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Quantitative Analysis of Iodine Thyroid and Gastrointestinal Tract Biokinetic Models Using MATLAB

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1. Introduction

This chapter quantitatively analyzed the biokinetic models of iodine thyroid and the gastrointestinal tract (GI tract) using MATLAB software. Biokinetic models are widely used to analyze the internally absorbed dose of radiation in patients who have undergone a nuclear medical examination, or to estimate the dose of I-131 radionuclide that is absorbed by a critical organ in patients who have undergone radiotherapy (ICRP-30, 1978). In the specific biokinetic model, human organs or tissues are grouped into many compartments to perform calculations. The defined compartments vary considerably among models, because each model is developed to elucidate a unique function of the human metabolic system.

The solutions to the time-dependent simultaneous differential equations that are associated with both the iodine and the GI tract model, obtained using the MATLAB default programming feature, yield much medical information, because the calculations that are made using these equations provide not only the precise time-dependent quantities of the radionuclides in each compartment in the biokinetic model but also a theoretical basis for estimating the dose absorbed by each compartment. The results obtained using both biokinetic models can help a medical physicist adjust the settings of the measuring instrumentation in the radioactive therapy protocol or the radio-sensitivity of the dose monitoring to increase the accuracy of detection and reduce the uncertainty in practical measurement.

In this chapter, MATLAB algorithms are utilized to solve the time-dependent simultaneous differential equations that are associated with two biokinetic models and to define the correlated uncertainties that are related to the calculation. MATLAB is seldom used in the medical field, because the engineering-based definition of the MATLAB parameters reduces its ease of use by unfamiliar researchers. Nevertheless, using MATLAB can greatly accelerate analysis in a practical study. Some firm recommendations concerning future studies on similar topics are presented and a brief conclusion is drawn.

2. Iodine thyroid model

2.1 Biokinetic model

The iodine model simulates the effectiveness of healing by patients following the post-surgical administering of ¹³¹I for the ablation of residual thyroid. Following initial treatment (a near-

total or total thyroidectomy), most patients are treated with ^{131}I for ablation of the residual thyroid gland (De Klerk *et al.*, 2000; Schlumberger 1998). However, estimates of cumulative absorbed doses in patients and people close to them remains controversial, despite the establishment of the criteria for applying the iodine biokinetic model to a healthy person from the ICRP-30 report. Conversely, the biokinetic model of iodine that is applied following the remnant ablation of the thyroid must be reconsidered from various perspectives, because the gland that is designated as dominant, the thyroid, in (near-) total thyroidectomy patients is the remnant gland of interest (Kramer *et al.*, 2002; North *et al.*, 2001).

According to the ICRP-30 report in the biokinetic model of iodine, a typical human body can be divided into five major compartments. They are (1) stomach, (2) body fluid, (3) thyroid, (4) whole body, and (5) excretion as shown in Fig. 1. Equations 1-4 are the simultaneous differential equations for the time-dependent correlation among iodine nuclides in the compartments

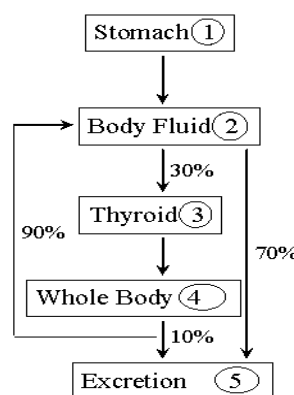


Fig. 1. Biokinetic model of Iodine for a standard healthy man. The model was recommended by ICRP-30.

$$\frac{d}{dt}q_{ST} = -(\lambda_R + \lambda_{ST})q_{ST} \quad (1)$$

$$\frac{d}{dt}q_{BF} = \lambda_{ST}q_{ST} - (\lambda_R + \lambda_{BF1} + \lambda_{BF2})q_{BF} + \lambda_{WB2}q_{WB} \quad (2)$$

$$\frac{d}{dt}q_{Th} = \lambda_{BF1}q_{BF} - (\lambda_R + \lambda_{Th})q_{Th} \quad (3)$$

$$\frac{d}{dt}q_{WB} = \lambda_{Th}q_{Th} - (\lambda_R + \lambda_{WB2} + \lambda_{WB1})q_{WB} \quad (4)$$

The terms q_i and λ_i are the time-dependent quantity of ^{131}I in all compartments and the decay constants between pairs of compartment, respectively (R: physical half life, ST: stomach, BF: body fluid, Th: thyroid, WB: whole body). Accordingly, the quantity of iodine nuclide in the stomach decreases regularly, whereas the quantity change inside the body fluid is complicated because the iodine can be transported from either stomach or whole body into the body fluid and then removed outwardly also from two channels (to thyroid or to excretion directly). The quantity change of iodine nuclides in either thyroid or whole

body is comparatively direct since only one channel is defined for inside or outside [Fig. 1]. Since the biological half-lives of iodine, as recommended by ICRP-30 for the stomach, body fluid, thyroid and whole body, are 0.029d, 0.25d, 80d and 12d, respectively, the corresponding decay constants for each variable can be calculated [Tab. 1]. Additionally, the time-dependent quantity of iodine in each compartment is depicted in Fig. 2, and the initial time is the time when the ¹³¹I is administered to the patient.

λ	coeff.	Derivation
λ_R	$0.0862 d^{-1}$	$\ln 2 / 8.0$
λ_{ST}	$24 d^{-1}$	$\ln 2 / 0.029$
λ_{BF1}	$0.832 d^{-1}$	$0.3 \times \ln 2 / 0.25$
λ_{BF2}	$1.940 d^{-1}$	$0.7 \times \ln 2 / 0.25$
λ_{Th}	$0.0058 d^{-1}$	$\ln 2 / 120$
λ_{WB2}	$0.052 d^{-1}$	$0.9 \times \ln 2 / 12$
λ_{WB1}	$0.0052 d^{-1}$	$0.1 \times \ln 2 / 12$

Table 1. The coefficients of variables for simultaneous differential equations as adopted in this work. The calculation results are theoretical estimations of the time-dependent quantity of iodine in various compartments for a typical body. Additionally, the decay constant for physical half-life of ¹³¹I is indicated as λ_R and the physical half-life is 8.0 d.

