THE IMPORTANCE OF PATIENT-SPECIFIC DOSE CALCULATIONS IN NUCLEAR MEDICINE

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As therapeutic uses of radionuclides in nuclear medicine increases, the use of patient-specific methods for calculation of radiation dose becomes more important. In this manuscript basic methods and resources for internal dose calculations are outlined, with a focus on how current changes and advances are making more accurate and detailed, patient-individualized dose calculations possible. Most current resources make use of standardized models of the human body representing median individuals, but the use of image-based and more realistic models will soon take their place, and will permit adjustments to represent individual patients and tailor therapy planning uniquely for each subject.

KEYWORDS : Radiation Dosimetry, Nuclear Medicine, Patient Safety, Therapy

1. INTRODUCTION

One of the important beneficial applications of the use of radiation is in the healing arts. Unlike in many other uses of radiation, the patient receives a direct benefit from the study, so evaluation of the risk/benefit relationship is more straightforward. An important example is the use of radiopharmaceuticals, i.e. nuclear medicine, in both diagnosis and therapy. Diagnostic uses of radiopharmaceuticals are well established, and are employed to evaluate a broad variety of patient conditions. Radiation doses for diagnostic agents are developed by studying the biokinetics of the radiopharmaceutical in preclinical and clinical studies. In the former case, extrapolation methods are applied to the values measured in the animal organs over time to humans, and in the latter case, the quantitative data observed in the human subjects can be used directly for input to dose calculations[1] (specific methods are described in more detail below). Once dose calculations have been generally accepted for a given diagnostic radiopharmaceutical, they are included with the product information distributed with the agent. Dose calculations are generally not performed for diagnostic radiopharmaceuticals on a subject-specific basis, except in some circumstances, for example, in pregnant women who may have been subjected to nuclear medicine procedures[2]. The most complete and authoritative listing of dose estimates for many radiopharmaceuticals is found in two publications of the International Commission on Radiological Protection (ICRP)[3,4]. Some examples of dose estimates given by the ICRP for several radiopharmaceuticals are shown in Table 1.

Therapeutic use of radiopharmaceuticals is also a well established and widely practiced science, treating thousands of patients daily, with generally good success rates against many forms of cancer. Diseases of the thyroid and bone marrow have been treated for decades with good success with radiopharmaceuticals[5]; currently many more radionuclides tagged to species such as radiolabeled antibodies and peptides are being tested and applied in therapy against a number of forms of cancer. The basic goal of all forms of radiation therapy (using external or internal radiation sources), is to deliver a lethal radiation dose to the unhealthy tissues of concern while avoiding or limiting the expression undesired effects in other normal tissues of the patient. Radioactive iodine (^{131}I) has been used for many years to treat benign thyroid disease with and without patient-specific treatment planning[6,7]. Treatment of thyroid cancer with ^{131}I NaI is the most common application of radionuclide therapy in nuclear medicine and has been in use for many decades. Patient therapy is most often based on administration of fixed levels of activity to all subjects, rather than targeting absorbed doses, although there have been exceptions[8,9]. Kobe et al[10]. evaluated the success of treatment of Graves' disease in 571 subjects, with the goal of delivering 250 Gy to the thyroid, with the end-point being the elimination of hyperthyroidism, evaluated 12 months after the treatment. Relief from hyperthyroidism was achieved in 96 % of patients who received more than 200

Table 1. Examples dose Estimates Given by the ICRP for Several Radiopharmaceuticals[3.4]

