INSTITUTE FOR MEDICAL PHYSICS

EFFECTIVE DOSE ESTIMATION AND RISK ASSESMENT IN PATIENTS TREATED WITH IODINE ^{131}I USING MONTE CARLO SIMULATION

Marina Zdraveska Kochovska, PhD medical physicist

Institute of pathophysiology and nuclear medicine, "Akademik I.Tadzer",

Medical faculty, Skopje

Ohrid, 2015

INTRODUCTION

- Oral administration of radioiodine has been commonly accepted procedure in nuclear medicine for treatment of hyperthyroid, and thyroid carcinoma patients.

- Whenever radiation is used in the treatment of patients dosimetry is essential.

- The facility in which treatment is performed must have appropriate standard criteria: educated personnel, radioiodine lab, radiotherapy room, radiation safety instruments, available procedures for waste handling, controlling spread of volatilized ^{131}I.

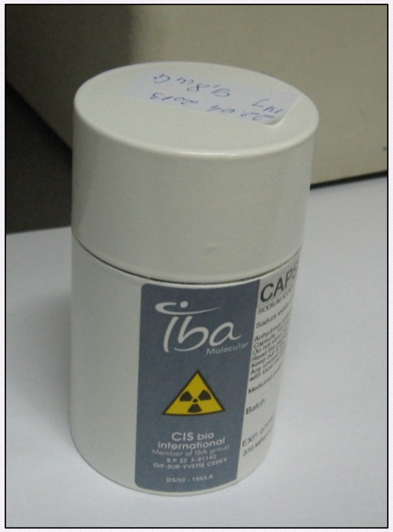
INTRODUCTION

- External dosimetry (dose rate meters and other conventional eq.)

- Internal dosimetry (gamma camera, scintillation probe, special software's: MCNP4b, MCNPX, GEANT 4, SIMIND, OLINDA, MIRD etc.)

- Radiation protection of patients, family and public members, workers, nurses and environment.

RECEIVING AND MEASURING THE CAPSULE

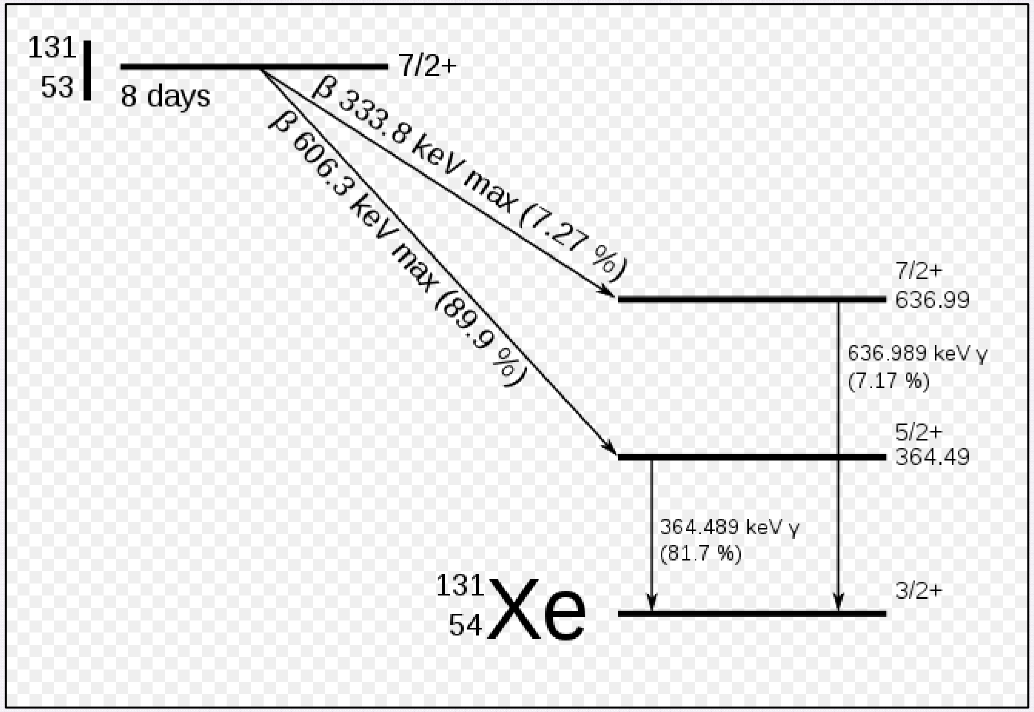


ROOM FOR PATIENTS TREATED WITH ^{131}I

^{131}I REVIEW

- Physical half-life of 8.06 days
- Beta emitter: max. energy 610 keV, average energy 193 keV tissue range 0.8 mm
- Gamma emitter: principal energy 365 keV (81%)

  94% of radiation dose is from the beta emissions.



- to minimize recurrence because the beta particles may destroy microscopic Ca
- to detect occult metastases
- to ablate residual normal Thyroid tissue.

NUCLEAR MEDICINE DOSIMETRY

The role of dosimetry within radionuclide therapy is threefold:

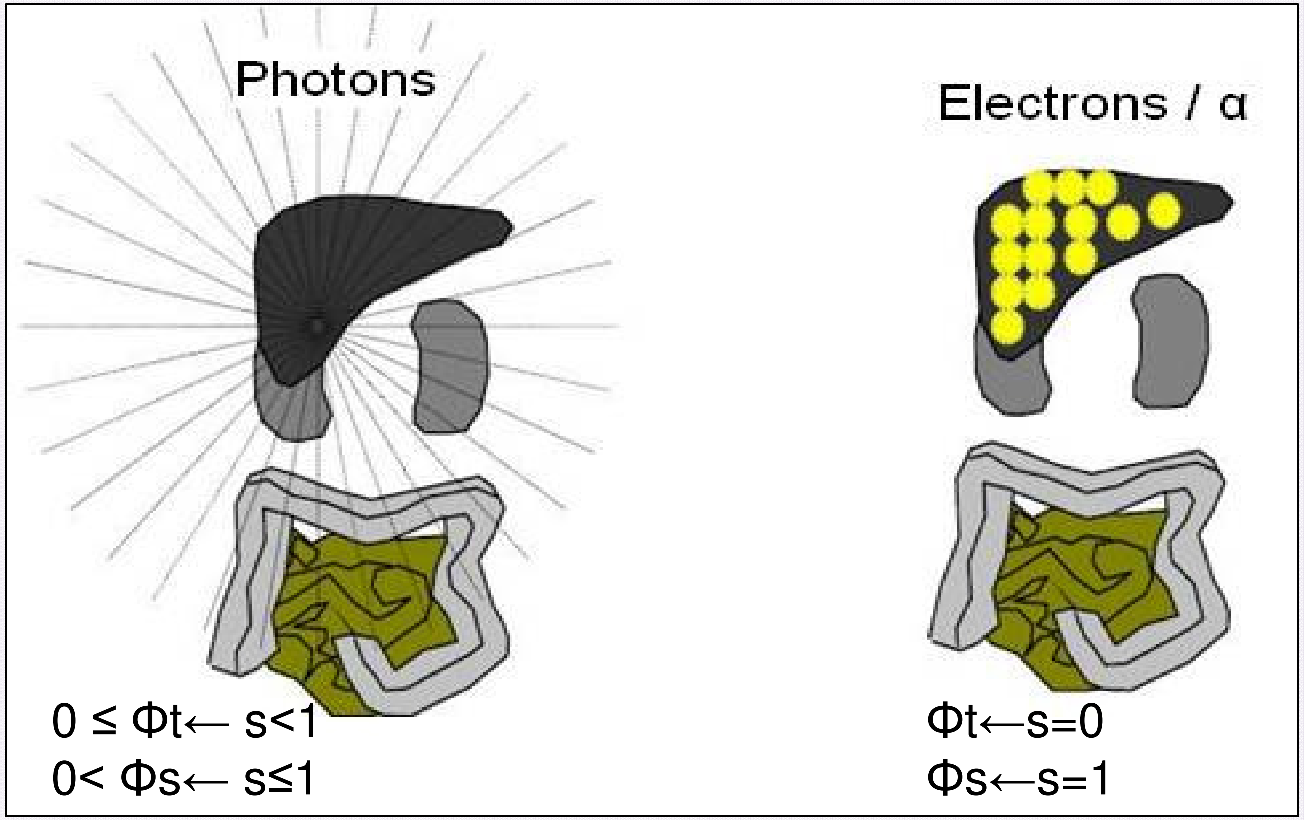
1)Radiation protection

2)Initial estimate of absorbed dose delivered to normal organs becomes mandatory requirement for the clinical introduction of new agents

