Determination of Residual Activity of 99 metastable Technetium (99mTc) in Urine Samples of Patients at University Teaching Hospital, Lusaka, Zambia.

By

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A Dissertation Submitted In Partial Fulfillment of the Requirements of the University of Zambia for the Award of Master of Science Degree in Clinical Pharmacy

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Notice

The practice of nuclear pharmacy is ever evolving and new research in nuclear isotopes is being expanded. This is broadening our existing knowledge on the safe use of radio isotopes both in diagnostic and therapeutic procedures. Therefore I, as the author of this work have checked with authorities and sources in the field of nuclear pharmacy in an effort to generate complete information that is up acceptable standards of pharmacy practice with regard to nuclear pharmacy. However, in view of the inevitable possibility of human error or changes in nuclear medicine sciences, I the author having been involved in the preparation of this research warrants that the information contained herein is in every aspect accurate or complete. I therefore disclaim all responsibility for any error or omissions whatsoever or for the results obtained from the use of all or part of the information contained herein. Readers are encouraged to confirm the information contained in this work with other reliable sources.

DECLARATION

I, **WINTER MUDENDA** hereby declare that the work on which this discussion is based is original, except where acknowledgement indicate otherwise.

Signed…….

Date: 8th August, 2014

Computer Number: **5831004849**

CERTIFICATE OF APPROVAL

The dissertation of WINTER MUDENDA has been approved as fulfilling the requirements for the award of Master's Degree in Clinical Pharmacy (Nuclear Pharmacy Specialty) by the University of Zambia.

Signature of examiner One……Date……..

Signature of examiner Two……Date……..

Signature of examiner Three……..... Date…….....

DEDICATION

To my late mom and dad who inspired in me a spirit of knowledge seeking and to my wife Loveness for putting up with the stress of this work.

ABSTRACT

INTRODUCTION

Ionizing radiation is the largest contributor to human exposure from manmade sources of radiation. Diagnostic and therapeutic procedures are routinely carried out in Zambia and patients are allowed home without measurement of the remaining amount of tracer in the body. Pharmacokinetic profiles of tracers in the body differ between individuals and in between 99metastable Technetium (99mTc) containing tracers. The pharmacokinetics of radioactive isotopes is dependent on the rate of decay which is characteristic to the isotope. Decay of radioactive elements in a biological system occurs by both biological and physical means and each of these have a distinct biological (T_b) and physical half-life (T_p). The effective half-life (T_e) is a combination of both the biological and physical half-lives. The effective half life is used to determine whether to allow home or to quarantine the patient after scanning with 99mTc containing tracers.

The aim of the study was to determine the residual activity of 99mTc in urine samples of patients at the University Teaching Hospital Department of Nuclear Medicine. The study also sought to establish whether the biological and effective half-life of 99mTc was affected when different pharmaceuticals were added to 99mTc for various scanning procedures.

METHODOLOGY

A prospective cross-sectional study that involved measuring amount of radioactivity from an on the spot urine sample of 22 patients with age ranging from 33 to 95 years who had just been scanned with 99mTc-MDP for bone metastases due to cancer of the prostate and cancer of the breast (15 males and 7 females respectively) and 13 patients (all females with age ranging from 22 to 51 years) scanned with sodium pertechnetate ($NaTcO_4^{-)}$ for thyroid disorders.

Pearson's correlation coefficient (r) was used to establish the relationship between independent and dependent variables (i.e. administered dose and biological and effective half life respectively).A p value < 0.05 was considered statistically significant.

PROCEDURE AND DATA COLLECTION

^{99m}Tc was eluted from the Molybdenum/Technetium generator and activity was measured after each elution. A pharmaceutical was added using aseptic technique according to the scan required i.e. methylene diphosphonate added to 99mTc solution, saline added to 99m-Tc solution and dimercapto succinic acid added to 99mTc solution. Patients were encouraged to hydrate before and after scanning process with 500-750ml of water. The activity to be administered was then withdrawn from the eluate vial and administered aseptically via the intravenous route.

Patients submitted on the spot urine samples immediately after each procedure and the activity measured instantly. Subsequent activity measurements were done at 30 minutes, 1 h, 1.5 h, 2 h, and 2.5 h using the same sample. Date of collection and volume of urine were also recorded.

Biological half-life was determined using the first order reaction equation;

$$T_b = 0.693 / k_d.$$

Where, T_b is the biological half-life and k_d is the biological decay constant obtained from the slope of the log activity vs. time curve which was linear. The slope which represented the decay constant (k_d) was determined from *x* and *y* values on the log (ln) residual activity vs. time graph as follows;

$$k_d = y_2 - y_1 / x_2 - x_1$$

Effective half-life was then calculated using the formula;

$$T_e = \frac{Tb \times Tp}{Tb + Tp}$$

RESULTS

The mean residual activity for 99m Tc-MDP and $NaTcO_4^-$ was (14.56 MBq and 3.84 respectively)

The mean administered dose of 99mTc-MDP was correlated with the mean biological half life T_b (r = 0.096) and mean effective half life T_e (r = -0.39). The mean administered dose of $NaTcO_4^-$ was correlated with mean biological half life T_b (r = 0.073) and mean effective half life T_e (r = 0.227).

The mean T_b of 99mTc-MDP (5.57 hrs, SD 0.962) was 5.4% longer than that of Na-TcO_4^-(5.27 hrs) and the mean T_e (2.88 hrs, SD 0.32) was 3.5 % longer than that of Na-TcO_4^-(2.78hrs)

The mean T_e of 99mTc-MDP(5.81 hrs, SD 0.618, 95% CI 4.57-7.04) in patients with bone metastases due to cancer of the prostate was 9.3% longer than in patients with thyroid disorders (5.27 hrs, SD 1.33 95%CI 2.66-7.87). The mean T_b in males with prostate cancer was longer than mean T_b in females with breast cancer.

CONCLUSION

The mean residual activity of 99mTc-MDP and $NaTcO_4^-$ in urine was low (14.46 and 3.84 MBq respectively) and it varied between patients and was independent of the administered dose.

T_b varied between individual patients and in between 99mTc-MDP and $NaTcO_4^-$ tracer groups

T_e and T_b was affected by the addition of different pharmaceuticals to 99mTc

In patients with thyrotoxicosis (Grave's disease) some doses of sodium pertechnetate were undetectable in urine samples. This was due to complete uptake of the $NaTcO_4^-$ by the toxic thyroid gland.

Key words: Administered dose, residual activity, biological half-life, effective half-life.