	Estimated Dose (mSv/MBq)					
	^{99m}Tc-MIBI Resting Subjects	^{99m}Tc-MIBI Exercise Subjects	^{99m}Tc-Tetrofosmin Resting Subjects	^{99m}Tc-Tetrofosmin Exercise Subjects	^{18}FDG	$^{13}NH_3$
Adrenals	7.5E-03	6.6E-03	3.4E-03	3.3E-03	1.2E-02	9.9E-03
Brain	5.2E-03	4.4E-03	3.9E-04	4.6E-04	2.8E-02	3.6E-03
Breasts	3.8E-03	3.4E-03	9.0E-04	1.0E-03	8.6E-03	3.5E-03
Gallbladder Wall	3.9E-02	3.3E-02	3.6E-02	2.7E-02	1.2E-02	6.5E-03
Lower Large Int. Wall	1.9E-02	1.6E-02	2.0E-02	1.5E-02	1.5E-02	3.4E-03
Small Intestine	1.5E-02	1.2E-02	1.5E-02	1.1E-02	1.3E-02	3.9E-03
Stomach Wall	6.5E-03	5.9E-03	3.7E-03	3.5E-03	1.1E-02	4.6E-03
Upper Large Int. Wall	2.7E-02	2.2E-02	2.7E-02	2.0E-02	1.2E-02	4.0E-03
Heart Wall	6.3E-03	7.2E-03	4.4E-03	4.8E-03	6.2E-02	2.3E-02
Kidneys	3.6E-02	2.6E-02	1.4E-02	1.1E-02	2.1E-02	1.8E-02
Liver	1.1E-02	9.2E-03	4.0E-03	3.3E-03	1.1E-02	1.3E-02
Lungs	4.6E-03	4.4E-03	2.0E-03	2.2E-03	1.0E-02	1.8E-02
Muscle	2.9E-03	3.2E-03	3.7E-03	4.1E-03	1.1E-02	3.3E-03
Ovaries	9.1E-03	8.1E-03	8.4E-03	7.6E-03	1.5E-02	3.7E-03
Pancreas	7.7E-03	6.9E-03	4.1E-03	3.9E-03	1.2E-02	6.6E-03
Red Marrow	5.5E-03	5.0E-03	2.9E-03	2.9E-03	1.1E-02	6.1E-03
Bone Surf	8.2E-03	7.8E-03	4.5E-03	4.8E-03	1.1E-02	7.4E-03
Skin	3.1E-03	2.9E-03	1.3E-03	1.4E-03	8.0E-03	2.0E-03
Spleen	6.5E-03	5.8E-03	3.0E-03	3.0E-03	1.1E-02	1.4E-02
Testes	3.8E-03	3.7E-03	2.4E-03	2.9E-03	1.2E-02	2.3E-03
Thymus	4.1E-03	4.0E-03	2.1E-03	2.4E-03	1.1E-02	6.1E-03
Thyroid	5.3E-03	4.4E-03	5.7E-03	4.8E-03	1.0E-02	5.7E-03
Urinary Bladder Wall	1.1E-02	9.8E-03	1.7E-02	2.6E-02	1.6E-01	8.5E-03
Uterus	7.8E-03	7.2E-03	7.2E-03	7.6E-03	2.1E-02	3.9E-03
Effective Dose	9.0E-03	7.9E-03	7.6E-03	7.0E-03	1.9E-02	7.0E-03

Gy, even for those with thyroid volumes greater than 40 ml; this represents a significant improvement over reported success rates for treatment planning using only a fixed administered activity approach. I-131 labeled meta-iodobenzylguanidine (mIBG) has been used for many years in the treatment of adult and paediatric neuroendocrine tumours, including phaeochromocytoma, paraganglioma and neuroblastoma, typically with administrations of 7.4 GBq to more than 30 GBq in adults[11-13]. Several monoclonal antibodies also have been developed or proposed for cancer treatment. Two products, ^{131}I-labeled Bexxar and ^{90}Y-labeled Zevalin have been approved by the United States Food and Drug Administration (USFDA) for treatment of relapsed or refractory B-cell non-Hodgkins lymphoma. Both employ the same anti-CD20 antibody but with the different radiolabels noted. Treatment with Bexxar is done with a target whole-body dose of 0.75 Gy[14] (with whole body dose being a surrogate for marrow dose). For Zevalin, dosimetry is not performed for individual subjects, although an imaging study is done with the ^{111}In labeled compound to evaluate general distribution of the compound[15]. Radiolabeled peptide therapy for neuroendocrine tumours has included the development of somatostatin analogues such as DOTA-DPhe(1)-Tyr(3)-octreotide (DOTATOC); some dosimetry studies have been reported[16,17].