- ^{131}I Bexxar – non Hodgkins lymphoma

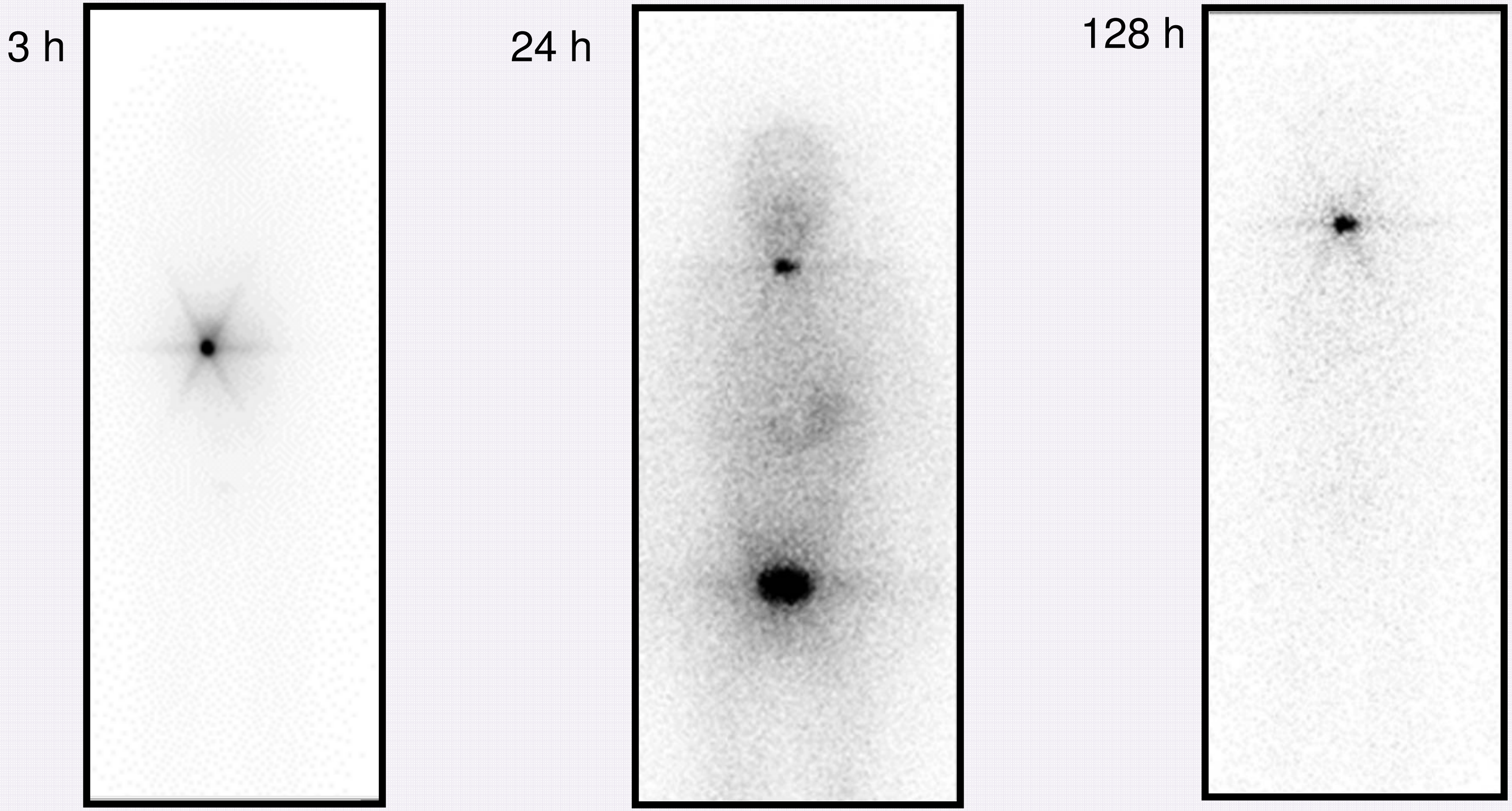
- ^{131}I MIBG – for neuroblastoma

3) Internal dosimetry is required to plan and optimize treatment



- Different tissue absorption properties of photons versus electrons or α- particle emissions of radio nuclide.
- Photon data are found in Reference Man (MIRD Pamphlet) which is well adapted for protection evaluation purposes.
- A large amount of radioactivity needlessly expose a part of stomach and other surrounding organs

- This fact was the main reason for additional risk estimation.
- As it is not possible to measure this doses directly the MC radiation transport calculations on anthropomorphic numerical phantoms seems quite suitable and good solution for this problem.



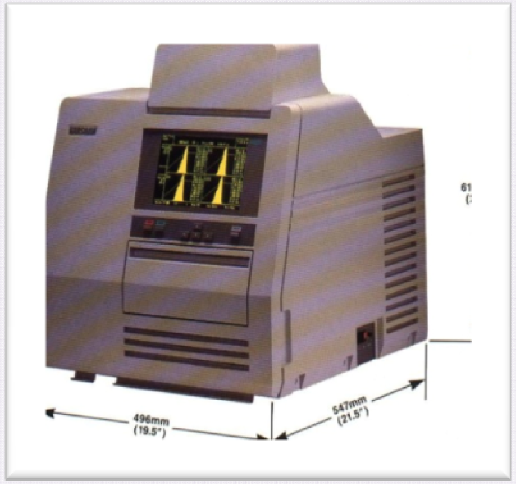
- ✓ To calculate dose equivalents, effective doses for internal organs under the risk during therapy application of radioiodine using numerical simulations
- ✓ To perform external measurements of dose rates of thyroid cancer and hyperthyroid patients at 0.25 m, 0.5 m, 1.0 m, and 2.0 m.
- ✓ To determinate additional risks of lifetime mortality of hyperthyroid and thyroid cancer patients.

MATERIAL AND METHODS

- In the study were analyzed thyroid cancer and hyperthyroid patients for 5 y (2007-2011).

- External measurements were performed with calibrated radiation survey meter – E range (0.45 keV-2 MeV).

TLD



Thermo Fisher Harshaw 6600

Mini rad series 1000 Morgan

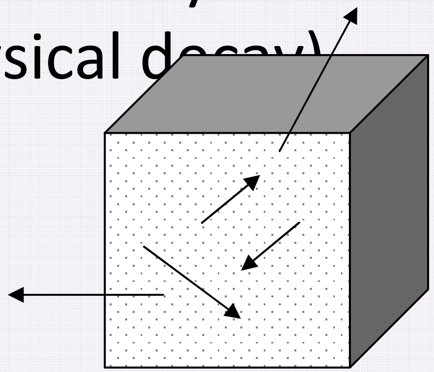
Internal dosimetry consideration

- Effective dose was calculated for 24 different activities (185 MBq up to 6105 MBq)
- Time 1 min and 15 min
- To calculate absorbed dose in an organ of interest we must know:
  - How many decays in organ
    - How much activity is in organ
    - How long activity is in organ
  - Energy from each decay
  - Fraction of decay energy deposited in organ
  - Mass of organ
  - Energy deposited from activity in other organs

Internal dosimetry consideration

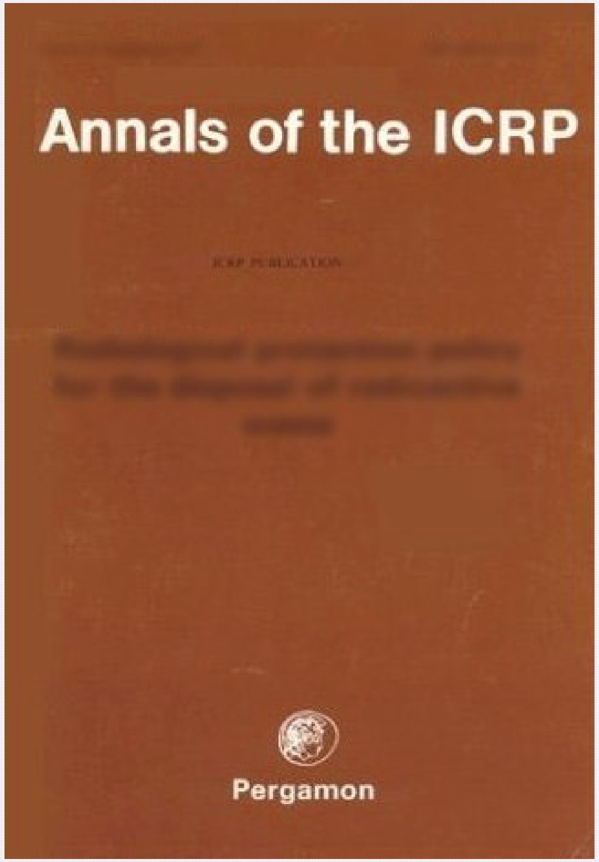
- The approach to dosimetry with internal emitters is based on a simple idealized phantom model of 70 kg reference man. The unique problem is that activity distributes spatially and temporally throughout the body. Each organ is both source and target and activity washes in and out and decays (Biological and physical decay).