2.2 MATLAB algorithms

Eqs 1-4 can be reorganized as below and solved by the MATLAB program.

$$\begin{bmatrix} dN_{ST} / dt \\ dN_{BF} / dt \\ dN_{Th} / dt \\ dN_{WB} / dt \end{bmatrix} = \begin{bmatrix} -(\lambda_{ST} + \lambda_R) & 0 & 0 & 0 \\ \lambda_{ST} & -(\lambda_{BF1} + \lambda_{BF2} + \lambda_R) & 0 & \lambda_{WB2} \\ 0 & \lambda_{BF} & -(\lambda_{Th} + \lambda_R) & 0 \\ 0 & 0 & \lambda_{Th} & -(\lambda_{WB1} + \lambda_{WB2} + \lambda_R) \end{bmatrix} \begin{bmatrix} N_{ST} \\ N_{BF} \\ N_{Th} \\ N_{WB} \end{bmatrix}$$

The MATLAB program is depicted as below;

```
#####
A=[-24.086 0 0 0;24 -2.859 0 0.052; 0 0.832 -0.0922 0; 0 0 0.0058 -0.144];
x0 = [1 0 0 0]';
B = [0 0 0 0]';
C = [1 0 0 0]';
D = 0;
for i = 1:101,
    u(i) = 0;
    t(i) = (i-1)*0.1;
end;
sys=ss(A,B,C,D);
[y,t,x] = lsim(sys,u,t,x0);
plot(t,x(:,1),'-',t,x(:,2),'-',t,x(:,3),'-',t,x(:,4),'-',t,x(:,2)+x(:,4),'-');
semilogx(t,x(:,1),'-',t,x(:,2),'-',t,x(:,3),'-',t,x(:,4),'-',t,x(:,2)+x(:,4),'-');
legend('ST','BF','Th','WB','BF+WB')
```

```

% save data
n = length(t);
fid = fopen('44chaineq.txt','w'); % Open a file to be written
for i = 1:n,
    fprintf(fid,'%20.16f %20.16f %20.16f %20.16f %20.16f
%20.16f\n',t(i),x(i,1),x(i,2),x(i,3),x(i,4),x(i,2)+x(i,4)); % Saving data
end
fclose(fid);
save 44chaineq.dat -ascii t,x
#####

```

Figure 2 plots the derived time-dependent quantities of iodine in various compartments in the biokinetic model. The solid dots represent either the sum of quantities in the body fluid and the whole body, or the thyroid gland. The practical measurement made regarding body fluid and whole body cannot be separated out, whereas the data concerning the thyroid gland are easily identified data collection.

2.3 Experiment

2.3.1 Characteristics of patients

Five patients (4F/1M) aged 37~46 years underwent one to four consecutive weeks of whole body scanning using a gamma camera following the post-surgical administration of ^{131}I for ablation of the residual thyroid. An iodine clearance measurement was made on all five patients before scanning to suppress interference with the data.

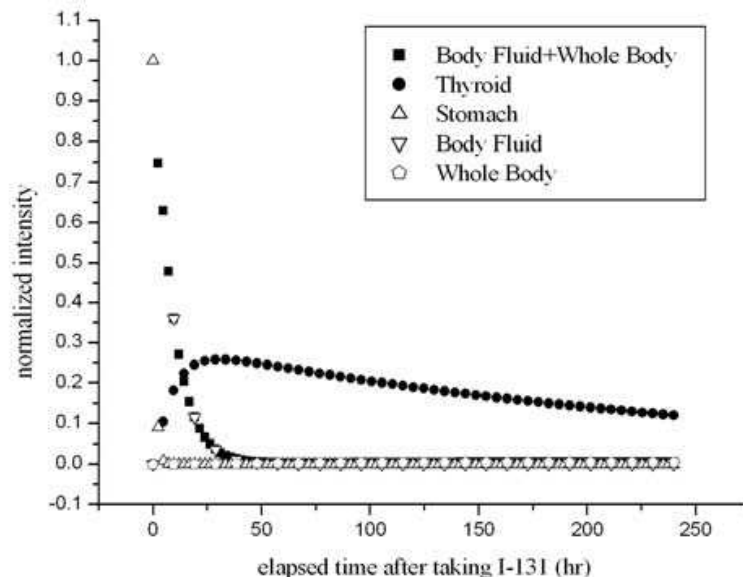


Fig. 2. The theoretical estimation for time-dependent quantities of iodine in various compartments of the biokinetic model.

2.3.2 Gamma camera

The gamma camera (SIEMENS E-CAM) was located at Chung-Shan Medical University Hospital (CSMUH). The gamma camera's two NaI $48 \times 33 \times 0.5 \text{ cm}^3$ plate detectors were positioned 5 cm above and 6 cm below the patient's body during scanning. Each plate was

connected to a 2"-diameter 59 Photo Multiplier Tube (PMT) to record the data. Ideally, the two detectors captured ~70% of the emitted gamma ray. Each patient scanned was given a 1.11GBq (30 mCi) ^{131}I capsule for thyroid gland remnant ablation. The ^{131}I capsule was carrier-free with a radionuclide purity that exceeded 99.9% and radiochemical purity that exceeded 95.0%. All radio pharmaceutical capsules were fabricated by Syncor Int., Corp. The coefficient of variance (%CV) of the activity of all capsules from a single batch was less than 1.0%, as verified by spot checks (Chen *et al.*, 2003). Therefore, the position-sensitive gamma ray emitted from the ^{131}I that was administered to patient could be analyzed and plotted.

2.3.3 Whole body scanning of patients

Each patient was treated with 1.11 GBq ^{131}I once weekly for four consecutive weeks, to ensure ablation of the residual thyroid gland. This treatment suppressed the rapid absorption of ultra high doses by normal organs. Post treatment ^{131}I was typically administered six weeks after the thyroidectomy operation. However, thyroid medication was discontinued during the sixth week to reduce the complexity of any side effects. Care was taken to ensure that drugs that were administered one week before scanning contained no iodine or radiographic contrast agent. Table 2 presents the measured data and the scanning schedule for the first subject for the first week. The schedules for other patients were similar, with only minor modifications. The final column in Tab. 2 presents data obtained from the thigh as ROI. This area was used to determine the pure background for the NaI counting system. Additionally, the body fluid and whole body compartments were treated as a single compartment and re-defined as "remainder" in the empirical evaluation since *in-vivo* measurements of these compartments were not separable. Therefore, the net counts for the ROI (either the remainder or the thyroid) were simply determined by subtracting either the count in the thigh region plus that in the thyroid areas or that in the thigh area only from the total counts from the entire whole body.

