measured activity. For reference or secondary standard activity meters this deviation is 0.5%. [14] The IAEA recommends the same values as the directive from the FANC. [4]

2.5 Sources of error

As already indicated, the apparent activity measured in the activity meter is influenced by several sources of errors, factors that give possible deviating results. This thesis does not investigate stochastic errors because the number of activity meters tested does not give a representative view. The factors investigated are systematic errors who can be minimised by following good practise. The sources of errors are listed and explained in this section. The methods to examine the magnitude of the influence are explained in the following chapters.

2.5.1 Electronics

The electro meter is the part of the activity meter that converts the current output (pA) of the ionization chamber into an indication of the activity (MBq) via the application of a calibration factor (pA/MBq). One source of uncertainty is the gain of the electro meter, which will change with time, resulting from normal electrical drift or ageing effects of electrical components. By executing the daily test the gain is checked and can be adjusted using the reference sources. The current induced in the chamber and measured by the electro meter is expected to be in a range from 10's of femto-amperes up to micro-amperes, a dynamic range of 10^8. It isn't unusual to expect deviation from linearity. To accommodate the range, some activity meters incorporate different linearity characteristics in each range, which may have separate gain adjustments.

2.5.2 Activity

The current output of the chamber depends on the number of positive ions which are collected on the electrode. As the activity of the source increases, the production rate of the ion pairs within the sensitive volume of the gas increases and with that probability of recombination of the positive ions with electrons. The point will be reached where, as the ion production rate increases, the rate of recombination becomes significant and a fraction of the expected current is lost. As shown in figure 2.4 the ratio of the measured activity to the true activity drops significantly when the activity of the sample reaches 10 GBq.

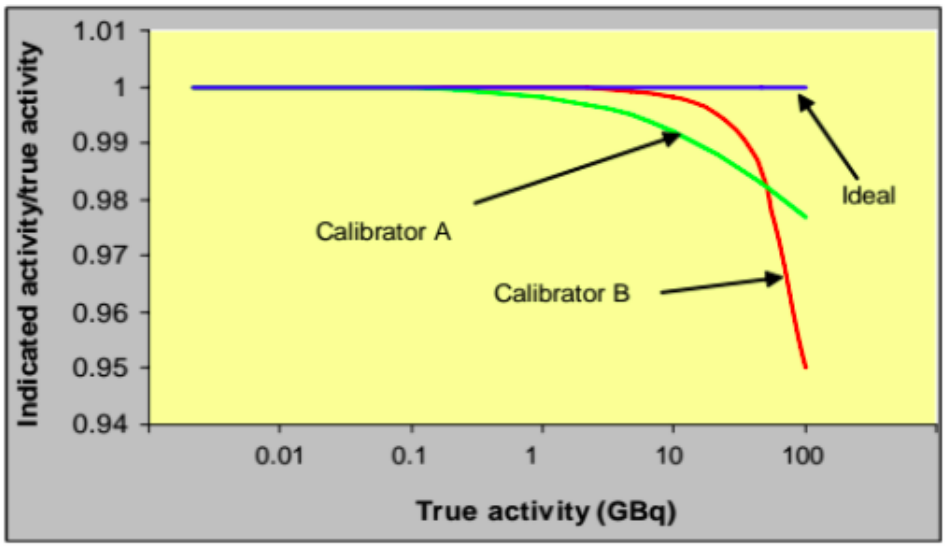


Figure 2.4: Effects of recombination [5]

When measuring activity, the background must always be considered. The fractional influence of the background is very little when measuring high activity but becomes significant when the activity of the sample is in the same order of magnitude as the background. The activity meters have a function to compensate the background. Whilst this simplifies the user's task, the feature can give erroneous results when the background level changes between measurements.

2.5.3 Ionisation chamber

The effect of local environment radiation can be reduced when shielding is used. However, this can induce a new source of error because of the backscatter effect. This effect will be most significant when isotopes are used that emit radiation with energy just above the K X-ray energy of the shielding, e.g. 80 keV for lead. The chamber wall between the sample and the chamber also influences the apparent activity. The chamber wall typically has a protective aluminum layer that cuts off all photons with an energy below 13 keV and attenuates other low energy photons [5]. For a secondary standard ionization chamber as the Fidelis, this protective aluminium layer is thinner resulting in a better sensitivity but more influence from background and geometry.
Another property from the ionization chamber affecting directly the measurement is the spatial sensitivity. The source will emit radiation in every direction. Hence, when the source is held at the opening like situation A in figure 2 the efficiency is approximately 50 percent. When held deeper in the ionization chamber the efficiency increases to 90 % in situation C. [3]

2.5.4 Radiopharmaceutical

The radiopharmaceutical will always be held in a container. This is obvious because liquid sources are used. As the shielding of the activity meter influences the measurement, the container has an even bigger influence. J. M. Calhoun et al. found that the response when ^{57}Co and ^{99m}Tc were measured in vials with plastic walls was higher, which is caused by the lower attenuation of plastic compared to glass. The data in the experiments demonstrated that as much as nine percent difference is possible in certain situations. The conclusion was that no matter which

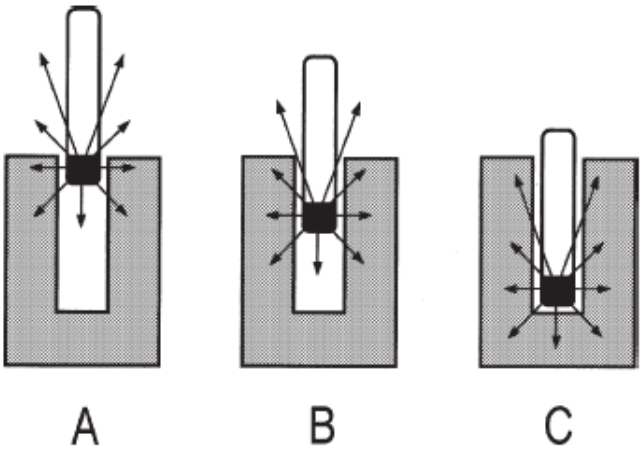


Figure 2.5: A point sourc placed in the well type ionisation chamber. [3]

calibrator was used, a calibration factor for each geometry should be determined to ensure the greatest accuracy. [15]
Every material has the property to attenuate radiation, the attenuation of photons through a medium is defined by the law of Lambert. Given by formula:

$$I_d = I_0.e^{-\mu.d}$$

Where I_d is the intensity of the photons outside the container with thickness d, I_0 the intensity of the photons inside the container. μ is the attenuation factor specific for the material. [16] The attenuation factor is dependent on the material and the energy of the photons passing through. In the nuclear medicine the measurement of activity is done in vials and syringes. These have a different composition of materials, which means that the attenuation factor differs and with that the intensity of the photons that pass through. The other factor that influences the attenuation is the thickness of the container. The thickness varies for example when a bigger syringe is used. The changes can be rather small but can still influence the apparent activity. The container material has also different properties concerning scatter. When photons pass through a material scatter is a commonly occurring phenomena to lose energy. When measuring β-emitting isotopes, the electrons will create bremsstrahlung which cause possible raise in the apparent activity. E.g. when Y-90 is placed on the other side of a lead plate or a plastic plate the radiation exposure behind a lead plate is bigger than the dose behind the plastic one. Another source of error connected to the radiopharmaceutical is the volume. When the same activity is inserted into 2 containers of identical shape but with different volumes, the self-absorption of the solution and the positioning in the ionization chamber is different, which result in a different measured activity.

Chapter 3

Gamma counter

Because of the need to assure the accuracy of the measurement and the need to trace the activity to a secondary standard, the gamma counter present in UZ Leuven is introduced in this thesis. The main reason is the completion of a chain of traceability to the primary standard via the secondary standard of the SCK, the Fidelis activity meter. This is done by referring the response of the gamma counter to the response of the Fidelis ionisation chamber. The Fidelis instrument is specified to be used as a secondary standard reference activity meter and can be used to check the accuracy of other activity meters.

For clinical routines, however, the Fidelis is less useful. The cost for the instrument and the maintenance, interface and the shielding causes the Fidelis to be less practical. The shielding around the ionisation chamber is lower to reduce the influence of backscatter from the wall of the chamber but the measurement is highly affected with background radiation from the environment. This is not a problem in a laboratory but in the clinical environment the background is elevated because more radioactive samples are present, resulting in unwanted deviations on the response.

The gamma counter available for the completion of the reference chain is the Perkin Elmer 1480 WIZARD 3", shown in figure 3.1. The gamma counter has a detector that consists of thallium activated, sodium iodide crystal of the end-well design. The crystal height is 80 mm (3.15") and diameter is 75 mm (3"), the detector measures almost in a 4 π direction because of the end-well design. Measuring samples in the gamma counter must be done in the containers specified for the gamma counter which eliminates any geometric influences and ensures an optimal counting efficiency. [17]

The output of the gamma counter is a file with information concerning the measurement and the sample, an example is shown in figure 3.2. The first line is the date and time of the measurement.The next group of lines state the protocol of the measurement, the limits for the duration and counts, the isotope setting and the date when the protocol was normalized. The following lines are the measured values. For each sample the position (POS) in the rack is given, the rack number (RACK), the index of the sample (BATCH) and the measured time (TIME). The next column is the amount of counts measured (COUNTS). This value is transformed to counts per minute (CPM) by decay correcting to the time in the first line and correcting for loss of counts due to the dead time (DT FACTOR), ERROR% is the variance on the counts, the column CLOCK gives the exact time of the start of the measurement.

The gamma counter is already in use in UZ Leuven by the radiopharmacy unit, where the gamma counter is mainly used for relative measurements. In the nuclear medicine department,

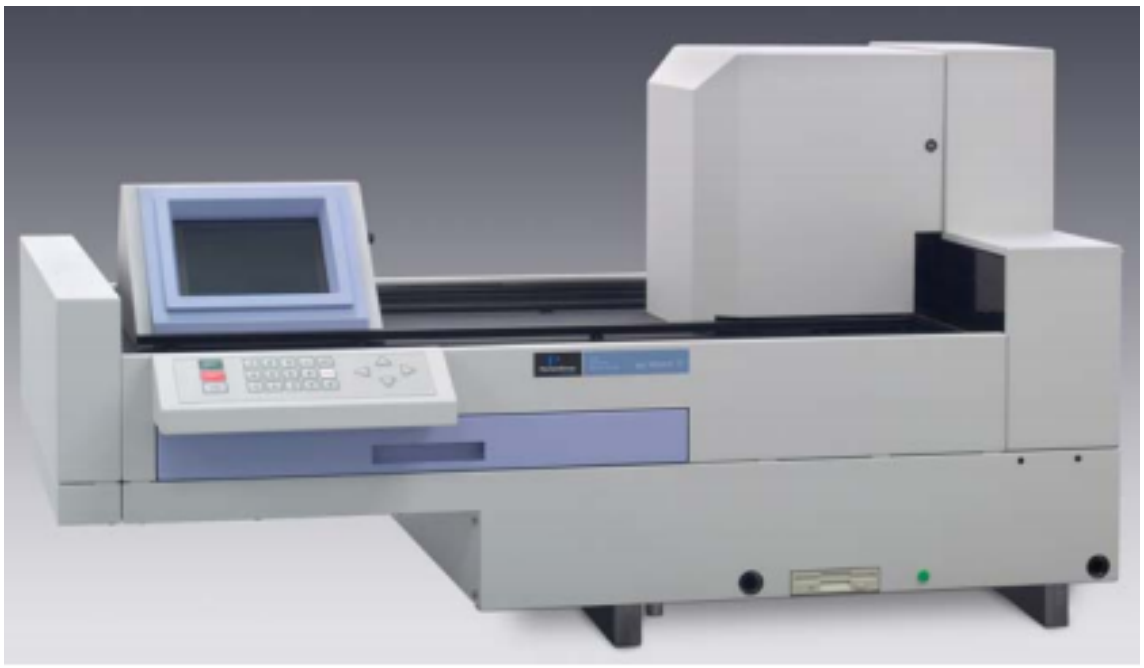


Figure 3.1: Perkin Elmer 1480 Wizard 3", the gamma counter used in this thesis [17]

it is desired to measure the exact activity. The gamma counter response must therefore be converted to the true activity of the sample. Using the counts per minute of the measurement, the activity in disintegrations per minute (DPM) can be determined using the efficiency (E):

$$DPM = CPM/E$$

The efficiency of the gamma counter for most isotopes is listed in the manual. In this dissertation, the efficiency of the gamma counter is referred to the measurement in the Fidelis, which is later explained.
When the response of the gamma counter is related to the Fidelis activity meter, the activity meter can be calibrated against the gamma counter. This results in a cross-calibration between the ionisation chamber and the gamma counter where the gamma counter is referred to the secondary standard ionisation chamber and the ionisation chambers in clinical routine are referred to the gamma counter.
The use as internal reference comes with the need to have a quality assurance (QA) program. The QA program is necessary to evaluate the performance of the gamma counter over time and to prove the conformance with the performance requirements. When the QA program is correctly used, the medical physicist can intervene when the performance decreases. Such a decrease is mainly due to the ageing of the gamma counter. Because of the ageing, the aluminium case can leak and the moisture will then slowly damage the hygroscopic crystal. This is a slow process and will cause the spectrum to shift. The QA program will indicate such a decrease and inform the medical physicist to start an intervention. This thesis will recommend a QA/QC program.

3.1 QA/QC program

Because the gamma counter 1480 WIZARD 3" will be used as an internal reference for the measured activity and the accuracy of the activity meters will be measured against the gamma counter, it is necessary that the gamma counter shows no lack in quality of its performance.

ASSAY 01-Dec-2016 10:43:30

Protocol id 28 F18B-1MI
Time limit 60
Count limit 99999999
Isotope F-18b
Protocol date 21-Sep-2015 16:18:11
Run id. 61

POS	RACK	BATCH	TIME	COUNTS	CPM	ERROR %	DT FACTOR	CLOCK
1	1	1	60	3716	3713.7	1.65	1.00090	10:43:32.1
2	1	2	60	25	6.8	76.96	1.00002	10:44:44.3
3	1	3	60	3490	3539.8	1.70	1.00088	10:45:55.7
4	1	4	60	23	4.9	104.19	1.00002	10:47:07.8
5	1	5	60	3373	3472.9	1.73	1.00085	10:48:19.8
11	2	6	60	14	-4.3	95.97	1.00002	10:49:49.2
12	2	7	60	15	-3.3	130.44	1.00002	10:51:01.1
13	2	8	60	22	4.1	126.55	1.00002	10:52:13.3
14	2	9	60	24	6.3	86.76	1.00002	10:53:25.4
15	2	10	60	18	-0.2	3095.57	1.00002	10:54:37.4

END OF ASSAY

Figure 3.2: example of the output file from the gamma counter

The assurance that the measurement of the gamma counter is accurate is given by executing a quality assurance and quality control program. The quality control consists of tests that indicate any possible deviation or miscalibrations. Like the QC of other devices in the clinical routine, the QC program of the gamma counter must be executed during the acceptance procedure and repeated in periodicity, given in this chapter.

3.1.1 Recommended QC program

Frequency of the tests [14]

This section discusses the periods in which the tests must be repeated to guarantee that the results are within the required accuracy. The tests that should be executed annually are the resolution, linearity and the verification of the settings of each isotope. The variables tested with these are dependant on the drift of the crystal and the accurate input of the values. Tests executed daily and monthly can indicate these drifts which is a sign to execute these tests again to determine if the measurements are erroneous. Without indication of drifts the tests should be executed annually and after each repair. The tests for constancy and reproducibility should be executed each month. The execution of all the above tests are done by a medical physicist.
The daily quality control exists off the background normalisation and the execution of a mechanical control. It is recommended to execute this control before the gamma counter is used. The execution can be done by any authorised personnel. When no damage is seen at first sight, a more detailed look must be done at the connectors, the buttons and the screen. When looking at the connectors, one must check if the connectors are correctly plugged in. After the verification that there is no damage, the gamma counter can be used. When starting up, the date and time is verified to be synchronised with the internal clock. The next test is the background normalisation. The execution is as follows:

1. remove all activity from the gamma counter and in the area around it

2. make a rack with the label "background norm"

3. place the rack and a rack with a stop label on the gamma counter and start an acquisition

4. remove the racks from the gamma counter

5. copy the results from the output file into the log file

Responsibilities

A physicist should take the responsibility for the calibration and obtaining machine maintenance of the gamma counter. The physicist must be aware of every work done on the device, whether it is by a representative of the manufacturer or authorized personnel of the hospital and what the effect is on the output of the device. The procedures for the QA of the device should be documented in detail and together with all the data of the quality assurance archived in logbooks. For the assurance of the performance, the QA results should be summarized and reviewed on a regular basis by the qualified physicist. [18]

3.1.2 Background normalisation

The measurement of the background has 2 goals: first to measure any contamination in the gamma counter and to determine the reaction of the device in absence of any radioactivity. To execute the background normalisation, all possible sources should be removed from the area. Then the label "Background Norm" is applied to a rack and the rack is placed on the gamma counter. An acquisition is started where the background is measured in the normal energy window (15 - 1000 keV) and in the extended energy window (15 - 2000 keV).
The background normalisation should be done daily and the results must be added to the logbooks (QCGammaCounter.xlsx). In these logbooks a trend is seen which should be constant over time. A higher value can indicate a contamination of the device or a source in the environment which causes a raise in the response. Measuring samples in the gamma counter when the background is elevated causes an overestimation of the activity which can cause e.g. a miscalibration of the activity meters. When the results are deviating from the constant, the area should be checked again for possible radioactive sources, which must be removed and the background normalisation should be executed again. When there are no sources in the area, the higher value indicates a contamination of de gamma counter and the decontamination or source removal procedure must be started.