Patient-specific dose calculations generally are not performed for either diagnostic or therapeutic applications

of radiopharmaceuticals, despite an ongoing trend towards patient-individualized approaches in drug delivery, chemotherapy planning and many other medical areas. In a review of the literature, Stabin[18] provided answers to standard objections to the use of patient-specific dose calculations in nuclear medicine therapy, addressing concerns such as that (1) performing such calculations is difficult and expensive, requiring too much effort, (2) there are no standardized methods for performing individualized dose calculations, and methods vary significantly among different institutions, (3), dose calculations calculated to date have had poor success in predicting tissue response and (4) with the level of difficulty involved, there must be some objective evidence that the use of radiation dose calculations provides positive benefit that justifies extra effort and cost. He concluded that "Continued objections to the use of patient-specific dose calculations are not supported by the available data in the literature, which clearly show that the routine implementation of such approaches are in the best interests of the patients treated, and are in the economic interests of the institution administering the treatment." and that "the time has come for this reasonable paradigm shift in the practice of nuclear medicine."[18]

2. DOSE CALCULATIONAL METHODS AND RESOURCES

A generic equation for the absorbed dose rate in an object uniformly contaminated with radioactivity (for example an organ or tissue with radiopharmaceutical uptake) may be shown as:

$$\dot{D}_T = \frac{k\, A_S \sum_i y_i\, E_i\, \phi_i}{m_T} \qquad (1)$$

where $\dot{D}_T$ = absorbed dose rate to a target region of interest (Gy/sec)
A_S = activity (MBq) in source region S
y_i = number of radiations with energy E_i emitted per nuclear transition
E_i = energy per radiation for the ith radiation (MeV)
ϕ_i = fraction of energy emitted n a source region that is absorbed in a target region
m_T = mass of the target region (kg)
k = proportionality constant (Gy-kg/MBq-sec-MeV)

The proportionality constant k includes the various factors that are needed to obtain the dose rate in the desired units, from the units employed for the other variables, and it is essential that this factor is properly calculated and applied. We may calculate cumulative dose, the time integral of the dose equation; generally, the only term

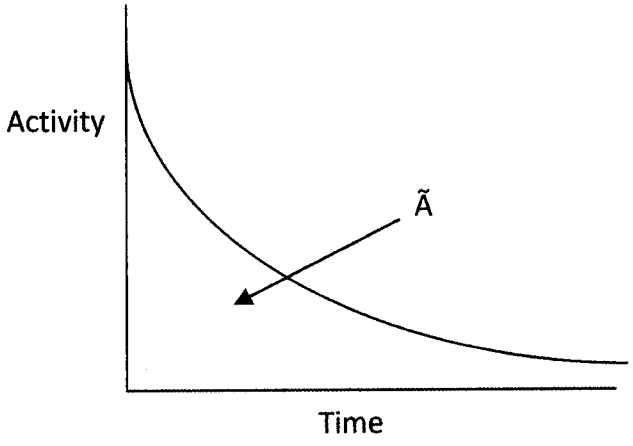

Fig. 1. Generalized Time/Activity Curve for Activity in an Organ

which depends on time is activity, so this is the only factor that has to be integrated. The integral of the time-activity curve, which is the area under that curve, is sometimes called the 'cumulated activity' (Ã), and it represents the total number of disintegrations that have occurred over time in a source region.

The equation for cumulative dose thus becomes:

$$D_T = \int \dot{D}_T\, dt = \frac{k\, \tilde{A}_S \sum_i y_i\, E_i\, \phi_i}{m_T} \qquad (2)$$

where D is the absorbed dose (Gy) and The quantity $\tilde{A}_S$ represents the integral of $A_S(t)$, the time-dependent activity term for activity in the organ:

$$\tilde{A}_S = \int_0^\infty \tilde{A}_S(t)\, dt = A_0 \int_0^\infty f_S(t)\, dt \qquad (3)$$

Here A_0 is the activity administered to the patient at time $t = 0$, and $f_S(t)$ is sometimes called the 'fractional distribution function' for the source region (fraction of administered activity present within the source region at time t). In many instances, the function $f_S(t)$ is given as a sum of exponential functions:

$$f_S(t) = f_1\, e^{-(\lambda_1+\lambda_P)t} + f_2\, e^{-(\lambda_2+\lambda_P)t} + \cdots + f_N\, e^{-(\lambda_N+\lambda_P)t} \qquad (4)$$

The terms $f_1 \ldots f_N$ represent the fractional uptake of the administered activity within the 1st to N^{th} compartments of the source region, $\lambda_1 \ldots \lambda_N$ represent the biological elimination constants for the compartments, and λ_P is the physical decay constant for the radionuclide of interest. Other functional expressions may be used to represent the fractional distribution function, but exponentials are

the ones most commonly encountered.