ACKNOWLEDGEMENTS

First and foremost, I would like to sincerely thank my principal supervisor Dr LT Muungo and co-supervisor Ms Mulape Kanduza for their support and valuable advice during the scientific orientation of my training. I am also greatly indebted to the study participants and members of staff at the nuclear medicine department of the University Teaching Hospital, Lusaka. Lastly I am thankful to my wife, Loveness for her support and putting up with the stresses associated with this work. Thank you all.

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ABBREVIATIONS

^{99}Mo	:	Molybdenum 99
^{99m}Tc	:	Metastable Technetium 99
ALARA	:	As Low As Reasonably Achievable
BSA	:	Body Surface Area
DMSA	:	Dimercapto succinic acid
DTPA	:	Diethylenetriamine pentaacetic acid
GBq	:	Giga Becquerel (one million Becquerels)
GFR	:	Glomerular Filtration Rate
IAEA	:	International Atomic Energy Agency
ICRP	:	International Committee on Radiation Protection
KeV	:	Kilo electron volt
m	:	Metastable state
MDP	:	Methylene diphosphonate
MIBI	:	2-methoxy isobutyl isonitrile
MIRD	:	Medical Internal Radiation Dose
NCRP	:	National Council on Radiation Protection and Measurement
NM	:	Nuclear Medicine
NRC	:	Nuclear Regulatory Commission
RAI	:	Radioactive iodine
ReFib	:	Reduced Fibrinogen
RhTSH	:	Recombinant Human Thyroid Stimulating Hormone
RN	:	Radionuclide

RP	:	Radiopharmaceutical
$\mathbf{t_{1/2}}$	:	Half life
$\mathbf{TcO^-_4}$	:	Pertechnetate ion
$\mathbf{T_b}$	:	Biological half life
$\mathbf{T_e}$	:	Effective half life
$\mathbf{T_p}$	:	Physical half life
UnFib	:	Unreduced Fibrinogen
UTH	:	University Teaching Hospital

1.0 INTRODUCTION

1.1 BACKGROUND

Ionizing radiation has become the largest contributor to human exposure from manmade sources of radiation. It accounts worldwide for about 90% of the total radiation dose from such sources. About two billion diagnostic x-ray examinations, thirty two million nuclear medicine procedures and five and a half million radiation therapy treatments are currently being carried out every year and the trend is on the increase. (IAEA, Malaga 2001).

Currently in Zambia, diagnostic nuclear medicine procedures are carried out routinely and after the procedure, the patients are allowed home without measurement of residual or remaining amount of tracer in the body.

This study aimed at determining how much activity of the tracer remained in the urine of patients that had just been scanned with 99 metastable Technetium containing tracers.

By so doing, radiation protection could have been optimized in accordance with the guidelines and fundamental principles of nuclear pharmacy practice.

Globally, studies have been done on other isotopes including radioactive iodine 131 to determine the residual body burden or activity using indirect methods. Effective half-life was calculated and used to determine whether to allow home or quarantine the patient after exposure (Ravichandran *et al*, 2010). Regionally the principal investigator could not find evidence of any studies so far conducted to determine residual activity of 99 metastable Technetium in urine samples after patients have been exposed to the tracer.

At the University Teaching Hospital Department of Nuclear Medicine, about 275 patients on average underwent different forms of nuclear medicine procedures between the years 2010 and 2012. Of these, 47 % received bone scans using Technetium with methylene diphosphonate

(99mTc-MDP), 30 % had thyroid scans using sodium pertechnetate Technetium (Na TcO_4^-), 7 % had static imaging of the kidney using 99 metastable Technetium with dimercapto succinic acid (99mTc-DMSA), 3.6 % had dynamic kidney studies using 99mTechnetium with diethylenetriamine pentaacetic acid (99mTc-DTPA) and 3 % received cardiac perfusion studies using 99 metastable Technetium with 2-methoxy isobutyl isonitrile (99mTc-MIBI). The radiological risks associated with diagnostic procedures are typically low but it is important to manage exposure of patients to radiation so that it is not higher than is required to produce the needed diagnostic information.

The levels of activity in radiopharmaceuticals or tracers administered clinically are governed primarily by the need to balance the effectiveness and safety of the medical procedure. This is achieved by choosing the minimum radiation dose delivered to the patient (referred to simply as 'dose') in order to achieve the desired objective which is either diagnostic image quality or therapeutic outcome. The Nuclear Regulatory Commission (NRC) has instituted the concept termed 'As Low as Reasonably Achievable' (ALARA) in order to reduce radiation exposure to individuals (Saha, 2006).

The fundamental safety objective is to protect people and the environment from harmful effects of ionizing radiation. According to the principles of radiation protection

(Principle V: Optimization of Protection), protection must be optimized to provide the highest level that can reasonably be achieved. Both the optimization of radiation and the limitation of doses and risks to individuals are necessary to achieve the desired level of safety. (IAEA, Vienna 2006).

In Zambia, radiation safety procedures are governed by the Ionizing Radiation Protection Act №16 of 2005 which provide protection of the patient, worker, the public and the environment

from the hazards arising from the use of devices or materials capable of producing ionizing radiation.

Decay of radioactive elements in a biological system occurs by both biological and physical means and each of these have a distinct half-life ($t_{1/2}$), the biological (T_b) and physical half-life (T_p). The effective half-life (T_e) is a combination of both the biological and physical half-lives (Saha, 2006).

Radioactive elements or isotopes tagged with appropriate ligands can be used for treatment and diagnostic purposes. They are administered orally or intravenously and distribute into a particular organ where an appropriate ligand facilitates uptake of the tracer. The radiation released from the tracer is then detected externally using a radioisotope probe or a special device called scintillation gamma camera.

In medical applications of tracers, there is need to estimate the radioactive body burden or residual activity or simply the remaining amount of tracer after a scan in order to ascertain radiation safety and minimize exposure to other people. There are two methods of monitoring for residual activity or radiation levels, indirect and direct method. Indirect monitoring is based on the determination of activity concentrations in biological samples obtained from the body, usually urine, feces, breath or blood or in physical samples taken from the work environment such as air or from contaminated surfaces. Direct methods involve in-vivo counting of emissions from the body. Direct methods require bio kinetic models for internal dosimetry but results can depend on the interpretation of rates of excretion from the body which can vary markedly over time and between individuals (IAEA Safety Standards, 2006).

By determining the biological half-life, the effective half-life of the tracer can then be calculated. Comparing with the normal values (Appendix 3) one is able to decide whether to quarantine the

patient or allow home immediately after a nuclear medicine procedure. The residual activity and exposure rates from biological samples serve as evidence based results and can be considered when designing a patient discharge protocol.

