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ORIGINAL PAPER

Validation of an in-house developed therapeutic dosimetric software tool for the treatment of ^{177}Lutetium-DOTATATE peptide receptor radionuclide therapy

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Abstract

Background Computer software for absorbed dose quantification has been used widely in nuclear medicine. Different software tools have been written to improve the dose assessment, especially in therapeutic nuclear medicine. Some software tools focusing on computational phantom models from the international commission of radiation protection and units (ICRP) whilst others on Monte Carlo simulated models. While many studies have investigated therapeutic nuclear medicine dosimetry. The authors have noticed that very few papers compare the therapeutic software tools to each other, hence a doctor of philosophy study was embarked on. The aim of our study was therefore to validate our in-house developed software tool Masterdose using the commercial software OLINDA/EXM 1.0 that was available in our department.

Methods Methodology was based on clinical patient data treated for neuroendocrine tumours with ^{177}Lutetium (Lu)-DOTATATE at a South African hospital. All patients underwent the same SPECT acquisition protocol and were corrected for scatter, partial volume, collimator-detector response, gamma camera calibration and attenuation. Correction factors were applied to images to convert counts to activity. The first cycle of peptide receptor radionuclide therapy (PRRT) for 11 single photon emission computed tomography (SPECT) patients were compared on the Masterdose and OLINDA/EXM 1.0 software tools at 1, 24, 72 and 168 h. Cumulated activity and the absorbed dose were compared for the two software tools. The absorbed dose difference was then compared using statistical Bland-Altman analysis.

Results Masterdose and OLINDA/EXM 1.0 had different peptide receptor radionuclide therapy methodologies. This led to different results obtained for the software tools. Cumulated activities of Masterdose and DTK was 10.5% and 10.9% for the kidneys and tumours respectively. On average tumour absorbed doses were nine-times that of the kidneys. Bland–Altman analysis show a non-systematic difference between the two software.

Conclusion On average the relative percentage difference between the cumulated activities and absorbed dose of the two software were 10.7%.

Keywords Software · Dosimetry · Therapeutic · PRRT · Quantification

1 Introduction

Radionuclides are used for therapeutic procedures in nuclear medicine, this treatment has been termed radiopharmaceutical therapy, which differs from external beam radiation therapy, since it uses radiolabelled therapeutic pharmaceutical agents [1]. It is therefore important to perform valid quantification of radionuclide dose in organs and tissues. Internal dosimetry is essential to evaluate the risk and benefit of these nuclear medicine procedures. Computer programs are needed to measure the dose to organs and tissues. Nuclear medicine has benefitted from advances in computer software and this gain was at a rapid

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pace [2]. Dose quantification using personal computer software in nuclear medicine was first developed in the early 1990's and was distributed to two thousand users worldwide [3]. Electronic dose calculations were formed by the Radiation Dose Assessment Resource (RADAR) group [4]. This data can be downloaded from the internet website www.doseinfo-radar.com. The MIRD committee of the United States Society of Nuclear Medicine developed the MIRD formulism which has gained acceptance in nuclear medicine [5–7]:

$$\overline{D}(r_T, T_D) = \sum_{rs} \widetilde{A}(r_s, T_D).S(r_T \leftarrow r_s) \quad (1)$$

where:

$\overline{D}\ (r_T, T_D)$ is the mean absorbed dose in Gy,

$\tilde{A}$ is the time-integrated activity (TIA) in Bq.s,

$r_T$represents the target region,

r_s represents the source organ,

and the 'S-value' which is the cumulated activity in the source organ in Gy/Bq.s

The formulism requires knowledge of the cumulated activities, which are numerical values obtained from quantified nuclear medicine images. The 'S-value' are Monte Carlo calculation estimates using anthropomorphic phantoms and are radionuclide specific. Fisher-Snyder [8, 9], developed the first anthropomorphic phantom of the human body through a combination of geometric shapes, spheres, cylinders, cones, etc. Cristy et al. [10], then developed a series of phantoms, which represented children and adults of both genders. Stabin et al. [11], developed the female phantom, at three stages of pregnancy and non-pregnant. Other models for organs and structures include the brain [12], eye [13], peritoneal cavity [13], prostate gland [11], bone [12], rectum [14] and tumours [15]. The specific absorbed fractions from the models were "electronically published" by Stabin et al. [16]. This software was written in basic programming language using Visual Basic from Microsoft Corporation, which was later migrated to Windows software [16].

To serve as quality check, a few studies have highlighted the need for development of in-house dosimetry software tools to validate results of commercially available ones [17–21]. An advantage of available dosimetry software packages is that they include image functionality or large databases for S-values. The disadvantage, however, is the exclusion of features for objective calculations of activity to administer, pertaining organ doses and its standard error [19]. Another disadvantage is that most software packages are only commercially available. Whether in-house or commercial, the demand for patient-specific dosimetry necessitates the development of computer software. While many studies have investigated therapeutic dosimetry using in-house or commercial software, comparison of these software is still an open issue. The importance of comparing software tools for accurate absorbed dose calculations are therefore not highlighted in current literature. Authors believe that software comparison studies will assist in predicting possible organ under dosage or over dosage for consequent therapy efficacy or radiation induced toxicity, respectively. Computed absorbed doses can play a role in the amount of activity injected and the actual activity distribution in the organ. The aim of our study was therefore to validate an in-house developed software tool Masterdose using a commercial software tool OLINDA/EXM 1.0 for targeted peptide receptor radionuclide ^{177}Lu-DOTATATE therapy.1

2 Materials and methods

We validated the clinical workflow for Masterdose and OLINDA/EXM 1.0; which included gamma camera acquisition calibration, SPECT acquisition, activity quantification, image volume of interest (VOI) segmentation, time-integrated activity curve (TIAC) fits and absorbed dose calculations as demonstrated in Fig. 1. The challenge in validating Masterdose using OLINDA/EXM 1.0, is that the two software did not address the same dosimetry workflow