A generalized expression for calculating internal dose may then be given as[19]:

$$D = N \times DF \tag{5}$$

where N is the number of nuclear transitions that occur in source region S (i.e. $\tilde{A}_S$ as given above), and DF is a 'dose factor'. The factor DF contains the decay data and 'absorbed fractions' (AFs), which are derived generally using Monte Carlo simulation of radiation transport in models of the body and its internal structures (organs, tumors, etc.):

$$DF = \frac{k \sum_i y_i E_i \phi_i}{m_T} \tag{6}$$

As written, the above equation gives only the dose from one source organ to one target organ, but it can be generalized to include contributions from multiple source regions:

$$D_T = \frac{k \sum_S \tilde{A}_S \sum_i y_i E_i \phi_i(T \leftarrow S)}{m_T} \tag{7}$$

The anthropomorphic models employed in the Monte Carlo studies to calculate values of ϕ have evolved from fairly simple geometric constructs to more realistic models that employ image-based methods (Figure 2).

This dose calculational scheme described above is implemented in the Radiation Dose Assessment Resource (RADAR) system[19] (www.doseinfo-radar.com), and in the OLINDA/EXM software code[22]. This has facilitated the standardization and widespread use of these standard models and calculational techniques by many users. The RADAR web site and OLINDA/EXM software currently provide dose factors for over 800 radionuclides for:

1) All source and target regions in the six models in the Cristy/Eckerman phantom series[23],
2) All source and target regions in the four models in the Stabin et al. pregnant female phantoms series[24],
3) All target regions in the Watson and Stabin peritoneal cavity model[25],
4) All target regions in the Stabin prostate gland model[26],
5) All source and target regions in the six models of the MIRD head and brain model[27],
6) All source and target regions in the MIRD regional kidney model[28], and
7) The unit density sphere models of Stabin and Konijnenberg[29].

3. IMAGE-BASED COMPUTATIONAL TOOLS

Several centers have implemented the use of image fusion techniques to develop three dimensional maps of

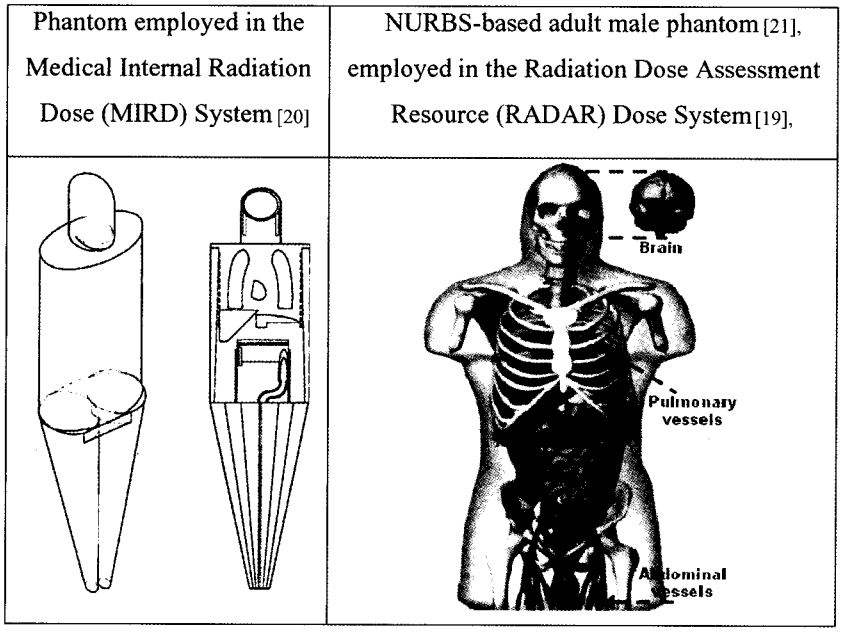

Fig. 2. Comparison of Traditional Body Models with those being used in Current Dose Modeling Efforts