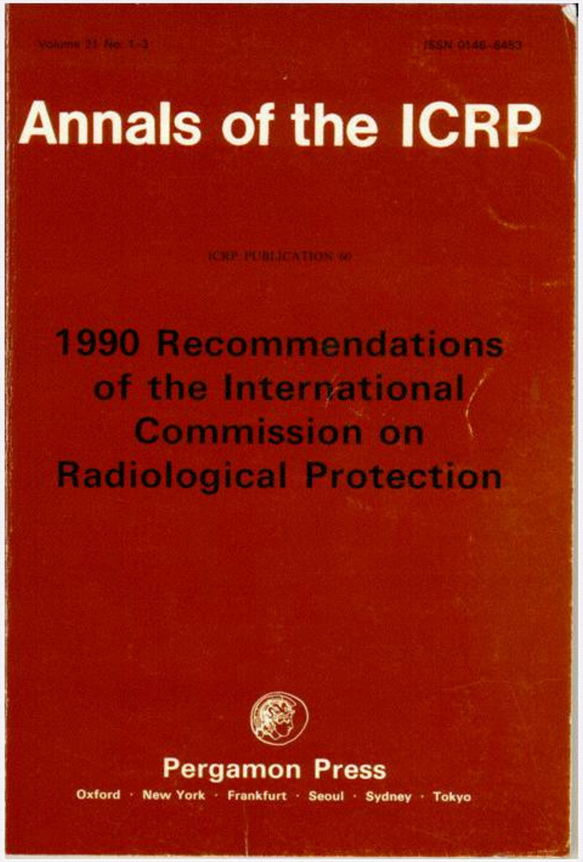
$$E = \sum w_T H_T = \sum w_T \sum w_R D_{T,R}$$

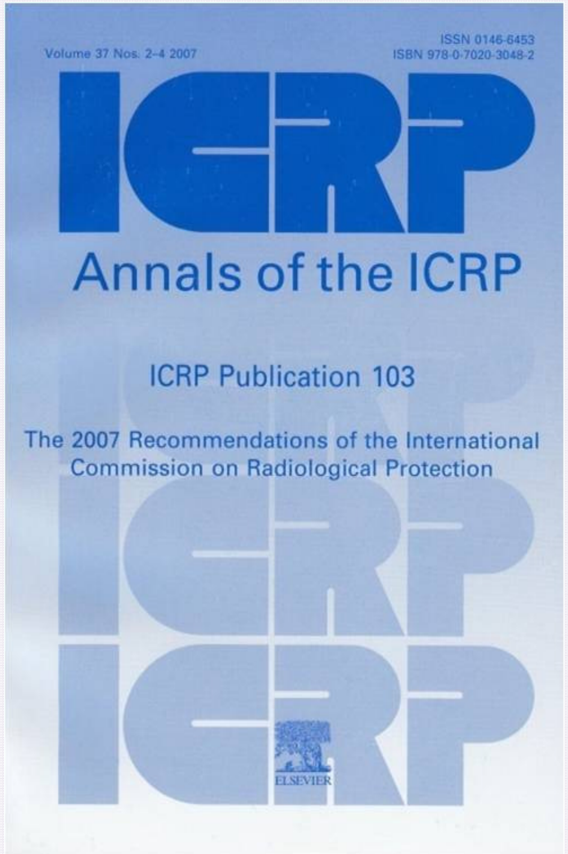


- Effective dose is calculated as a weighted sum of absorbed doses to organs

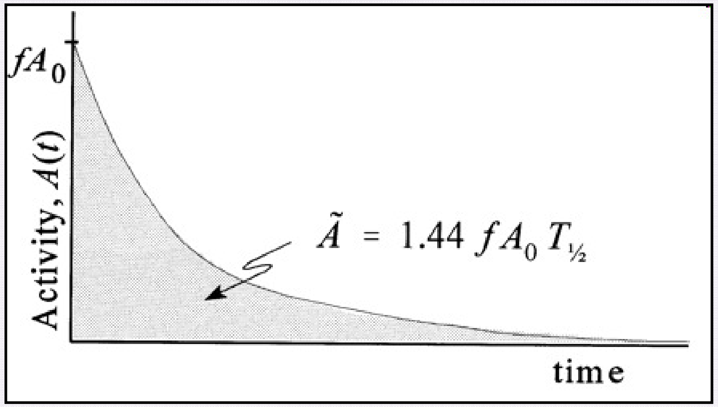
Weights are defined in ICRP 30 (1979), ICRP 60 (1990) and ICRP 103 (2007) (mathematical approach for RP purposes of workers)







➢The MIRD committee gives mathematical approach to assess dose and risk to patients from radiopharmaceuticals and they figured out the **cumulative activity Ã** for each radiopharmaceutical used in NM



➢ $\tilde{A}_T = A_0 \bullet f_h \bullet 1.44\, T_e$

- A_0 (MBq) = initial activity taken into body
- T_e - "effective" half-life
- f_h - fraction of A_0 deposited into organ of concern

$$S = \frac{k \sum_i n_i E_i \phi_i}{m}$$

- By MC simulation for each radionuclide are figured “S” values which relate the absorbed dose in each target organ per disintegration in each source organ. S values are tabulated in MIRD pamphlet

- **Assumption**: Iodine capsule is administered on empty stomach, it takes 15 minutes before absorption starts, point source.

- **Input data**: Nuclear and radiological data, geometry, materials, source, history.

1. Nuclear data of ^{131}I

- **Gama photons** **364 keV (81 %) main pik**
  637 keV (7.3 %)
  284 keV (6.1 %)
- **Beta yield** **192 keV (89 %)**
  96.6 keV (7.36 %)
  69.4 keV (2.12 %)
- **Gama constant** 7,647 E-5 mSv/hr per MBq per 1.0 m
- **Physical Half life** T1/2 - 8.02 days
- **Biological Half life** 27 -138 days
- **Effective Half life** 7.6 days
- **Specific activity** 4,600 TBq/g
- **Spectrum**

2. Radiological data

- **Radio toxicity**: 4,76 x 10^{-7} Sv/Bq ingested ^{131}I or 2,92 x10^{-7} Sv/Bq inhaled ^{131}I
- **Target organ**: Thyroid gland
- **Critical organ**: Stomach
- **Radiological hazard**: external and internal exposure
- Ingestion, inhalation, contamination
- HVL – (3 mm); TVL – (11 mm)

3. Geometry

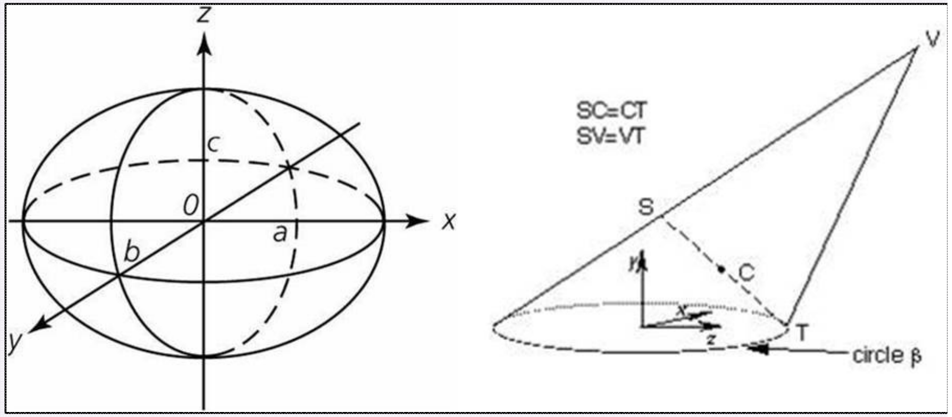
- point source in the middle of sphere of soft tissue
- Self absorption is negligible

➢**Geometry of phantom -** elliptical cylinder (trunk and arms) two truncated circular cones (legs and feet), circular cylinder on which sits elliptical cylinder capped by half an ellipsoid representing the neck and head.