3.1.3 Mechanical evaluation

The mechanical evaluation is a visual verification of the device. The first examination is a verification of the condition of the connectors and the correct connections. Afterwards the device is checked for any damage on the buttons or the screen. When the visual verification is successful, the device can be started.
The next step is the confirmation of the date and time on the gamma counter. The clock should be synchronised with the internal reference clock in the UZ Leuven. Any deviation can cause an erroneous correction for decay when the gamma counter is used together with other devices. The deviation becomes very important when isotopes are used with a short lifetime. Important

here is the change from summer- to wintertime, this is not changed automatically and the user should adjust the time.
The recommended period for a mechanical evaluation is daily and can be executed by any authorised personnel. When damage is noticed or when the deviation of the time exceeds 1 minute, the medical physicist should be warned.

3.1.4 Sensitivity check

The review of the sensitivity evaluates the constancy and precision of the gamma counter. The aim of this test is to control the efficiency of detection. This is done with measuring calibrated sources in the stated settings. [19] The measured values are filed in the logbook and a trend should be seen in time which corresponds to the decay of the source. A different value can indicate a loss in detection efficiency. this means that the crystal is possibly damaged and the manufacturer should be contacted.
The test should be executed monthly and the results are filed in the logbook[1]. The sources used during the execution are calibrated sources with long-lived radionuclides, in this case ^{129}I and ^{68}Ge. The protocol used for the measurement of ^{68}Ge is 'Ge-68B', the protocol for the measurement of ^{129}I is protocol 'I-129'. The ^{68}Ge sources must frequently be replaced. The sources are replaced one by one so that the reliability of this test can be guaranteed. In the logbook, the measurement(counts, CPM, error and DT-factor) is filed together with the date and time of the measurement, UZ-code assigned to the reference source.

3.1.5 Reproducibility

The reproducibility gives a measure of the counting efficiency and the variation that can exist when 2 identical sources are measured. The aim of the verification of reproducibility is the confirmation that repetitive measurements give the same result, when the executor manipulates the sources or not. The test is done by measuring a reference sources 10 times in the same circumstances. The reference source should have an activity exceeding 10000 CPM and the loss of activity due to decay during the measurement is lower than 10%. The counting efficiency is checked by a chi-square test. Where the value of the chi-square is calculated with:

$$\chi^2 = \frac{\sum_{i-1}^{n}(N_i - \bar{(}N))^2}{\bar{N}}$$

The values for n, N_i and $\bar{N}$ are respectively the number of measurement (10), the measured counts and the mean over the measurements. The recommended period for repetition is monthly and is executed by the medical physicist. The chi-square test is successful when the value is between 3.3 and 16.9 when 10 measurements are executed. [19]

3.1.6 Settings

The settings are set during the installation. It is recommended to annually check the settings for the most common isotopes used in clinical routine. During this check, the window for each isotope is checked if this is correctly set around the peak and a normalisation is executed. When research and literature recommends different values than inserted during the installation the values can be changed during this test. It is recommended to save the values inserted in the

[1] QCGammaCounter.xlsx

device in the logbook, in case the settings are removed or the device needs a reset. The check on the settings is a verification on the calibration, which is related to the PM tube. When the calibration drift becomes excessive, the PMT gain should be adjusted [17]. The gamma counter has the setting to set a dynamic range around the peak. During the normalisation, the peak energy is determined and the region of interest is set around this peak. This setting is useful when the peak is shifted caused by the ageing of the crystal. However, when a sample that is contaminated, e.g. ^{123}I with a ^{125}I contaminant, the region of interest is shifted and the result can be erroneous. It is therefore recommended to determine a static region of interest based on the spectrum extracted from the gamma counter and analysed on the PC.

3.1.7 Linearity

The gamma counter possesses a dead time, this is the period that the device is insensitive to pulses. This causes a loss of detection above a certain amount of CPM. The software of the gamma counter corrects automatically for the dead time, which is accurate up to a certain level. The test for linearity evaluates the range where the gamma counter can measure accurately and the capability of the software to correct for dead time errors.
The gamma counter has, according to the manual, a maximum error of 1% if the number of counts is less than 2.10^6 DPM. [17] With the linearity check, the aim is to check how the gamma counter reacts when a source is measured in the interval between 0 to 2.10^6 DPM. It is recommended to determine how the gamma counter reacts to a source with even more activity. Hence, a sample with more activity must be measured. This gives a view of the behaviour of the gamma counter above the limits stated in the manual. Together with the high values, very low values are measured at the end of the test. This visualises the minimal activity that can be measured reliable. Additional the influence of the background radiation is seen in the low activity region.
The gamma counter has the setting to measure high activity samples. In this setting samples with 30.10^6 DPM can be measured accurately. The test for linearity can be extended to determine the accuracy in this setting by measuring a sample with an activity above 30.10^6 DPM with the label attached for high activity samples. Because the response to different energies can deviate, it is recommended to execute the linearity for more than one isotope.

3.1.8 Resolution

Because of the ageing of the gamma counter, it can occur that the humidity in the casing causes a fading of the crystal. The crystal is a hygroscopic NaI crystal and will therefore attract water molecules. This will cause a decrease of counting efficiency. This decrease of counting efficiency and the fading can be evaluated with the resolution. The resolution is determined using the full-width half medium (FWHM) and the energy of the peak. To determine the resolution the spectrum is extracted from the gamma counter. The extraction of the spectrum can be done with the following steps:

1. SYSTEM: operation mode: store assay spectra YES
2. FILES: Spectra:
    - Operation: send to disk

- Protocol: choose the spectra you want
- Format: EXCEL

3. Do operation

4. readout of the floppy disk via PC

The file can be transformed to an excel file where the spectrum is drawn in a graph and analyzed. The resolution should be calculated annually. [19] The resolution is also strongly affected when the crystal is partially cracked due to the internal tension. This will not necessary result in a decrease of counting efficiency. By evaluation the resolution, a possible defect can thus be detected even though the counting efficiency shows no decrease.

3.1.9 Volume Dependence

The manual of Perkin Elmer states that a volume variance between 0 and 20 ml causes a maximum deviation of 1% measuring the isotope ^{59}Fe [17]. This is not evaluated in this thesis. ^{59}Fe is an isotope that emits mainly two photons with energy 1099,245 keV and 1291,59 keV. These are relative high energy photon, the influence of a volume variance is therefore very small. It is recommended to determine the influence of volume variation with isotopes emitting lower energy photons, e.g. ^{18}F, ^{99m}Tc, ^{123}I.

3.2 Reference chain

The gamma counter is used to trace the response of the activity meter to a secondary standard and to have a reference value for the experiments. The opportunity was given to relate the gamma counter measurements to the Fidelis in the SCK because of a series of experiments at the department in UZ Leuven executed by Carbutti et al. [20] During the series of experiments, activity in several recipients were measured. The samples were kept aside and when decayed enough to be measured in the gamma counter the activity concentration was determined in CPM/g. It is assumed that the density of the solutions are 1 g/ml, the results are therefore in CPM/ml. This value and the result from Carbutti et al. [20] give the conversion factor needed to relate the result of the gamma counter to the actual activity. The value from the gamma counter is then used as reference for the activity meters in clinical routine.
The values were made available for the isotopes ^{18}F and ^{99m}Tc. The activity measured by the Fidelis was transformed to the concentration as well as the measured CPM in the gamma counter. After correcting for decay was the factor MBq/CPM determined. The Fidelis is calibrated for the Schott vials. Hence 2 factors are given, the factor resulting from the measurement in the Schott vial and the factor considered as overall factor of the recipients. The factors for ^{18}F are 0,0500 Bq/CPM in a Schott vial and 0,0406 Bq/CPM as the overall factor. The factors for ^{99m}Tc are 0,0328 Bq/CPM and 0,0310 Bq/CPM for the Schott vial and the overall factor respectively. The conversion for ^{123}I was not computed due to the ^{125}I contaminant which causes the gamma counter to normalize around the wrong peak. For ^{111}In the measurements of the Fidelis were unavailable. Hence for ^{123}I and ^{111}In the conversion is based on the manual which provides an efficiency factor that can be used for the conversion. This is for ^{123}I: 0,0208 Bq/CPM and For ^{111}In: 0,0201 Bq/CPM.

As part of the establishment of the traceability chain, it is necessary to add the verification of the conversion factors to the quality assurance program. The verification should be executed for each isotope that is measured during clinical routines. Because the gamma counter measures in a range between 0 and 2 million CPM and the Fidelis in a range 0.001 MBq up to 75 GBq. [21] The method to verify the conversion factor is; measuring samples in the Fidelis activity meter and afterwards, when enough decayed in the gamma counter. After the decay correction, the conversion factor can be evaluated, as is done in this thesis. An other method involves diluting the sample, which introduces an extra undesired uncertainty.

Chapter 4

Methods

The sources of errors that are discussed in chapter 2 will be evaluated in this thesis, more precise the influences introduced by the followed routine are evaluated. During the routine, the daily test is already executed and any defect in the electro meter is checked and it is approved to measure activity. The influences that mainly cause the deviation of the response are the position in the chamber, the volume of the sample and the choice of the recipient. For this thesis, the goal is to determine the deviation in the apparent activity against the nominal activity. The deviation is defined as:

$$\text{deviation} = \frac{A_{App} - A_{Nom}}{A_{Nom}}$$

The nominal activity $[A_{Nom}]$ is the activity given by the manufacturer or the one obtained by measurement with the gamma counter. The apparent activity $[A_{App}]$ is the response of the activity meter. From the determined deviation, this thesis will recommend correction factors that should be applied in certain geometries. The executed experiments determine the influence of the 3 factors: volume, height and container type. These experiments will be explained in detail in this section. Additional, the activity meters are tested for reproducibility and energy response.

Before executing the experiments, the daily test is done. The daily test is a check-up that no drag is shown that indicates a defect. The test is an automated test by the activity meter where the only task for the user is the insertion of the correct sources. The test controls the following parameters: HV supply, display, zero adjust, background and accuracy and constancy of the activity meter. Detailed descriptions can be found in the manuals of the meters. During the daily test a first miscalibration was seen. The reference source ^{133}Ba shows a 10% deviation due to a wrong calibration factor. The reference source is placed in a container different from the 5 ml NIST ampoule and this has a clear effect on the measurement. Correcting these errors is the main goal in this thesis and the tests are therefore the determination of the accuracy in changing geometries.

4.1 Samples

The thesis has the goal to determine the correction needed for the most used isotopes in the commonly used recipients. The experiments in this thesis are executed with the isotopes ^{18}F, ^{99m}Tc, ^{111}In and ^{123}I in the recipients:

- Terumo 2,5 ml syringe

- BD 3 ml syringe
- BD 5 ml syringe
- BD 10 ml syringe
- vial: Scott vial for ^{99m}Tc and ^{18}F and the vial for ^{111}In and ^{123}I is the one that contains the solution when it is delivered.

In certain experiments like the volume experiment, it may be useful to know the measures of the recipients. The measures are given in table 4.1.

Table 4.1: Measures of the recipients used during experiments, in cm

	10 ml	5 ml	3 ml	1 ml	2,5 ml	Schott	Mallinckrodt
height	8,30	6,40	6,80	8,50	5,00	4,80	5,00
contour	5,40	4,60	3,60	2,40	3,50	7,80	7,20
radius	0,86	0,73	0,57	0,38	0,56	1,24	1,15
distance/ml	0,60	0,88	1,70	5,20	1,56	0,25	0,34

The isotopes that are measured have all different energies in a range between 22 keV and 511 keV and an overview of the influence in function of the energy can be made. ^{18}F decays by beta plus transition for 96,86%. The main emission are 511 keV photons. ^{99m}Tc emits for 88,5% a single photon of 140,5 keV. ^{111}In disintegrates through EC and emits mainly 4 photons: 22,98 keV and 23,17 keV K-X-rays for 23,65% and 44,47% and 90,61% 171,28 keV and 94,12% 245,35 keV photons respectively. ^{123}I disintegrates also by electron capture emitting K-X-rays of energy 27,2 and 27,47 keV for 24,69% and 45,98% together with a 158,97 keV photon for 83,25%. [22] [23] It can be predicted that photons of lower energy are more influenced by the geometry than high energy photons. This will be examined in this thesis and if this prediction is correct, the influence on ^{18}F measurements should be the smallest and ^{123}I measurements are the most influenced by geometric changes because the fraction low-energy photons is the highest of the isotopes.

4.2 Energy response

The energy response of an activity meter is the relation between the calibration factors and the response, as explained in chapter 2. This relation should be the same for each radionuclide in the same activity meter and the calibration factor can then be determined using this relation. In this thesis, the relation will be computed in the 3 ways explained in chapter 2: the method described by Zimmerman, the method described by Capintec and the method described by Veenstra. From the computed relations, the calibration factors are calculated and compared to the calibration factor given by the manufacturer.
First the samples are measured in the activity meter using a series of calibration factors. Then the relationship is computed as done in the method described by Zimmerman. The response ratio (R) is taken from the response of the meter to the true activity. Then a fit is calculated between the inverse of the response ratio and the calibration factors(CF) used. This gives the following relation:

$$R^{-1} = a * \mathrm{CF} + b$$

This relation is solved for R = 1 which gives the calibration factor that should be used according to the method described by Zimmerman.
The method described by Veenstra uses the response ratio: the true activity over the response in the ^{99m}Tc setting. In this master's thesis the fit is made of the relation between calibration factor and the response ratio against the ^{99m}Tc setting and the relation between the CF and the response ratio against the ^{18}F setting.
The last method is the method described in the manual of Capintec. The calculation is based on the response ratio of the sample over the response ratio of a certified ^{60}Co source.
The regression is made on the relation using each method and from these regressions the calibration factors are calculated and compared to the calibration factors used at the moment.

4.3 Isosensitivity

Because of the uniform emission of radiation, the most accurate way to measure a radioactive substance is by an ionisation chamber that encloses the sample completely. The activity meters used in the clinical practice are re-entrant well type chambers, this means that the chambers are always open at the top. Hence, radiation is lost through that opening. The fraction of radiation lost through the opening is related to the angle between the edges of the ionisation chamber and the source. This angle is related to the depth of the sample and it is expected that the loss of radiation is minimal when the sample is at the bottom. This expectation is confirmed by literature. Figure 4.1 shows the sensitivity map of a typical ionisation chamber. The sensitivity map indicates that the best height to measure is a few cm above the bottom. The reason why the sensitivity is higher in this region than the expected region is because the anode is positioned at the bottom of the chamber, which means that the geometry in this part of the chamber differs causing this region to be less sensitive. [5] The sensitivity map is confirmed by the manual of the Veenstra devices. According to the manual the best height to masure is between 5 and 13 cm above the bottom, where the sensitivity is maximal and nearly height-independent. The figure from the manual, shown in 4.1 , shows that the error in this range stays within 2%. [24]

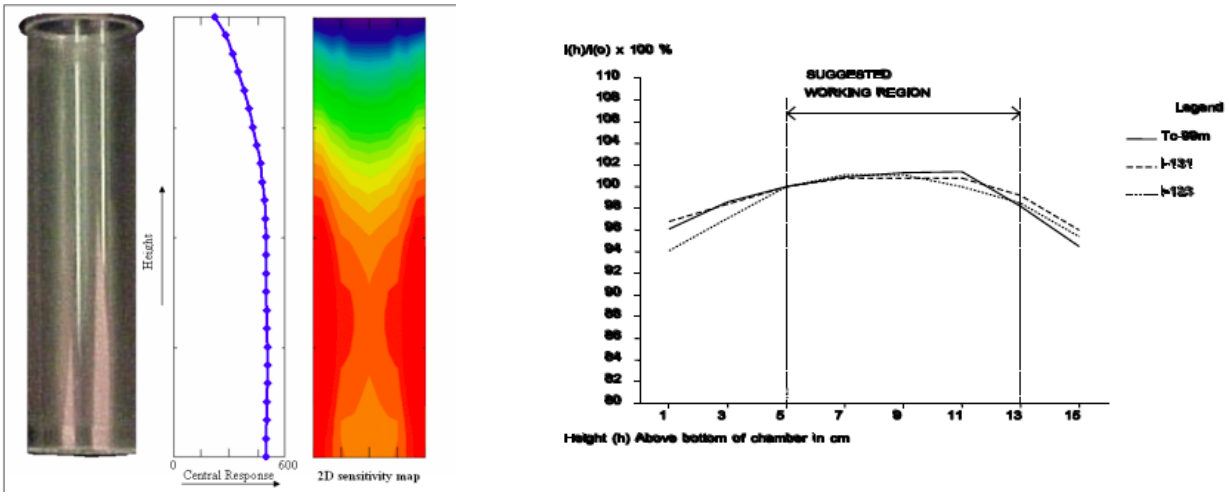


Figure 4.1: Spatial dependance of the ionization chamber: Sensitivity map of a typical ionisation chamber (Left), Height dependance of the VIK-202 (Right)

The experiment is creating a depth profile for the devices used in clinical routine. The method is described by Santos et [25]. This is not a time consuming or complex test, therefore it is appropriate for a semester periodicity. The depth profile of the activity meter is measured using a quasi-point source of ^{99m}Tc. An acrylic device as shown in figure 4.2 is used, this device is equiped with an opening and cap at the end as can be seen in figure 4.2. In this opening a small amount ^{99m}Tc solution is inserted to create a quasi-point source that has an activity measurable by the chamber. The dipper and well liner are taken out of the chamber and the acrylic device is inserted using the set-up shown in figure 4.2. The acrylic device has a ruler attached so the depth can be measured easily. The following step is measuring at different distances from the bottom to the top of the ionisation chamber. From the measurement a curve of apparent activity can be proposed giving the depth profile. [26] The reference plane is the bottom, the first measurement is in the center of this plane. Then the point source is displaced along the longitudinal axis with steps of 1 cm. Each measurement is corrected for decay and the depth profile of the ionisation chamber is proposed.