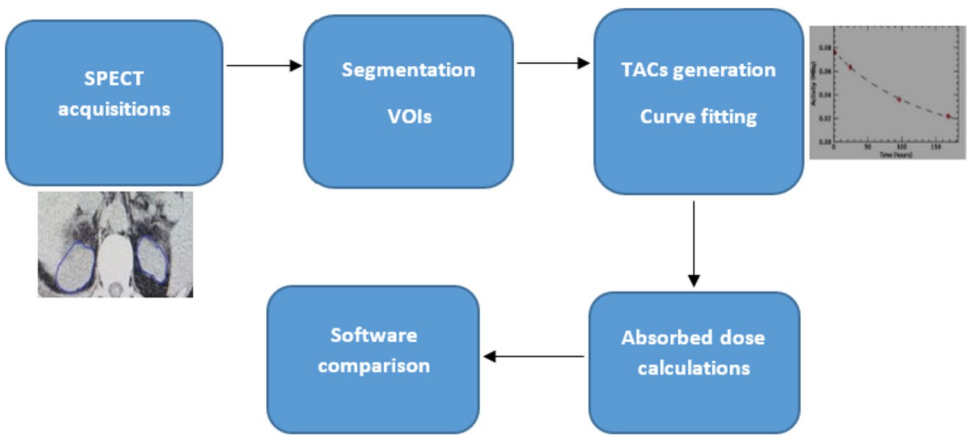


Fig. 1 Dosimetry workflow of the study

chain steps, this was similar to what was experienced by Mora-Ramirez et al. [22]. The OLINDA/EXM 1.0 does not propose steps for image quantification. In order to proceed in this study, the Dosimetry Toolkit® (DTK) on the Xeleris® software by GE Healthcare [23] was used to quantify counts and then transferred to OLINDA/EXM 1.0. To reduce uncertainties in each dosimetry workflow step and allow fair comparison, this study only compared the cumulated activity and absorbed dose for the two software tools.

All SPECT quantification were performed using full rotation mode (360^0) with 30 s per projection. All acquisitions were performed with a 128×128 matrix which had pixel size of 4×4 mm^2 and the energy discriminatory window was $\pm 15\%$. The ordered subsets expectation maximisation (OSEM) algorithm was used for SPECT reconstruction. This algorithm had default settings of eight subsets, four iterations and a Hann filter with a cut-off of 0.85. Gamma camera acquisition calibration, either SPECT or planar, was performed using the same acquisition protocol as the patients. A total of 11 SPECT images in DICOM format with a biopsy proven well-differentiated neuroendocrine tumour (NET) was loaded on each software tool and the kidney with spherical tumour delineated manually or automatically. Most "fine-tuning" of the organs were done manually, the time activity curves created, fitting models applied and the mass dependent S-value time-integrated activity curve (TIAC) calculated. This was done for the first peptide receptor radionuclide ^{177}Lu-DOTATATE patient cycle. All patients were scheduled to receive an activity of 7.4 GBq of peptide receptor ^{177}Lu-DOTATATE in 50 mL of saline for the cycle. All patients were also pretreated with 1500–2000 mL of lysine amino acid mixture over a period of four hours as well as intravenous injections of 8 mg each of Ondansetron and Corticosteroids prior to administration of peptide receptor ^{177}Lu-DOTATATE therapy. Quantified counts on the kidneys and tumours were compared for the time-points of 1, 24, 72 and 168 h. Peptide receptor radionuclide lutetium-177 therapeutic methods to correct for scatter, partial volume, collimator-detector response, attenuation and correction factor (CF) as discussed in the literature, were applied to all DICOM images [20, 21].

The relative percentage difference (RPD), as demonstrated in Eq. (2), was then used to determine differences in the cumulated activity:

$$RPD = \frac{Q_{Masterdose} - Q_{DTK}}{Q_{DTK}} \quad (2)$$

where; $Q_{Masterdose}$ = cumulated activity on Masterdose, Q_{DTK} = cumulated activity on DTK

Bland–Altman analysis was also used to compare the absorbed dose difference between Masterdose and OLINDA/EXM 1.0. This was done by plotting the difference between the two software on the Y-axis and the mean on the X-axis. The bias (b) was calculated as the mean of the difference between Masterdose and OLINDA/EXM 1.0, with the lower and upper limits of agreement were calculated using Eqs. (3) and (4).

$$LL = b - 1.96 \times SD \quad (3)$$

$$UL = 1.96 \times SD \quad (4)$$

where, LL and UL = lower limit and upper limit of agreement respectively, SD = standart deviation.

The S-values and organ masses from OLINDA/EXM 1.0 were incorporated into Masterdose, hence no comparative analysis performed and is demonstrated in the Appendix Tables 4, 5, 6 and 7.

Table 1 Data of NETs patients treated with ^{177}Lu-DOTATATE

ID	Gender (M/F)	NET site
1	F	Glomus
2	F	Rectum
3	F	Bronchial
4	F	Pancreas
5	F	GIT
6	M	Pancreas
7	M	Jejunum
8	M	Pancreas
9	M	Pancreas
10	M	Carcinoid
11	M	Pancreas

3 Results

The ^{177}Lu-DOTATATE patient data used in this study is given in Table 1.

The patient population presented in this study had advanced disease. These patients had prior surgeries, chemotherapy and biological therapies with further treatment options being limited. The Eastern Cooperative Oncology Group (ECOG) [24] performance status mean was 0. Demonstrating that all patients were fully active and able to carry all pre-disease performance without restriction.

The organ masses after manual delineation on CT for the kidneys are demonstrated in Table 2. Men organ mass was

Table 2 Manual delineated masses for the kidneys

Parameter	Kidney mass (g)
Minimum	272
Maximum	475
Mean	357

Table 3 Analysis criteria for the computational software tools

Author	Software	Workflow (2D/3D)	ROI/VOI segmentation	TIAC fitting	Dose Parameter
Van Wyk et al. 2022 [18]	Masterdose	2D and 3D	ROI and VOI (manual/automatic)	Trapezoidal method	Absorbed dose
Stabin et al. 2005 [19]	OLINDA/EXM 1.0	2D	GE Dosimetry Toolkit® (DTK)	Exponential fitting model	Absorbed dose per activity

larger than that of women, as reported by similar studies [25, 26]. Kidney masses have been shown to vary up to a factor of three between patients.

Table 3 gives the dosimetry analysis of computational software tools. Of note is the varying TIAC fitting used by the different software.

Computer software tools are needed due to the difficult nature in measuring absorbed dose to organs and tissues [27]. Both software tools were able to create a TIAC.

The cumulated activities from Masterdose and OLINDA/EXM1.0 are demonstrated in Fig. 2a and b.

The largest cumulated activities were found in tumours compared to the kidneys for both software. The tumour uptake was on average nine-times that of the kidneys for both software. The VOIs delineation, quantification steps and fitting parameters have a direct impact on the results displayed in Fig. 2. On average the RPD between the cumulated activities of Masterdose and DTK was 10.5% and 10.9% for the kidneys and tumours respectively.