➢ The stomach wall was defined with equation Eckerman et al. 1996:

$$\left(\frac{x-8}{4}\right)^2 + \left(\frac{y+4}{3}\right)^2 + \left(\frac{z-35}{8}\right)^2 \leq 1$$

$$\left(\frac{x-8}{3.387}\right)^2 + \left(\frac{y+4}{2.387}\right)^2 + \left(\frac{z-35}{7.387}\right)^2 \geq 1$$



➢ phantom tissue were recognized: skeletal, lung and all other soft tissue with Densities: 1.4 gcm^{-3}, 1.04 gcm^{-3} and 0.296 gcm^{-3} (Eckerman et al. 1996)

(ICRP 70, ICRP 89 and ICRU 46 defined composition of the tissue)

➢ Soft tissue 10.6 % H + 11.5 % C + 2.2 % N + 75.1 % O + 0.1 % Na + 0.1 % P + 0.1 % S + 0.2 % Cl + 0.1 % K.

➢Application of MCNP software package

➢ MCNP 4b radiation transport code was used, (gamma ray transport is taken into consideration beside beta particles in case of ^{131}I).

Application	Tally	Remarks
Only for beta	*F8	
Distribution of gamma dose in different organs	*F8, F6	Calculation of absorbed energy in organ MeV/g per disintegration
Local dose distribution into the stomach	*F8, F6, F2	F2 gama flux on the surface conversion coefficient-flux ICRP 74

➢ Tally give the absorbed energy in organs in unit MeV/g per disintegration

➢ Total number of histories 1 000 000

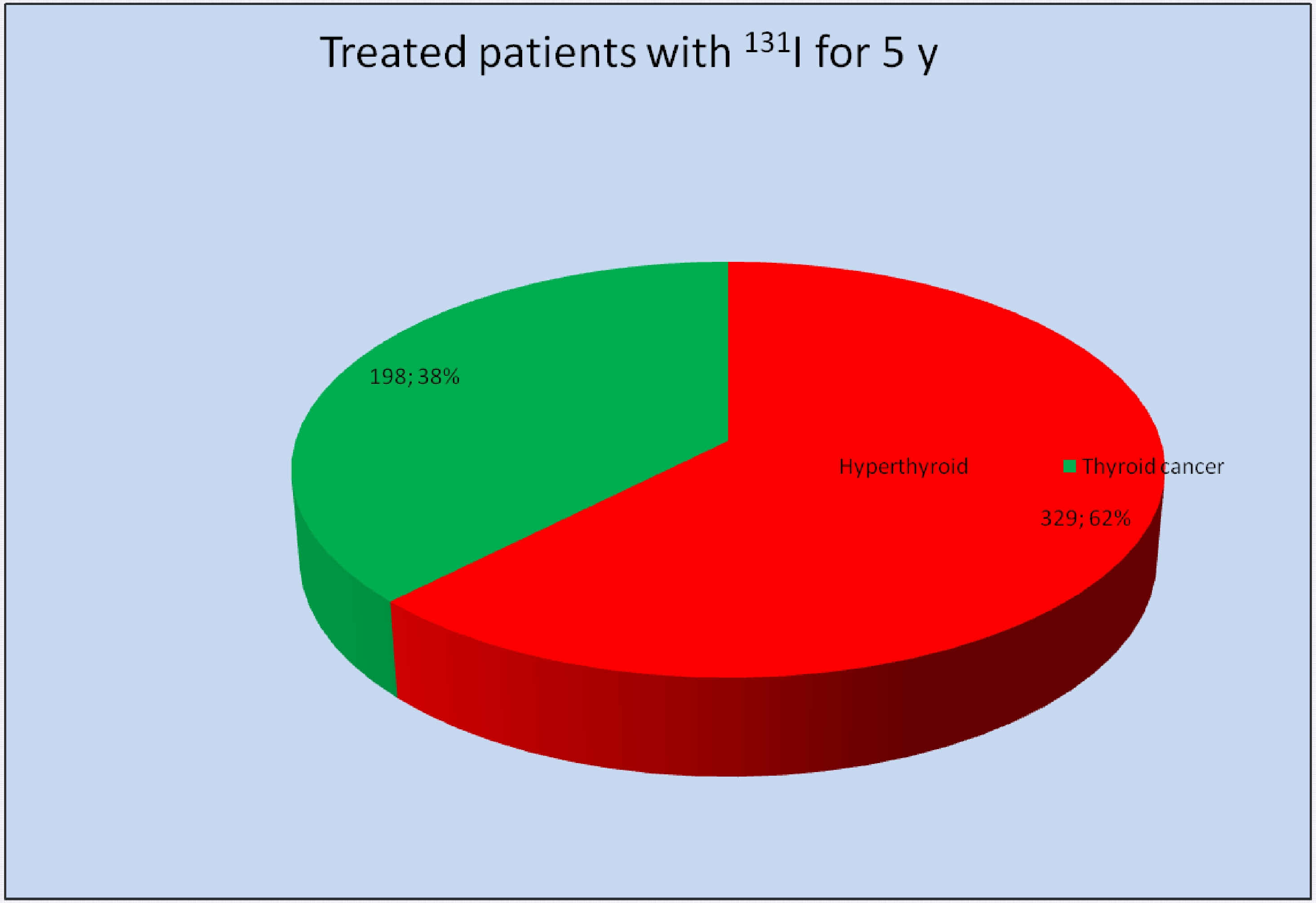
➢ relative uncertainty of simulation was < 5% and sphere symmetry estimated uncertainties for calculation of local stomach doses are less than 0.01% and are negligible

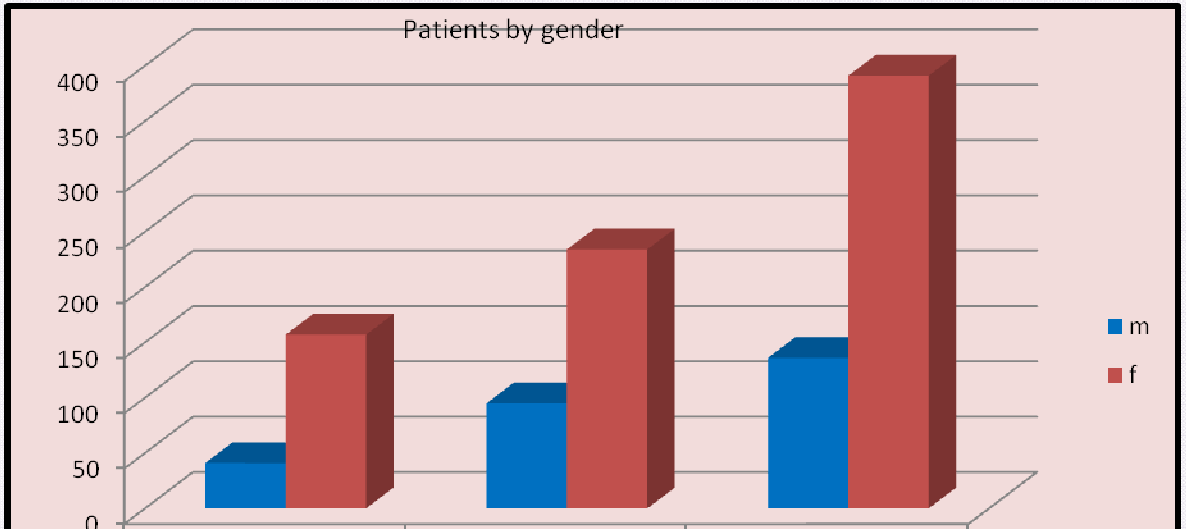
Risk assessment

- The gained results of effective dose equivalent intended to be directly proportional to the risk from exposure.

- The significant uptake of iodine by stomach and other organs carries additional risks of probabilistic fatal occurrences in them as compare to other organs.