2.4 Data analysis

Data for each patient are analyzed and normalized to provide initial array in MATLAB output format to fit the optimal data for Eqs. 1-4. Additionally, to distinguish between the results fitted in MATLAB and the practical data from each subject, a value, Agreement (AT), is defined as

$$AT = \sqrt{\frac{\sum_{i=1}^n [Y_i(\text{nor. iten.}) - Y_i(\text{MATLAB})]^2}{N}} \times 100\% \quad (5)$$

where $Y_n(\text{nor. iten.})$ and $Y_n(\text{MATLAB})$ are the normalized intensity that were practically obtained from each subject in the n^{th} acquisition, and that data computed using MATLAB, respectively. N is defined to be between 11 and 17, corresponding to the different counting schedules of the subjects herein.

An AT value of zero indicates perfect agreement between analytical and empirical results. Generally, an AT value of less than 5.00 can be regarded as indicating excellent consistency between computational and practical data, whereas an AT within the range 10.00-15.00 may still offer reliable confidence in the consistency between analytical and empirical results (Pan *et al.*, 2000; 2001). Table 3 shows the calculated data for five subjects over four weeks of whole body scanning. As shown in Tab. 3, the $T_{1/2}(\text{thy.})$ and $T_{1/2}(\text{BF})$ are changed from 80d and 0.25d to $0.66 \pm 0.50\text{d}$ and $0.52 \pm 0.23\text{d}$, respectively. Yet, the branching ratio from the body

fluid compartment to either the thyroid compartment ($I_{thy.}$) or the excretion compartment ($I_{exc.}$) is changed from 30% or; 70%, respectively to $11.4 \pm 14.6\%$ or; $88.4 \pm 14.6\%$, respectively. A shorter biological half-life ($80d \rightarrow 0.66d$) and a smaller branching ratio from body fluid to remnant thyroid gland ($30\% \rightarrow 11.4\%$) also reveal the rapid excretion of the iodine nuclides by the metabolic mechanism in thyroidectomy patients.

Figure 3 presents the results computed using MATLAB along with practical measurement for various subjects, to clarify the evaluation of the ^{131}I nuclides of either the thyroid compartment or the remainder. As clearly shown in Fig. 3, the consistency between each calculated curve and practical data for various subjects reveals not only the accuracy of calculation but also the different characteristics of patients' biokinetic mechanism, reflecting the real status of remnant thyroid glands.

2.5 Discussion

Defining the biological half-life of iodine in the thyroid compartment without considering the effects of other compartments in the biokinetic model remains controversial. For healthy people, the thyroid compartment dominates the biokinetic model of iodine. In contrast, based on the analytical results, for (near) total thyroidectomy patients, both the body fluid and the thyroid dominate the revised biokinetic model. Additionally, the biological half-life of iodine in the thyroid of a healthy person can be evaluated directly using the time-dependent curve. The time-dependent curve for thyroidectomy patients degrades rapidly because of iodine has a short biological half-life in the remnant thyroid gland. Withholding iodine from the body fluid compartment of thyroidectomy patients rapidly increases the percentage of iodine nuclides detected in subsequent *in-vivo* scanning.

counting No.	elapsed time(hrs)	whole body	thyroid	thigh
1	0.05	21504618	355224	101133
2	0.25	19894586	434947	219306
3	0.5	22896468	754599	308951
4	0.75	23417836	834463	298034
5	1.00	23645836	944563	316862
6	2.00	21987448	1014885	311113
7	3.00	18901178	1124704	260065
8	4.00	18997956	1329043	245960
9	5.00	19006712	1297005	242498
10	6.00	16861720	1247396	204844
11	7.00	16178016	1334864	191212
12	8.00	14884935	1222750	175766
13	32.00	7810032	1080369	70999
14	56.00	3709699	949135	17926
15	80.00	2100217	673606	7377
16	104.00	1639266	540182	4627
17	128.00	1477639	429230	5457

Table 2. The time schedule for, and measured data from, whole body scanning of patient case 5. The last column presents data for the thigh area. This specific area simulated the pure background for the NaI counting system.

In a further examination of the theoretical biokinetic model, since 90% of the administered ^{131}I to the whole body (compartment 4) feeds back to the body fluid (compartment 2) and only 30% of the administered ^{131}I in the body fluid flows directly into the thyroid (compartment 3) [Fig. 1], the cross-links between compartments make obtaining solutions to Eqs. 1-4 extremely difficult. Just a small change in the biological half-life of iodine in the thyroid compartment significantly affects the outcomes for all compartments in the biokinetic model. Moreover, the effect of the stomach (compartment 1) on all compartments is negligible in this calculation because the biological half-life of iodine in the stomach is a mere 0.029 day (~40min). The scanned gamma camera counts from the stomach yield no useful data two hours after I-131 is administered, since almost 90% of all of the iodine nuclides are transferred to other compartments. Therefore, analysis of the calculated ^{131}I nuclides in the biokinetic model remains in either the remainder or the thyroid compartment only (Chen *et al.*, 2007).

Case No.	week	$T_{1/2}(\text{thy.})$ (d)	$T_{1/2}(\text{BF})(\text{d})$	$I_{\text{thy}}(\%)$	$I_{\text{exc}}(\%)$	AT_{thy}	AT_{BF}
ICRP-30		80	0.25	30	70		
1	1	1.10	0.65	12.5	87.5	1.74	31.22
	2	0.50	0.50	5.0	95.0	0.60	12.58
	3	0.50	0.50	5.0	95.0	0.60	12.10
	4	0.50	0.50	5.0	95.0	0.55	6.23
2	1	1.70	1.20	55.0	45.0	4.34	7.56
	2	1.25	0.80	32.5	67.5	5.24	25.38
	3	1.10	0.55	12.5	87.5	3.21	30.13
	4	0.50	0.30	5.0	95.0	1.20	35.90
3	1	0.15	0.40	5.0	95.0	0.53	8.93
	2	0.15	0.40	5.0	95.0	0.22	2.07
	3	0.15	0.40	5.0	95.0	0.10	3.64
	4	0.15	0.40	5.0	95.0	0.70	7.56
4	1	0.25	0.25	5.0	95.0	0.62	27.65
5	1	1.25	0.50	5.0	95.0	1.74	5.79
Average		0.66 ± 0.50	0.52 ± 0.23	11.4 ± 14.6	88.4 ± 14.6	1.52 ± 1.54	14.05 ± 11.01

Table 3. The reevaluated results for five patients in this work. The theoretical data quoted from ICRP-30 report is also listed in the first row for comparing.