The absorbed doses for Masterdose and OLINDA/EXM 1.0 are demonstrated in Fig. 3a and b.

On average the RPD between the absorbed doses of Masterdose and OLINDA/EXM 1.0 was 10.5% and 10.9% for the kidneys and tumours respectively. Following the similar trend by the cumulated activities.

The Bland–Altman analysis for the kidney and tumour absorbed doses are demonstrated in Figs. 4 and 5.

For the kidneys, a particular trend is seen that the calculated absorbed doses were almost consistently higher that the bias or systematic error of 0.2 Gy. However, the tumour Bland–Altman analysis show a non-systematic difference, as calculated absorbed doses were distributed evenly around the bias of 1.9 Gy. None of the cases quantified received a kidney absorbed dose of 23.0 Gy, which is considered the external radiotherapy limit [28].

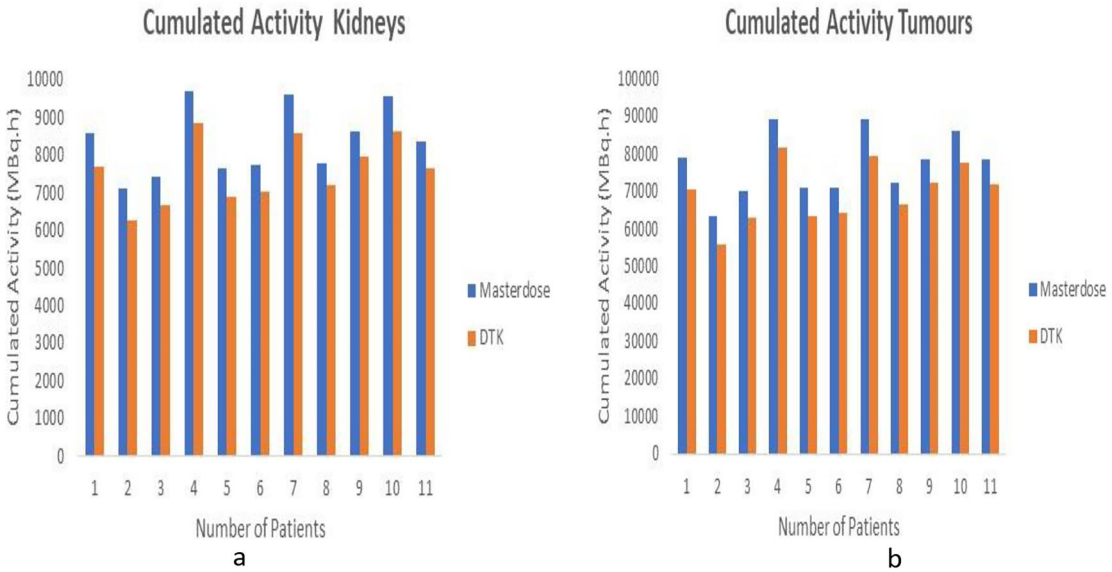


Fig. 2 Cumulated activities for the (**a**) kidneys and (**b**) tumours



Fig. 3 Absorbed doses for the (**a**) kidneys and (**b**) tumours

4 Discussion

There was a lack of standardized peptide receptor radionuclide therapy methodology between the Masterdose and OLINDA/EXM 1.0 software tools. According to GE recommendations, planar acquisition should be performed to obtain the CF [23]. Therefore Masterdose used a SPECT CF and OLINDA/EXM a planar CF. The relative percentage difference in the accumulated activity could be attributed to the different CFs used. Using a planar CF for SPECT cases, even though recommended by the vendor, is not ideal, the in-air CF for DTK did not adequately approximate patient scatter and attenuation conditions. The Masterdose SPECT calibration factor correctly accounted for scatter and attenuation corrections since the volumetric phantom "mimicked" the patient. Similar studies deemed an overall percentage difference of less than 10% between software dose as acceptable [25, 26].