Total number of treated patients - 527



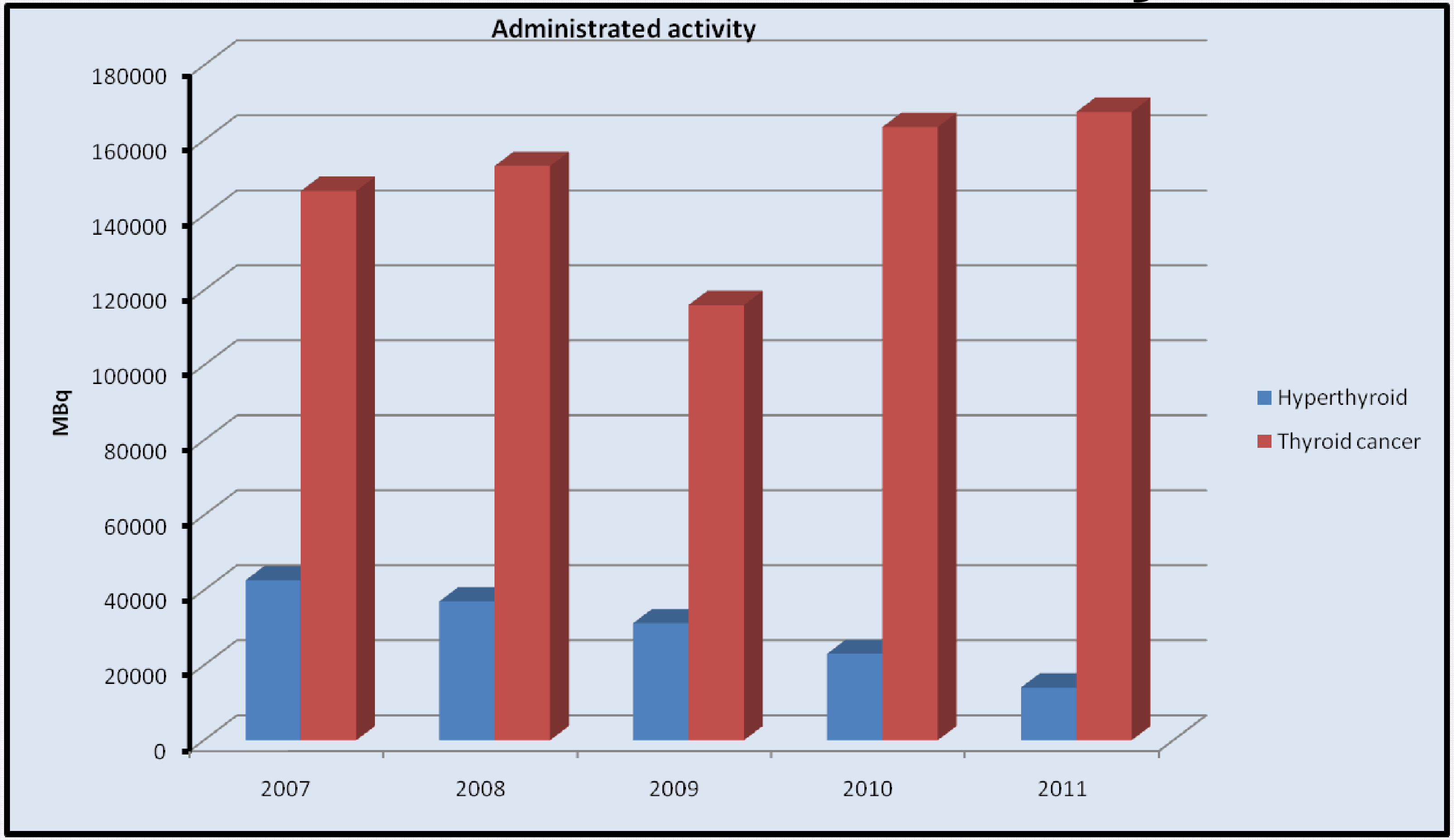


	Thyroid cancer	Hyperthyroid	Total
m	41	95	136
f	157	234	391

- The female patients are more affected by thyroid disease for both groups: 71.1% fm / 28.9% m for hyperthyroid
  79.3% fm / 20.7% m for thyroid cancer
  Total ratio m/fm **1/2.8**

  - *Tzavara et. al 677 pt. thyroid cancer 75% fm*
  - *R. Sciuto et al. Cohort 1503 pt. fm 78.6%/21.4% m*
  - *Brig Anand et al. 70 pt. m/fm ratio was 1/2.2*

Administered activity



- Totally administered activity for 5 years was 894 GBq (148 GBq/746 GBq)

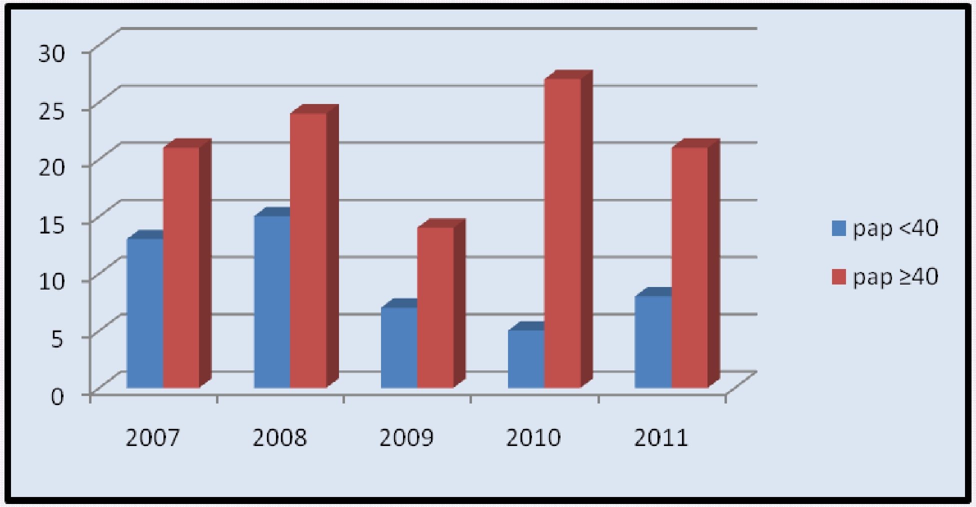
➢The majority of well differentiated malignancies manifested between 3 and 5 decade of life

-Mean age was (44±5) y

-(median 45, range 17-74)

-30.9% of the patients with papillary carcinoma were aged under 40

Age of patients



Diagnosis	World (%)	Results (%)
Papillary carcinoma	60-80	79
Follicular carcinoma	5-25	20
Medullar carcinoma	5-10	1.5
Anaplastic carcinoma	4-10	1

70.2% male and 80.2% female The difference between male and fm for the type of cancer was not statistically significant ($p=0.84$)

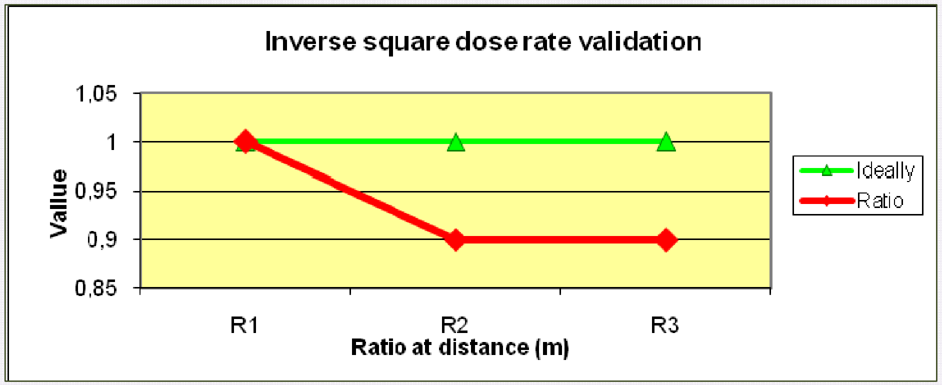
Our results are in consonance with other reported studies in world literature.