Blood was not used for analysis because it is the first compartment a tracer distributes into following intravenous administration and serves to deliver the tracer to the target organ. Urine is the end biological fluid of excretion and contains the residual amounts of the tracer. The choice of biological sample to analyze was dependent not only on the major route of excretion but also on such factors as ease of collection, analysis and interpretation. Therefore urine was the most convenient and non-invasive biological sample to analyze.

Patients were availed with the following information leaflet before receiving 99m Tc.

PATIENT INFORMATION LEAFLET ON 99 METASTABLE TECHNETIUM (^{99m}Tc)

Read all the information in this leaflet before you are given this medicine.

Keep this leaflet. You may need to read it again.

If you have further questions, please ask your doctor or pharmacist

If any of the side effects gets serious or if you notice any side effects not listed in this leaflet please tell your doctor or pharmacist.

1. **WHAT IS 99 METASTABLE TECHNETIUM(^{99m}Tc) AND WHAT IS IT USED FOR**

   99mTc is a radioactive isotope and is used as a tracer for diagnostic purposes only.

   It is produced from radioactive Molybdenum (^{99}Mo). The sterile generator allows for the separation and collection of ^{99m}Tc injection.

   This product, when injected, temporarily collects in a particular organ of the body.

   It can also be used for the preparation of other radiopharmaceuticals or tracers.

Because the substance contains a small amount of radioactivity, it can be detected from outside the body using a special camera and a picture known as a scan can then be taken. This scan will show exactly the distribution of the radioactivity within the organ and the body. This can give the physician valuable information about the structure and function of that organ.

2. BEFORE YOU ARE GIVEN THE SOLUTION OF ^{99m}Tc

Do not use the solution:

If you are allergic or hypersensitive to sodium pertechnetate (^{99m}Tc) or any other ingredients of the solution.

The use of 99mTc involves the administration of small amounts of radioactivity. The risk this involves is very small and your doctor will not consider carrying out the investigation unless he believes that the risk is outweighed by the potential benefit of the study.

Because some cases of allergic type reactions have been reported after administration of ^{99m}Tc you should tell your doctor if you have an allergic disease.

Taking other medicines:

Some other medicines may affect the quality of the results obtained from ^{99m}Tc examinations such as methotrexate.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medication including medicines obtained without a prescription.

Pregnancy and breastfeeding:

Ask your doctor or pharmacist for advice before taking any medicines.

It is important to tell your physician if there is any possibility that you are pregnant.

Special consideration is given to the use of tracers during pregnancy.

Your physician will only use this product if he considers that the benefits outweigh the risks.

Tell your doctor if you are breastfeeding as the investigation may be delayed until breastfeeding is completed or he may ask you to stop breastfeeding for a short while until the radioactivity is no longer in your body.

3. ANY OTHER EFFECTS

Apart from the injection, the tracer itself causes no effect and you will not feel anything nor feel sleepy and you can go about your normal activities afterwards. However if you have any complications or feel very uncomfortable during and after the procedure please inform the doctor or radiographer immediately.

As the gamma rays are similar to X-rays, there are small risks associated with being exposed to radiation. However, the radiation decays away or diminishes over a period of time and the total amount of radiation involved is kept to a minimum. You will be required to take a lot of water before and after the procedure.

While in the department you will be requested to use the special toilet for nuclear medicine patients.

4. FINALLY

Please remember that the isotope preparation required for this examination is ordered especially for you. If you are not able to attend, please let the department know in good time, so that it can be used for someone else.

Some of your questions should have been answered by this leaflet.

Make sure you are satisfied that you have received enough information about the procedure.

For any further information and questions please contact the doctor or pharmacist at the department of nuclear medicine.

1.2 RATIONALE OF STUDY

In the working environment of the Nuclear Medicine laboratory at UTH, radiation protection measures that exist include operator shielding, patient and staff protection during tracer administration, minimizing exposure time and distance from the source of radiation. No procedures are done to measure or determine the residual body activity or remainder of the administered tracer after radiation in biological fluids. After a nuclear medicine procedure there is no definite and evidence based discharge protocol to follow regarding quarantine time and discharge of patients who have just received radioactive tracers. Patients may end up exposing other members of the family and public to unwanted radiation. In order to determine the residual activity, on the spot urine samples were analyzed after each examination. The residual activity so measured would then help determine whether the patient could be quarantined to allow the tracer to decay to its first half life or allow them home without undue exposure of radiation to others.

1.3 SIGNIFICANCE OF THE STUDY

Despite 99mTc being the most widely used tracer in diagnostic procedures, there was no assessment done to estimate residual body activity in biological samples at UTH. Usual diagnostic doses of tracers were typically low and so was the associated risk. However there was need to provide scientific evidence on the actual amount being excreted in urine. With different pharmaceuticals added, the pharmacokinetic profiles of 99mTc changes and this affects the amount of radioisotope eliminated from the body via the kidneys and other organs of excretion. If the elimination can not sufficiently occur before the tracer reaches its half life, 99mTc

undergoes decay into 99Tc with a half life of 279 years and this could cause deleterious effects on the body.

Beneficiaries

1. **The patient**: The study provided proof that residual dose of 99mTc-MDP and $NaTcO_4^-$ can be measured in urine samples and accordingly patients can be evidently advised on the amounts remaining in their body.
2. **The profession**: The study was the first of its kind by a pharmacist in the nuclear medicine department. It therefore provides a basis for other similar studies on radioactive isotopes used in diagnostic and therapeutic procedures using urine samples.
3. **Policy**: The study provides evidence that such studies on imported radioactive elements can be done using locally available instruments. Therefore more isotopes could be imported for a variety of scanning procedures with patient safety assured.

Therefore there is need to establish an evidence based discharge protocol for individual patients based on the residual dose and effective half life in order to reduce the risk of radiation exposure to others.

1.4 AIM OF STUDY

The aim of the study was to determine the residual activity of ^{99m}Tc in urine samples of patients with prostate and breast cancer and those with thyroid disorders at the University Teaching Hospital. The study also sought to establish whether the biological and effective half-life of ^{99m}Tc was affected when different pharmaceuticals were added to ^{99m}Tc for various scanning procedures.

1.5 SPECIFIC OBJECTIVES

i. To measure the residual dose of ^{99m}Tc-MDP

ii. To determine the biological half-life of ^{99m}Tc-MDP

iii. To determine the effective half-life of ^{99m}Tc-MDP

iv. To measure the residual dose of sodium Pertechnetate-^{99m}Tc

v. To determine the biological half-life of Sodium Pertechnetate-^{99m}Tc

vi. To determine the effective half-life of Sodium Pertechnetate-^{99m}Tc

1.6 RESEARCH QUESTIONS

i. Is the residual activity of ^{99m}Tc low enough to allow for discharge of patients soon after scanning?

ii. Are the biological and effective half-lives of ^{99m}Tc affected when different pharmaceuticals are added to ^{99m}Tc?