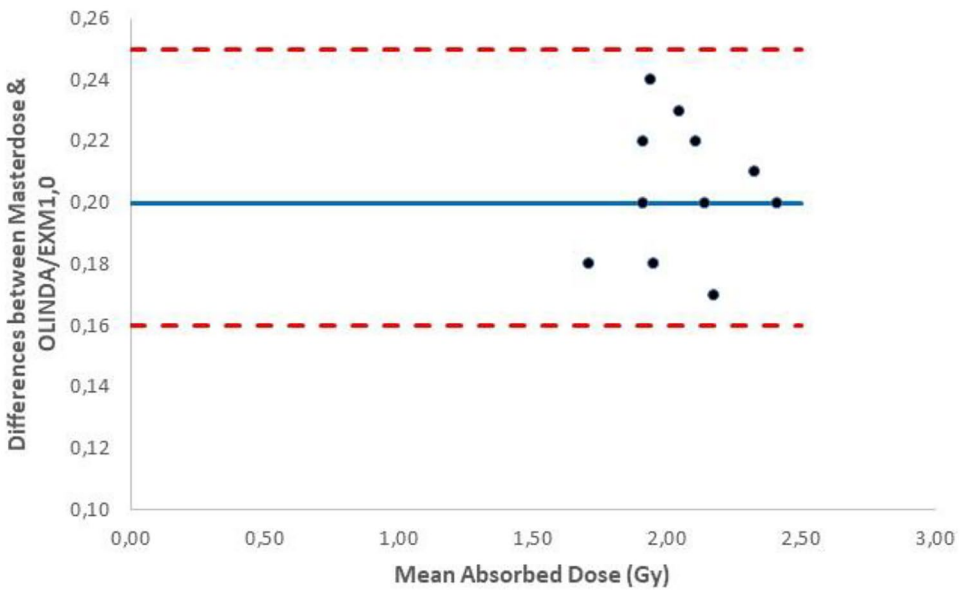


Fig. 4 Bland–Altman analysis of the kidney absorbed dose for the two software

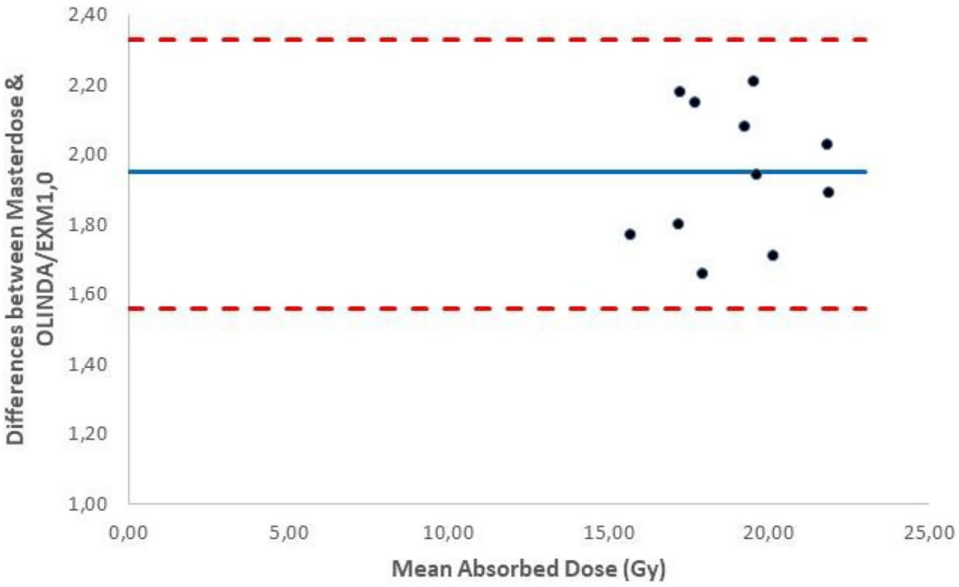


Fig. 5 Bland–Altman analysis of the tumour absorbed dose for the two software

Comparison of software in this study was just outside this limit, however, one should consider use of CFs as discussed extensively earlier as a large contribution to this error. Although not explicitly studied in this research, the authors could have used a SPECT generated CF for the DTK software, going against vendor recommendations, as performed by Mora-Ramirez et al. [22]. This would have produced an RDP of 3.2% between Masterdose and OLINDA/EXM 1.0, which would be well within the 10%.

The largest cumulated activities were found in tumours compared to the kidneys for both software. The tumour uptake was on average nine-times that of the kidneys for both software, demonstrating the therapeutic clinical environment. Clinicians could therefore have escalated absorbed doses to the tumours whilst sparing the kidneys. The VOIs delineation, quantification steps and fitting parameters have a direct impact on the results displayed in Fig. 2. Although not explicitly investigated in this comparison of software, studies have shown that trapezoid methods will be influenced by random and systematic errors [29]. The selection of four data time points in our study assisted in reducing these types of errors, as trapezoidal curve fitting improves with more data points. Mora-Ramirez et al. [22] made the observation that it is difficult to compare time-activity curve fitting performances of software at this stage, due to non-identical activity maps. This prevented authors from implementing the same approach for the software compared and is a development which needs to be addressed in the near future. Therefore, this study did not compare the fitting performance of the trapezoidal and mono-exponential function, which could have added to the RPD of software comparison.

It should be noted that only self-absorbed doses were reported in this study. Self-absorbed dose is the dominant contributor for ^{177}Lu according to the ICRP [30]. The electron emission dominates the self-absorbed dose of ^{177}Lu, due to its short range in soft tissue and bone. Absorbed doses were spread throughout the Bland–Altman plot, with only three kidney and one tumour calculated absorbed doses within correlation of agreement. All absorbed doses were within the limits of agreement of 0.5 Gy and 3.9 Gy for the kidneys and tumours respectively.

5 Conclusion

The Masterdose and OLINDA/EXM 1.0 software tools compared have different therapeutic approaches. This led to variations in the radiopharmaceutical therapeutic approach and affected the clinical evidence derived from this paper. Our paper has estimated uncertainties during the CF, and activity quantification of Masterdose and OLINDA/EXM 1.0.

Appendix 1

Tables 4

Table 4 S-factors for ^{177}Lu Adult Male (mGy/MBq.s) [19]