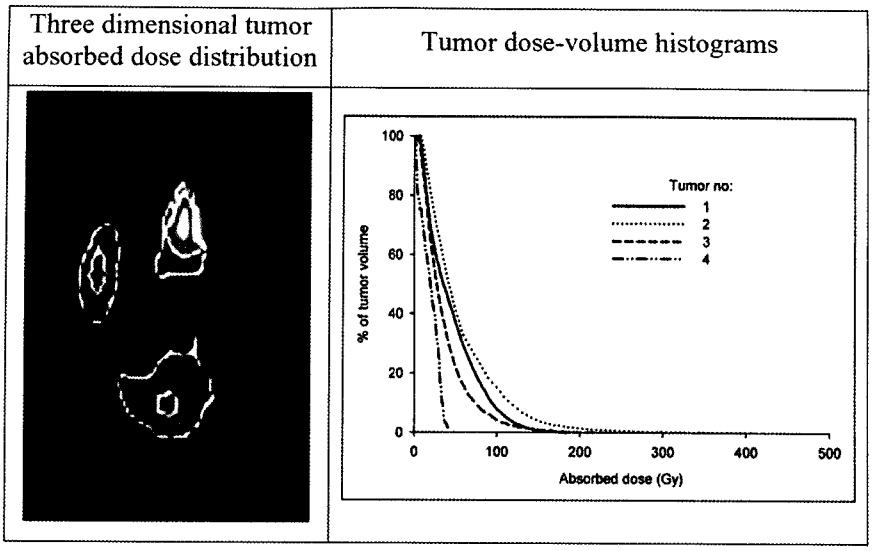

Fig. 3. Three Dimensional Tumor Absorbed dose Distributions (left) and Dose-Volume Histograms (Right) from the 3D-ID Code[36]

dose, instead of only average organ dose estimates from standard models, as are generally available. This suggests that treatment planning for internal emitters may soon be far more sophisticated and similar to that used in external beam therapy for individualized patient therapy planning. Examples include the 3D-ID code from the Memorial Sloan-Kettering Cancer Center[30], the SIMDOS code from the University of Lund[31], the RTDS code at the City of Hope Medical Center[32], the RMDP code from the Royal Marsden Hospital[33], the DOSE3D code[34], and the PEREGRINE code[35]. Figure 3 shows an example of the capabilities of the 3DID code.

4. CONCLUSIONS

Radiation dose calculations for radiopharmaceuticals have been standardized by the implementation and dissemination of tools like the RADAR web site[19] and the OLINDA/EXM software[22]. Current efforts suggest a move towards more image-based and patient-specific methods in internal dose calculations for therapeutic applications in nuclear medicine (e.g. the 3D-ID code[36]. Current evidence in the literature strongly supports the idea that patient-specific dose calculations are needed to improve patient outcomes when internal emitters are used in therapy, as is commonly accepted in external radiation therapy[18].

REFERENCES

[1] M.G. Stabin Internal Radiation Dosimetry. Nuclear Medicine, 2nd Ed., Vol 1, Chapter 22, 313-331, edited by RE Henkin, D Bova, GL Dillahay, JR Halema, SM Karesh, RH Wagner, AM Zimmer. Mosby, St. Louis, MO (2006).

[2] M.G. Stabin, R. Blackwell, R.L. Brent, E. Donnelly, V.A. King, K. Lovins, M. Stovall. Fetal Radiation Dose Calculations. ANSI N13.54-2008, American National Standards Institute, Washington, DC (2008).

[3] International Commission on Radiological Protection. ICRP Publication 53: Radiation Dose to Patients from Radiopharmaceuticals, 53, Pergamon, New York (1989).

[4] International Commission on Radiological Protection. Radiation Dose To Patients From Radiopharmaceuticals. ICRP Publication 80, Pergamon, New York (2000).

[5] United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and Effects of Ionizing Radiation. UNSCEAR 2000 Report to the General Assembly, United Nations Scientific Committee on the Effects of Atomic Radiation (2000).

[6] C. Canzi, F. Zito, F. Voltini, E. Reschini, P. Gerundini. Verification of the agreement of two dosimetric methods with radioiodine therapy in hyperthyroid patients. *Medical Physics* 33(8) 2860-2867 (2006).

[7] T. Carlier, P.Y. Salaun, M.B. Cavarec, F. Valette, A. Turzo, M. Bardies, Y. Bizais, O. Couturier. Optimized radioiodine therapy for Graves' disease: Two MIRD-based models for the computation of patient-specific therapeutic I-131 activity. *Nuclear Medicine Communications* 27(7) 559-566 (2006).