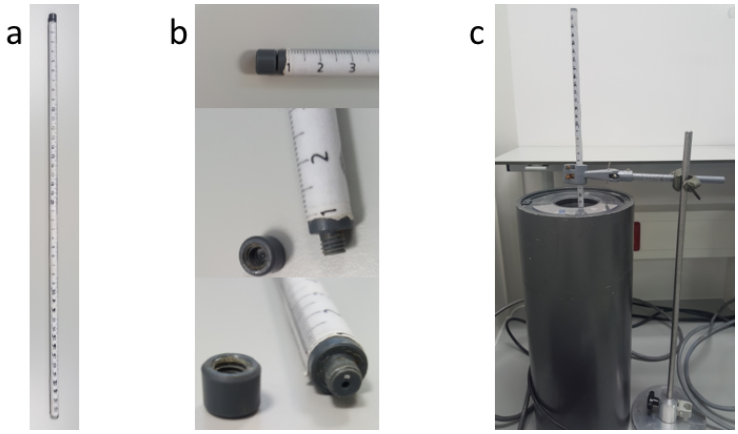


Figure 4.2: Set-up for the experiment to determine the influence of position. (a) Acrylic device;(b) close up on the opening and cap; (c) the set-up during measurements

Because the influence of the height is evaluated, it is important to know where the source is located inside the chamber. This is displayed in figure 4.3, where the most important measures of the ionisation chamber are specified. The syringes will hang at a depth of 9,7 cm which is at 17,5 cm above the bottom.

4.4 Reproducibility

If a sample is measured 2 times in the same geometry, the response of the activity meter is the same. However due the background variations, small geometric changes, etc. is this not true in practice. Reproducibility is the measure for efficiency of the activity meter and gives the variation of the result. The reproducibility in the standard deviation in a series of measurements and the test is executed as follows: 10 measurements are taken with the source in the same place, the source is kept inside the chamber. Then 10 measurements are taken with re-entering the sample in between 2 measurements. The mean is taken and the standard deviation. The relative standard variation is evaluated against the demanded 2% maximum of the FANC. The test is done for all isotopes tested in this thesis.

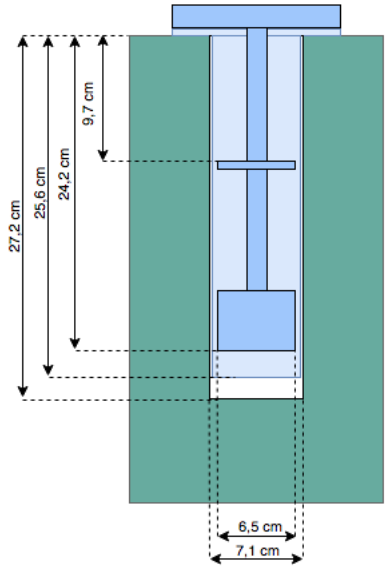


Figure 4.3: Measures of the ionisation chamber

4.5 Volume sensitivity

When diluting and dispensing the sample, the activity spreads over a larger volume, changing the position higher in the chamber. Additionally, the self-absorption is different and the contact area with the container wall is enlarged, allowing the particles to move closer to the sensitive volume of the chamber. The influence of the volume is tested with 4 isotopes: ^{18}F, ^{99m}Tc, ^{123}I and ^{111}In. To test the sensitivity to volume changes a concentrated solution is measured in the chamber. The solution is then diluted with physiological water, holding the activity constant but changing the volume.

The following steps are executed for the volume dependence test in a vial. 1 ml concentrated solution is inserted in a vial. The activity is measured and the weight is taken. 1 ml physiological water is added and the solution is measured and weighted. This step is repeated 9 times. From the response of the chamber a curve is drawn in function of volume. The diluted solutions are then used as stock solution for the experiment concerning the container influence. The experiment is then repeated in syringes of 1 ml, 3 ml, 5 ml, 10 ml. The physiological water is added in steps of resp. 0.1 ml, 0.4 ml, 0.6 ml and 1ml. The response is then drawn in function of volume. Santos et al. concluded from their experiments that the deviation can be ascribed to the height . Hence, the relationship between response and height in the chamber is also drawn. [25]

4.6 Influence of the recipient

The container used during the measurement is often dependent on the type of isotope and the use of the radiopharmaceutical. The experiment executed to survey performance for measurement of ^{123}I activity by Jacobson shows that the magnitude of the influence of the container type is bigger than the influence of the other factors. [9]. 'Determining the influence of every container is impracticable, thus a questionnaire was used to determine the most used containers in the clinical routine. five were chosen to be examined: the Terumo 2,5 ml syringe, the 3 ml, 5 ml, 10

ml BD syringes and a vial, either the Mallinckrodt or the Scott vial.
To determine the influence of the containers a stock solution is made. This is the solution resulting from the volume experiment ro efficiently using of the product. The stock solution is divided in the 5 recipients, each recipient has approximately 2 ml solution to minimize the volume influence. From each recipient, the weight is taken before and after application of the solution, the activity concentration is calculated when the solution is measured using their calibration factor. The result is compared with the known activity concentration provided by the gamma counter, which give the correction factor for each recipient.

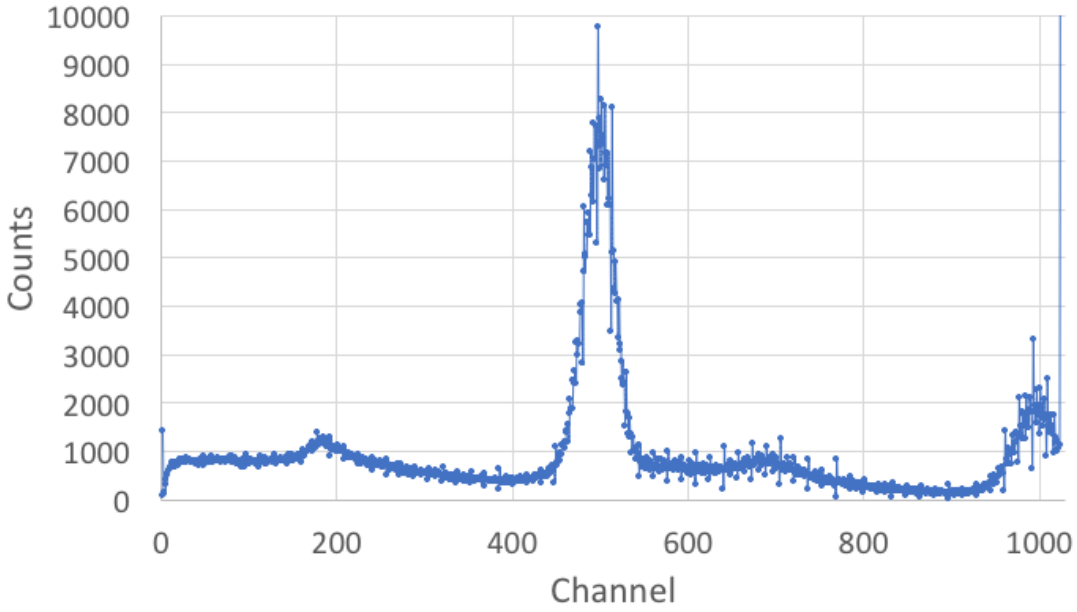
4.7 QA gamma counter

Linearity

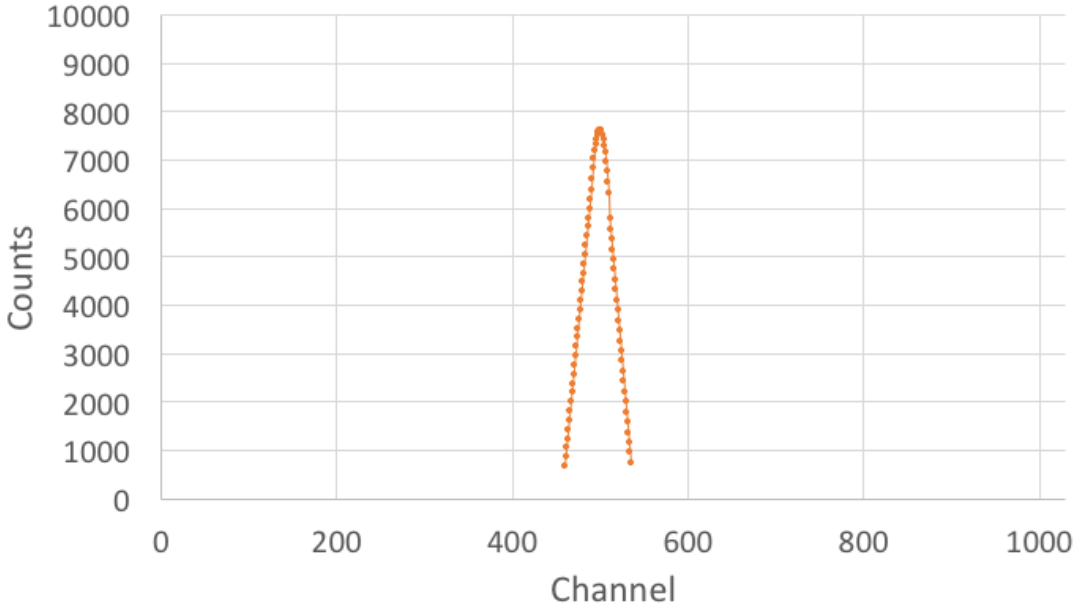
For this thesis, the linearity is tested with ^{18}F within a range that exceeds the 2.10^6 DPM. The test is executed by placing a number of samples with an activity above 2.10^6 DPM on the gamma counter and starting the acquisition without a STOP rack. To stall between the measurements, a rack of empty tubes is added. The gamma counter will then continuously count the samples. A regression analysis is executed on the response over time. From this regression, the decay constant is determined and evaluated against the theoretic value. The deviation of the response is compared to a fit based on the regression, the deviation between these curves should be 1% in the range 0-2.10^6 DPM.

Resolution

The resolution is calculated with templates designed in this thesis. Spectra are read into the Excel-file and the peak is analysed. A spectrum of ^{18}F is shown in figure 4.4a. The spectra has a peak with a rough surface and should be smoothed. This is done by fitting the peak with 3 functions: first the top of the peak is fitted with a polynomial regression and the walls of the peak are fitted with linear functions. The result is a peak shown in figure 4.4b In this way the peak is smoothed out. From the fitted functions, the maximum is calculated and with this value the peak position can be calculated and the energies where the spectrum crosses the half-maximum. The FWHM is the distance between these energies and the resolution is calculated by dividing the FWHM by the peak energy. One remark on this calculation is that the region of interest should extent when the peak energy raises because the FWHM increases with the energy.



(a) The spectrum measured



(b) the smoothed peak

Figure 4.4: The spectrum of ^{18}F measured by the gamma counter 1480 WIZARD 3" and the smooth peak

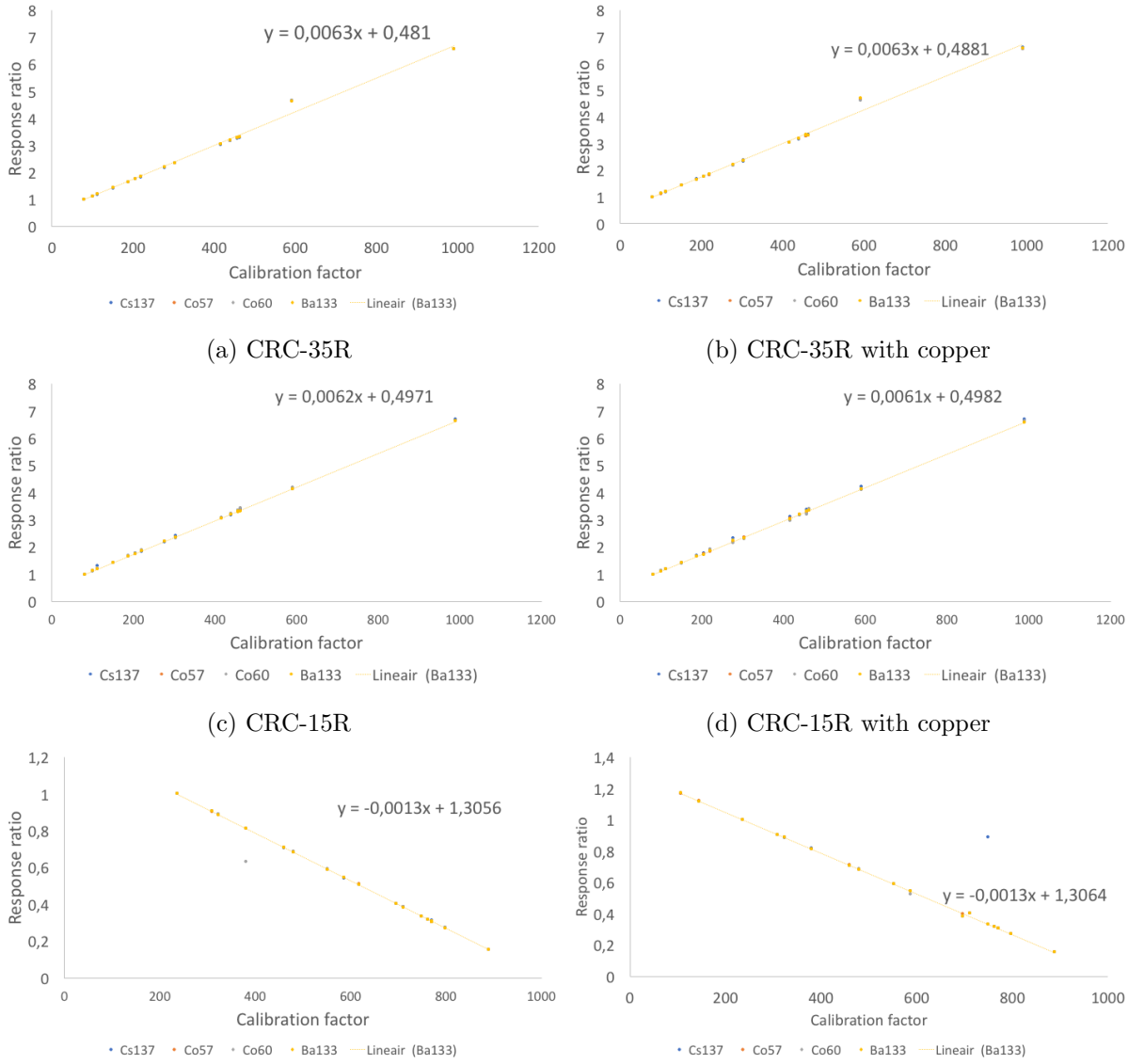
Chapter 5

Results

The results of the experiments are shown as graphs or in summary tables. The full list of values is listed in the appendix. As an extra angle, the experiments are executed with a copper sleeve and without copper sleeve. There is a big difference in the copper sleeve of the Capintec and Veenstra model. The copper sleeve of Capintec has the same shape as the well-liner in the chamber. The Veenstra model, however, is smaller and encases the sample closely, it is especially designed for vials. The use of the copper sleeve will give an interesting angle on the magnitude of the influences when an extra layer is added. The copper sleeve will reduce the measured activity because photons with lower energies will be stopped by the sleeve. Another effect is the scatter and bremsstrahlung in the sleeve. The influence of the copper sleeve will be briefly discussed at the end of each experiment.

5.1 Energy response

The goal of the experiment is to evaluate the relationship between calibration factors and the response given by the manuals. The evaluation is done by fitting the response ratio against the calibration factors as described by Zimmerman [11] and the manuals [7] [6] evaluate these relations and calculate the calibration factor for the used isotopes. For each activity meter, a sensitivity curve is drawn in figure 5.1. The apparent activity in each setting and each device can be found in the appendix. In these curves the relation is fitted of the response ratio against the CF. In the sensitivity curve of the CRC-35R there is 1 point that is not on the curve, this is the calibration factor corresponding to ^{133}Ba. As already mentioned was the activity of the ^{133}Ba reference source deviation around 10%, the miscalibration is in this test confirmed.
The calculation of the calibration factor is done with the 3 methods. The first method used, is the method described by Zimmerman. The response ratio is the apparent activity over the true activity. From inverse of these values and the calibration factors is a relationship fitted that is shown in table 5.1. The relationship is computed using reference sources of ^{57}Co, ^{60}Co, ^{137}Cs and ^{133}Ba. The relationship is different for each isotope because the reference value (the true activity) differs from isotope to isotope. The second method is the one from the Veenstra manual. Where the ratio is: the response using the calibration factor over the response using the ^{99m}Tc CF. Table 5.2 shows the relations using the isotopes. The relations match each other closely. To extend the experiment, the ratio using the response with the ^{18}F CF is used instead of the ^{99m}Tc CF. The resulting relations are shown in table 5.3. The relations between the calibration factor and the response ratio for the veenstra VIK-202 are in good agreement with



(a) CRC-35R

(b) CRC-35R with copper

(c) CRC-15R

(d) CRC-15R with copper

(e) VIK-202

(f) VIK-202 with copper

Figure 5.1: sensitivity curves of the activity meters

the formula given in the manual. From the fit using the ^{99m}Tc setting, the calibration factor can be determined. This is done for the 4 reference sources and shown in table 5.4. The third method is described in the manuals of Capintec. The values are related to the output of the ^{60}Co reference source. The formula given in the manual will be taken for this method because only 4 values are known to fit the relation, which is not sufficient. The resulting calibration factors are tabulated in table 5.5

Table 5.1: The calibration curve of the calibration factor in function of the ratio of the apparent activity to the true activity using the method described by Zimmerman

	^{137}Cs	^{57}Co	^{60}Co	^{133}Ba
CRC-35R	CF = 309,55.R - 71,39	CF = 182,50.R - 74,21	CF = 983,29.R - 74,13	CF = 699,73.R - 73,59
CRC-35R with copper	CF = 263,22.R - 72,43	CF = 94,52.R - 73,88	CF = 943,37.R - 75,49	CF = 182,56.R - 73,79
CRC-15R	CF = 314,53.R - 60,89	CF = 187,37.R - 79,97	CF = 1008,67.R - 80,10	CF = 745,83.R - 80,64
CRC-15R with copper	CF = 272,88.R - 80,21	CF = 97,59.R - 80,21	CF = 958,36.R - 77,59	CF = 188,39.R - 81,05
VIK-202	CF = 237,40.R + 299,01	CF = 136,91.R + 298,44	CF = 752,88.R + 295,24	CF = 489,67.R + 298,65
VIK-202 with copper	CF = 235,30.R + 253,00	CF = 125,59.R + 212,24	CF = 891,05.R + 208,12	CF = 210,89.R + 211,12