	Adrenals	Brain	Breasts	GB Cont	LLI Cont	SI Cont	StomCont	ULI Cont	HeartCon	Hrt Wall	Kidneys	Liver	Lungs	Muscle
Adrenals	1.46E-03	1.39E-10	1.35E-08	8.58E-08	6.60E-09	1.97E-08	7.50E-08	2.42E-08	6.88E-08	7.66E-08	2.01E-07	1.22E-07	6.38E-08	3.11E-08
Brain	1.39E-10	1.73E-05	9.72E-10	5.81E-11	6.70E-12	1.60E-11	1.78E-10	1.89E-11	1.01E-09	8.55E-10	5.71E-11	2.65E-10	2.24E-09	6.15E-09
Breasts	1.35E-08	9.72E-10	6.84E-05	8.69E-09	7.68E-10	2.24E-09	1.55E-08	2.50E-09	6.83E-08	7.44E-08	5.70E-09	1.91E-08	6.48E-08	1.20E-08
Gallbladder Wall	9.31E-08	5.68E-11	9.19E-09	2.15E-04	1.67E-08	1.19E-07	8.20E-08	2.08E-07	2.71E-08	3.17E-08	1.08E-07	2.41E-07	2.02E-08	3.28E-08
LLI Wall	5.95E-09	5.71E-12	8.08E-10	1.49E-08	8.35E-05	1.62E-07	2.40E-08	5.93E-08	1.26E-09	1.54E-09	1.50E-08	4.06E-09	1.01E-09	3.68E-08
Small Intestine	1.97E-08	1.60E-11	2.24E-09	1.25E-07	2.00E-07	2.82E-05	5.48E-08	3.49E-07	4.31E-09	5.69E-09	5.77E-08	3.14E-08	3.76E-09	3.08E-08
Stomach Wall	7.58E-08	9.23E-11	1.62E-08	8.03E-08	3.47E-08	5.82E-08	4.64E-05	7.79E-08	4.54E-08	7.13E-08	6.93E-08	3.98E-08	3.22E-08	2.99E-08
ULI Wall	2.35E-08	1.93E-11	2.27E-09	2.13E-07	8.35E-08	3.78E-07	7.17E-08	5.17E-05	6.18E-09	7.71E-09	5.77E-08	5.05E-08	5.02E-09	3.03E-08
Heart Wall	7.66E-08	8.55E-10	7.44E-08	2.75E-08	1.67E-09	5.69E-09	6.43E-08	8.21E-09	2.68E-05	7.58E-05	2.12E-08	6.41E-08	1.21E-07	2.53E-08
Kidneys	2.01E-07	5.71E-11	5.70E-09	1.03E-07	1.93E-08	5.77E-08	7.42E-08	5.72E-08	1.71E-08	2.12E-08	8.03E-05	8.13E-08	1.80E-08	2.73E-08
Liver	1.22E-07	2.65E-10	1.91E-08	2.25E-07	4.94E-09	3.14E-08	3.97E-08	5.07E-08	5.81E-08	6.41E-08	8.13E-08	1.29E-05	5.47E-08	2.09E-08
Lungs	6.43E-08	2.25E-09	6.52E-08	1.86E-08	1.42E-09	3.77E-09	2.97E-08	4.70E-09	1.28E-07	1.22E-07	1.81E-08	5.63E-08	2.39E-05	2.61E-08
Muscle	3.11E-08	6.15E-09	1.20E-08	3.16E-08	3.38E-08	3.08E-08	2.77E-08	2.93E-08	2.45E-08	2.53E-08	2.73E-08	2.09E-08	2.59E-08	8.72E-07
Ovaries	9.92E-09	6.67E-12	7.94E-10	2.84E-08	3.51E-07	2.54E-07	1.54E-08	2.11E-07	1.49E-09	2.01E-09	1.89E-08	1.03E-08	1.75E-09	3.93E-08
Pancreas	3.00E-07	1.62E-10	1.69E-08	1.83E-07	1.32E-08	3.77E-08	3.44E-07	4.37E-08	7.04E-08	9.56E-08	1.37E-07	1.06E-07	4.66E-08	3.42E-08
Red Marrow	6.85E-08	2.75E-08	1.57E-08	2.79E-08	5.67E-08	4.86E-08	2.08E-08	3.91E-08	3.03E-08	3.03E-08	4.74E-08	2.31E-08	3.07E-08	2.53E-08
Osteogenic Cells	6.88E-08	7.85E-08	2.00E-08	2.71E-08	4.59E-08	3.61E-08	2.50E-08	3.10E-08	3.90E-08	3.90E-08	4.07E-08	3.07E-08	4.24E-08	4.68E-08
Skin	9.53E-09	1.16E-08	2.15E-08	8.79E-09	1.00E-08	8.36E-09	9.58E-09	8.79E-09	9.58E-09	1.05E-08	1.11E-08	1.02E-08	1.13E-08	1.63E-08
Spleen	1.26E-07	2.24E-10	1.25E-08	3.41E-08	1.66E-08	2.70E-08	2.15E-07	2.74E-08	3.24E-08	4.39E-08	1.85E-07	1.97E-08	4.52E-08	2.87E-08
Testes	5.20E-10	7.62E-13	0.00E+00	2.14E-09	3.95E-08	7.00E-09	9.96E-10	5.70E-09	1.87E-10	2.23E-10	1.05E-09	5.30E-10	1.35E-10	2.77E-08
Thymus	1.61E-08	2.19E-09	6.75E-08	4.20E-09	6.68E-10	1.48E-09	1.04E-08	1.74E-09	2.47E-07	2.04E-07	5.08E-09	1.61E-08	7.75E-08	2.94E-08
Thyroid	2.24E-09	3.69E-08	8.01E-09	8.10E-10	9.34E-11	1.55E-10	8.68E-10	2.72E-10	1.33E-08	1.14E-08	1.06E-09	2.60E-09	2.35E-08	3.24E-08
Urinary Bladder Wall	2.28E-09	2.82E-12	4.53E-10	1.24E-08	1.37E-07	5.77E-08	5.17E-09	4.31E-08	7.19E-10	6.10E-10	5.61E-09	3.51E-09	4.61E-10	3.86E-08
Uterus	5.88E-09	5.77E-12	8.95E-10	3.05E-08	1.42E-07	2.30E-07	1.32E-08	1.07E-07	1.55E-09	1.81E-09	1.72E-08	8.99E-09	1.30E-09	3.94E-08
Total Body	3.58E-07	3.45E-07	3.39E-07	6.64E-08	2.22E-07	2.92E-07	1.27E-07	1.86E-07	1.40E-07	3.56E-07	3.54E-07	3.54E-07	3.50E-07	3.48E-07

	Ovaries	Pancreas	Red Mar	CortBoneS	TrabBone	CortBone	TrabBone	Spleen	Testes	Thymus	Thyroid	UB Cont	Uterus	TotBody
Adrenals	9.92E-09	3.00E-07	6.74E-08	2.99E-08	2.99E-08	2.99E-08	2.99E-08	1.26E-07	5.20E-10	1.61E-08	2.24E-09	2.74E-09	5.88E-09	3.57E-07
Brain	6.67E-12	1.62E-10	2.30E-08	3.34E-08	3.34E-08	3.34E-08	3.34E-08	2.24E-10	7.62E-13	2.19E-09	3.69E-08	2.78E-12	5.77E-12	3.45E-07
Breasts	7.94E-10	1.69E-08	1.47E-08	8.91E-09	8.91E-09	8.91E-09	8.91E-09	1.25E-08	0.00E+00	6.75E-08	8.01E-09	4.45E-10	8.95E-10	3.39E-07
Gallbladder Wall	2.76E-08	2.15E-07	3.09E-08	1.20E-08	1.20E-08	1.20E-08	1.20E-08	3.43E-08	2.09E-09	7.62E-09	8.59E-10	1.00E-08	3.06E-08	3.59E-07
LLI Wall	3.12E-07	1.17E-08	5.51E-08	2.02E-08	2.02E-08	2.02E-08	2.02E-08	1.23E-08	5.47E-08	5.27E-10	7.88E-11	1.60E-07	1.36E-07	3.58E-07

Table 4 (continued)