RESULTS FROM EXTERNAL DOSE RATE MEASUREMENTS

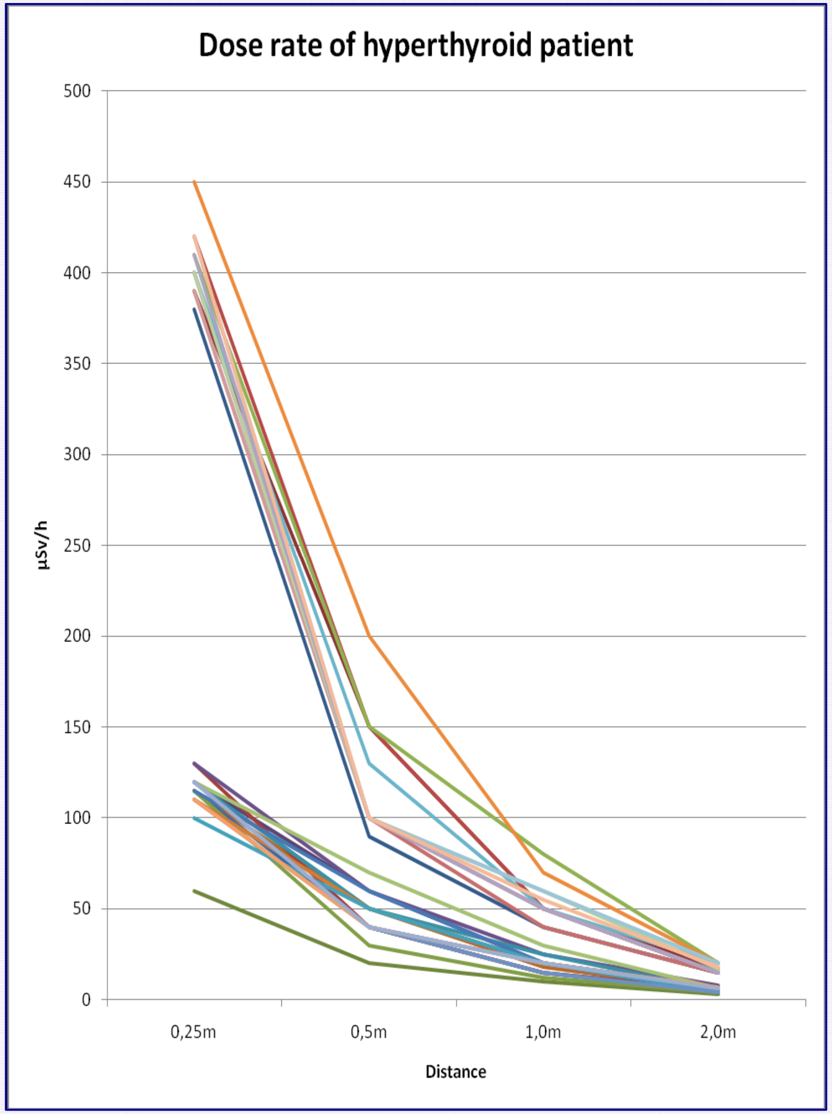
In order to validate the dose rate results of the survey meter, dose rate test was performed with activity of 1100 MBq ^{99m}Tc.

Activity MBq	Dose rate µSv/h	Dose rate µSv/h	Dose rate µSv/h	Dose rate µSv/h
	0.25 m	0.5 m	1.0 m	2.0 m
1100	420	110	30	7

r^1	r^2	r^3	$R1=r^1/4$	$R2=r^2/16$	$R3=r^3/64$
3.82	14.00	60.00	**1.0**	**0.9**	**0.9**



RESULTS FROM EXTERNAL DOSE RATE MEASUREMENTS



For hyperthyroid patients we recommend detailed instruction for further behavior for the next seven days, to protect their close family members

Coefficients at distances (m)			
0.25 m	0.5 m	1.0 m	2.0 m
0,34	0,36	0,44	0,30

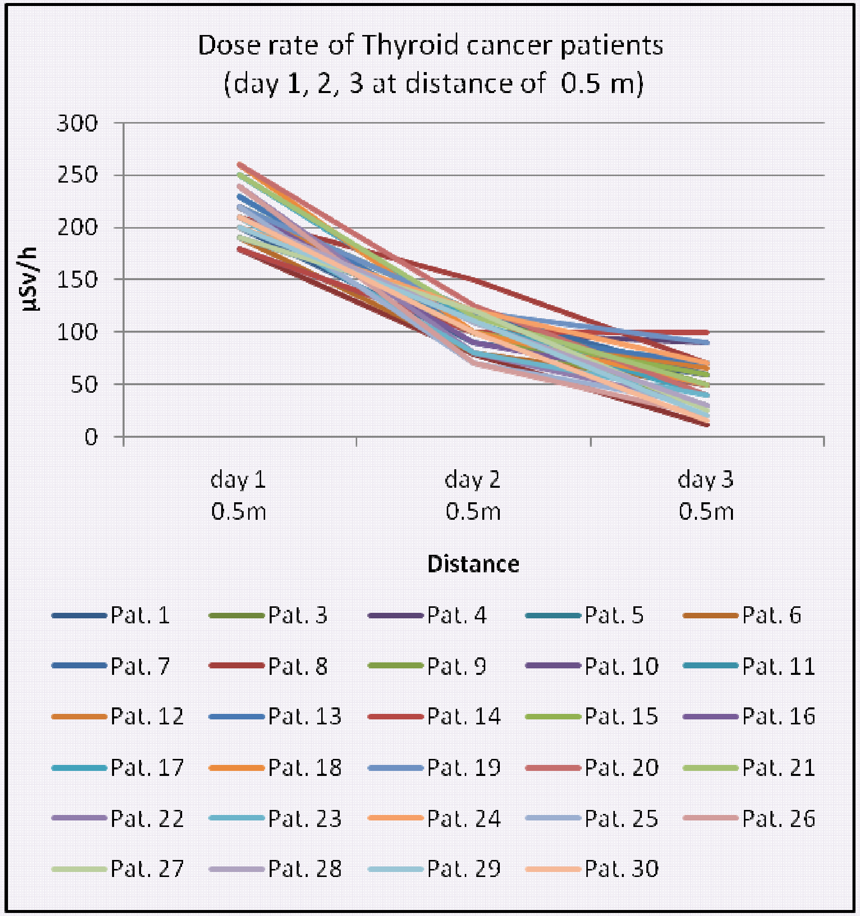
The correlation coefficients were positive and in range 0.30 to 0.44 not significant

RESULTS FROM EXTERNAL DOSE RATE MEASUREMENTS

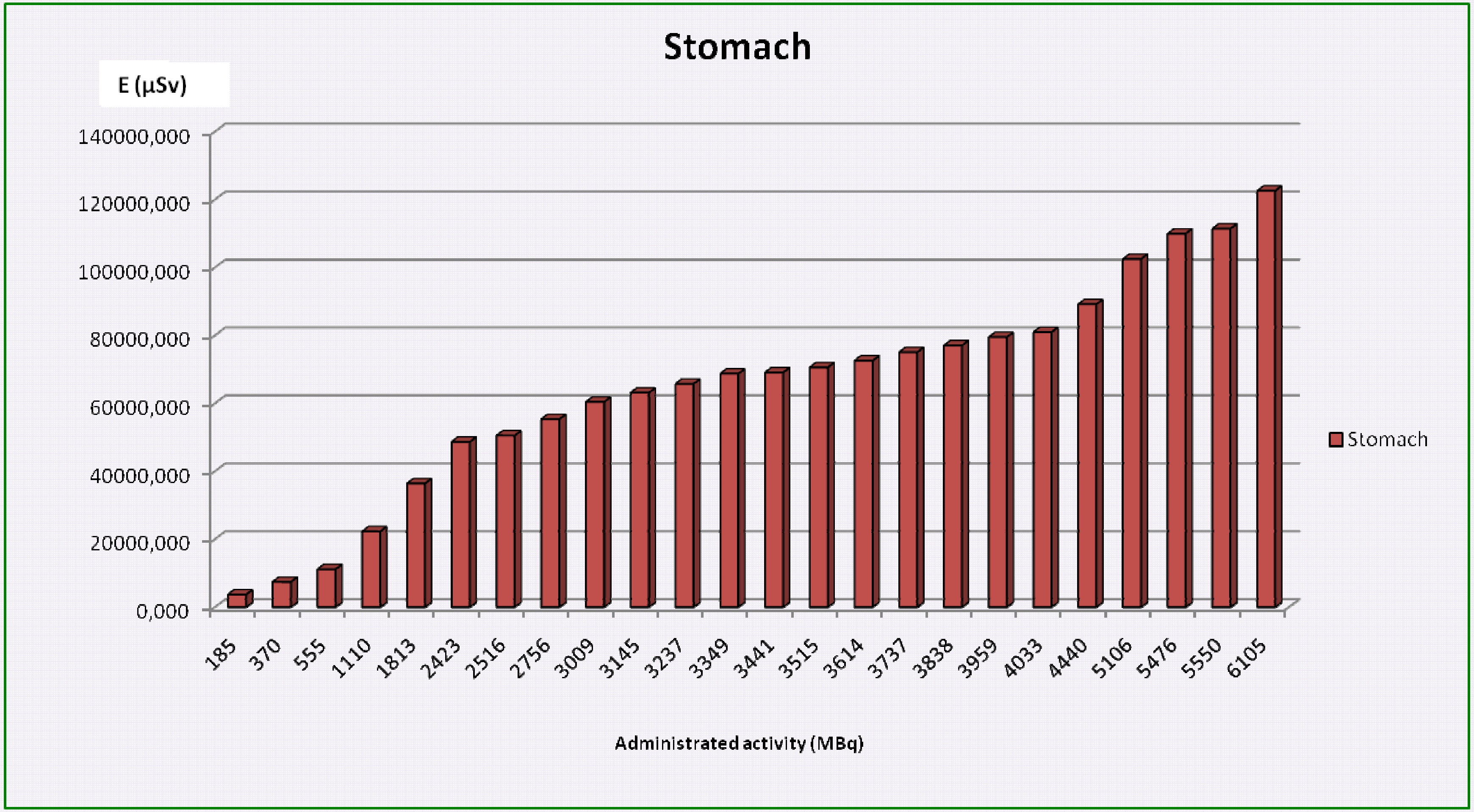
DR for hyperthyroid patients treated for AFTA are higher than DR for thyroid cancer pts. at the day of release from hospital