Table 5.2: The calibration curve of the calibration factor in function of the ratio of the response to the response with ^{99m}Tc CF

	^{137}Cs	^{57}Co	^{60}Co	^{133}Ba
CRC-35R	CF = 158,16.R - 71,39	CF = 158,52.R -74,21	CF = 158,59.R -74,13	CF = 158,32.R -73,59
CRC-35R with copper	CF = 157,68.R - 72,43	CF = 158,63.R - 73,88	CF = 158,85.R - 75,49	CF = 157,45.R - 73,79
CRC-15R	CF = 157,69.R - 60,89	CF = 162,10.R - 79,97	CF = 160,82.R - 80,10	CF = 162,29.R - 80,64
CRC-15R with copper	CF = 160,50.R - 80,209	CF = 162,52.R - 80,21	CF = 162,59.R - 77,59	CF = 162,81.R - 81,05
VIK-202	CF =-771,40.R +1007,56	CF = -771,50.R +1007,49	CF =-786,62.R +1007,96	CF =-771,23.R + 1006,95
VIK-202 with copper	CF =-707,31.R + 989,99	CF = -771,23.R +1007,83	CF =-770,05.R +1005,46	CF =-769,83.R +1005,971

Table 5.3: The calibration curve of the calibration factor in function of the ratio of the response to the response with ^{18}F CF

	^{137}Cs	^{57}Co	^{60}Co	^{133}Ba
CRC-35R	CF = 477,75.R - 71,39	CF = 481,85.R - 74,21	CF = 483,58.R - 74,13	CF = 482,12.R - 73,59
CRC-35R with copper	CF = 500,32.R - 72,43	CF = 504,02.R - 73,88	CF = 506,88.R - 75,49	CF = 502,33.R - 73,79
CRC-15R	CF = 499,90.R - 60,89	CF = 516,77.R - 79,97	CF = 518,74.R - 80,10	CF = 517,23.R - 80,64
CRC-15R with copper	CF = 498,38.R - 80,209	CF = 494,21.R - 80,21	CF = 480,52.R - 77,59	CF = 491,42.R - 81,05
VIK-202	CF =-245,50.R +1007,56	CF =-245,00.R +1007,49	CF =-250,22.R +1007,96	CF = -244,60.R + 1006,95
VIK-202 with copper	CF =-225,39.R +989,99	CF =-245,38.R +1007,83	CF =-245,67.R +1005,46	CF = -244,08.R + 1005,97

Table 5.4: The calibrationfactors for the isotopes: ^{137}Cs, ^{60}Co, ^{57}Co and ^{133}Ba using the fit according to the Veenstra manual

	CRC-35R	CRC-35R+copper	CRC-15R	CRC-15R+copper	VIK-202	VIK-202 + copper
Cs-123	237	190	245	196	604	568
^{57}Co	109	20	110	18	302	115
^{60}Co	909	865	933	876	876	876
^{133}Ba	627	109	663	108	814	474

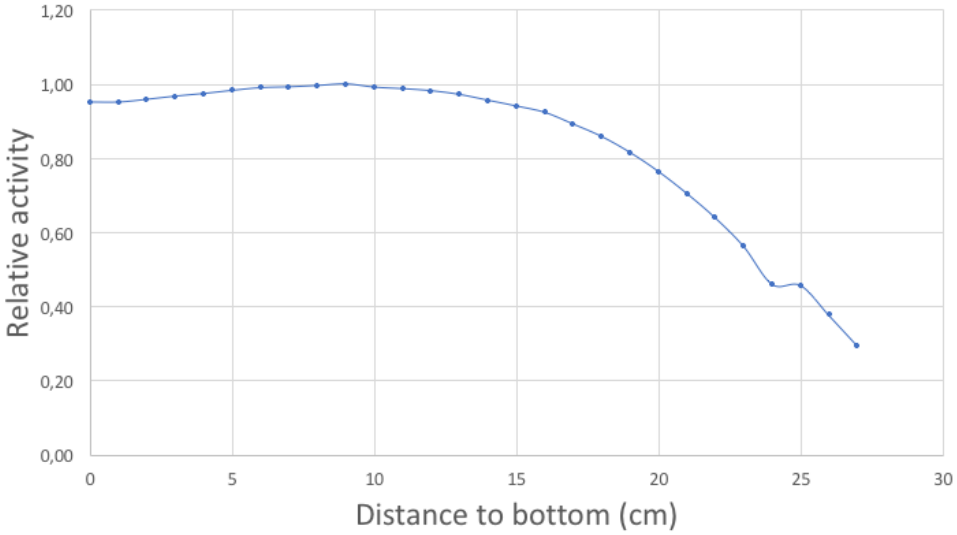
Table 5.5: The calibration factors for the isotopes: ^{137}Cs, ^{60}Co, ^{57}Co and ^{133}Ba using the equation given in the Capintec manual

	CRC-35R	CRC-35R+copper	CRC-15R	CRC-15R+copper	VIK-202	VIK-202 + copper
^{137}Cs	255	217	268	219	260	254
^{57}Co	114	22	114	23	113	68
^{60}Co	990	990	990	990	990	990
^{133}Ba	681	123	707	124	627	171

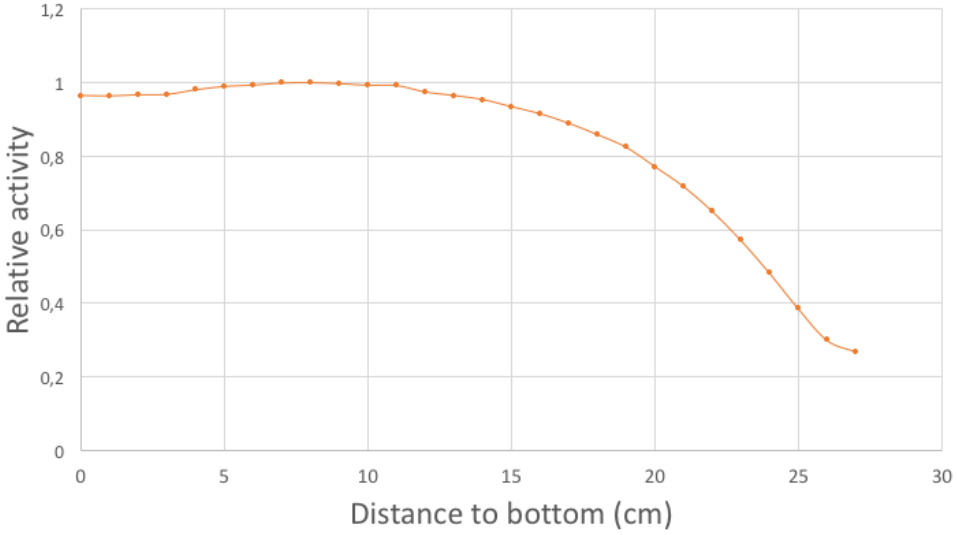
5.2 Isosensitivity

The spatial sensitivity, dependence on the position of the detectors is determined by displacing a quasi-point source ^{99m}Tc and the acrylic device in the ionization chamber. The result is a depth profile of the response. Figure 5.2a and 5.2b give respectively the profile of the Capintec CRC-15R and CRC-35R. The apparent activity is normalized to the maximum value of the measurements. Figure 5.2c shows the depth profile of the Veenstra VIK-202 model.
The depth profile of the Capintec CRC-15R, figure 5.2a, shows that the hotspot of the chamber is between 5 and 12 cm from the bottom with a minimum of 98%. Between the bottom and 14 cm above the maximum loss of activity is 5%. This meets the standards of FANC. At a distance of 14 cm the fault is 4 %. Placing the source more than 14 cm above the bottom gives a deviation above the accepted 5%.

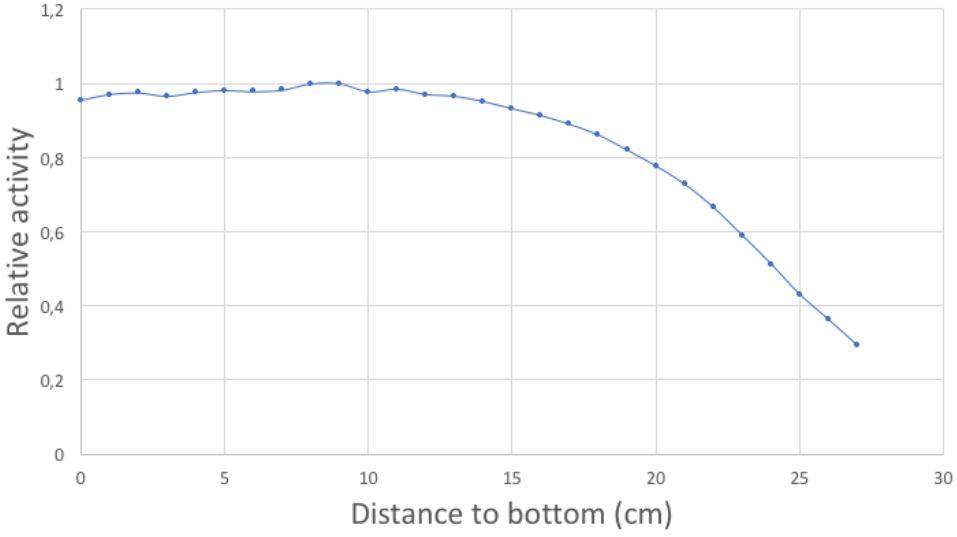
The depth profile of the Capintec CRC-35R, from figure 5.2b, shows a response that is nearly the same as the Capintec CRC-15R. Where there is a maximum deviation of 2% between 4 cm en 11 cm and a deviation of maximum 5 % between the bottom and 14 cm. Again, above 14 cm the response is deviating above the limit of 5%.
As seen in figure 5.2c the response of the VIK-202 of Veenstra is similar to the Capintec models. With a maximum deviation of 2% between 5 and 11 cm and a maximum 5% deviation between the bottom and 14 cm. Above the 14 cm the response deviates above the accepted 5%.



(a) Capintec CRC-15R



(b) Capintec CRC-35R



(c) Veenstra VIK-202

Figure 5.2: Depth profiles of the ionisation chambers

5.3 Reproducibility

As already explained the test is done using 2 methods, the first where the source is kept in the activity meter and the second where the source is re-entered in the activity meter. The test is done with the Capintec CRC-15R and Capintec CRC-35R. The results are shown in the tables 5.6 and 5.7. The true activity, measured activity and mean can be found in the appendix.

Table 5.6: relative standard deviation of the Capintec CRC-15R response

	Cs137	^{133}Ba	^{60}Co	^{57}Co	^{123}I	^{111}In	^{99m}Tc	^{18}F
no reenter	0,55%	0,23%	0,64%	0,13%	0,20%	0,18%	0,12%	0,19%
reenter	1,49%	1,65%	1,83%	1,04%	1,20%	0,79%	1,05%	1,14%

Table 5.7: relative standard deviation of the Capintec CRC-35R response

	Cs137	^{133}Ba	^{60}Co	^{57}Co	^{123}I	^{111}In	^{99m}Tc	^{18}F
no reenter	0,39%	0,00%	0,00%	0,09%	0,25%	0,36%	0,49%	0,26%
reenter	1,92%	1,91%	3,15%	1,98%	0,90%	0,65%	0,87%	1,05%

When looking at the results the deviation when measured without re-entering is always under 1%. The deviation when the source is re-entered, is larger and can have a maximum of 3,15%. The accepted deviation, according to the decree of FANC, is 2%. This deviation is exceeded in the CRC-35R activity meter with more than 1% for the ^{60}Co source. This source had an activity of 1,7 MBq, the lowest of all the sources in this experiment. The other measurements are all kept within the accepted range.

5.4 Volume sensitivity

The apparent activity measured when varying the volume is shown in figure 5.3 and figure 5.4. figure 5.3 shows the dependence of the apparent activity in vials for the isotopes ^{123}I, ^{111}In, ^{18}F, ^{99m}Tc. Figure 5.4 shows the influence of the volume in syringes for ^{99m}Tc and ^{18}F. All values are normalized to the value of the concentrated solution where the experiment is started with. This approach eliminated the influence of the container and position in the chamber.

The influence of the volume in vials, as can be seen in figure 5.3 has no effect on the measurement of ^{99m}Tc. In the measurement of ^{18}F there is a slight reduction of the apparent activity when the solution is diluted. The aparent activity when measuring ^{111}In and ^{123}I is higher when the sample is diluted.

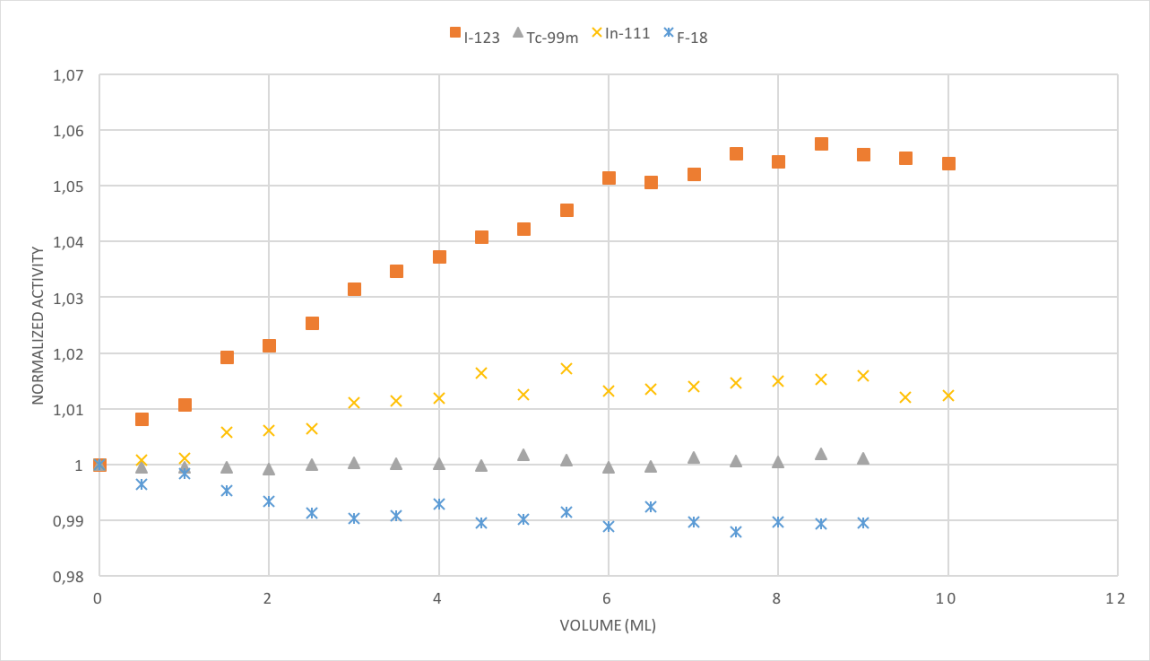
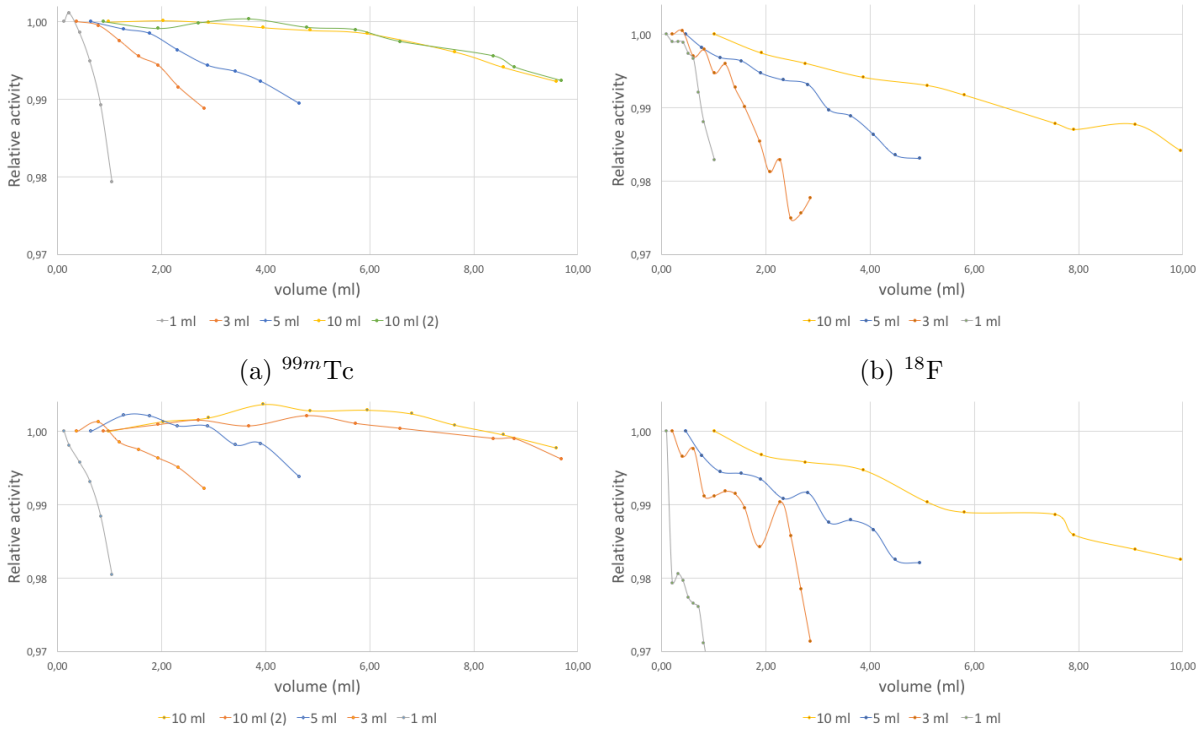


Figure 5.3: Volume dependence of CRC-55tR



(a) ^{99m}Tc

(b) ^{18}F

(c) ^{99m}Tc using the copper sleeve

(d) ^{18}F using the copper sleeve

Figure 5.4: Volume dependence in syringes in function of the volume

As can be seen in figure 5.4, the dilution of the sample in a syringe will also influence the apparent activity. Figure 5.4 also shows the variance in response versus the volume when a copper sleeve is used. No great reduction is seen, hence the volume dependence can not be altered by inserting a copper sleeve. The reduction per ml is the most remarkable in a 1 ml syringe and the least changing in a 10 ml vial. The relative variation for the 1 ml syringe between the concentrated solution and the maximum diluted solution is 2,07% for ^{99m}Tc and 1,96% for ^{99m}Tc using the

copper sleeve, 1,72% for ^{18}F and 3,45% for ^{18}F with copper sleeve. In the 10 ml syringe the variation between the zero volume added and the maximum diluted solution is 0,76% for ^{99m}Tc and 0,38% using a copper sleeve and for ^{18}F: 1,59% and 1,75% using the copper sleeve. The variation per ml in the 10 ml syringe is thus less than one tenth smaller than in the 1 ml syringe.