	Ovaries	Pancreas	Red Mar	CortBoneS	TrabBone	CortBone	TrabBone	Spleen	Testes	Thymus	Thyroid	UB Cont	Uterus	TotBody
Small Intestine	2.54E-07	3.77E-08	5.04E-08	1.57E-08	1.57E-08	1.57E-08	1.57E-08	2.70E-08	7.00E-09	1.48E-09	1.55E-10	5.88E-08	2.30E-07	3.59E-07
Stomach Wall	1.55E-08	3.50E-07	2.25E-08	1.09E-08	1.09E-08	1.09E-08	1.09E-08	2.12E-07	1.46E-09	9.72E-09	1.30E-09	6.08E-09	1.47E-08	3.55E-07
ULI Wall	2.28E-07	4.42E-08	4.26E-08	1.38E-08	1.38E-08	1.38E-08	1.38E-08	2.82E-08	5.22E-09	1.74E-09	2.72E-10	4.30E-08	1.13E-07	3.58E-07
Heart Wall	2.01E-09	9.56E-08	2.97E-08	1.57E-08	1.57E-08	1.57E-08	1.57E-08	4.39E-08	2.23E-10	2.04E-07	1.14E-08	6.50E-10	1.81E-09	3.55E-07
Kidneys	1.89E-08	1.37E-07	4.71E-08	1.73E-08	1.73E-08	1.73E-08	1.73E-08	1.85E-07	1.05E-09	5.08E-09	1.06E-09	6.04E-09	1.72E-08	3.53E-07
Liver	1.03E-08	1.06E-07	2.45E-08	1.34E-08	1.34E-08	1.34E-08	1.34E-08	1.97E-08	5.30E-10	1.61E-08	2.60E-09	3.47E-09	8.99E-09	3.54E-07
Lungs	1.75E-09	4.67E-08	3.05E-08	1.85E-08	1.85E-08	1.85E-08	1.85E-08	4.57E-08	1.35E-10	7.95E-08	2.37E-08	3.26E-10	1.30E-09	3.50E-07
Muscle	3.93E-08	3.42E-08	2.53E-08	2.08E-08	2.08E-08	2.08E-08	2.08E-08	2.87E-08	2.77E-08	2.94E-08	3.24E-08	3.59E-08	3.94E-08	3.47E-07
Ovaries	2.72E-03	1.06E-08	5.78E-08	1.80E-08	1.80E-08	1.80E-08	1.80E-08	1.06E-08	0.00E+00	6.56E-10	8.84E-11	1.45E-07	4.21E-07	3.61E-07
Pancreas	1.06E-08	2.53E-04	4.05E-08	1.78E-08	1.78E-08	1.78E-08	1.78E-08	3.63E-07	8.53E-10	1.61E-08	2.25E-09	4.13E-09	1.07E-08	3.60E-07
Red Marrow	5.78E-08	3.87E-08	1.19E-05	5.60E-08	4.32E-06	5.60E-08	2.48E-06	2.34E-08	7.48E-09	2.29E-08	2.19E-08	2.19E-08	3.76E-08	2.67E-07
Osteogenic Cells	4.18E-08	4.13E-08	5.58E-06	1.33E-05	1.70E-05	3.17E-06	8.17E-06	3.14E-08	2.44E-08	3.11E-08	4.95E-08	2.49E-08	3.10E-08	1.08E-06
Skin	8.70E-09	8.36E-09	1.21E-08	1.37E-08	1.37E-08	1.37E-08	1.37E-08	1.01E-08	2.94E-08	1.28E-08	1.27E-08	1.11E-08	8.36E-09	3.36E-07
Spleen	1.06E-08	3.63E-07	2.48E-08	1.35E-08	1.35E-08	1.35E-08	1.35E-08	1.31E-04	7.14E-10	9.53E-09	2.33E-09	2.69E-09	7.25E-09	3.54E-07
Testes	0.00E+00	8.53E-10	8.51E-09	1.13E-08	1.13E-08	1.13E-08	1.13E-08	7.14E-10	6.10E-04	7.43E-11	1.04E-11	1.05E-07	0.00E+00	3.47E-07
Thymus	6.56E-10	1.61E-08	2.35E-08	1.34E-08	1.34E-08	1.34E-08	1.34E-08	9.53E-09	7.43E-11	1.14E-03	4.26E-08	2.85E-10	6.11E-10	3.51E-07
Thyroid	8.84E-11	2.25E-09	2.07E-08	2.10E-08	2.10E-08	2.10E-08	2.10E-08	2.33E-09	1.04E-11	4.26E-08	1.15E-03	3.91E-11	8.34E-11	3.51E-07
Urinary Bladder Wall	1.49E-07	4.27E-09	2.45E-08	1.08E-08	1.08E-08	1.08E-08	1.08E-08	2.55E-09	1.05E-07	2.89E-10	3.95E-11	5.74E-05	3.52E-07	3.57E-07
Uterus	4.21E-07	1.07E-08	4.16E-08	1.35E-08	1.35E-08	1.35E-08	1.35E-08	7.25E-09	0.00E+00	6.11E-10	8.34E-11	3.42E-07	3.03E-04	3.61E-07
Total Body	3.62E-07	3.61E-07	3.53E-07	3.49E-07	3.49E-07	3.49E-07	3.49E-07	3.54E-07	3.47E-07	3.51E-07	3.52E-07	6.74E-08	3.62E-07	3.49E-07

Appendix 2

Table 5

Table 5 S-factors for ^{177}Lu Adult Female (mGy/MBq.s) [19]