2.0 LITERATURE REVIEW

Effective half-life of a radioactive element is the period during which the quantity of that element in a biological system is reduced to half its original amount due to interactions of radioactive decay and excretion due to biological processes.

At the study time there was no available literature locally on studies done using biological samples to determine the effective half-life of radioisotopes used for either diagnostic or therapeutic procedures.

After intravenous administration of sodium pertechnetate Tc-99m, the early distribution of pertechnetate is similar to that of iodide ion in terms of concentration in the thyroid gland. Plasma protein binding of pertechnetate Tc-99m is weak and reversible. It readily accumulates in urine. The renal clearance is approximately 10 milliliters of plasma per minute. In a normal resting adult it has a biological half-life of two days.

Technetium has versatile coordination chemistry and allows for a large number of ligands to complex with it. By using different ligands in the radiopharmaceutical formulation a wide range of radiopharmaceuticals can be made and used in many diagnostic procedures (Winfield and Richards, 1998).

99mTc-MDP is a widely used RP in metastatic bone scans. $99m^{5+}$Technetium-DMSA is excreted in urine via glomerular filtration and tubular secretion. Plasma clearance is about ten minutes. Plasma protein binding of ^{99m}Tc-DMSA is about 75% in 6 hours and urinary excretion is 37% in 24 hrs. Renal retention of Tc-DMSA in both kidneys amounts to nearly 24% of the administered dose one hour after injection (Saha, 2006)

99mTc-DMSA was introduced in 1974 and is still the agent of choice in static renal scintigraphy. Despite its frequent use, little is known about the mechanism of renal uptake.

It has been shown that the tracer is concentrated in the proximal tubular cells of the kidneys. ^{99m}Tc-DMSA could enter the proximal tubular cell either by glomerular filtration and subsequent reabsorption or by direct uptake from the peritubular capillaries.

Because Tc-DMSA is largely bound to plasma proteins it is generally assumed that GF is insignificant and that the uptake takes place at the peritubular side of the cell (M.J de Lange *et al*, 1988). They found that there was low renal uptake and a high concentration of ^{99m}Tc-DMSA in the urine of patients with the Fanconi syndrome and other forms of tubular reabsorption dysfunction that are accompanied by proteinuria.

In vivo scintigraphic studies were performed in four mice bearing an abscess or Ehrlich tumor after an intravenous injection of Tc-99m unreduced fibrinogen (Tc-99mUnFib) or Tc-99m reduced fibrinogen (Tc-99mReFib) solutions. Sequential scintigrams of mice bearing abscess revealed that the Tc-99mUnFib was rapidly excreted in urine (Yoshiharo *et al* 1996). The blood clearance of Tc-99m ReFib was found to be slower than that of Tc-99mUnFib. From this we deduce that addition of a compound to 99mTc affects its renal clearance.

Khalil WM *et al* in 2000 compared GFR obtained by modified Gate's method for 99mTc-MDP with those obtained by means of 99mTc-DTPA. Thirty five adults (23 males and 12 females) with age ranging from 18 to 70 were enrolled. They underwent renal studies with 99mTc-MDP and 99mTc-DTPA to evaluate bone metastases. They were given adequate hydration with 500 to 750 ml of water for 30 minutes. Gamma camera was used to measure activity. Data was analyzed using time-activity curves. Data was presented as means and standard deviations. Statistical analysis of GFR values obtained with 99mTc-MDP and 99mTc-DTPA percent uptake was done by linear regression analysis. Correlation between the tracers was evaluated with Pearson's correlation coefficient. Statistical significance was defined as $p < 0.001$. The results of renal

handling by 99mTc-MDP were sufficiently similar to those of 99mTc-DTPA. In our study 35 patients were analyzed and similar statistical methods to those used by Khalil W M *et al* were employed.

In Japan, H. Inoue et al from the Kurume University of Medicine reported that Technetium excreted by patients injected with radioisotopes was detected in sludge and supernatant fluid from the processing pool in Kurume sewerage treatment plant. There is a strong possibility that 99mTc released from nuclear medicine department into the local sewer system finds its way to sewer ponds of Lusaka in a similar manner.

When Technetium is released to the environment, the pertechnetate ion (TcO_4^-) which is the main chemical form of Tc is readily absorbed in the human body through agricultural products.

H. Inoue *et al* used ion exchange paper membrane consisting of trimethylhydroxypropylammonium ion exchange groups bound onto cellulose fibres to separate the pertechnetate ion. The $^{99m}Tc\ O_4^-$ was detected using the gamma scintillation counter (Armeshan Pharmacia Biotech: 1470 Wizard, NJ) and a liquid scintillation counter (Beckman LS 6500, CA).

Patients who received radioactive iodine 131 for the treatment of differentiated carcinoma of the thyroid and thyrotoxicosis were taken up for study between 2006 and 2009. Measurement of exposure rates using a hand held gamma survey meter at 5 centimeter distance at the stomach and neck levels, then at 1 meter and 2 meter distances respectively were taken. The mean half time of clearance of tracer was estimated and was at variance with normal values (Ravichandran *et al*, 2010). The nuclear regulatory commission specifies that patients be discharged when body burden falls below 1100 MBq (30 mCi). (IAEA, Nov 2006).

Ravichandran *et al* conducted a study where whole body retentions of radioactive iodine 131 were measured in patients (n=254) and repeated quantitative whole body scans and measurements of the urinary excretion of Iodine131 were performed in 30 of these patients. The radioactivity of each sample was measured in a calibrated gamma counter-LKB 1282 Compu Gamma; Wallac.

The results showed that effective half-life (T_e) was not dependent on administered activity (3.7 or 1.1 GBq). This fact was also demonstrated in our study. A longer mean T_e was associated with male sex ($p = 0.02$), a higher serum creatinine level ($p = 0.0001$), a follicular histology of thyroid cancer ($p= 0.016$) and a higher serum thyroglobulin level ($p=0.018$) and the presence of metastases ($p=0.03$).

Ravichandran *et al* concluded that the longer mean T_e was mainly due to delayed renal excretion of Iodine 131 and resulted in dose estimates higher than the data in report 53 of the International Commission on Radiological Protection which were obtained from healthy euthyroid subjects.