5.5 Influence of the recipient

In chapter 2 was stated that the container of the radioactive substance influences the measurement through the attenuation of the material, bremsstrahlung and scatter. The attenuation of glass is larger than the attenuation of plastic, thus there is a difference between the measurement in a vial and a syringe. Additional there is a difference in scatter and bremsstrahlung. This is confirmed by the results which can be seen in table 5.8 where the apparent activity in different containers is given. The reference used is the activity determined by the measurement of the gamma counter and the deviation is the difference between the activity concentration and this reference value.

Table 5.8: Apparent activity concentration in the different recipients in Mbq/ml

^{111}In	reference(GC)	activityconc.	deviation(%)	activityconc. with copper	deviation(%)
terumo	1,84	2,11	0,15	1,04	-0,44
BD 3 ml	1,87	2,11	0,13	1,03	-0,45
BD 5 ml	1,86	2,09	0,13	1,04	-0,44
BD 10 ml	1,93	2,07	0,07	1,05	-0,46
vial	1,83	1,66	-0,09	0,95	-0,48
^{123}I	reference(GC)	activityconc.	deviation(%)	activityconc. with copper	deviation(%)
terumo	2,96	3,54	0,19	0,77	-0,74
BD 3 ml	2,98	3,50	0,17	0,77	-0,74
BD 5 ml	2,97	3,42	0,15	0,78	-0,74
BD 10 ml	2,99	3,35	0,12	0,78	-0,74
vial	2,89	2,03	-0,30	0,66	-0,77
^{99m}Tc	reference(GC)	activityconc.	deviation(%)	activityconc. with copper	deviation(%)
terumo	24,51	25,72	0,05	16,27	-0,34
BD 3 ml	24,45	26,02	0,06	16,40	-0,33
BD 5 ml	24,36	26,22	0,08	16,44	-0,33
BD 10 ml	24,24	26,29	0,08	16,36	-0,33
vial	24,03	25,78	0,07	15,49	-0,36
^{18}F	reference(GC)	activityconc.	deviation(%)	activityconc. with copper	deviation(%)
terumo	80,11	75,79	-0,05	71,20	-0,11
BD 3 ml	76,83	76,47	0,00	71,66	-0,07
BD 5 ml	73,58	76,76	0,04	72,04	-0,02
BD 10 ml	74,39	77,00	0,04	71,91	-0,03
vial	77,25	73,83	-0,04	68,20	-0,12

For each isotope the reference value, the measured value and the deviation is given. The results show that the measurement in syringes result in higher apparent activity than the measurement in vials. Measuring ^{18}F gives the lowest deviations and the results are even within the regulatory standard of 5%. ^{99m}Tc is overestimated in all recipients. ^{123}I and ^{111}In are overestimated in syringes by 12-19% and 7-15% and underestimated in vials by respectively 30% and 9%. The

type of containers is not the only factor deviating the results. When using a syringe to measure the activity, the position is different by approximately 10 cm. As discussed earlier, this will affect the measurement. There is also a deviation difference seen between syringes of the same type but with different size. The deviation seen in the table show the problem that was meant to be investigated in this thesis and the need for corrections when measuring the activity in different containers.
A first angle that is looked at is the use of a copper sleeve. The copper sleeve has an influence on the measurement as a container wall. The influence is seen in Table 5.8, the copper sleeve causes a reduction in the measured activity up to an apparent activity that is 20% of the true activity. The copper sleeve has a bigger influence on the radionuclides that emit low energy photons than isotopes with high energy photons. With the reduction of the apparent activity is a reduction seen in the variation in the measurements of ^{111}In and ^{123}I where the range [1,66-2,11] was reduced to [0,95-1,05] for In-123 and [2,03-3,54] to [0,66-0,78] for ^{123}I. The variation of the apparent activity was not influenced in the measurements of ^{99m}Tc and ^{18}F.

5.6 QA gamma counter

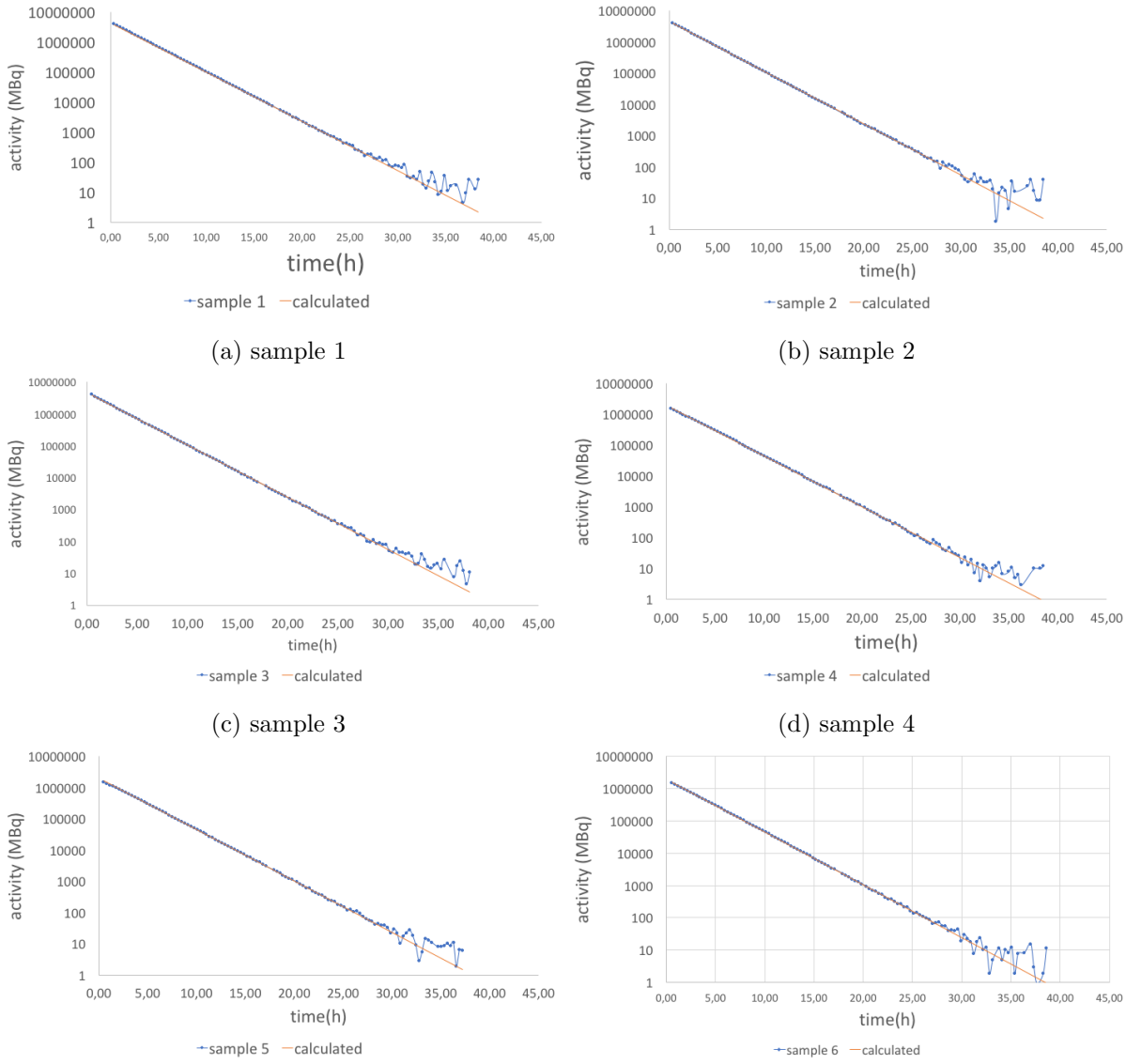
5.6.1 Linearity

The linearity is tested with 6 samples of ^{18}F, sample 1, 2 and 3 with protocol '10 ^{18}F 1min' and sample 4, 5 and 6 with protocol '28 ^{18}FM 1MI'. Protocol '10 ^{18}F 1min' measures in an energy window of 15-2000 keV, this means that the spectrum has 2 peaks, the 511 keV annihilition photons and the sum peak at 1022 keV. Protocol '28 ^{18}FB 1MI' measures in an energy window 15-1000 keV, this excludes the sum peak and measures therefore in a narrow window only around the 511 keV. Figure 5.5 shows the CPM in function of the time in semi-log graph.
The response of the gamma counter is fitted and the slope is the measured decay constant, this should be within 1% of the theoretical value. Table 5.9 gives the decay constants from each sample. The values for the decay constant extracted from the figure 5.5 in the samples are within the 1% of the theoretic value. This confirms the manuals statement concerning the linearity.

Table 5.9: Decay constants measured in the samples 1 to 6

sample	decay constant
theory [22]	0,3790
sample 1	0,3777
sample 2	0,3777
sample 3	0,3769
sample 4	0,3789
sample 5	0,3775
sample 6	0,3769

The deviation of the measurement is calculated for sample 1 and is shown in figure 5.6. The measurement started with nearly 4 million CPM this is above the maximum CPM indicated by the manual. The dead time factor is 1,4979 for this measurement. The deviation of the measurement is below 1%. The linearity of the gamma counter is therefore up to 4 million



(a) sample 1

(b) sample 2

(c) sample 3

(d) sample 4

(e) sample 5

(f) sample 6

Figure 5.5: semi-log graph of the decay ^{18}F measured in the Perkin Elmer gamma counter 1480 WIZARD 3"

CPM. Also from this measurement it can be concluded that the correction for dead time is accurate up to a factor of 1,50. This is also confirmed in the other samples. In the graph it can be seen that the deviation raises above 1% when 551,6 CPM are measured. The values where the deviation raises above 1% in the other samples are between 200 and 400 CPM. Possible cause of this deviation is the background fluctuations. Hence, the linearity with an maximum error of 1% is achieved in the range 551-4.10^6 DPM.

5.6.2 Resolution

The resolution is calculated for ^{129}I, ^{68}Ge, ^{18}F and ^{99m}Tc. The spectra are shown in figure 5.7. From the spectra the resolution is calculated, which is:

- ^{129}I: 34,27%
- ^{68}Ge: 8,94%
- ^{18}F (1-2000 keV window):8,54%

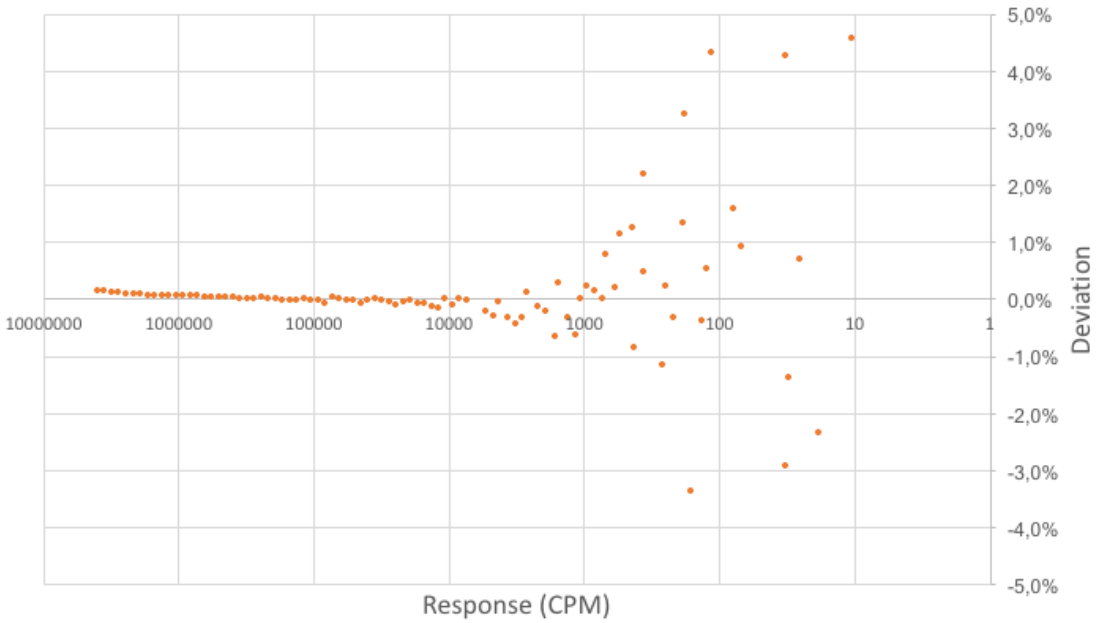
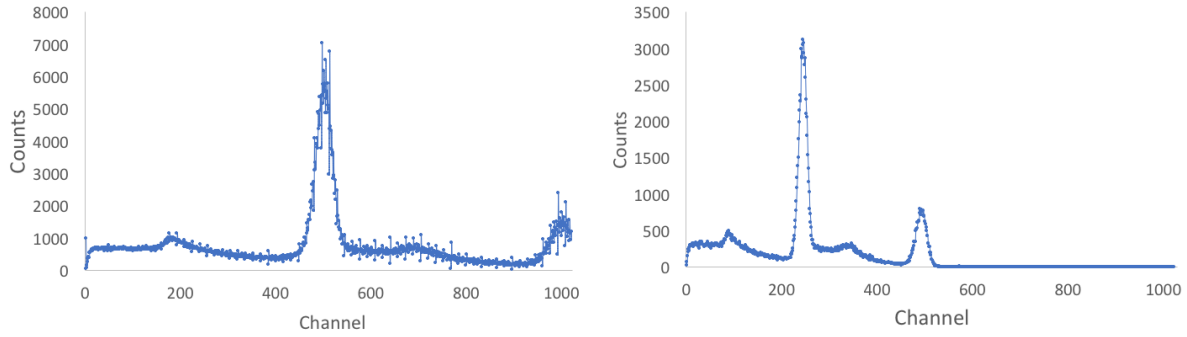


Figure 5.6: deviation of the response of the linearised measurement in sample 1

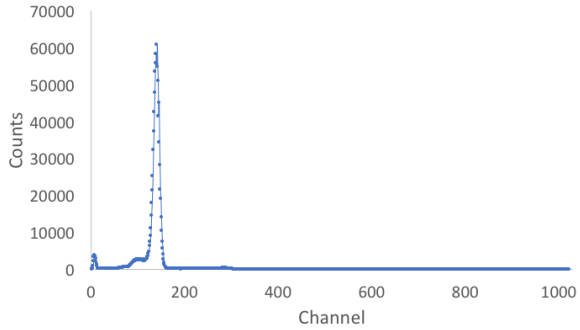
- ^{18}F (1-1000 keV window,1 min):8,77%
- ^{18}F (1-1000 keV window,10 min):8,47%
- ^{99m}Tc: 10,62%

The manual gives 2 values for the resolution, the resolution of ^{125}I is 28% and for ^{137}Cs the resolution is 8%. The resolution is determined by the FWHM divided by the energy of the peak. The relation between the resolution and the energy of the peak is an inverse relation. The resolution of isotopes emitting high energy photons is thus better than low energy photons.

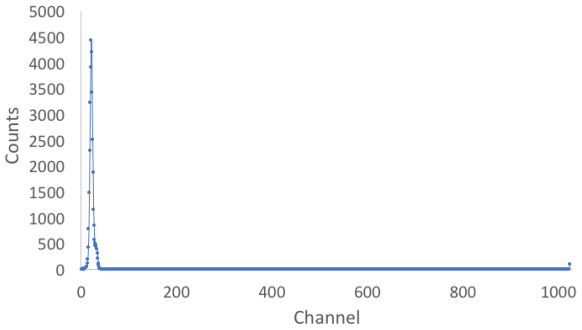


(a) ^{68}Ge spectrum

(b) ^{18}F spectrum



(c) ^{99m}Tc spectrum



(d) ^{129}I spectrum

Figure 5.7: Spectra measured by the gamma counter 1480 WIZARD 3" and the smooth peak

Chapter 6

Discussion

6.1 Energy response

The relation between the calibration factor and the response of the activity meter is computed in 3 possible ways. The first method is the one described by Zimmerman where the calibration factor is in function of the response ratio of the measured activity over the true activity. This gave functions that were different for each isotope and is therefore hard to use. Using the method described by the Veenstra manual, where the calibration factor is in function of the ratio of the response in the correct setting over the response in the setting for ^{99m}Tc. This gave similar functions for each isotope and can therefore be generalized and used for the calculation and correction of calibration factors. These functions are given in table 6.1.

Table 6.1: functions recommended to use to determine the calibration factors

	function without copper sleeve	function using the copper sleeve
CRC-35R	CF =158,40.R^{-1}-73,33	CF = 158,15.R^{-1}-73,90
CRC-15R	CF =160,72.R^{-1}-75,40	CF = 162,11.R^{-1}-79,77
VIK-202	CF = -775,19.R+ 1007,49	CF = -754,60.R+1002,31

Because of the reference chain that is made using the gamma counter, the true activity of each sample is known by correcting the measured value. This gives the opportunity to adjust the calibration factor to the geometry used for the measurement. The only thing to do is the measurement in the ^{99m}Tc setting and filling in the response together with the true activity.