	Adrenals	Brain	Breasts	GB Cont	LLI Cont	SI Cont	StomCont	ULI Cont	HeartCon	Hrt Wall	Kidneys	Liver	Lungs	Muscle
Adrenals	1.69E-03	2.28E-10	1.67E-08	1.11E-07	1.02E-08	2.83E-08	8.93E-08	3.25E-08	7.67E-08	8.36E-08	2.68E-07	1.44E-07	8.58E-08	3.90E-08
Brain	2.28E-10	2.04E-05	1.01E-09	1.36E-10	1.51E-11	3.26E-11	1.89E-10	3.89E-11	9.28E-10	7.97E-10	1.11E-10	3.43E-10	2.24E-09	6.17E-09
Breasts	1.67E-08	1.01E-09	6.67E-05	1.13E-08	1.24E-09	2.69E-09	2.05E-08	3.70E-09	8.85E-08	9.32E-08	6.94E-09	2.48E-08	7.00E-08	1.53E-08
Gallbladder Wall	1.20E-07	1.38E-10	1.21E-08	2.39E-04	2.85E-08	1.49E-07	1.17E-07	2.69E-07	3.86E-08	4.10E-08	1.21E-07	2.85E-07	2.80E-08	3.85E-08
LLI Wall	7.01E-09	1.23E-11	1.15E-09	2.31E-08	8.86E-05	2.09E-07	3.12E-08	8.38E-08	2.12E-09	2.64E-09	1.91E-08	6.55E-09	2.31E-09	4.37E-08
Small Intestine	2.83E-08	3.26E-11	2.69E-09	1.53E-07	2.42E-07	3.20E-05	7.19E-08	4.27E-07	7.25E-09	8.19E-09	7.50E-08	4.04E-08	6.54E-09	3.83E-08
Stomach Wall	9.44E-08	2.16E-10	2.20E-08	1.07E-07	4.71E-08	7.49E-08	5.26E-05	1.06E-07	6.36E-08	9.73E-08	7.79E-08	5.93E-08	4.48E-08	3.70E-08
ULI Wall	3.20E-08	3.87E-11	4.34E-09	2.66E-07	1.05E-07	4.72E-07	9.26E-08	5.72E-05	9.07E-09	1.05E-08	7.02E-08	6.51E-08	7.69E-09	3.41E-08
Heart Wall	8.36E-08	7.97E-10	9.32E-08	3.96E-08	3.29E-09	8.19E-09	8.67E-08	1.10E-08	2.97E-05	9.96E-05	2.66E-08	8.64E-08	1.58E-07	3.25E-08
Kidneys	2.68E-07	1.11E-10	6.94E-09	1.23E-07	2.44E-08	7.50E-08	8.05E-08	6.87E-08	2.39E-08	2.66E-08	8.73E-05	9.61E-08	2.63E-08	3.38E-08
Liver	1.44E-07	3.43E-10	2.48E-08	2.80E-07	7.68E-09	4.04E-08	5.87E-08	6.65E-08	8.12E-08	8.64E-08	9.61E-08	1.75E-05	7.52E-08	2.69E-08
Lungs	8.67E-08	2.29E-09	7.07E-08	2.66E-08	2.37E-09	6.58E-09	4.29E-08	8.01E-09	1.72E-07	1.61E-07	2.65E-08	7.67E-08	2.99E-05	3.45E-08
Muscle	3.90E-08	6.17E-09	1.53E-08	3.88E-08	4.16E-08	3.83E-08	3.49E-08	3.68E-08	3.12E-08	3.25E-08	3.38E-08	2.69E-08	3.41E-08	1.42E-06
Ovaries	9.18E-09	1.20E-11	1.18E-09	4.35E-08	4.64E-07	3.17E-07	2.24E-08	2.61E-07	2.76E-09	3.34E-09	2.61E-08	1.46E-08	2.28E-09	4.78E-08
Pancreas	3.52E-07	2.19E-10	2.03E-08	2.38E-07	2.04E-08	5.17E-08	4.10E-07	6.14E-08	9.03E-08	1.15E-07	1.65E-07	1.34E-07	6.52E-08	4.36E-08
Red Marrow	7.79E-08	3.74E-08	1.68E-08	3.05E-08	7.19E-08	5.73E-08	2.38E-08	4.63E-08	3.10E-08	2.95E-08	5.55E-08	2.68E-08	3.53E-08	3.10E-08
Osteogenic Cells	8.75E-08	9.53E-08	2.46E-08	3.42E-08	5.65E-08	4.56E-08	3.34E-08	3.93E-08	4.62E-08	4.41E-08	5.26E-08	4.08E-08	5.42E-08	5.68E-08
Skin	1.18E-08	1.39E-08	2.54E-08	1.03E-08	1.23E-08	1.05E-08	1.21E-08	1.06E-08	1.25E-08	1.28E-08	1.35E-08	1.27E-08	1.31E-08	1.93E-08
Spleen	1.79E-07	3.00E-10	1.42E-08	4.93E-08	2.09E-08	3.69E-08	2.40E-07	3.65E-08	4.19E-08	5.53E-08	2.29E-07	2.95E-08	6.04E-08	3.67E-08
Thymus	1.60E-08	2.45E-09	9.03E-08	1.08E-08	1.07E-09	2.28E-09	1.43E-08	2.41E-09	2.59E-07	2.19E-07	6.23E-09	2.10E-08	9.71E-08	3.70E-08
Thyroid	3.24E-09	1.61E-08	1.09E-08	1.56E-09	1.98E-10	3.90E-10	2.26E-09	5.24E-10	1.92E-08	1.49E-08	1.29E-09	3.81E-09	3.13E-08	3.19E-08
Urinary Bladder W	3.75E-09	5.98E-12	8.27E-10	1.92E-08	1.63E-07	7.99E-08	6.86E-09	5.62E-08	1.42E-09	1.53E-09	1.01E-08	5.37E-09	9.85E-10	5.19E-08
Uterus	9.34E-09	1.34E-11	1.26E-09	4.20E-08	1.91E-07	2.81E-07	2.07E-08	1.41E-07	2.91E-09	3.49E-09	2.17E-08	1.24E-08	2.33E-09	4.78E-08
Total Body	4.62E-07	4.44E-07	4.39E-07	7.73E-08	2.89E-07	3.75E-07	1.64E-07	2.40E-07	1.58E-07	4.54E-07	4.57E-07	4.57E-07	4.53E-07	4.43E-07

	Ovaries	Pancreas	Red Mar	CortBoneS	TrabBone	CortBone	TrabBone	Spleen	Thymus	Thyroid	UB Cont	Uterus	TotBody
Adrenals	9.18E-09	3.52E-07	7.86E-08	3.81E-08	3.81E-08	3.81E-08	3.81E-08	1.79E-07	1.60E-08	3.24E-09	3.47E-09	9.34E-09	4.60E-07
Brain	1.20E-11	2.19E-10	3.46E-08	4.00E-08	4.00E-08	4.00E-08	4.00E-08	3.00E-10	2.45E-09	1.61E-08	4.16E-12	1.34E-11	4.45E-07
Breasts	1.18E-09	2.03E-08	1.68E-08	1.09E-08	1.09E-08	1.09E-08	1.09E-08	1.42E-08	9.03E-08	1.09E-08	7.71E-10	1.26E-09	4.38E-07
Gallbladder Wall	4.58E-08	2.85E-07	2.79E-08	1.49E-08	1.49E-08	1.49E-08	1.49E-08	5.39E-08	9.54E-09	1.56E-09	1.66E-08	4.78E-08	4.62E-07

Table 5 (continued)