Coefficients, n=30, at distance of 0.50 m		
day 1	day 2	day 3
0,48	0,35	0,24

The correlation coefficients were positive and in range 0.24 to 0.48 not significant



RESULTS from effective dose for stomach



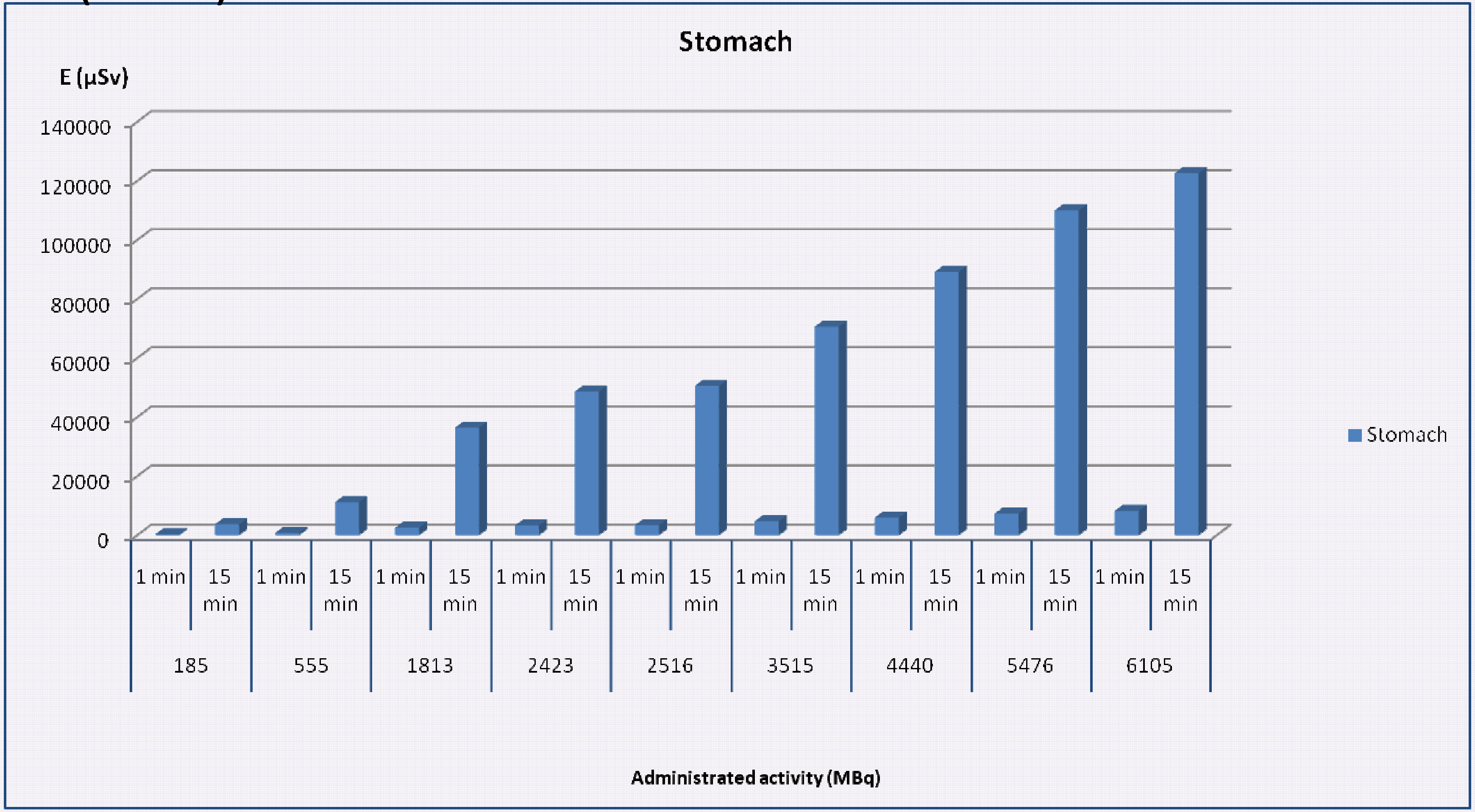
E=122,9 mSv

A=6105 MBq

Effective doses in stomach for 1 min and 15 minutes

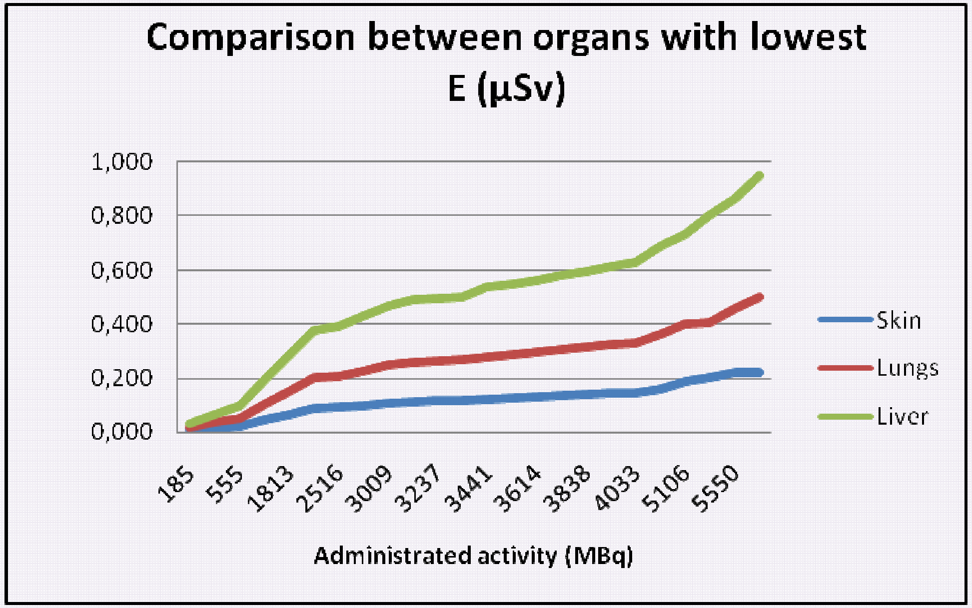
E(15min) = 122.9 mSv

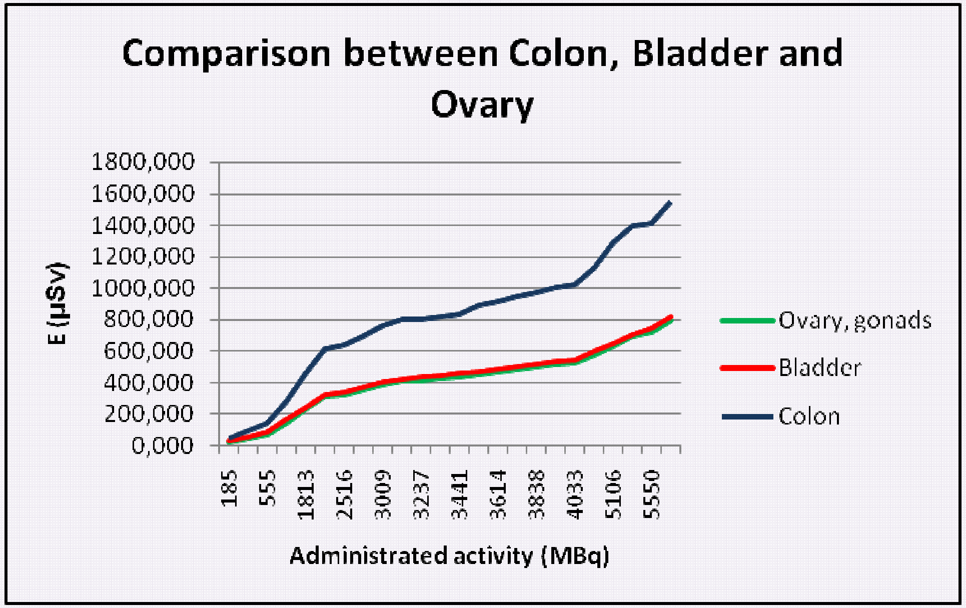
E(1min) = 8.2 mSv



Effective doses in surrounding organs

E (skin) = 0.2 μSv
E (lung) = 0.5 μSv
E (Liver) = 0.9 μSv





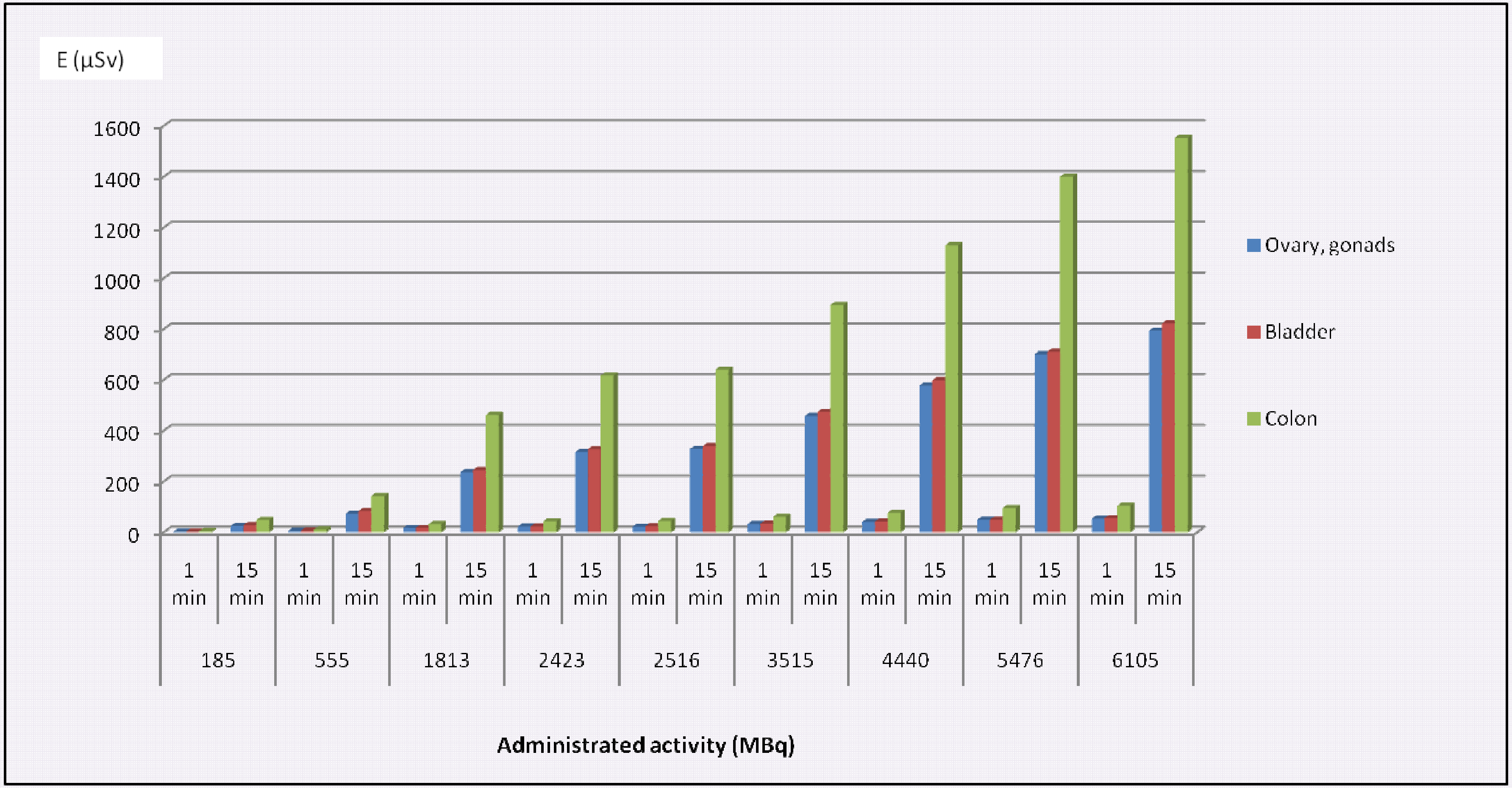
E (ovary) = 793 μSv
E (bladder) = 821 μSv
E (Colon) = 1552 μSv