6.2 Isosensitivity

Figure 6.1 shows the depth profile of the CRC-35R, CRC-15R and VIK202 combined. In this graph 3 lines are added. The deviation 5% line defines a region where the deviation is maximum 5%. The deviation 10% line defines the region where the deviation is not more than 10%. The third line is the position where the syringes are hanged in the chamber. These marks can be used for position optimization inside an activity meter and as a tool for accepting test, e.g. in a QC or in a performance verification after a repair. Thus, should be determined for an activity meter during the accepting procedure. [25] Figure 6.2 shows the correlation between the depth profile with the position of the liquid column of the syringes. The figures shows that the liquid column is placed for a part in the region between the 5% and 10% line. This results in a deviation of

more than 5%.

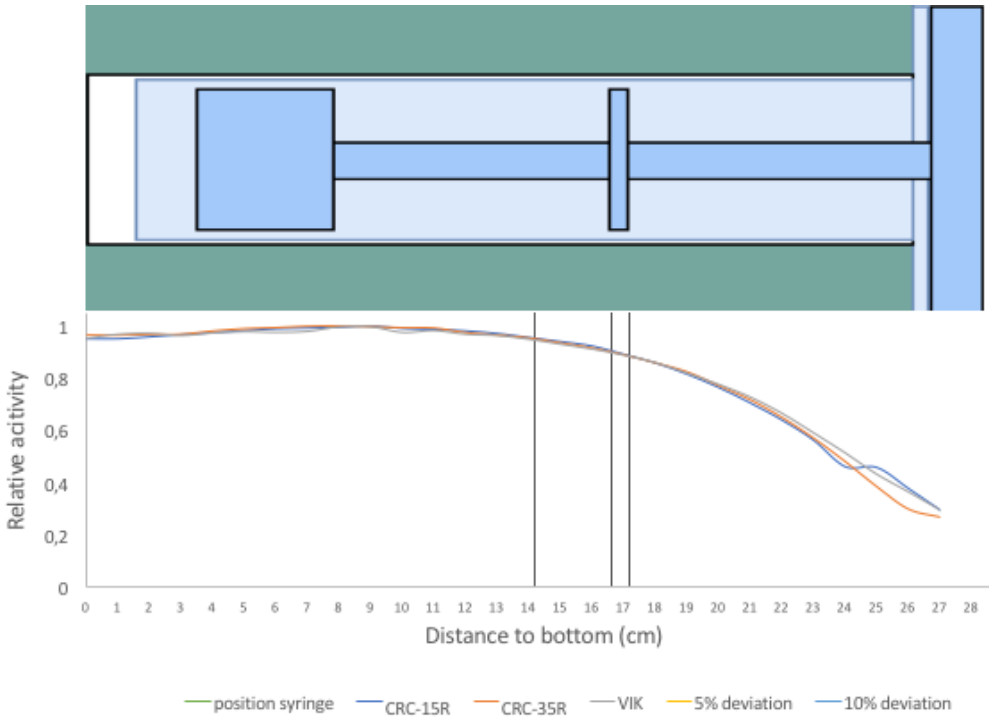


Figure 6.1: summarized depth profile of 3 activity meters with the indication of 5 % and 10 % deviation.

The resulting depth profile with the correlation to the syringes (6.2) shows that there is a correction needed when measuring the syringes. This correction can be made either mechanical where the dipper is adjusted and the liquid column is placed entirely beneath the 5% mark or the response should be corrected for the loss in efficiency above the 5% mark. The relation between the ratio of apparent activity (A_{App}) over true activity (A_{True}) and the height in the chamber (x) can be fitted with a polynomial regression. The fit is given by:

$$\frac{A_{App}}{A_{True}} = 6.10^{-5}.x^3 + 4.10^{-4}.x^2 + 6.10^{-2}.x + 0,9529$$

Using this polynomial regression the correction for position can be determined for each vial and syringe because the position is known of the vial and syringe or can be measured using a ruler. The measures of the recipients used in this thesis are given in the methods. For each recipient is the correction calculated for some situations and shown in table 6.2.

Table 6.2: corrections for most common recipients with different volumes

Recipient	10 ml BD	5 ml BD	3 ml BD	1 ml BD	2,5 ml TERUMO	Schott vial	Mallinckrodt vial
Position	9,2 cm	11,1 cm	10,7 cm	9,0 cm	12,5 cm	4,0 cm	4,0 cm
quasi point	1,005	1,013	1,011	1,004	1,028	1,021	1,021
1ml	1,006	1,017	1,018	1,017	1,039	1,020	1,020
2ml	1,007	1,022	1,028	–	1,055	1,019	1,019
5ml	1,012	1,043	–	–	–	1,017	1,016
10ml	1,030	–	–	–	–	1,014	1,012

This equation gives opportunity to correct for the position in the chamber to a maximum deviation due to position of 2% between the bottom and 23 cm height.

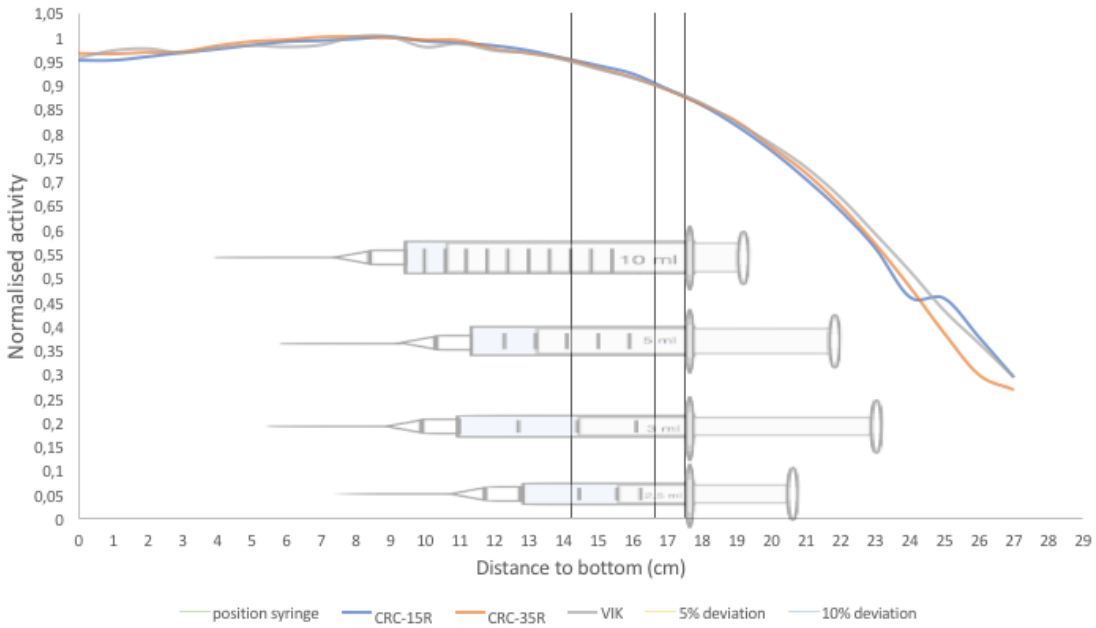
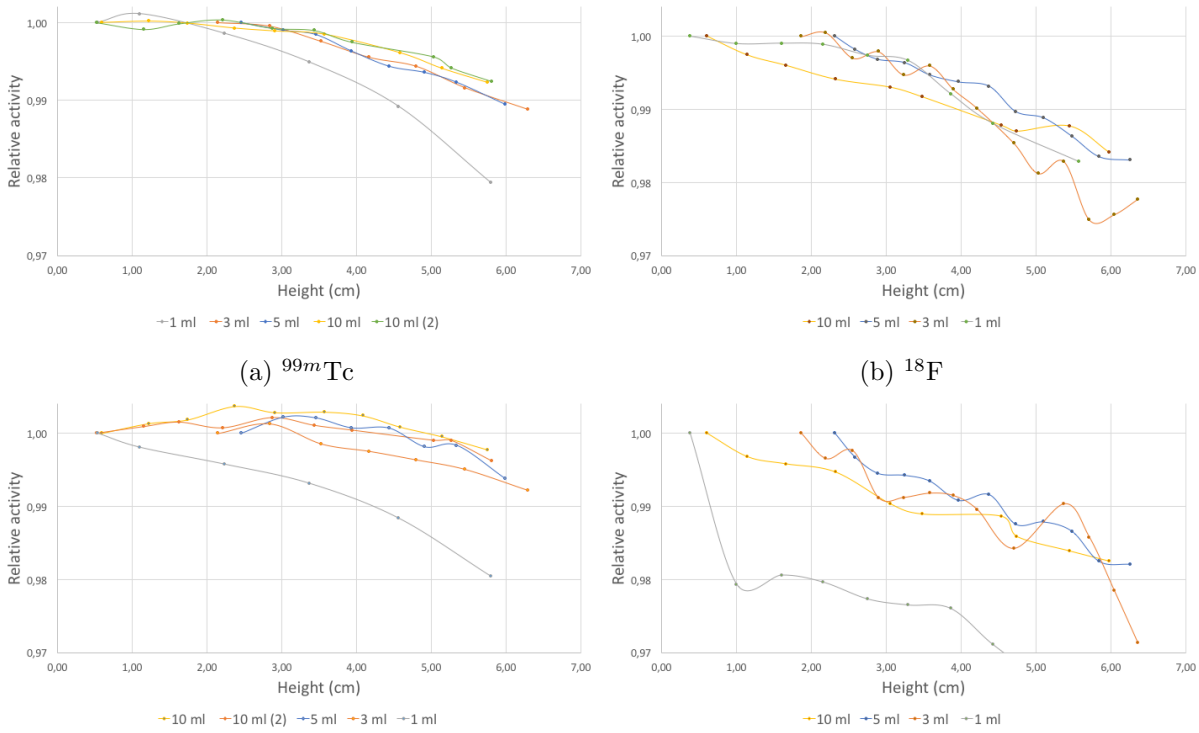


Figure 6.2: summarized depth profile of 3 activity meters with the indication of 5 % and 10 % deviation.

6.3 Volume sensitivity

The volume influence is determined for 4 radionuclides: ^{123}I, ^{111}In, ^{18}F and ^{99m}Tc. ^{123}I decays through electron capture and the main photons emitted are 27 keV and 159 keV. ^{111}In decays also through electron capture and its main photons are 23 keV, 171 keV and 245 keV. Both ^{123}I and ^{111}In show a positive relation with the dilution of the sample. ^{99m}Tc disintegrates through emission of a 140 keV photons and shows a negligible change when the solution is diluted. ^{18}F emits a positive β-particle that converts to 2 511 keV photons after collision with an electron, the response to the measurement of ^{18}F has a slight negative relation with the dilution. From the results a phenomenon is visible: when the sample is diluted the lower energy emitters will reach the chamber and the high energy emitters will pass through the chamber. A reduction was seen in the influence of the volume when a copper sleeve was used. It is therefore recommended to measure ^{123}I and ^{111}In using the copper sleeve.

The influence of volume was also measured in syringes. The results show a clear variation in each syringe. Santos et al. [25] had the same phenomena in their experiment. After defining the spatial sensitivity and the 5 % and 10 % deviation lines, they concluded that the liquid column rests in the region around these lines. [25] Hence it is considered that the deviation is due to the position of the liquid column, the deviation is calculated in function of the length of the liquid column and shown in figure 6.3. In this figure, the normalised apparent activity is in function of the length of the liquid column, which is the distance between the bottom of the syringe and the stopper of the syringe. The origin of the graph is chosen to be at the bottom of the 10 ml syringe in the chamber. The other syringes are related to this position.



(a) ^{99m}Tc

(b) ^{18}F

(c) ^{99m}Tc using the copper sleeve

(d) ^{18}F using the copper sleeve

Figure 6.3: Volume dependence in syringes in function of the length of the liquid column

The figure shows clearly that the variation of the function is nearly the same is all syringes for ^{99m}Tc as well as for ^{18}F and it seems that the variation follows the depth profile of the ionization chamber. The conclusion drawn from these phenomena is that the ideal procedure is to move the measuring position in such a way that the entire liquid column would rest inside the 5% region. Because a dipper is used for these measurements, it is necessary to correct for the measurement. When the response is corrected with the fit from the isosensitivity, the results will show a constant value over the volume.

The same change is seen with a copper sleeve is the chamber. A different variation is seen in the 1 ml syringe were the activity drops in the first dilution but the variation after this jump is the same as the other syringes, which can indicate that during the first measurement, an elevated background was present. The influence of the volume on the measurement of ^{99m}Tc while using the copper sleeve is lower in magnitude than the influence without the copper sleeve.

No pure negative beta-emitters are evaluated in this thesis but are important in isotope therapies and will therefore be mentioned. Proper measurement of the activity is important for the safe and accurate dosing in these therapies. Siegel et al. recommend that a single calibrated dial setting is determined individually and says that volume correction factors should not be necessary when measuring the activity of Y-90-ibritumomab tiuxetan. [27]

6.4 Influence of the recipient

When measuring a sample from a stock solution, the apparent activity in a vial is often not the same as the apparent activity in a syringe. This is previously concluded during measurements and other experiments and confirmed by the results in this thesis. Due to attenuation, scatter and bremsstrahlung the measurement is influenced by the container wall, which is different in

the different recipients. It is chosen that the reference value is determined with the gamma counter using the conversion factor calculated during the experiments of Carbutti et al. [20] The method for the determination of the reference value is explained in chapter 3. From the results, it becomes clear that correction factors are needed. The correction factors for the used recipients are given in table 6.3a and table 6.3b. The corrections also differ for recipients of the same material and manufacturer in relation with the size of the container, this is due the little differences in the container wall together with deviations due to the position in the chamber. The difference in correction can be related to the energy of the emitted photons. The isotopes ^{123}I and ^{111}In have an emission that contains low energy X-rays. These X-rays are attenuated more in the vial than in the syringe causing a large reduction when the sample is measured in a vial. The correction for ^{18}F is given but is not necessary because the values are within the range determined by the regulatory standards. The correction for the TERUMO syringe is however strongly recommended because the deviation is 5%. Any influence of the background for example can cause the deviation to exceed the regulatory standard. The isotope ^{99m}Tc is overestimated in all recipients but the range is small, this gives the opportunity to generalize the correction to 0,93. This is sufficient to meet the standards required by the FANC. For the ^{111}In and ^{123}I the correction factors given in the table must be used to comply with the standards maintained by the FANC.

When using the copper sleeve, the results show a large reduction in the activity. This is due to the attenuation of the copper sleeve. The use of the copper sleeve becomes interesting when looking at the range of the corrections or deviations in chapter 4. For the isotopes that are influenced by the container type, ^{111}In and ^{123}I, the range becomes smaller which indicates that the influence of the container type is much lower. The influence on the other radionuclides, ^{99m}Tc and ^{18}F is not sufficient to conclude that the copper sleeve will influence the measurement in a positive way.

Table 6.3: Recommended correction factors for the isotopes: ^{111}In, ^{123}I, ^{99m}Tc and ^{18}F

(a) Without copper sleeve

	^{111}In	^{123}I	^{99m}Tc	^{18}F
terumo	0,84	0,87	1,15	1,05
BD 3ml	0,89	0,85	1,13	1,00
BD 5ml	0,89	0,87	1,13	0,96
BD 10ml	0,93	0,89	1,07	0,97
vial	1,09	1,29	0,94	1,05

(b) With the copper sleeve

	^{111}In	^{123}I	^{99m}Tc	^{18}F
terumo	1,77	3,84	1,51	1,13
BD 3 ml	1,81	3,87	1,49	1,07
BD 5 ml	1,78	3,79	1,48	1,02
BD 10 ml	1,84	3,83	1,48	1,03
vial	1,91	4,40	1,55	1,13

Because it is not practicable and time consuming to search, calculate and apply for every measurement the correction needed to determine the true activity, the copper sleeve can be useful to narrow the number of corrections for ^{111}In and ^{123}I using a mean correction factor. For measurements of ^{111}In this means that a correction factor 1,81 is applied on the measurements (table 6.4). All the apparent activities are corrected within the maximum deviation of $\pm$ 5%. Hence it can be concluded that the corrections for the influence of the recipient in the measurement of ^{111}In can be narrowed to the correction factor 1,81 when the copper sleeve is used. For ^{123}I the mean correction factor is 3,80. Applying this correction to the measurements results in an apparent activity in syringes deviation less than 5% but the apparent activity still needs to be corrected with a factor 1,12. (Table 6.4) Hence for ^{123}I there are 2 correction factors

needed 3,80 for the syringes and 4,36 for the vial. When applying a mean correction factor to the results without the copper sleeve, the apparent activities still show a range that is too wide. Hence this method can only be applied when the copper sleeve is used.

Table 6.4: ratio of apparent activity using the copper sleeve and reference activity after correcting with the mean correction factor (1,81 for ^{111}In and 3,80 for ^{123}I)

	^{111}In	^{123}I
terumo	1,03	1,00
BD 3ml	1,01	0,99
BD 5ml	1,02	1,01
BD 10ml	0,99	1,00
vial	0,95	0,87

Chapter 7

Conclusion

The nuclear medicine department uses radioactive isotopes for diagnosing or treating cancer. The activity of the isotope is measured before administration with the activity meter. During experiments and accuracy evaluations, it occurred that a deviation is seen that exceeded the maximum 5% regulatory standard. Which was mainly due to a change in geometry. This thesis determined the influence of 3 geometric factors on the response of the activity meter: the volume, the container and the position in the ionisation chamber.

For the influence of the position, the isosensitivity was measured of the ionisation chamber which resulted in 2 regions: one region where the deviation was maximum 5% which was the area between the bottom and 14 cm above the bottom and one region where the deviation was lower than 10%, the area between the bottom and 17 cm high. The dipper holds the syringes at a height of 17,5 cm. Hence the liquid column is placed mainly in the region between the 5% and 10% mark. It is therefore suggested to adjust the dipper to locate the full liquid column inside the 5% region. Because the dipper is a standard device, a correction of the result can be made using the regression executed in this thesis. The formula gives opportunity to correct for the position in the chamber so the deviation due to position is maximum $\pm$ 2% between the bottom and 23 cm height.