3. Gastrointestinal tract model

The gastric emptying half time (GET) of solid food in 24 healthy volunteers is evaluated using the gamma camera method. The GET of solids is used to screen for gastric motor disorders and can be determined using many approaches, among which the gamma camera survey is simple and reliable. Additionally, scintigraphic gastric emptying tests are used extensively in both academic research and clinical practice, and are regarded as the gold-standard for evaluating gastric emptying (Minderhoud *et al.*, 2004; Kim *et al.*, 2000). The GET can also be estimated by monitoring the change in the concentration of an ingested tracer in the blood, urine, or breath, since the tracer is rapidly absorbed only after it leaves the stomach. The tracer, the paracetamol absorption approach and the ^{13}C -octanoate breath test (OBT), all support convenient means of evaluating GET. However, the breath test yields

only a convolution index of GE, although it requires no gamma camera and can be performed at the bedside (Sanaka *et al.*, 1998; 2006).

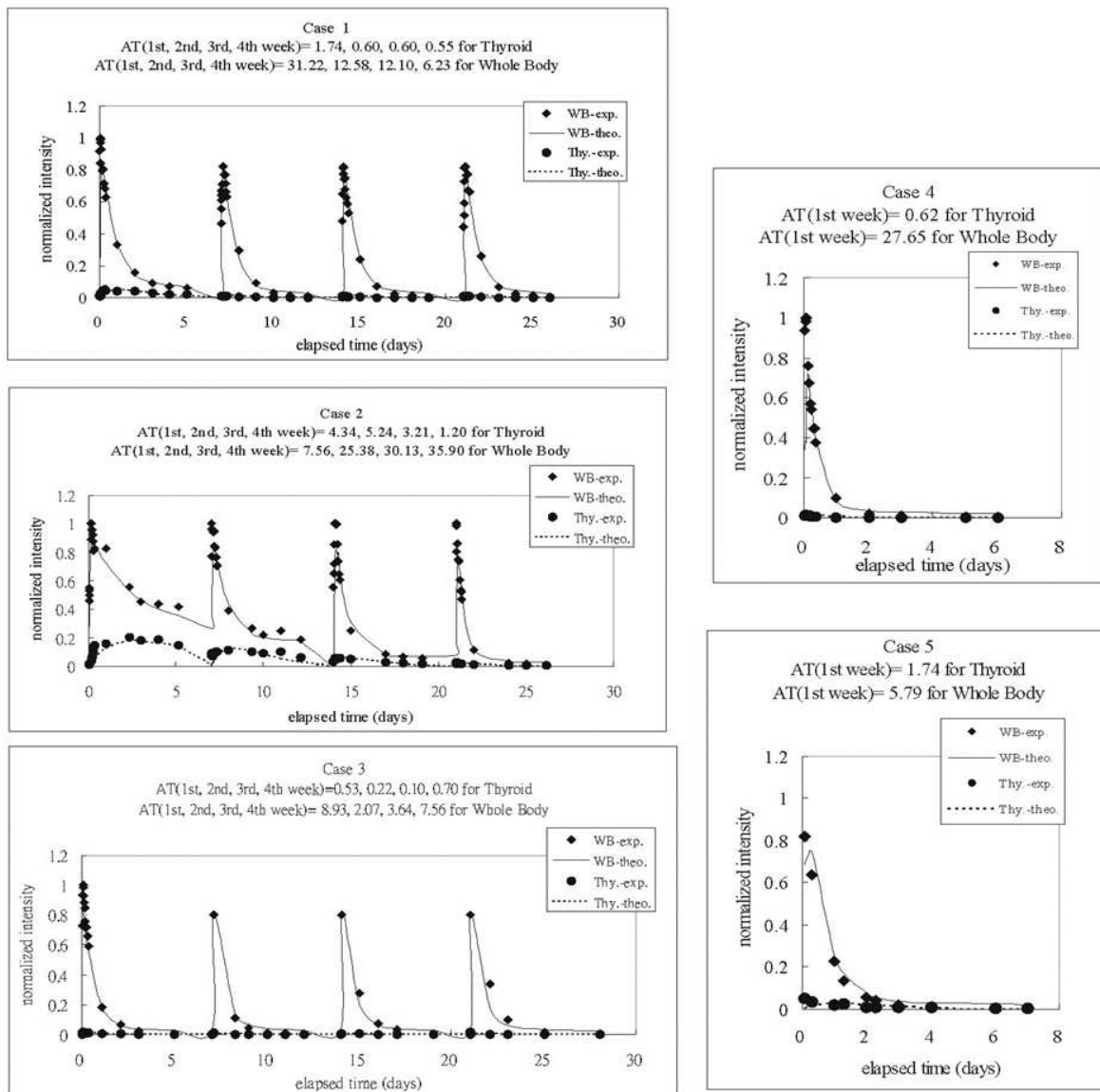


Fig. 3. The time-dependent intensity of either whole body plus body fluid compartments or thyroid compartment from the optimized results of revised biokinetic model of iodine. The various data from *in-vivo* scanning of 5 patients are also included.

The use of a gamma camera to survey the absorption by subjects of Tc-99m radionuclide-labeled products satisfies the criteria for the application of the GI tract biokinetic model, because the short physical half life of Tc-99m is such that a limited dose is delivered. In this study, the revised GET of solids is determined from several *in-vivo* measurements made of healthy volunteers. Twenty-four healthy volunteers underwent a 5 min. scan from neck to knee once every 30 min. for six hours using a gamma camera. Measured data were analyzed and normalized as input data to a program in MATLAB. The revised GET of solids for volunteers differed significantly from those obtained using a theoretical simulation that was based on the ICRP-30 recommendation.

3.1 Biokinetic model

According to the ICRP-30 report, the biokinetic model of the GI tract divides a typical human body into five major compartments, which are (1) stomach (ST), (2) small intestine (SI), (3) upper large intestine (ULI), (4) lower large intestine (LLI), and (5) body fluid (BF), as shown in Fig. 4. Equations 6-9 are the simultaneous differential equations that specify the time-dependent correlation among the quantities of the radio-activated Tc-99m nuclides in the compartments.