In euthyroid patients treated with recombinant human Thyroid Stimulating Hormone (rhTSH), the mean T_e was shorter by 30% than in hypothyroid patients who underwent withdrawal. This treatment decreases the radiation dose delivered to extra thyroidal tissues and permits a shorter and more predictable length of hospitalization (Herve *et al*, 2008). In this study we demonstrated that effective half-life can be longer due to delayed renal clearance and that different disease conditions and gender have an influence on the mean effective half-life.

Radiation can cause deleterious effects in living systems if diagnostic isotopes are not cleared from the body beyond their half life. It is therefore important to assess the effects in humans for a given number of nuclear medicine procedures involving administration of tracers. The damaging effects arise from absorption of radiation energy by tissues.

The damage depends on a number of factors such as;

1. The activity of administered tracer.
2. The physical and biological half-life of the tracer.
3. The pharmacokinetics of the tracer in the body,
4. The fraction of energy released per disintegration from a source region that is absorbed in the particular target volume and
5. The shape, composition and location of the target organs (Saha 2006).

3.0 METHODOLOGY

3.1 STUDY POPULATION

All patients receiving 99mTc tagged tracers for bone, thyroid and kidney scans at UTH Nuclear Medicine Department during the study period and met the eligibility criteria.

3.2 TARGET POPULATION

All patients receiving diagnostic doses of 99m Tc at UTH.

3.3 INCLUSION CRITERIA

Men and women above 18 years of age.

Patients with all conditions of the thyroid.

Patients receiving radioactive iodine for treatment of hyperthyroidism and those with thyroid carcinoma.

Patients with bone metastases from breast and prostate cancer.

All grades of renal dysfunction (mild, moderate and severe).

3.4 EXCLUSION CRITERIA

Pregnant women and breastfeeding mothers and persons under the age of 18.

3.5 STUDY TYPE

Prospective, Cross sectional

3.6 SAMPLE SIZE

The estimated percentage of patients receiving ^{99m}Tc scans at University Teaching Hospital Nuclear Medicine Department was 85 % of all that were attended to. With degree of confidence at 95% and confidence interval between 80 % and 90 %, the sample size was calculated as follows:

$$N = \frac{1.96^2 P(100-P)}{d^2}$$

Where P is the prevalence, d is the width of the confidence interval

$N = 1.96^2.85(100-85)/10^2 = 50$

3.7 SAMPLING METHOD

A convenient sample of patients who were available at the time of study was selected. The number of participants for each group was allocated according to probability proportionate to size (bone scan 22, thyroid scan 13 patients respectively)

3.8 PATIENT INFORMATION

All patients under study were allocated a data sheet bearing date, age, sex, type of scan, activity administered, duration of scan, time sample collected, volume of urine and subsequent activity readings (Appendix 5). A patient consent form containing information on radiation procedure and the benefits of measuring the activity in urine before allowing the patient home was administered. Patients were also told that the procedure was part of normal patient care process.

3.9 STUDY SITE

The study was conducted at the University Teaching Hospital, Department of Nuclear Medicine laboratory.

3.10 MATERIALS and INSTRUMENTATION

Molybdenum/Technetium sterile generator ('Moly generator') to produce gamma radiation of mean energy 140 keV, 18 or 10 GBq, graduated urine bottles, alcohol swabs, cotton wool, and isopropyl alcohol 70% for the aseptic collection of urine samples. Sterile and pyrogen free normal saline 0.9%, eluate vials, mineral water, oral and written information concerning Tc and radiation protection.

Dose calibrator (model: Atom Lab 930 SN 1282006), Well counter with sodium iodide crystal detector (model: Capintec CRC-15R, Ramsey NJ. SN 158555).

Vial and syringe shields, personnel protective equipment (sterile gowns, surgical gloves and masks) and Radiation Survey Meter.

3.11 PROCEDURE AND DATA COLLECTION

^{99m}Tc was eluted from the Molybdenum/Technetium generator and activity was measured after each elution. A pharmaceutical was added using aseptic procedure according to the scan required i.e. methylene diphosphonate added to 99mTc solution, saline added to 99m-Tc solution and dimercapto succinic acid added to 99mTc solution. Patients were encouraged to hydrate with 500-750ml of water before and after scanning process. The activity to be administered was then withdrawn from the eluate and administered aseptically via the intravenous route.

Patients submitted on the spot urine samples immediately after each procedure and the activity measured instantly.

Subsequent activity measurements were done at 30 minutes, 1 h, 1.5 h, 2 h, and 2.5 h intervals using the same sample. Date of collection and volume of urine were also recorded.

Biological half-life was determined using the first order reaction equation;

$$\mathbf{T_b = 0.693 / k_d.} \qquad \text{(Hr)} \qquad \text{(Equation 1)}$$

Where, T_b is the biological half-life and k_d is the biological decay constant obtained from the slope of the log activity vs. time curve which was linear. The slope which represents the decay constant (k_d) was determined from *x* and *y* values on the log (ln) residual activity vs. time graph as follows;

$$\mathbf{k_d = y_2 - y_1 / x_2 - x_1} \qquad (hr^{-1}) \qquad \text{(Equation 2)}$$

Effective half-life was calculated using the formula;

$$\mathbf{T_e} = \frac{\boldsymbol{Tb \times Tp}}{\boldsymbol{Tb + Tp}} \qquad \text{(Hr)} \qquad \text{(Equation 3)}$$

Where; T_e, T_b and T_p are the effective, biological and physical half-lives of ^{99m}Tc respectively.

3.12 RESEARCH VARIABLES

Table 1: Variables of the study

VARIABLE	TYPE OF VARIABLE	DATA TYPE:NOTES
Administered dose	Independent	Numerical, continuous. Calculated according to the patients BSA(m^2)
Biological half life	Dependent	Numerical. Estimated from the slope of the regression line; $y = mx - c$
Effective half life	Dependent	Numerical and continuous. Dependent on the values of T_b and T_p
Residual activity	Dependent	Numerical, continuous. Activity detected in urine and was declining exponentially with time

4.0 ETHICAL CONSIDERATIONS

Ethical clearance to conduct the study was obtained from the University of Zambia Biological Research and Ethics Committee. Permission to conduct the study at the department of nuclear medicine was obtained from UTH management. Confidentiality was maintained by number and letter coding of patients and urine samples. The procedure did not harm the patients in any way as it was non-invasive and collection of urine samples for analysis was done as part of normal patient care process. Patient informed consent was obtained after explanation of the procedures and the risks of exposure of radiation to other people.

5.0 RESULTS

Table 2

Administered activity for 99mTc-MDP and $NaTcO_4^-$ in prostate and breast cancer patients.