[8] E. E. Furhang, S. M. Larson, P. Buranapong, J. L. Humm. "Thyroid cancer dosimetry using clearance fitting", *Journal of Nuclear Medicine*, 40(1):131-136 (1999).

[9] H. R. Maxon, S. R. Thomas, R. C. Samaratunga. "Dosimetric considerations in the radioiodine treatment of macrometastases and micrometastases from differentiated thyroid cancer", *Thyroid*, 7(2):183-187, (1997).

[10] C. Kobe, W. Eschner, F. Sudbrock, I. Weber, K. Marx, M. Dietlein, H. Schicha. "Graves' disease and radioiodine

therapy: Is success of ablation dependent on the achieved dose above 200 Gy" *Nuklearmedizin*, 47:14, (2007).
[11] C. A. Hoefnagel. "Nuclear medicine therapy of neuroblastoma", *Quarterly Journal of Nuclear Medicine*, 43 (4):336-343 (1999).
[12] K. K. Matthay, C. Panina, J. Huberty, D. Price, D. V. Glidden, H. R. Tang, R. A. Hawkins, J. Veatch, B. Hasegawa. "Correlation of tumor and whole-body dosimetry with tumor response and toxicity in refractory neuroblastoma. treated with I-131-MIBG", *Journal of Nuclear Medicine*, 42(11):1713-1721 (2001).
[13] M. N. Gaze, Y. C. Chang, G. D. Flux, R. J. Mairs, F. H. Saran, S. T. Meller. "Feasibility of dosimetry-based high-dose I-131-meta-iodobenzylguanidine with topotecan as a radiosensitizer in children with metastatic neuroblastoma", *Cancer Biotherapy and Radiopharmaceuticals*, 20(2):195-199 (2005).
[14] R. L. Wahl, S. Kroll, K. R. Zasadny. "Patient-specific whole-body dosimetry: Principles and a simplified method for clinical implementation", *Journal of Nuclear Medicine*, 39(8):14S-20S (1998).
[15] G. A. Wiseman, C. A. White, R. B. Sparks, W. D. Erwin, D. A. Podoloff, D. Lamonica, N. L. Bartlett, J. A. Parker, W. L. Dunn, S. M. Spies, R. Belanger, T. E. Witzig, B. R. Leigh. "Biodistribution and dosimetry results from a phase III prospectively randomized controlled trial of Zevalin (TM) radioimmunotherapy for low-grade, follicular, or transformed B- cell non-Hodgkin's lymphoma", *Critical Reviews in Oncology Hematology*, 39(1-2):181-194 (2001).
[16] M. Cremonesi, M. Ferrari, M. Chinol, M. Bartolomei, M.G. Stabin, E. Sacco, M. Fiorenza, G. Tosi, G. Paganelli. "Dosimetry in radionuclide therapies with Y-90-conjugates: the IEO experience", Quarterly Journal of Nuclear Medicine, vol. 44, no. 4, pp. 325-332, 2000
[17] Barone R., Walrand S., Valkema R., Kvols L., Smith C., Krenning E. P., Jamar F., & Pauwels S. "Correlation between acute red marrow (RM) toxicity and RM exposure during Y-90-SMT487 therapy", *Journal of Nuclear Medicine*, 43(5):1267 (2002).
[18] M.G. Stabin The Case for Patient-Specific Dosimetry in Radionuclide Therapy. *Cancer Biotherapy & Radiopharmaceuticals*, 23 (3): 273-284 (2008).
[19] M.G. Stabin and J. A. Siegel. Physical Models and Dose Factors for Use in Internal Dose Assessment. *Health Physics*, 85(3):294-310 (2003).
[20] W. Snyder, M. Ford, G. Warner. Estimates of specific absorbed fractions for photon sources uniformly distributed in various organs of a heterogeneous phantom. MIRD Pamphlet No. 5, revised, Society of Nuclear Medicine, New York (1978).
[21] J.P. Segars. Development and Application of the New Dynamic NURBS-based Cardiac-Torso (NCAT) Phantom, Ph.D. Dissertation, The University of North Carolina (2001).