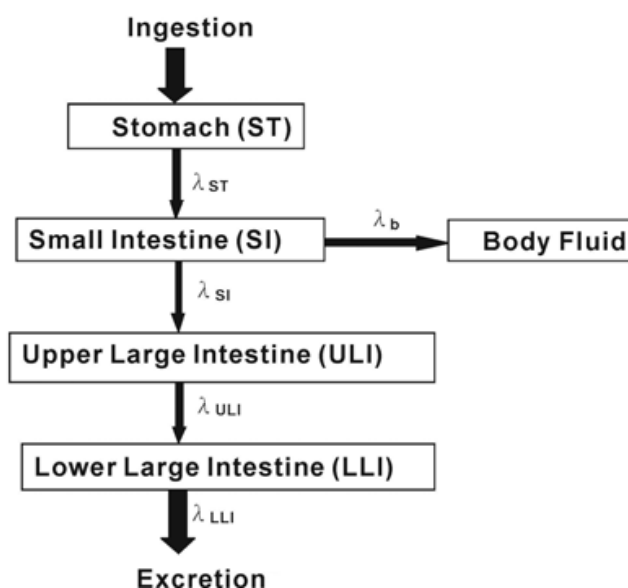


Fig. 4. Biokinetic model of Gastric Intestine Tract for a standard healthy man. The model is recommended by the ICRP-30 report.

$$\frac{d}{dt}q_{ST} = -(\lambda_{ST} + \lambda_R) \cdot q_{ST} \tag{6}$$

$$\frac{d}{dt}q_{SI} = -(\lambda_{SI} + \lambda_b + \lambda_R) \cdot q_{SI} + \lambda_{ST} \cdot q_{ST} \tag{7}$$

$$\frac{d}{dt}q_{ULI} = -(\lambda_{ULI} + \lambda_R) \cdot q_{ULI} + \lambda_{SI} \cdot q_{SI} \tag{8}$$

$$\frac{d}{dt}q_{LLI} = -(\lambda_{LLI} + \lambda_R) \cdot q_{LLI} + \lambda_{ULI} \cdot q_{ULI} \tag{9}$$

The terms q_i and λ_i are defined as the time-dependent quantities of radionuclide, Tc-99m, and the biological half-emptying constants, respectively, for the compartments. λ_R is the physical decay constant of the Tc-99m radionuclide.

Since the biological half lives of Tc-99m, given by ICRP-30, in the stomach, small intestine, upper large intestine and lower large intestine are 0.029d, 0.116d, 0.385d and 0.693d, respectively, the corresponding half-emptying constants can be calculated, and are presented in Fig. 4. Additionally, λ_b is the metabolic removal rate and equals $[f_1 \times \lambda_{SI} / (1 - f_1)]$. This term varies with the chemical compound and is 0.143 for Tc-99m nuclides.

λ	Half-emptying constant	Derivation
λ_R	2.77 d ⁻¹	(ln2 / 6.0058) × 24
λ_{ST}	24 d ⁻¹	ln 2 / 0.029
λ_{SI}	6 d ⁻¹	ln 2 / 0.116
λ_{ULI}	1.8 d ⁻¹	ln 2 / 0.385
λ_{LLI}	1 d ⁻¹	ln 2 / 0.693
λ_b	1 d ⁻¹	0.143×6 / (1-0.143)

Table 4. The coefficients of variables for simultaneous differential equations as adopted in this work. The calculation results are theoretical estimations of the time-dependent quantity of Tc-99m in various compartments for a typical body. Additionally, the decay constant for physical half life of Tc-99m is indicated as λ_R and the physical half-life is 6.0058 h.

3.2 MATLAB algorithms

Eqs 6-9 can be reorganized again as below and solved by the MATLAB program.

$$\begin{bmatrix} dN_{ST} / dt \\ dN_{SI} / dt \\ dN_{ULI} / dt \\ dN_{LLI} / dt \end{bmatrix} = \begin{bmatrix} -(\lambda_{ST} + \lambda_R) & 0 & 0 & 0 \\ \lambda_{ST} & -(\lambda_{SI} + \lambda_b + \lambda_R) & 0 & 0 \\ 0 & \lambda_{SI} & -(\lambda_{ULI} + \lambda_R) & 0 \\ 0 & 0 & \lambda_{ULI} & -(\lambda_{LLI} + \lambda_R) \end{bmatrix} \begin{bmatrix} N_{ST} \\ N_{SI} \\ N_{ULI} \\ N_{LLI} \end{bmatrix}$$

The MATLAB program is depicted as below;

```
#####
A=[-26.77 0 0 0;24 -9.77 0 0; 0 6 -4.57 0; 0 0 1.8 -3.77];
x0 = [1 0 0 0]';
B = [0 0 0 0]';
C = [1 0 0 0];
D = 0;
for i = 1:101,
    u(i) = 0;
    t(i) = (i-1)*0.01;
end;
sys=ss(A,B,C,D);
[y,t,x] = lsim(sys,u,t,x0);
plot(t,x(:,1),'-',t,x(:,2),'-',t,x(:,3),'-',t,x(:,4),'-',t,x(:,2)+x(:,3)+x(:,4),'-');
semilogx(t,x(:,1),'-',t,x(:,2),'-',t,x(:,3),'-',t,x(:,4),'-',t,x(:,2)+x(:,3)+x(:,4),'-');
legend('ST','SI','ULI','LLI','SI+ULI+LLI')
% save data
n = length(t);
fid = fopen('gi44chaineq.txt','w'); % Open a file to be written
for i = 1:n,
    fprintf(fid,'%10.8f %20.16f %20.16f %20.16f %20.16f
%20.16f\n',t(i),x(i,1),x(i,2),x(i,3),x(i,4),x(i,2)+x(i,3)+x(i,4)); % Saving data
end
```

```
fclose(fid);
save gi44chaineq.dat -ascii t,x
#####
```

Figure 5 shows the time-dependent amount of Tc-99m in each compartment, and the initial time is defined as the time when a Tc-99m dose is administered to the volunteer. The results can be calculated and plotted using a program in MATLAB.

3.3 Experiment

3.3.1 Characteristics of volunteers

Twenty-four healthy volunteers (13F/11M) aged 19~75 years underwent six continuous hours of whole body scanning using a gamma camera after they had ingested Tc-99m-labeled phytate with solid food.