Diagnosis	Administered activity(MBq) Dose Range	Number of patients	Radiopharmaceutical
Prostate cancer	622-1233	15	99m Tc-MDP
Breast cancer	626-986	7	99m Tc-MDP
Thyroid disorders	81.8-118.2	13	Na Tc O_4^-

Table 2 shows details of administered activity dose ranges for both 99m Tc-MDP and $NaTcO_4^-$ and the corresponding disease condition. Patients with prostate (15 patients) and breast cancer (7 patients) received higher doses than those with thyroid disorders (13 patients).

Table 3

99mTc-MDP Results

Qualitative data	Administered dose(MBq)	Residual activity in urine(MBq)	Biological half life T_b(hr)	Effective half life T_e(hr)
Mean	860.09	14.56	5.57	2.88
Standard deviation	170.12	14.49	0.96	0.32

The values in the table represent details of mean administered dose to all the sampled patients both with prostate and breast cancer. The residual activity was measured form on the spot urine at 30 minutes, 1hr, 1.5 hrs, 2 hrs intervals using the same urine sample. Biological half life was determined from the log (ln) activity versus time curve. Effective half live was calculated using equation 3. The data are means ±SD for 22 patients who received 99m Tc-MDP.

Table 4

$NaTcO_4^-$ Results

Qualitative data	Administered dose(MBq)	Residual activity in urine(MBq)	Biological half life(hr) T_b	Effective half life(hr)T_e
Mean	97.57	3.84	5.27	2.78
Standard deviation	7.41	2.96	1.33	0.37

The values represent details of administered dose, residual activity, biological and effective half lives for Na-Tc O_4^- in all the sampled patients with thyroid disorders. The residual activity was measured form on the spot urine at 30 minutes, 1hr, 1.5 hrs, 2 hrs intervals using the same urine sample. Biological half life was determined from the log activity versus time curve. Effective half live was calculated using equation 3.

Table 5

Mean biological half lives of 99mTc-MDP and Na-TcO_4^-

Radiopharmaceutical	Mean T_b(hrs)	Standard Deviation	95% CI
99mTc-MDP	5.57	0.96	4.5-6.10
Na-TcO_4^-	5.27	1.33	2.66-7.87

The values in the table represent mean biological half life of 99mTc-MDP in comparison to $NaTcO_4^-$ with the respective 95% confidence intervals. The mean T_b of 99mTc-MDP was longer than that of $NaTcO_4^-$(5.57 and 5.27 hrs respectively).

Table 6

Mean effective half lives of 99mTc-MDP and Na-TcO_4^-

Radiopharmaceutical	Mean Te(hrs)	Standard Deviation	95% CI
99mTc-MDP	2.88	0.32	2.24-3.15
Na-TcO_4^-	2.78	0.37	2.04-3.52

Table 5 shows comparison between the mean effective half lives of 99mTc-MDP and Na-TcO_4^- standard deviations and respective 95% confidence intervals. Mean T_e for 99mTc-MDP was longer than that of $NaTcO_4^-$

Table 7

Mean T_b and T_e values for 99mTc-MDP based on gender

Gender	Mean T_b(hrs)	SD	95% CI	Mean T_e(hrs)	SD	95% CI
Males with prostate cancer (15patients)	5.81	0.61	4.57-7.05	2.95	0.16	2.61-3.29
Females with breast cancer (7patients)	5.04	1.36	2.30-7.78	2.71	0.50	1.69-3.73
% Difference	13.3			8.1		

Values represent mean T_b and T_e values for 99mTc-MDP for males with prostate cancer and for females with breast cancer. The data are means ±SD of T_b for 15 males and 7 females. The results indicate that T_b (5.81 hrs) in males with prostate cancer was 13% longer than in females (5.04hrs) with breast cancer. The mean T_e for prostate cancer patients was 8.1% longer than in patients with breast cancer.

6.0 DISCUSSION

In this study, the following were the findings in relation to the specific objectives set out in the study:

99m Tc-MDP

The mean administered activity for 99mTc-MDP was 860.09 MBq and this yielded a mean residual activity of 14.56 MBq in urine (Table 2). This resulted in a mean biological half life of 5.57 hours (SD 0.96, 95% CI 4.85-6.10). The mean effective half life 99mTc-MDP was found to be 2.88 hours (SD 0.32, 95% CI 2.61-3.0). The normal effective half life value for 99mTc-MDP is 6 hrs. The Pearson's correlation coefficient(r) between administered dose and biological half life was r = 0.094 and between administered dose and effective half life r = 0.175 .This was indicative of a strong relationship between independent and dependent variables i.e. administered dose and biological and effective half lives respectively. The amount of activity initially administered had no influence on the residual activity in urine. This has also been demonstrated by Ravichandran *et al* in 2010.

In this study the mean biological and effective half lives were averaged over measured values and represented along with the range. This was so because of many variables such as administered activities, various age groups of patients (ranging from 33 to 95 years) and gender. Males with prostate cancer (15 patients) had a mean T_b of 5.81hrs (SD 0.618, 95% CI 4.57-7.05) which was 13.3 % longer than in females with breast cancer (7 patients) with mean T_b 5.04 hrs (SD1.369, 95% CI 2.30-7.05). Mean T_e of 2.95 hrs (SD 0.168, 95% CI 2.61-3.29) in males with prostate cancer was 8.1% longer than in females with breast cancer, mean T_e of 2.71 hrs (SD 0.508, 95% CI 1.69-3.73)

Na Tc O_4^-

All the patients that received thyroid scans were females (13 patients). Only three out of the 13 patients had their urine samples detectable. The remaining ten patients had thyrotoxicosis (Grave's disease) and therefore $NaTcO_4^-$ was completely taken up rendering very negligible amounts in urine which the well counter could not detect. The mean administered activity for Na Tc O_4^- was 97.56 MBq and the mean residual activity in urine samples was 3.84 MBq (Table 4). The resultant mean biological half life T_b was 5.27 hrs (SD 1.33, 95% CI 2.61-7.93). The mean effective half life of $NaTcO_4^-$ was 2.78 hrs (SD 0.378, 95% CI 2.03-3.53 $p>0.05$). There was a negative correlation between administered dose and biological half life for $NaTcO_4^-$ ($r = -0.398$) and a positive correlation between administered dose and effective half life ($r = 0.227$). The normal range of T_e for $NaTcO_4^-$ is 2.8-5.5hrs. Therefore effective half life for sodium pertechnetate was within range.