	Ovaries	Pancreas	Red Mar	CortBoneS	TrabBone	CortBone	TrabBone	Spleen	Thymus	Thyroid	UB Cont	Uterus	TotBody
LLI Wall	4.09E-07	1.60E-08	7.16E-08	2.48E-08	2.48E-08	2.48E-08	2.48E-08	1.82E-08	8.68E-10	1.60E-10	2.01E-07	1.73E-07	4.62E-07
Small Intestine	3.17E-07	5.17E-08	5.90E-08	1.95E-08	1.95E-08	1.95E-08	1.95E-08	3.69E-08	2.28E-09	3.90E-10	7.62E-08	2.81E-07	4.58E-07
Stomach Wall	2.32E-08	4.18E-07	2.43E-08	1.47E-08	1.47E-08	1.47E-08	1.47E-08	2.34E-07	1.62E-08	2.59E-09	7.14E-09	2.00E-08	4.58E-07
ULI Wall	2.96E-07	6.09E-08	5.01E-08	1.65E-08	1.65E-08	1.65E-08	1.65E-08	3.60E-08	3.11E-09	5.27E-10	5.94E-08	1.50E-07	4.61E-07
Heart Wall	3.34E-09	1.15E-07	3.02E-08	1.91E-08	1.91E-08	1.91E-08	1.91E-08	5.53E-08	2.19E-07	1.49E-08	1.19E-09	3.49E-09	4.58E-07
Kidneys	2.61E-08	1.65E-07	5.64E-08	2.34E-08	2.34E-08	2.34E-08	2.34E-08	2.29E-07	6.23E-09	1.29E-09	8.46E-09	2.17E-08	4.55E-07
Liver	1.46E-08	1.34E-07	2.74E-08	1.72E-08	1.72E-08	1.72E-08	1.72E-08	2.95E-08	2.10E-08	3.81E-09	5.11E-09	1.24E-08	4.56E-07
Lungs	2.29E-09	6.59E-08	3.64E-08	2.38E-08	2.38E-08	2.38E-08	2.38E-08	6.11E-08	9.90E-08	3.15E-08	8.94E-10	2.34E-09	4.53E-07
Muscle	4.78E-08	4.36E-08	3.10E-08	2.54E-08	2.54E-08	2.54E-08	2.54E-08	3.67E-08	3.70E-08	3.19E-08	4.40E-08	4.78E-08	4.47E-07
Ovaries	2.16E-03	1.85E-08	7.13E-08	2.22E-08	2.22E-08	2.22E-08	2.22E-08	1.40E-08	1.03E-09	1.30E-10	1.88E-07	5.52E-07	4.63E-07
Pancreas	1.85E-08	2.81E-04	4.20E-08	2.21E-08	2.21E-08	2.21E-08	2.21E-08	4.38E-07	1.88E-08	2.85E-09	5.05E-09	1.51E-08	4.63E-07
Red Marrow	7.08E-08	4.11E-08	1.05E-05	6.81E-08	4.51E-06	6.81E-08	2.63E-06	2.86E-08	2.44E-08	2.48E-08	2.82E-08	5.19E-08	3.30E-07
Osteogenic Cells	5.28E-08	5.11E-08	7.53E-06	1.77E-05	2.27E-05	4.20E-06	1.09E-05	4.15E-08	3.79E-08	5.61E-08	3.12E-08	3.97E-08	1.46E-06
Skin	1.04E-08	1.04E-08	1.52E-08	1.72E-08	1.72E-08	1.72E-08	1.72E-08	1.22E-08	1.59E-08	2.98E-08	1.37E-08	1.08E-08	4.34E-07
Spleen	1.40E-08	4.38E-07	2.93E-08	1.79E-08	1.79E-08	1.79E-08	1.79E-08	1.60E-04	1.19E-08	3.04E-09	4.36E-09	1.10E-08	4.56E-07
Thymus	1.03E-09	1.88E-08	2.48E-08	1.65E-08	1.65E-08	1.65E-08	1.65E-08	1.19E-08	1.19E-03	6.85E-08	4.99E-10	9.77E-10	4.53E-07
Thyroid	1.30E-10	2.85E-09	2.51E-08	2.39E-08	2.39E-08	2.39E-08	2.39E-08	3.04E-09	6.85E-08	1.40E-03	8.20E-11	1.77E-10	4.46E-07
Urinary Bladder W	1.86E-07	5.82E-09	2.82E-08	1.44E-08	1.44E-08	1.44E-08	1.44E-08	4.63E-09	5.08E-10	8.35E-11	7.60E-05	4.01E-07	4.59E-07
Uterus	5.52E-07	1.51E-08	5.19E-08	1.70E-08	1.70E-08	1.70E-08	1.70E-08	1.10E-08	9.77E-10	1.77E-10	4.12E-07	2.99E-04	4.62E-07
Total Body	4.64E-07	4.65E-07	4.54E-07	4.50E-07	4.50E-07	4.50E-07	4.50E-07	4.58E-07	4.52E-07	4.48E-07	8.58E-08	4.64E-07	4.49E-07

Appendix 3

Table 6

Table 6 Masses for Adult Male phantom [19]

Target Organ	Mass (g)
Adrenals	1.63E+01
Brain	1.42E+03
Breasts	3.51E+02
Gallbladder Wall	1.05E+01
LLI Wall	1.67E+02
Small Intestine	6.77E+02
Stomach Wall	1.58E+02
ULI Wall	2.20E+02
Heart Wall	3.16E+02
Kidneys	2.99E+02
Liver	1.91E+03
Lungs	1.00E+03
Muscle	2.80E+04
Ovaries	8.71E+00
Pancreas	9.43E+01
Red Marrow	1.12E+03
Osteogenic Cells	1.20E+02
Skin	3.01E+03
Spleen	1.83E+02
Testes	3.91E+01
Thymus	2.09E+01
Thyroid	2.07E+01
Urinary Bladder Wall	4.76E+01
Uterus	7.90E+01
Total Body	7.37E+04

Appendix 4

Table 7

Table 7 Masses for Adult Female phantom [19]

Target Organ	Mass (g)
Adrenals	1.40E+01
Brain	1.20E+03
Breasts	3.60E+02
Gallbladder Wall	8.00E+00
LLI Wall	1.60E+02
Small Intestine	6.00E+02
Stomach Wall	1.40E+02
ULI Wall	2.00E+02
Heart Wall	2.40E+02
Kidneys	2.75E+02
Liver	1.40E+03
Lungs	8.00E+02
Muscle	1.70E+04
Ovaries	1.10E+01
Pancreas	8.50E+01
Red Marrow	1.30E+03
Osteogenic Cells	9.00E+01
Skin	1.79E+03
Spleen	1.50E+02
Thymus	2.00E+01
Thyroid	1.70E+01
Urinary Bladder Wall	3.59E+01
Uterus	8.00E+01
Total Body	5.69E+04

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Data availability The authors make this data available to the journal.

Code availability This study was part of a PhD, the code can only be made available after 5 years.

Declarations

Ethical approval Sefako Makgatho Health Sciences University Research Ethics Committee approved this study, SMUREC Ethics Reference Number: SMUREC//M/114/2018: PG.

Consent to participate Not applicable.

Consent for publication All authors consent to the publication.

Conflicts of interest The authors declare that they have no conflicts of interest.

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