3.3.2 Tc-99m-labeled phytate solid food

The test meal comprised solid food and a cup of 150 ml water that contained 5% dextrose. The solid food was two pieces of toast and a two-egg-omelet. The two eggs were broken, stirred and mixed with 18.5 MBq (0.5 mCi) Tc-99m-labeled phytate. Each omelet was baked in an oven for 20 min at 250 °C, and then served to a volunteer. Each volunteer had fasted for at least eight hours before eating the meal and finished it in 20 minutes, to avoid interference with the data.

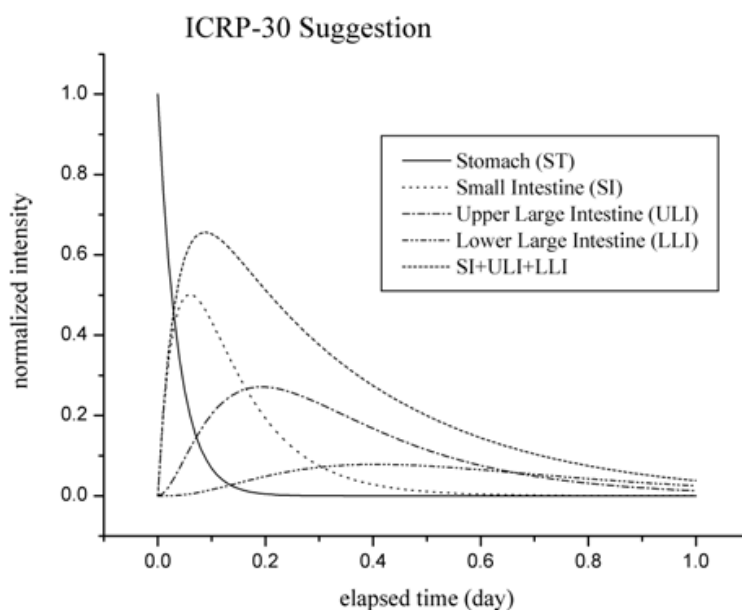


Fig. 5. The theoretical estimation for time-dependent amounts of Tc-99m in various compartments of the biokinetic model.

3.3.3 Gamma camera

The gamma camera (SIEMENS E-CAM) was located at the Department of Nuclear Medicine, TaiChung Veterans General Hospital (TVGH). The camera's two NaI (48×33×0.5 cm³) plate detectors were positioned 5 cm above and 6 cm below the volunteer's body during scanning. Each plate was connected to a 2"-diameter 59 Photo Multiplier Tube (PMT) to record data. The two detectors captured ~70% of the emitted gamma rays.

3.3.4 Whole body scanning of volunteers

Each volunteer underwent his/her first gamma camera scan immediately after finishing the meal. The scan protocol was as follows; supine position, energy peak of 140 keV (window: 20%), LEHS collimator, 128×128 matrix, and scan speed of 30 cm/min. over a distance of 150 cm (~5 min. scan from neck to knee) for 5 min. every half hour. The complete scan took six hours. Thirteen sets of data were recorded for every volunteer for analysis. The regions of interest (ROIs) of the images in the subsequent analysis were (1) whole body, WB, (2) stomach, ST, and (3) small intestine, upper large intestine and lower large intestine, SI+ULI+LLI. The data that were obtained from SI could not be separated from those obtained from ULI or LLI, whereas the data for ST were easily distinguished during the collection of data. Therefore, the SI, ULI, and LLI data were summed in the data analysis.

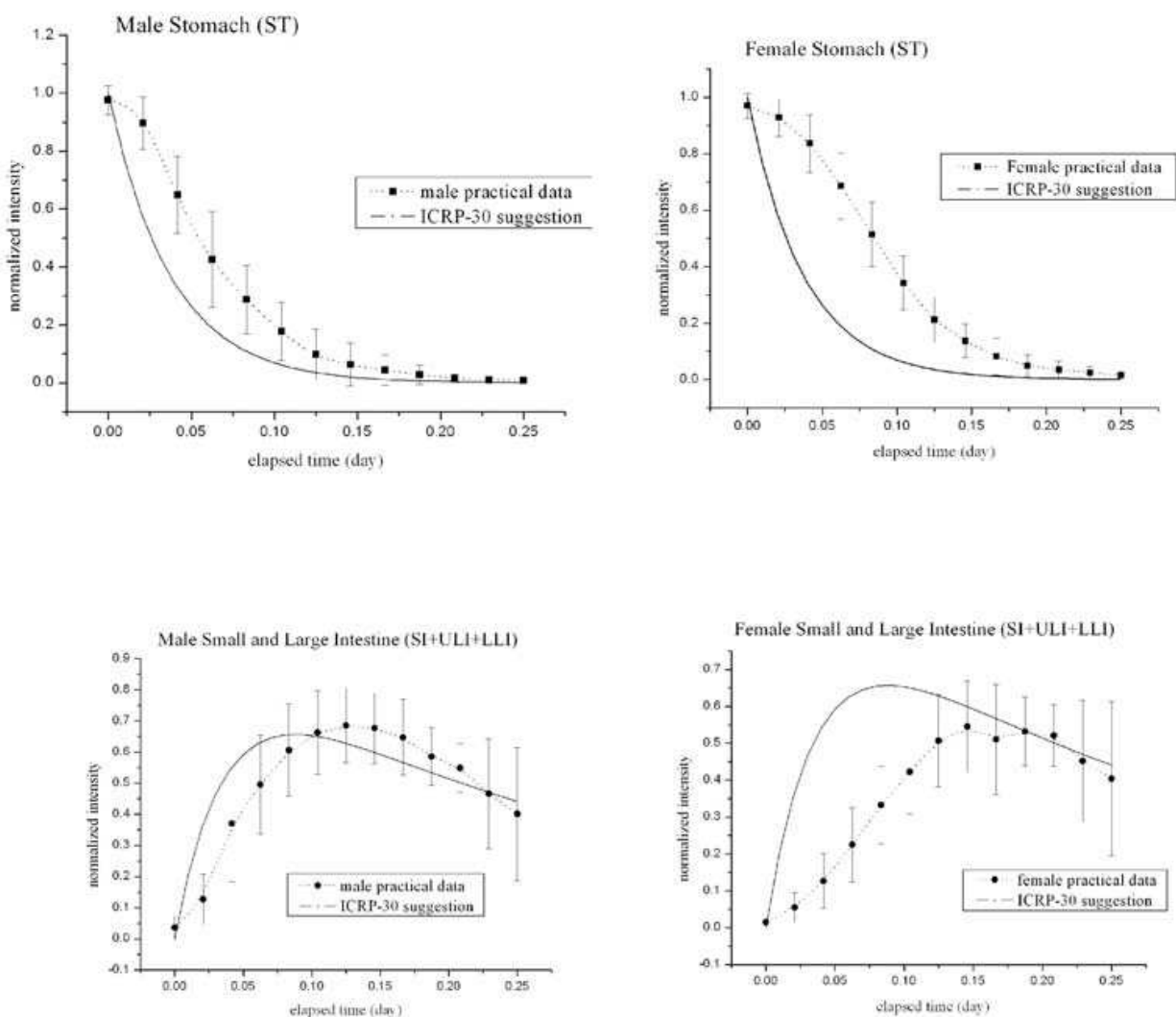


Fig. 6. The time dependent curve of ST and SI+ULI+LLI for males and females, respectively. The inconsistency in comparing the theoretical calculation and practical evaluation is significant.