99mTc-MDP vs. $NaTcO_4^-$

The mean biological half life for 99mTc-MDP was 5.4 % longer than that of Na-TcO_4^- and mean effective half life of 99mTc-MDP was about 3.5% longer than that of Na-TcO_4^-. However these were not statistically significant ($p>0.05$)

These differences in the mean T_b and T_e of 99mTc between the two groups indicate that the T_e and T_b are affected by addition of MDP to 99mTc. The mean biological half life was reduced fourfold from the normal value for 99m Tc (24hrs) with the addition of a pharmaceutical ligand and effective half life was reduced by 41%($p<0.0001$) . The normal T_e is 6.0hrs for 99mTc-MDP and 3.6 hrs for $NaTcO_4^-$

With $NaTcO_4^-$ all 10 patients with Graves' disease had undetectable urine samples. The reason was that the uptake and concentration of pertechnetate ion in the thyroid glands is similar to that of physiological iodine. In this case sodium pertechnetate was quickly up taken by the hyperactive thyroid leaving negligible amounts in urine. These activities could not be detected by the well counter (model: Capintec CRC-15R, Ramsey NJ. SN 158555).

7.0 CONCLUSION

Residual activity of 99mTc in urine was low and it differed between patients and in between tracer groups .These differences were attributed to variations in renal clearance of 99mTc by individual patients. The mean residual activities of 14.56 MBq for 99mTc-MDP and 3.84 MBq for $NaTcO_4^-$ were lower than the recommended radiation absorbed doses for bone and thyroid (appendix 2). These residual activities were lower than those a person living in the USA would receive annually from background radiation and natural sources.

This makes 99mTc-MDP ideal for bone scan. Both 99mTc-MDP and $NaTcO_4^-$ are considered safe and therefore there is no justification to quarantine the patients after a scan. In summary this study demonstrated that the mean T_e in patients with bone metastases due to cancer of the prostate and breast cancer was longer than in patients with thyroid disorders. A longer mean T_e was associated with the male sex due to delayed emptying of bladder contents as a result of urethral constriction in prostate cancer.

However, patients must be advised to take plenty fluids during and after scanning and encouraged to void frequently. The study further shows that varied administered doses yielded varied residual activities. There was no relationship between administered dose

and residual activity. The amount of activity excreted in urine was dependent on a patients' renal clearance, the duration of the scan and possible presence of other biological materials in urine.

RECOMMENDATIONS

For health physics purposes the results obtained still give an estimate of how much activity remains in urine samples of patients after radiation procedures.

Such studies are recommended especially where high doses of activity are being administered such as in radiotherapy before patients are allowed home.

8.0 STUDY LIMITATIONS.

99mTc-DMSA in urine was not sampled due very low doses of tracer patients in the study period received.

The initial sample size of 50 participants could not be achieved as the molybdenum generator availability was not consistent and the well counter could not detect low administered doses of $NaTcO_4^-$

This was a unicenter study as UTH is the only centre that administers radioisotopes and therefore the results could not be extrapolated to a larger population.

9.0 DISPOSAL OF RADIOACIVE WASTE

All waste generated during and after the study was treated as regulated radioactive waste material and disposed of according to local guidelines which included allowing isotopes to decay in storage and releasing into local sewer system.

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11.0 APPEDICES

11.1 APPENDIX 1

DEFINITIONS

1. Becquerel (Bq). A unit of radioactivity. One Becquerel is equal to one disintegration per second.
2. Biological half-life (T_b): The time by which one half of an administered dosage of a substance is eliminated by biological processes such as urinary and fecal excretion.
3. Curie (Ci): A unit of activity. A curie is defined as 3.7 $x10^{10}$ disintegrations per second.
4. Decay constant (λ): The fraction of atoms of a radioactive element decaying per unit time. It is expressed as $\lambda = 0.693/t_{1/2}$ where $t_{1/2}$ is the half-life of the radionuclide.
5. Dosage: A general term for the amount of a radiopharmaceutical administered in micro curies or millicuries, or Becquerels.
6. Dosimetry: The calculation or measurement of radiation absorbed doses.
7. Effective half-life (T_e): Time required for an initial administered dosage to be reduced to one half due to both physical decay and biological elimination of a radionuclide. It is given by $T_e = T_p \times T_b/T_p + T_b$, where T_e is the effective half-life, and T_p and T_b are the physical and biological half-lives, respectively.
8. Elution: A method of ‘‘washing out’’ an adsorbed substance from a solid adsorbing matter (such as ion-exchange resin) with a liquid.
9. Erg: The unit of energy or work done by a force of 1 dyne through a distance of 1 cm.

10. Generator: A device in which a short-lived daughter is separated chemically and periodically from a long-lived parent adsorbed on adsorbent material. For example, ^{99m}Tc is separated from ^{99}Mo from the Moly generator by eluting with normal saline.

11. Gray (Gy): The unit of radiation dose in SI units. One gray is equal to100 rad.

12. Half-life ($t_{1/2}$): A unique characteristic of a radionuclide, defined by the time during which an initial activity of a radionuclide is reduced to one half. It is related to the decay constant λ by $t_{1/2} = 0.693/\lambda$.

13. Isomeric transition (IT): Decay of an excited state of a nuclide to another lower excited state or the ground state.

It is equal to 2.58×10^{-4} C/kg air.

14. Labeled compound: A compound whose molecule is tagged with a radionuclide

15. Ligand: An ion or molecule attached to a metallic atom by coordinate bonding and allows for selective binding

16. Metastable state (m): An excited state of a nuclide that decays to another excited state or the ground state with a measurable half-life.

17. Rad: The unit of radiation absorbed dose. One rad is equal to 100 ergs of radiation energy deposited per gram of any matter, or 10^{-2} J/kg of any medium.

18. Radiopharmaceutical: A radioactive drug that can be administered safely to humans for diagnostic and therapeutic purposes.

19. Roentgen Equivalent Man (rem): A dose equivalent defined by the absorbed dose (rad) times the relative biological effectiveness or quality factor or radiation weighting factor of the radiation in question.

20. Roentgen: The quantity of x ray or gamma radiations that produces one electrostatic unit of positive or negative charge in 1 cm^3 of air at 0°C and 760 mm Hg pressure.

21. Scintillation scanning or imaging: Recording of the distribution of radioactivity in the body or a section of the body with the use of a detector.

22. Sievert (Sv): The unit of dose equivalent and equal to100 rem.

23. Specific Activity: The amount of radioactivity per unit mass of a radionuclide or labeled compound.

24. Tracer: A radionuclide or a compound labeled with a radionuclide that may be used to follow its distribution or course through a chemical, physical, or metabolic process.