[22] M. G. Stabin, R. B. Sparks, E. Crowe. OLINDA/EXM: The Second-Generation Personal Computer Software for Internal Dose Assessment in Nuclear Medicine. *J Nucl Med* 46 1023-1027 (2005).
[23] M. Cristy and K. Eckerman.Specific absorbed fractions of energy at various ages from internal photons sources. ORNL/TM-8381 V1-V7. Oak Ridge National Laboratory, Oak Ridge, TN (1987).
[24] M. Stabin, E. Watson, M. Cristy, J. Ryman, K. Eckerman, J. Davis, D. Marshall., K. Gehlen. Mathematical models and specific absorbed fractions of photon energy in the nonpregnant adult female and at the end of each trimester of pregnancy. ORNL Report ORNL/TM-12907 (1995).
[25] E.E. Watson, M.G. Stabin, J.L. Davis, K.F. Eckerman. A Model of the Peritoneal Cavity for Use in Internal Dosimetry. *J Nucl Med* 30:2002-2011 (1989).
[26] M.G. Stabin. A Model of the Prostate Gland for Use in Internal Dosimetry. J Nucl Med 35(3):516-520 (1994).
[27] L. Bouchet, W. Bolch, D. Weber, H. Atkins, J. Poston, Sr. MIRD Pamphlet No 15: Radionuclide S values in a revised dosimetric model of the adult head and brain. *J Nucl Med* 40:62S-101S (1999).
[28] L.G. Bouchet, W.E. Bolch, H.P. Blanco, B.W. Wessels, J.A. Siegel, D.A. Rajon, I. Clairand, G. Sgouros. MIRD Pamphlet No. 19: Absorbed Fractions and Radionuclide S Values for Six Age-Dependent Multiregion Models of the Kidney. *J. Nucl. Med.* 44: 1113-1147 (2003).
[29] M.G. Stabin, M. Konijnenberg. Re-evaluation of absorbed fractions for photons and electrons in small spheres. *J Nucl Med* 41:149-160 (2000).
[30] K.S. Kolbert, G. Sgouros, A.M. Scott, J.E. Bronstein, R.A. Malane, J. Zhang, H. Kalaigian, S. McNamara, L. Schwartz, S.M. Larson. Implementation and evaluation of patient-specific three-dimensional internal dosimetry. *J. Nucl. Med.* 38: 301-308 (1997).
[31] Y. K. Dewaraja, S.J. Wilderman, M. Ljungberg, K.F. Koral, K. Zasadny, M. S. Kaminiski. Accurate Dosimetry in 131I Radionuclide Therapy Using Patient-Specific, 3-Dimensional Methods for SPECT Reconstruction and Absorbed Dose Calculation. *J. Nucl. Med.* 2005 46: 840-849 (2005).
[32] A. Liu, L. Williams, G. Lopatin, D. Yamauchi, J. Wong, A. Raubitschek. A radionuclide therapy treatment planning and dose estimation system. *J Nucl Med* 40:1151-1153 (1999).
[33] M. J. Guy, G. D. Flux, P. Papavasileiou, M. A. Flower, R. J. Ott. RMDP: A dedicated package for I-131 SPECT quantification, registration and patient-specific dosimetry, *Cancer Biotherapy and Radiopharmaceuticals*, 18(1): 61-69, (2003).
[34] I. Clairand, M. Ricard, J. Gouriou, M. Di Paola, B. Aubert. DOSE3D: EGS4 Monte Carlo code-based software for internal radionuclide dosimetry. *J. Nucl. Med.* 40: 1517-1523 (1999).
[35] J. Lehmann, C. Hartmann Siantar, D.E. Wessol, C.A. Wemple, D. Nigg, J. Cogliati, T. Daly, M.A. Descalle, T. Flickinger, D. Pletcher, G. Denardo. Monte Carlo treatment planning for molecular targeted radiotherapy within the MINERVA system. *Phys Med Biol.* Mar 7;50(5):947-58 (2005).
[36] G. Sgouros, K.S. Kolbert, A.Sheikh, K.S. Pentlow, E.F. Mun, A.Barth, R.J. Robbins, S.M. Larson. Patient-Specific Dosimetry for 131I Thyroid Cancer Therapy Using 124I PET and 3-Dimensional-Internal Dosimetry (3D-ID) Software. *J Nucl Med* 45: 1366-1372, (2004).