3.4 Data analysis

Table 5 shows the results that were obtained for 24 healthy volunteers. The first row includes theoretical recommendations in the ICRP-30 report for comparison. The results are grouped into male and female, and each volunteer is indicated. The GET is the effective half life of Tc-99m in the stomach. It equals the reciprocal of the sum of the reciprocal of the biological half life and that of the radiological half life ($GET^{-1} = T_{1/2eff}(ST)^{-1} = [T_{1/2}(Tc-99m)^{-1} + T_{1/2}(ST)^{-1}]$). The biological half lives in the stomach $T_{1/2}(ST)$ and small intestine $T_{1/2}(SI)$ in

Case No.	Sex	$T_{1/2}(ST)$ Min.	$T_{1/2}(SI)$ Min.	$T_{1/2}(ULI)$ Min.	$T_{1/2}(LLI)$ Min.	$T_{1/2}(b)$ Min.	AT_{ST} %	AT_{LSI} %
ICRP-30		41.8	167.0	554.5	998.0	998.0		
1	F	166.4	199.6	554.5	998.0	1.0E+05	8.4	7.5
2	F	142.6	199.6	554.5	998.0	1.0E+05	10.5	7.3
3	F	110.9	166.4	554.5	998.0	1.0E+05	5.9	7.6
4	F	142.6	199.6	554.5	998.0	1.0E+05	5.9	3.6
5	F	124.8	199.6	554.5	998.0	1.2E+04	11.3	6.9
6	F	166.4	199.6	554.5	998.0	1.0E+05	9.8	8.5
7	F	99.8	332.7	554.5	998.0	1.0E+05	12.7	17.0
8	F	142.6	249.5	554.5	998.0	1.0E+05	14.5	10.6
9	F	99.8	249.5	554.5	998.0	1.0E+05	10.9	14.9
10	F	199.6	166.4	554.5	998.0	1.0E+05	11.9	10.1
11	F	99.8	166.4	554.5	998.0	1.0E+05	8.2	7.6
12	F	124.8	166.4	554.5	998.0	1.0E+05	14.2	9.6
13	F	166.4	199.6	554.5	998.0	1.0E+05	15.8	8.6
Average (1~13)		137.4 ±31.3	207.3 ±46.9	554.5	998.0	9.3E+04± 2.4E+04	10.8± 3.1	9.2 ±3.5
14	M	83.2	199.6	554.5	998.0	1.0E+05	12.1	13.3
15	M	99.8	249.5	554.5	998.0	1.0E+05	11.4	16.3
16	M	99.8	166.4	554.5	998.0	1.0E+05	7.6	8.6
17	M	99.8	249.5	554.5	998.0	1.0E+05	8.1	15.7
18	M	62.4	166.4	554.5	998.0	3.3E+04	3.3	6.5
19	M	142.6	124.8	554.5	998.0	1.0E+05	11.5	6.9
20	M	76.8	166.4	554.5	998.0	1.0E+05	3.7	5.1
21	M	45.4	166.4	554.5	998.0	5.0E+04	10.9	9.6
22	M	62.4	166.4	554.5	998.0	1.0E+05	10.3	9.7
23	M	90.7	166.4	554.5	998.0	1.0E+05	13.8	13.9
24	M	52.5	998.1	554.5	998.0	1.0E+05	10.9	14.4
Average (14~24)		76.7 ±23.0	256.3 ±248.9	554.5	998.0	8.9E+04± 2.4E+04	9.3 ±3.4	10.5 ±4.0

Table 5. The evaluated results for 24 healthy volunteers in this work. The Theoretical recommendation from ICRP-30 report is also listed in the first row for comparing. Either AT_{ST} or AT_{LSI} indicates the curve fitting agreement between theoretical estimation and practical measurement for stomach (ST) or small intestine (SI) + upper large intestine (ULI) + lower large intestine (LLI).

males are 76.7 ± 23.0 min. and 256.3 ± 248.9 min. respectively, and in females are 137.4 ± 31.3 min., 207.3 ± 46.9 min, respectively. Therefore, the GET and $T_{1/2\text{eff}}(\text{SI})$ for males are 63.2 ± 18.9 min. and 149.8 ± 145.1 min. and those for females are 99.5 ± 22.6 min. and 131.6 ± 29.8 min., respectively. The values of both $T_{1/2}(\text{ULI})$ and $T_{1/2}(\text{LLI})$ that were used in the program calculation were those suggested in the ICRP-30 report. The calculated $T_{1/2}(\text{b})$ 10,000, is greatly higher than that, 998, recommended by the original ICRP-30 report. The increased half life, associated with metabolic removal (around an order of magnitude greater than its suggested value), indicates that only a negligible amount of Tc-99m phytate is transported to the body fluid (BF).

Both AT_{ST} and AT_{LSI} reveal consistency between the measured and estimated fitted curves for ST and SI+ULI+LLI [Eq. 5]. The ATs are around 3.6~16.3; the average ATs for males are 9.3 ± 3.4 and 10.5 ± 4.0 and those for females are 10.8 ± 3.1 and 9.2 ± 3.5 [Tab. 5, last two columns]. Twenty-six correlated data are used in the program in MATLAB to find an optimal value of Tc-99m quantities for each volunteer ($13 \times 2 = 26$, ST and SI+ULI+LLI). Equations 6-9 must be solved simultaneously and include all four compartments of the GI tract biokinetic model [cf. Fig. 4]. Figure 6 plots the time-dependent curves of ST and SI+ULI+LLI for males and females. The inconsistency between the theoretical and empirical values is significant.