11.2 APPENDIX 2

RADIATION ABSORBED DOSES IN ADULTS FOR VARIOUS RADIOPHARMACEUTICALS

Radiopharmaceutical	Organ	Dose	
		Rad/mCi	mGy/GBq
99mTc-DMSA	Kidney	0.630	170.3
99mTc-DTPA	Kidney	0.0201	24.3
99mTc-MDP	Bone	0.035	9.5
99mTc-Pertechnetate	Thyroid	0.130	35.1

11.3 APPENDIX 3

OCCUPATIONAL SAFETY AND ENVIRONMENTAL HEALTH RADIONUCLIDE

SAFETY DATA SHEET FOR ^{99m}Tc

PHYSICAL DATA

99mTc

Physical half-life: 6.02 hours

Biological half-life: 24.00 hours

Effective half-life: 4.80 hours

Specific activity: 5,243,820 Curies/gram ("carrier free"/pure Tc 99m)

3.4×10^6 Curies/gram (99m Tc–Pertechnetate form)

Gamma energies: 140.51 keV (89.1%)

99mTc-MDP

Biological half life: 6.0Hrs

Effective half life: 3.0 hrs

$NaTcO_4^-$

Biological half life: 6.0 hrs

Effective half life: 3.6 hrs

11.4 APPENDIX 4

PATIENT CONSENT FORM

Patient Code/ID Number: _____

Date: ……/……/ …….

Dear participant,

My name is Winter Mudenda and I am a postgraduate student of pharmacy carrying out a study in Nuclear Pharmacy.

You will receive an injection of a small amount of radioactive tracer material namely 99 metastable Technetium into your body for the purpose of a diagnostic scan.

As part of normal patient care process you are requested to voluntarily submit an on the spot urine sample after the process to allow for determination of the amount of tracer remaining in your body. This will also help protect others from the radiation. All information will be kept confidential and you may decline the procedure if you so wish.

Please sign or thumb print below for consent.

Signed ……..

Thumbprint

Principal Investigator: Winter Mudenda

UTH Pharmacy Department

P/Bag RW 1X, Lusaka.

Cell phone: 0966 951913

Note: In case of any questions please contact:

The Chairperson

University Of Zambia Biomedical Research Ethics Committee

Ridgeway campus

P.O. Box 50110

Lusaka, Zambia

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11.5 APPENDIX 5

PATIENT DATA SHEET

Date:	Age:	Sex:	Patient Code:
Diagnostic scan			
Tracer/Radiopharmaceutical			
Activity administered (MBq)			
Time tracer administered			
Duration of scan			
Volume of urine collected(ml)			
Time urine collected			

URINE ACTIVITY READINGS:

Reading	Time	Activity (MBq)	Time	Log Activity(ln)
1st	15 min			
2nd	30 min			
3rd	1 hr			
4th	2 hrs.			
5th	3 hrs.			

Urine sample collected by:……. Signed:…….

Readings taken by:…….. Signed:……

Data entered by : Signed:

11.6 APPENDIX 6

11.6 APPENDIX 6

CERTIFICATES and LETTERS OF APPROVAL

EXTRACTS FROM SPSS ANALYSIS

Pearson correlation between biological half life for 99mTc-MDP and $NaTcO_4^-$

		Tb(99mTc-MDP)	Tb(NaTcO4-)
Tb(99mTc-MDP)	Pearson Correlation	1	.392
	Sig. (2-tailed)		.744
	N	22	3
Tb(NaTcO4-)	Pearson Correlation	.392	1
	Sig. (2-tailed)	.744	
	N	3	3

Correlations between effective half life of 99mTc-MDP and $NaTcO_4^-$

		T_e (NaTcO4-)	T_e (99mTc-MDP)
Te(NaTcO4-)	Pearson Correlation	1	.200
	Sig. (2-tailed)		.872
	N	3	3
Te(99mTc-MDP)	Pearson Correlation	.200	1
	Sig. (2-tailed)	.872	
	N	3	22

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.750E2[a]	266	.339	.[b]	
Likelihood Ratio	111.053	266	1.000	1.000	
Fisher's Exact Test	408.215			1.000	
Linear-by-Linear Association	.193	1	.660	.[b]	.[b]
N of Valid Cases	22				

a. 300 cells (100.0%) have expected count less than 5. The minimum expected count is .05.

b. Cannot be computed because there is insufficient memory.

Linear regression analysis: Administered dose and mean biological half life

Variables Entered/Removed

Model	Variables Entered	Variables Removed	Method
1	Administered Dose[a]	.	Enter

a. All requested variables entered.

b. Dependent Variable: Mean Biological Half Life

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.096[a]	.009	-.040	.98155

a. Predictors: (Constant), Administered Dose

ANOVA[b]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	.179	1	.179	.186	.671[a]
	Residual	19.269	20	.963		
	Total	19.448	21			

a. Predictors: (Constant), Administered Dose

b. Dependent Variable: Mean Biological Half Life

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	5.102	1.103		4.626	.000
	Administered Dose	.001	.001	.096	.431	.671

Regression analysis: Residual dose vs. biological half-life for 99mTc-MDP

Variables Entered/Removed[b]

Model	Variables Entered	Variables Removed	Method
1	Tb 99mTc-MDP	.	Enter

a. All requested variables entered.

b. Dependent Variable: Biological half life of 99mTc-MDP

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.094[a]	.009	-.041	.98168

a. Predictors: (Constant), Residual dose of 99mTc-MDP

b. Dependent Variable: Biological half life of 99mTc-MDP

ANOVA[b]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	.174	1	.174	.180	.676[a]
	Residual	19.274	20	.964		
	Total	19.448	21			

a. Predictors: (Constant), Residual Dose of 99mTc MDP

b. Dependent Variable: Tb

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	5.477	.300		18.245	.000	4.851	6.1
	Residual Dose of 99mTc MDP	.006	.015	.094	.424	.676	-.025	.0

a. Dependent Variable: Mean biological half life of 99mTc-MDP

Residuals Statistics

	Minimum	Maximum	Mean	Std. Deviation	N
Predicted Value	5.4825	5.8087	5.5682	.09093	22
Residual	-3.38939	1.33407	.00000	.95803	22
Std. Predicted Value	-.942	2.645	.000	1.000	22
Std. Residual	-3.453	1.359	.000	.976	22

Regression analysis between mean Residual activity of 99mTc-MDP and Effective Half-life

ANOVA[b]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	.068	1	.068	.635	.435[a]
	Residual	2.150	20	.108		
	Total	2.219	21			

a. Predictors: (Constant), Residual Activity

b. Dependent Variable: Effective half-life

Coefficients

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval f B	
		B	Std. Error	Beta			Lower Bound	Upper Bou
1	(Constant)	2.820	.100		28.126	.000	2.611	3.0
	Res Activity	.004	.005	.175	.797	.435	-.006	.0

a. Dependent Variable: effective half-life of 99mTc-MDP