For the volume sensitivity, it can be concluded from the results that the main influence is due to the isosensitivity. In the test for volume sensitivity in a vial the change never causes the activity to exceeds a 5% deviation. For the isotope ^{123}I however is the deviation 5% when the vial is completely filled, this is the limit demanded by the FANC and thus no correction should be applied.

The influence of the recipient has, as predicted from the literature, the biggest influence on the apparent activity. For each recipients evaluated in this thesis is a correction given. Because searching and calculating the correction for each recipient is unpracticable and time consuming, it is tried narrow the number of correction factors. The deviation in the measurements of ^{18}F never exceeds the 5% deviation limit and therefore no correction is needed. The apparent activity of the ^{99m}Tc solution is overestimated in each recipient. When correcting with a factor 1,0694 all the results will be within the demanded $\pm$ 5%. For ^{123}I and ^{111}In is the variation in syringes and vials remarkable and the corrections are certainly needed. The option to use the copper sleeve is evaluated and from the measurements,the conclusion can be drawn that measuring ^{111}In using a copper sleeve will need only the correction factor, 1,81, to convert the values within the accepted range. For ^{123}I the copper sleeve did not result in an uniform correction but gave a more uniform result for the syringes. It is therefore recommended to measure ^{123}I with the

copper sleeve with the correction factors of 3,80 and 4,36 for the syringes and vials respectively. The gamma counter is used as a internal reference during this thesis and could be used in the future as an internal reference for the activity meters and to check the their accuracy. It is therefore recommended to implement a QA/QC program similar to the one described in this thesis. The gamma counter measures CPM instead of Bq. Using the Fidelis activity meter the conversion is calculated for ^{18}F and ^{99m}Tc, values for ^{123}I and ^{111}In are determined using the manual. The conversion factors are for ^{123}I 0,0208 Bq/CPM, for ^{111}In 0,0201 Bq/CPM, for ^{99m}Tc 0,0328 Bq/CPM and for ^{18}F 0,0500 Bq/CPM. Other conversion factors can be calculating by making a stock solution which is measured in the Fidelis activity meter and in the gamma counter.

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Appendix

A Reproducibility

Table 1: values for the reproducibility without re-entering the source in the CRC-15R in MBq

	Cs137	^{133}Ba	^{60}Co	^{57}Co	^{123}I	^{111}In	^{99m}Tc	^{18}F
1	7,98	8,13	1,703	83,6	26	23,3	10,68	45,7
2	7,97	8,17	1,678	83,5	25,9	23,3	10,7	45,7
3	7,96	8,15	1,699	83,7	26	23,2	10,67	45,7
4	8,02	8,13	1,703	83,5	25,9	23,3	10,69	45,7
5	7,96	8,13	1,71	83,4	26	23,3	10,68	45,6
6	7,93	8,15	1,705	83,7	26	23,3	10,7	45,6
7	7,96	8,1	1,72	83,5	25,9	23,3	10,68	45,5
8	7,9	8,14	1,703	83,5	25,9	23,2	10,68	45,6
9	8,01	8,15	1,711	83,4	25,9	23,3	10,66	45,5
10	7,88	8,13	1,697	83,6	25,9	23,3	10,69	45,5
Mean	7,96	8,14	1,70	83,54	25,94	23,28	10,68	45,61
Deviation	0,044	0,019	0,011	0,107	0,052	0,042	0,013	0,088
Rel. dev	0,55%	0,23%	0,64%	0,13%	0,20%	0,18%	0,12%	0,19%

Table 2: values for the reproducibility with re-entering the source in the CRC-15R in MBq

	^{137}Cs	^{133}Ba	^{60}Co	^{57}Co	^{123}I	^{111}In	^{99m}Tc	^{18}F
1	8	8,1	1,703	83,4	25,9	23,3	10,52	43,7
2	7,79	8,14	1,717	84,4	26,2	23,3	10,48	43,7
3	8,05	8,13	1,702	83,7	26,5	23,9	10,39	43,6
4	8,06	8,55	1,687	80,9	26,8	23,4	10,84	44,9
5	8,29	8,1	1,7	83,4	26,4	23,6	10,57	43,5
6	7,97	8,15	1,69	83,6	25,8	23,4	10,5	43,9
7	7,93	8,27	1,707	83,3	25,8	23,5	10,55	43,3
8	8,05	8,08	1,701	83,7	26,2	23,3	10,51	43,2
9	7,97	8,1	1,726	83,5	25,9	23,3	10,49	43,1
10	7,99	8,13	1,802	83,6	26,2	23,6	10,53	43,2
Mean	8,01	8,18	1,71	83,35	26,17	23,46	10,54	43,61
Deviation	0,119	0,135	0,031	0,866	0,313	0,185	0,111	0,497
rel. Dev	1,49%	1,65%	1,83%	1,04%	1,20%	0,79%	1,05%	1,14%

Table 3: values for the reproducibility without re-entering the source in the CRC-35R in MBq

	^{137}Cs	^{133}Ba	^{60}Co	^{57}Co	^{123}I	^{111}In	^{99m}Tc	^{18}F
1	8,1	9,5	1,7	84	25,3	23	10,63	45,6
2	8,1	9,5	1,7	83,9	25,3	22,9	10,7	45,6
3	8,1	9,5	1,7	84	25,3	23	10,68	45,6
4	8,1	9,5	1,7	84,1	25,2	22,8	10,77	45,5
5	8,0	9,5	1,7	84	25,4	23	10,7	45,5
6	8,1	9,5	1,7	84	25,2	22,9	10,62	45,4
7	8,1	9,5	1,7	84,1	25,3	23	10,65	45,4
8	8,1	9,5	1,7	83,9	25,3	22,9	10,74	45,3
9	8,1	9,5	1,7	84	25,3	22,8	10,61	45,4
10	8,1	9,5	1,7	83,9	25,2	23	10,67	45,3
Mean	8,09	9,50	1,70	83,99	25,28	22,93	10,68	45,46
Deviation	0,032	0,000	0,000	0,074	0,063	0,082	0,052	0,117
rel. Dev	0,39%	0,00%	0,00%	0,09%	0,25%	0,36%	0,49%	0,26%

Table 4: values for the reproducibility with reentering the source in the CRC-35R in MBq

	^{137}Cs	^{133}Ba	^{60}Co	^{57}Co	^{123}I	^{111}In	^{99m}Tc	^{18}F
1	8	9,5	1,7	84,2	25,3	23	10,44	43,1
2	7,95	10,09	1,7	84	25,2	23	10,54	43,2
3	8,02	9,4	1,8	80,3	25,3	23,3	10,54	42,8
4	7,93	9,48	1,6	87,8	25,4	23	10,49	43,7
5	7,83	9,58	1,8	84,4	25,7	23,2	10,67	43,9
6	7,92	9,5	1,7	83,7	25,9	23	10,44	43,4
7	7,96	9,49	1,7	84	25,2	22,9	10,51	43,3
8	8,43	9,52	1,7	84,4	25,2	22,9	10,68	42,8
9	7,93	9,49	1,7	84	25,3	22,8	10,46	42,6
10	7,96	9,51	1,7	83,9	25,2	23,2	10,39	42,4
Mean	7,99	9,56	1,71	84,07	25,37	23,03	10,52	43,12
Deviation	0,153	0,183	0,054	1,689	0,228	0,149	0,091	0,453
rel. Dev	1,92%	1,91%	3,15%	1,98%	0,90%	0,65%	0,87%	1,05%

B Isosensitivity

Table 5: values for the depth profile of CRC-15R

distance (cm)	date and time	app. activity (MBq)	corr. activity (MBq)	relative activity
0	16:45:05	6	6,00	95,13%
1	16:46:50	5,98	6,00	95,13%
2	16:47:25	6,02	6,05	95,87%
3	16:47:45	6,07	6,10	96,73%
4	16:48:05	6,11	6,15	97,43%
5	16:48:20	6,16	6,20	98,28%
6	16:48:45	6,2	6,24	98,99%
7	16:49:05	6,21	6,26	99,22%
8	16:49:20	6,23	6,28	99,58%
9	16:49:50	6,25	6,31	100,00%
10	16:50:15	6,19	6,25	99,12%
11	16:50:40	6,16	6,23	98,72%
12	16:51:10	6,12	6,19	98,17%
13	16:51:45	6,05	6,13	97,16%
14	16:52:00	5,95	6,03	95,60%
15	16:52:20	5,85	5,93	94,05%
16	16:52:35	5,74	5,82	92,33%
17	16:53:00	5,54	5,63	89,18%
18	16:53:15	5,33	5,42	85,84%
19	16:53:35	5,06	5,14	81,55%
20	16:53:50	4,74	4,82	76,43%
21	16:54:05	4,37	4,45	70,49%
22	16:54:30	3,96	4,03	63,93%
23	16:54:50	3,48	3,55	56,22%
24	16:55:10	2,85	2,91	46,07%
25	16:55:20	2,83	2,89	45,76%
26	16:55:40	2,33	2,38	37,70%
27	16:56:00	1,82	1,86	29,47%

Table 6: values for the depth profile of the Capintec CRC-35R

distance (cm)	date and time	app. activity (MBq)	corr. activity (MBq)	relative activity
0	16:59:00	5,91	6,07	96,54%
1	16:59:20	5,9	6,06	96,43%
2	17:00:00	5,91	6,08	96,72%
3	17:00:40	5,91	6,09	96,85%
4	17:01:10	5,98	6,17	98,09%
5	17:01:30	6,03	6,22	98,97%
6	17:01:45	6,05	6,25	99,35%
7	17:02:05	6,08	6,28	99,90%
8	17:02:35	6,08	6,29	100,00%
9	17:02:55	6,06	6,27	99,73%
10	17:03:15	6,03	6,25	99,30%
11	17:03:35	6,02	6,24	99,20%
12	17:04:00	5,91	6,13	97,47%
13	17:04:15	5,85	6,07	96,53%
14	17:04:30	5,78	6,00	95,42%
15	17:04:50	5,66	5,88	93,50%
16	17:05:05	5,54	5,76	91,56%
17	17:05:25	5,38	5,60	88,97%
18	17:05:45	5,19	5,40	85,88%
19	17:06:00	4,98	5,19	82,45%
20	17:06:15	4,66	4,85	77,19%
21	17:06:30	4,33	4,51	71,76%
22	17:06:55	3,92	4,09	65,01%
23	17:07:20	3,44	3,59	57,10%
24	17:07:40	2,9	3,03	48,17%
25	17:07:55	2,32	2,42	38,55%
26	17:08:25	1,804	1,89	30,01%
27	17:09:25	1,616	1,69	26,93%

Table 7: values for the depth profile of the Veenstra VIK-202

distance (cm)	date and time	app. activity (MBq)	corr. activity (MBq)	relative activity
0	16:10:00	7,474	7,47	95,55%
1	16:10:25	7,589	7,60	97,10%
2	16:10:55	7,612	7,63	97,49%
3	16:11:20	7,538	7,56	96,62%
4	16:11:40	7,613	7,64	97,64%
5	16:12:05	7,646	7,68	98,14%
6	16:12:20	7,621	7,66	97,87%
7	16:12:45	7,645	7,69	98,26%
8	16:13:15	7,771	7,82	99,97%
9	16:13:40	7,767	7,82	100,00%
10	16:14:10	7,592	7,65	97,84%
11	16:14:30	7,641	7,71	98,54%
12	16:14:50	7,526	7,60	97,11%
13	16:15:10	7,483	7,56	96,62%
14	16:15:30	7,368	7,45	95,20%
15	16:15:50	7,214	7,30	93,27%
16	16:16:05	7,067	7,15	91,41%
17	16:16:25	6,88	6,97	89,05%
18	16:16:45	6,652	6,74	86,15%
19	16:17:05	6,333	6,42	82,07%
20	16:17:20	5,998	6,08	77,77%
21	16:17:40	5,616	5,70	72,86%
22	16:18:00	5,129	5,21	66,59%
23	16:18:20	4,547	4,62	59,07%
24	16:18:40	3,949	4,02	51,33%
25	16:19:00	3,313	3,37	43,09%
26	16:20:05	2,785	2,84	36,30%
27	16:20:25	2,249	2,29	29,33%
28	16:20:45	1,822	1,86	23,78%

C Volume sensitivity

C.1 vial

Table 8: Table of results from volume dependence experiment in a vial with ^{18}F (reference time: 11/05/17 09:00)

volume (ml)	date and time	app. activity (MBq)	corr. activity (MBq)	relative activity
0	11/05/17 10:35	439	800,03	100,00%
0,5	11/05/17 10:42	419	798,94	99,86%
1	11/05/17 10:44	411	797,00	99,62%
1,5	11/05/17 10:49	400	796,36	99,54%
2	11/05/17 10:54	387	796,46	99,55%
2,5	11/05/17 10:56	382	796,58	99,57%
3	11/05/17 11:00	372	795,58	99,44%
3,5	11/05/17 11:02	366	794,38	99,29%
4	11/05/17 11:06	358	795,22	99,40%
4,5	11/05/17 11:08	352	793,09	99,13%
5	11/05/17 11:14	340	794,39	99,30%
5,5	11/05/17 11:17	332	791,79	98,97%
6	11/05/17 11:21	325	792,00	99,00%
6,5	11/05/17 11:23	320	793,90	99,23%
7	11/05/17 11:27	313	793,48	99,18%
7,5	11/05/17 11:29	309	795,39	99,42%
8	11/05/17 11:33	300	793,24	99,15%
8,5	11/05/17 11:35	297	794,03	99,25%
9	11/05/17 11:38	292	793,93	99,24%
9,5	11/05/17 11:40	289	794,09	99,26%

Table 9: Table of results from volume dependence experiment in a vial with ^{18}F using the copper sleeve (reference time: 11/05/17 09:00)

volume (ml)	date and time	app. activity (MBq)	corr. activity (MBq)	relative activity
0	11/05/17 10:35	404	740,13	1,00
0,5	11/05/17 10:41	389	739,40	1,00
1	11/05/17 10:45	378	737,65	1,00
1,5	11/05/17 10:48	372	735,95	0,99
2	11/05/17 10:52	362	734,88	0,99
2,5	11/05/17 10:57	350	734,09	0,99
3	11/05/17 10:59	346	736,87	1,00
3,5	11/05/17 11:03	337	734,52	0,99
4	11/05/17 11:05	332	735,14	0,99
4,5	11/05/17 11:09	324	733,08	0,99
5	11/05/17 11:12	318	733,27	0,99
5,5	11/05/17 11:18	306	732,47	0,99
6	11/05/17 11:20	302	733,63	0,99
6,5	11/05/17 11:24	294	732,48	0,99
7	11/05/17 11:26	291	733,45	0,99
7,5	11/05/17 11:31	282	732,03	0,99
8	11/05/17 11:33	279	734,22	0,99
8,5	11/05/17 11:36	274	734,86	0,99
9	11/05/17 11:37	271	733,73	0,99
9,5	11/05/17 11:40	267	735,96	0,99

Table 10: Table of results from volume dependence experiment in a vial with ^{123}I (reference time:20/12/16 18:00)

volume (ml)	date and time	app. activity (MBq)	corr. activity (MBq)	relative activity
0	20/12/16 15:35	24,7	21,77	100,00%
0,5	20/12/16 15:45	24,7	21,95	100,83%
1	20/12/16 15:47	24,7	22,01	101,08%
1,5	20/12/16 15:52	24,8	22,19	101,92%
2	20/12/16 15:55	24,8	22,24	102,14%
2,5	20/12/16 15:59	24,8	22,33	102,55%
3	20/12/16 16:01	24,9	22,46	103,15%
3,5	20/12/16 16:05	24,9	22,53	103,47%
4	20/12/16 16:08	24,9	22,59	103,74%
4,5	20/12/16 16:12	24,9	22,66	104,09%
5	20/12/16 16:13	24,9	22,69	104,23%
5,5	20/12/16 16:17	24,9	22,77	104,56%
6	20/12/16 16:19	25	22,89	105,14%
6,5	20/12/16 16:22	24,9	22,88	105,07%
7	20/12/16 16:24	24,9	22,91	105,21%
7,5	20/12/16 16:28	24,9	22,99	105,58%
8	20/12/16 16:36	24,7	22,96	105,44%
8,5	20/12/16 16:39	24,7	23,03	105,76%
9	20/12/16 16:42	24,6	22,98	105,56%
9,5	20/12/16 16:46	24,5	22,97	105,50%
10	20/12/16 16:49	24,4	22,95	105,41%

Table 11: Table of results from volume dependence experiment in a vial with ^{111}In (reference time:24/11/16 18:00)

volume (ml)	date and time	app. activity (MBq)	corr. activity (MBq)	relative activity
0	23/11/16 16:19	23,4	17,95	100,00%
0,5	23/11/16 16:23	23,4	17,97	100,08%
1	23/11/16 16:25	23,4	17,98	100,12%
1,5	23/11/16 16:27	23,5	18,06	100,58%
2	23/11/16 16:29	23,5	18,06	100,61%
2,5	23/11/16 16:31	23,5	18,07	100,64%
3	23/11/16 16:33	23,6	18,15	101,10%
3,5	23/11/16 16:35	23,6	18,16	101,15%
4	23/11/16 16:38	23,6	18,17	101,19%
4,5	23/11/16 16:39	23,7	18,25	101,65%
5	23/11/16 16:41	23,6	18,18	101,25%
5,5	23/11/16 16:44	23,7	18,26	101,72%
6	23/11/16 16:45	23,6	18,19	101,32%
6,5	23/11/16 16:47	23,6	18,20	101,36%
7	23/11/16 16:49	23,6	18,20	101,39%
7,5	23/11/16 16:54	23,6	18,22	101,46%
8	23/11/16 16:55	23,6	18,22	101,50%
8,5	23/11/16 16:57	23,6	18,23	101,53%
9	23/11/16 17:00	23,6	18,24	101,58%
9,5	23/11/16 17:03	23,5	18,17	101,20%
10	23/11/16 17:05	23,5	18,18	101,23%