3.5 Discussion

Unlike the thyroid biokinetic model, which includes a feedback loop between the body fluid compartment and the whole body compartment, the GI Tract biokinetic model applies exactly the direct chain emptying principle, and assumes that no equilibrium exists between the parent and daughter compartments, because the parent's (ST) biological half emptying time is shorter than the daughter's (SI+ULI+LLI) biological half emptying time. The unique integration of parent's and daughter's biological half emptying times also reflects the unpredictability of the real GET of the gastrointestinal system. Therefore, a total of 13 groups of data were obtained for each volunteer over six continuous hours of scanning and input to the program in MATLAB to determine the complete correlation between ST and SI+ULI+LLI. Simplifying either the biokinetic model or the calculation may generate errors in the output and conclusion. Very few studies have addressed the time-dependent curve for SI+ULI+LLI, because this curve is not a straight line that is associated with a particular emptying constant (slope) [Fig. 6]. Any two or three sets of discrete measurements cannot provide enough data to yield a conclusive result. The optimal fitted time-dependent SI+ULI+LLI curve is a polynomial function of fourth or fifth order. Therefore, the data must be measured discretely in five or six trials to draw conclusions with a satisfactory confidence level.

The biological half emptying time of SI dominates the time-dependent curve of SI+ULI+LLI, since the SI biological half emptying time, $T_{1/2}(\text{SI})$, fluctuates markedly, whereas the values of both $T_{1/2}(\text{ULI})$ and $T_{1/2}(\text{LLI})$ contribute inconsiderably to solve the simultaneous differential equations in the program in MATLAB [cf. Tab. 5]. Additionally, a close examination of the time-dependent SI+ULI+LLI curve of either males or females reveals that quantities of Tc-99m radionuclides in the SI compartment for males more rapidly approaches saturation than does that for the females, and so the biological half emptying time is shorter in males [cf. Fig. 6]. However, the analyzed results concerning GETs herein do not support this claim (female: 207.3 ± 46.9 min.; male: 256.3 ± 248.9 min.) because the extent of changes of the SI (daughter compartment) is governed by the chain emptying rate from the ST (parent compartment), and the $T_{1/2}(\text{ST})$ for males (76.7 ± 23.0 min.) is shorter than that for females (137.4 ± 31.3 min.). Restated, the correct interpretation of the results must be based on the GI Tract biokinetic model and satisfy the simultaneous differential equations, Eqs. 6-9.

4. Recommendation and conclusion

Both the effective half-life of iodine in either the thyroid or the body fluid compartment of (near) total thyroidectomy patients and the gastric emptying half time of solid food in 24 healthy volunteers (11M/13F) were determined using the *in-vivo* gamma camera method. The real images that were captured using the gamma camera provide reliable information for biokinetic model-based analysis, since the easy and accurate positioning feature enables the time-dependent quantities of cumulated gamma rays in various biokinetic compartments to be determined.

MATLAB is rarely used in the medical field because of its complicated demanding programming. However, its powerful ability to define time-dependent simultaneous differential equations and to derive optimal numerical solutions can accelerate correlative analyses in most practical studies. Notably, only an appropriate definition at the beginning of study can ensure a reliable outcome that is consistent with practical measurements. The application of a simplistic or excessively direct hypothesis about any radiological topic can yield very erroneous results.

4.1 Iodine thyroid model

The revised values of T_{eff} of iodine in the thyroid compartment were initially obtained from computations made for each subject using the iodine biokinetic model and averaged over all five subjects. The T_{eff} of iodine in the thyroid compartment was revised from the original 7.3d to 0.61d, while that of iodine in the body fluid compartment was increased from 0.24d to 0.49d. The I_{thy} and I_{exc} were revised from the original 30% and 70% to 11.4% and 88.4%, respectively following *in-vivo* measurement. The differences between the results of the original and the revised iodine biokinetic models were used AT to determine the biological half-life of iodine in the thyroid and the remainder. The T_{eff} of the integrated remainder (both body fluid and whole body compartments) remained around 5.8d, since the body fluid and whole body compartment were inseparable in practical scanning of the whole body. The different effective half lies of radioiodine nuclides in thyroidectomy patients had to be considered in evaluating effective dose.

4.2 Gastrointestinal tract model

The results obtained using the program in MATLAB were based on four time-dependent simultaneous differential equations that were derived to be consistent with the measured gamma ray counts in different compartments in the GI Tract biokinetic model. The GET and $T_{1/2\text{eff}}(\text{SI})$ for males thus obtained were 63.2 ± 18.9 min. and 149.8 ± 145.1 min. and those for females were 99.5 ± 22.6 min. and 131.6 ± 29.8 min. The calculated $T_{1/2}(\text{b})$, 10,000 was greatly higher than that, 998, recommended by the original ICRP-30 report. The fact that the half life associated with metabolic removal, $T_{1/2}(\text{b})$, was around ten times the original value implied that a negligible amount of Tc-99m phytate was transported to the body fluid.

5. Acknowledgement

The authors would like to thank the National Science Council of the Republic of China for financially supporting this research under Contract No. NSC~93-2213-E-166-004. Ted Knoy is appreciated for his editorial assistance.

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Applications of MATLAB in Science and Engineering

Edited by Prof. Tadeusz Michalowski

ISBN 978-953-307-708-6

Hard cover, 510 pages

Publisher InTech

Published online 09, September, 2011

Published in print edition September, 2011

The book consists of 24 chapters illustrating a wide range of areas where MATLAB tools are applied. These areas include mathematics, physics, chemistry and chemical engineering, mechanical engineering, biological (molecular biology) and medical sciences, communication and control systems, digital signal, image and video processing, system modeling and simulation. Many interesting problems have been included throughout the book, and its contents will be beneficial for students and professionals in wide areas of interest.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Chia Chun Hsu, Chien Yi Chen and Lung Kwang Pan (2011). Quantitative Analysis of Iodine Thyroid and Gastrointestinal Tract Biokinetic Models Using MATLAB, Applications of MATLAB in Science and Engineering, Prof. Tadeusz Michalowski (Ed.), ISBN: 978-953-307-708-6, InTech, Available from:
<http://www.intechopen.com/books/applications-of-matlab-in-science-and-engineering/quantitative-analysis-of-iodine-thyroid-and-gastrointestinal-tract-biokinetic-models-using-matlab>

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