Table 12: Table of results from volume dependence experiment in a vial with ^{99m}Tc (reference time:31/03/17 09:00)

volume (ml)	date and time	app. activity (MBq)	corr. activity (MBq)	relative activity
0	11/05/17 10:35	439	800,03	100,00%
0,5	11/05/17 10:42	419	798,94	99,86%
1	11/05/17 10:44	411	797,00	99,62%
1,5	11/05/17 10:49	400	796,36	99,54%
2	11/05/17 10:54	387	796,46	99,55%
2,5	11/05/17 10:56	382	796,58	99,57%
3	11/05/17 11:00	372	795,58	99,44%
3,5	11/05/17 11:02	366	794,38	99,29%
4	11/05/17 11:06	358	795,22	99,40%
4,5	11/05/17 11:08	352	793,09	99,13%
5	11/05/17 11:14	340	794,39	99,30%
5,5	11/05/17 11:17	332	791,79	98,97%
6	11/05/17 11:21	325	792,00	99,00%
6,5	11/05/17 11:23	320	793,90	99,23%
7	11/05/17 11:27	313	793,48	99,18%
7,5	11/05/17 11:29	309	795,39	99,42%
8	11/05/17 11:33	300	793,24	99,15%
8,5	11/05/17 11:35	297	794,03	99,25%
9	11/05/17 11:38	292	793,93	99,24%
9,5	11/05/17 11:40	289	794,09	99,26%

Table 13: Table of results from volume dependence experiment in a vial with ^{99m}Tc using the copper sleeve (reference time: 31/03/17 09:00)

volume (ml)	date and time	app. activity (MBq)	corr. activity (MBq)	relative activity
0	10:31:40	136,5	162,75	1,0000
0,5	10:34:50	135,6	162,67	0,9995
1	10:40:50	134,2	162,85	1,0006
1,5	10:42:45	133,7	162,84	1,0005
2	10:46:20	132,8	162,86	1,0007
2,5	10:48:50	132,3	163,03	1,0017
3	10:51:20	131,8	163,19	1,0027
3,5	10:53:05	131,5	163,37	1,0038
4	10:56:25	130,8	163,54	1,0049
4,5	11:00:30	129,8	163,57	1,0050
5	11:02:35	129,4	163,72	1,0059
5,5	11:04:55	128,9	163,82	1,0065
6	11:06:40	128,5	163,86	1,0068
6,5	11:09:10	128	164,01	1,0077
7	11:10:35	127,8	164,20	1,0089
7,5	11:13:40	127,1	164,27	1,0093
8	11:15:30	126,7	164,33	1,0097
8,5	11:18:30	126,1	164,49	1,0107

C.2 syringe

Table 14: Table of results from volume dependence experiment in a 10 ml BD syringe with ^{99m}Tc

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
15:18:50	9,1811	0,98	0,59	142,82	295,47	1,0000
15:21:40	10,2356	2,04	1,22	142,07	295,52	1,0002
15:23:20	11,0985	2,90	1,74	141,58	295,45	0,9999
15:26:55	12,1551	3,96	2,38	140,52	295,26	0,9993
15:30:00	13,0489	4,85	2,91	139,64	295,15	0,9989
15:31:50	14,157	5,96	3,58	139,09	295,02	0,9985
15:37:05	15,8372	7,64	4,58	137,37	294,33	0,9961
15:39:05	16,7688	8,57	5,14	136,57	293,74	0,9941
15:41:30	17,789	9,59	5,76	135,69	293,20	0,9923

Table 15: Table of results from volume dependence experiment in a 10 ml BD syringe with ^{99m}Tc using the copper sleeve

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
15:19:35	9,1811	0,98	0,59	88,6	183,56	1,0000
15:21:10	10,2356	2,04	1,22	88,45	183,81	1,0013
15:24:30	11,0985	2,90	1,74	87,93	183,90	1,0018
15:27:50	12,1551	3,96	2,38	87,53	184,24	1,0037
15:29:25	13,0489	4,85	2,91	87,19	184,08	1,0028
15:32:20	14,157	5,96	3,58	86,71	184,10	1,0029
15:33:45	15,0086	6,81	4,09	86,43	184,00	1,0024
15:35:55	15,8372	7,64	4,58	85,94	183,72	1,0009
15:39:40	16,7688	8,57	5,14	85,21	183,48	0,9995
15:41:00	17,789	9,59	5,76	84,84	183,15	0,9977

Table 16: Table of results from volume dependence experiment in a 10 ml BD syringe with ^{99m}Tc (2)

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
15:53:05	9,181	0,88	0,53	120,66	266,58	1,0000
15:56:45	10,226	1,93	1,16	119,71	266,35	0,9991
15:58:00	11,0111	2,71	1,63	119,51	266,55	0,9999
16:00:40	11,979	3,68	2,21	118,96	266,68	1,0004
16:03:00	13,0928	4,80	2,88	118,30	266,39	0,9993
16:06:10	14,0247	5,73	3,44	117,55	266,32	0,9990
16:07:30	14,8783	6,58	3,95	117,07	265,91	0,9975
16:10:30	16,68	8,38	5,03	116,18	265,41	0,9956
16:11:30	17,0793	8,78	5,27	115,79	265,03	0,9942
16:13:55	17,9822	9,69	5,81	115,05	264,56	0,9924

Table 17: Table of results from volume dependence experiment in a 10 ml BD syringe with ^{99m}Tc using the copper sleeve(2)

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
15:54:45	9,181	0,88	0,53	74,88	165,97	1,0000
15:55:30	10,226	1,93	1,16	74,84	166,12	1,0009
15:58:45	11,0111	2,71	1,63	74,42	166,22	1,0015
16:00:10	11,979	3,68	2,21	74,16	166,09	1,0007
16:04:00	13,0928	4,80	2,88	73,72	166,32	1,0021
16:05:30	14,0247	5,73	3,44	73,43	166,15	1,0011
16:08:00	14,8783	6,58	3,95	73,03	166,04	1,0004
16:10:00	16,68	8,38	5,03	72,65	165,81	0,9990
16:12:00	17,0793	8,78	5,27	72,37	165,80	0,9990
16:13:25	17,9822	9,69	5,81	71,97	165,34	0,9962

Table 18: Table of results from volume dependence experiment in a 5 ml BD syringe with ^{99m}Tc

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
14:42:50	6,204	0,64	2,46	99,44	191,99	1,0000
14:46:10	6,839	1,27	3,02	98,71	191,81	0,9990
14:47:50	7,3351	1,77	3,46	98,34	191,70	0,9985
14:52:00	7,876	2,31	3,93	97,35	191,29	0,9964
14:54:15	8,4493	2,88	4,44	96,74	190,92	0,9944
14:58:00	8,9884	3,42	4,91	95,97	190,76	0,9936
14:59:50	9,4772	3,91	5,34	95,51	190,52	0,9923
15:04:00	10,2103	4,64	5,99	94,48	189,98	0,9895

Table 19: Table of results from volume dependence experiment in a 5 ml BD syringe with ^{99m}Tc using the copper sleeve

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
14:43:35	6,204	0,64	2,46	62,02	119,92	1,0000
14:45:50	6,839	1,27	3,02	61,89	120,18	1,0022
14:49:20	7,3351	1,77	3,46	61,47	120,17	1,0021
14:51:05	7,876	2,31	3,93	61,18	120,01	1,0008
14:55:10	8,4493	2,88	4,44	60,7	120,00	1,0007
14:56:45	8,9884	3,42	4,91	60,36	119,69	0,9981
15:00:40	9,4772	3,91	5,34	59,92	119,72	0,9983
15:03:15	10,2103	4,64	5,99	59,35	119,17	0,9938

Table 20: Table of results from volume dependence experiment in a 3 ml BD syringe with ^{99m}Tc

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
14:18:00	4,1605	0,38	2,14	61,38	112,99	1,0000
14:21:15	4,5715	0,79	2,84	60,97	112,94	0,9995
14:24:10	4,9774	1,19	3,53	60,51	112,72	0,9976
14:27:20	5,3542	1,57	4,17	60,02	112,49	0,9955
14:29:10	5,7235	1,94	4,80	59,74	112,36	0,9944
14:32:00	6,1103	2,33	5,46	59,25	112,04	0,9916
14:34:20	6,6026	2,82	6,29	58,82	111,73	0,9888

Table 21: Table of results from volume dependence experiment in a 3 ml BD syringe with ^{99m}Tc using the copper sleeve

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
14:18:55	4,1605	0,38	2,14	38,53	71,05	1,0000
14:21:55	4,5715	0,79	2,84	38,36	71,15	1,0013
14:24:50	4,9774	1,19	3,53	38,04	70,95	0,9986
14:26:30	5,3542	1,57	4,17	37,88	70,88	0,9975
14:29:45	5,7235	1,94	4,80	37,6	70,80	0,9964
14:31:25	6,1103	2,33	5,46	37,43	70,70	0,9950
14:35:05	6,6026	2,82	6,29	37,06	70,50	0,9922

Table 22: Table of results from volume dependence experiment in a 1 ml BD syringe with ^{99m}Tc

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
13:43:55	2,9250	0,13	0,54	22,52	38,83	1,0000
13:48:55	3,0239	0,23	1,10	22,33	38,88	1,0011
13:50:10	3,2229	0,43	2,23	22,22	38,78	0,9986
13:55:05	3,4216	0,63	3,37	21,93	38,63	0,9949
13:59:45	3,6311	0,84	4,56	21,61	38,41	0,9892
14:01:20	3,8480	1,05	5,80	21,33	38,03	0,9793

Table 23: Table of results from volume dependence experiment in a 1 ml BD syringe with ^{99m}Tc using the copper sleeve

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
13:44:55	2,9250	0,13	0,54	14,21	24,55	1,0000
13:48:20	3,0239	0,23	1,10	14,09	24,50	0,9981
13:50:50	3,2229	0,43	2,23	13,99	24,45	0,9958
13:55:50	3,4216	0,63	3,37	13,82	24,38	0,9931
13:58:15	3,6311	0,84	4,56	13,69	24,26	0,9884
14:02:05	3,8480	1,05	5,80	13,48	24,07	0,9804

Table 24: Table of results from volume dependence experiment in a 10 ml BD syringe with ^{18}F

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
15:50:30	9,1856	1,02	0,6117	63,10	843,85	1,0000
15:54:25	10,0839	1,92	1,15068	61,40	841,68	0,9974
15:55:45	10,9296	2,76	1,6581	60,8	840,51	0,9960
15:59:40	12,0412	3,88	2,32506	59,2	838,89	0,9941
16:01:55	13,2664	5,10	3,06018	58,30	837,97	0,9930
16:05:00	13,9744	5,81	3,48498	57,1	836,86	0,9917
16:06:20	15,7253	7,56	4,53552	56,4	833,59	0,9878
16:08:45	16,0768	7,91	4,74642	55,5	832,91	0,9870
16:10:35	17,2498	9,08	5,45022	54,9	833,50	0,9877
16:12:55	18,1269	9,96	5,97648	53,9	830,47	0,9841

Table 25: Table of results from volume dependence experiment in a 10 ml BD syringe with ^{18}F using the copper sleeve

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
15:51:10	9,1856	1,02	0,6117	58,9	791,01	1,00
15:53:55	10,0839	1,92	1,15068	57,70	788,47	1,00
15:56:15	10,9296	2,76	1,6581	56,8	787,70	1,00
15:59:10	12,0412	3,88	2,32506	55,7	786,81	0,99
16:02:30	13,2664	5,10	3,06018	54,3	783,35	0,99
16:04:20	13,9744	5,81	3,48498	53,6	782,26	0,99
16:06:40	15,7253	7,56	4,53552	52,8	782,03	0,99
16:08:20	16,0768	7,91	4,74642	52,1	779,83	0,99
16:11:05	17,2498	9,08	5,45022	51,1	778,27	0,98
16:12:25	18,1269	9,96	5,97648	50,6	777,17	0,98

Table 26: Table of results from volume dependence experiment in a 5 ml BD syringe with ^{18}F

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
15:15:35	6,1194	0,47	2,31	36,2	388,28	1,0000
15:18:50	6,4273	0,78	2,58	35,4	387,58	0,9982
15:20:25	6,7752	1,12	2,89	35	387,05	0,9968
15:23:05	7,1779	1,53	3,24	34,4	386,88	0,9964
15:24:40	7,5610	1,91	3,58	34	386,22	0,9947
15:27:20	7,9995	2,35	3,97	33,4	385,85	0,9937
15:28:40	8,4647	2,81	4,38	33,1	385,62	0,9931
15:31:30	8,8650	3,21	4,73	32,4	384,28	0,9897
15:32:50	9,2912	3,64	5,10	32,1	383,95	0,9888
15:35:55	9,7236	4,07	5,48	31,4	382,96	0,9863
15:37:30	10,1350	4,48	5,84	31	381,88	0,9835
15:40:00	10,6057	4,95	6,26	30,5	381,71	0,9831

Table 27: Table of results from volume dependence experiment in a 5 ml BD syringe with ^{18}F using the copper sleeve

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
15:16:05	6,1194	0,47	2,31	33,9	364,76	1,0000
15:17:55	6,4273	0,78	2,58	33,4	363,57	0,9967
15:20:55	6,7752	1,12	2,89	32,7	362,76	0,9945
15:22:20	7,1779	1,53	3,24	32,4	362,66	0,9942
15:25:10	7,5610	1,91	3,58	31,8	362,38	0,9935
15:26:45	7,9995	2,35	3,97	31,4	361,41	0,9908
15:29:25	8,4647	2,81	4,38	30,9	361,70	0,9916
15:30:50	8,8650	3,21	4,73	30,5	360,23	0,9876
15:33:30	9,2912	3,64	5,10	30	360,34	0,9879
15:35:25	9,7236	4,07	5,48	29,6	359,87	0,9866
15:38:00	10,1350	4,48	5,84	29	358,38	0,9825
15:39:35	10,6057	4,95	6,26	28,7	358,23	0,9821

Table 28: Table of results from volume dependence experiment in a 3 ml BD syringe with ^{18}F

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
14:19:30	4,0373	0,21	1,86	23,9	179,87	1,0000
14:22:15	4,2322	0,41	2,20	23,5	179,96	1,0005
14:28:35	4,4436	0,62	2,55	22,5	179,34	0,9970
14:33:00	4,6473	0,82	2,90	21,9	179,50	0,9979
14:35:25	4,8422	1,02	3,23	21,5	178,93	0,9947
14:38:35	5,0514	1,23	3,59	21,1	179,15	0,9960
14:40:20	5,2358	1,41	3,90	20,8	178,56	0,9927
14:43:00	5,4199	1,60	4,21	20,4	178,10	0,9902
14:48:05	5,7088	1,89	4,71	19,66	177,25	0,9854
14:50:50	5,8997	2,08	5,03	19,24	176,50	0,9812
14:52:35	6,1028	2,28	5,38	19,06	176,79	0,9829
14:55:30	6,3020	2,48	5,71	18,56	175,35	0,9749
14:57:25	6,4970	2,67	6,05	18,35	175,48	0,9756
14:59:35	6,6837	2,86	6,36	18,14	175,86	0,9777

Table 29: Table of results from volume dependence experiment in a 3 ml BD syringe with ^{18}F using the copper sleeve

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
14:20:10	4,0373	0,21	1,86	22,4	169,30	1,0000
14:21:45	4,2322	0,41	2,20	22,1	168,71	0,9965
14:29:15	4,4436	0,62	2,55	21,1	168,89	0,9976
14:31:15	4,6473	0,82	2,90	20,7	167,79	0,9911
14:35:55	4,8422	1,02	3,23	20,1	167,81	0,9912
14:37:50	5,0514	1,23	3,59	19,87	167,91	0,9918
14:40:55	5,2358	1,41	3,90	19,48	167,85	0,9914
14:42:20	5,4199	1,60	4,21	19,27	167,53	0,9896
14:47:25	5,7088	1,89	4,71	18,56	166,62	0,9842
14:53:20	6,1028	2,28	5,38	17,99	167,66	0,9903
14:55:00	6,3020	2,48	5,71	17,72	166,89	0,9858
14:58:05	6,4970	2,67	6,05	17,25	165,66	0,9785
15:00:15	6,6837	2,86	6,36	16,89	164,44	0,9713

Table 30: Table of results from volume dependence experiment in a 1 ml BD syringe with ^{18}F

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
13:41:55	2,9385	0,10	0,38	15,22	90,34	1,0000
13:44:10	3,0475	0,21	1,00	14,99	90,25	0,9990
13:49:00	3,1524	0,32	1,60	14,54	90,25	0,9990
13:51:50	3,2490	0,41	2,15	14,28	90,24	0,9989
13:55:45	3,3548	0,52	2,76	13,91	90,10	0,9974
13:57:35	3,4493	0,61	3,29	13,74	90,04	0,9967
14:01:25	3,5490	0,71	3,86	13,35	89,63	0,9921
14:04:00	3,6483	0,81	4,43	13,08	89,26	0,9881
14:09:20	3,8493	1,01	5,57	12,58	88,79	0,9828

Table 31: Table of results from volume dependence experiment in a 1 ml BD syringe with ^{18}F using the copper sleeve

time	weight(g)	volume(ml)	hoogte(cm)	activity(MBq)	corr. act.(MBq)	rel. act.
13:40:40	2,9385	0,10	0,38	14,66	86,33	1,0000
13:45:20	3,0475	0,21	1,00	13,94	84,55	0,9793
13:48:10	3,1524	0,32	1,60	13,71	84,65	0,9806
13:52:35	3,2490	0,41	2,15	13,32	84,57	0,9796
13:55:05	3,3548	0,52	2,76	13,08	84,37	0,9773
13:58:30	3,4493	0,61	3,29	12,79	84,30	0,9765
14:00:40	3,5490	0,71	3,86	12,61	84,26	0,9760
14:04:50	3,6483	0,81	4,43	12,22	83,83	0,9710
14:06:55	3,7511	0,91	5,01	12,01	83,48	0,9670
14:08:40	3,8493	1,01	5,57	11,86	83,36	0,9655

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