Effective doses of ovary, bladder and colon for 1 min and 15 min

A = 6105 MBq

1 min E= 0,15 mSv

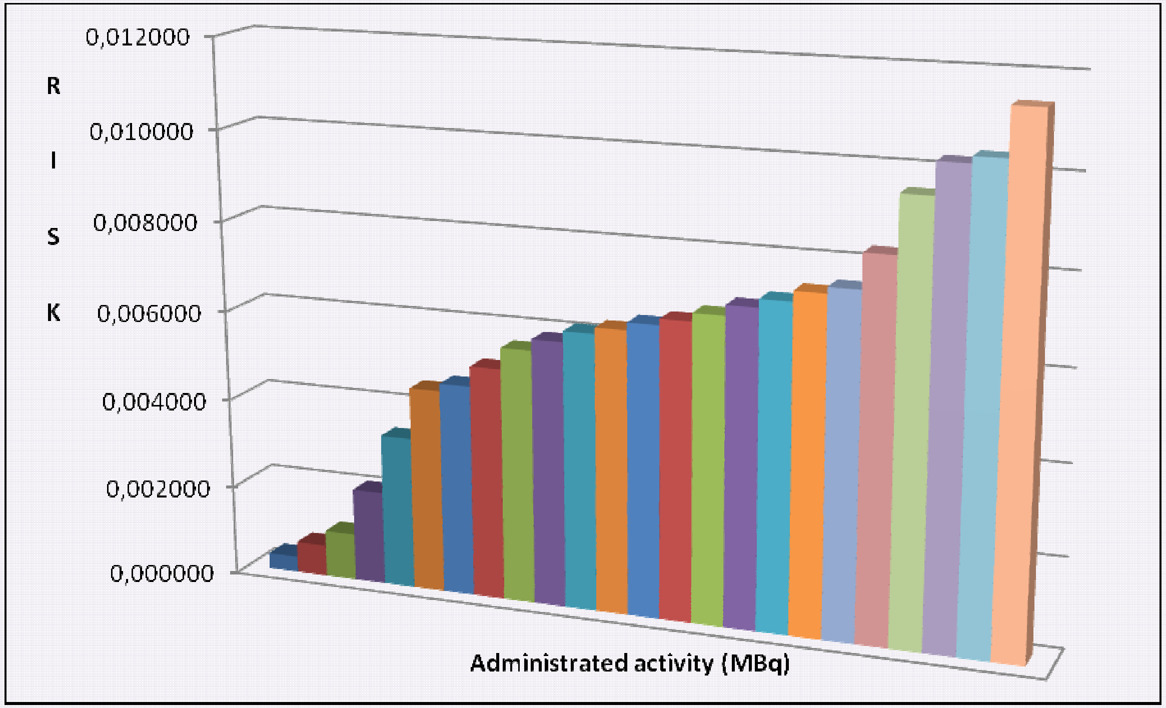
15 min E= 1,55 mSv



Risk assessment

MC method gives good opportunity and reliable tool for risk assessment.

Organ	Risk coefficient [$10^{-2}Sv^{-1}$]
Bladder	0.30
Bone surface	0.05
Colon	0.80
Liver	0.15
Lungs	0.85
Ovary, gonads	0.10
Skin	0.02
Stomach	1.10



ICRP gives lifetime fatal cancer probability coefficients for specific organs. The lowest value is for bone surface $0.05x10^{-2}$ and highest for stomach $1.10x10^{-2}$

Risk assessment

MBq	Time (min)	Bladder	Colon	Ovary, gonads	Stomach
185	1 min	1.00×10^{-9}	0.90×10^{-7}	0.80×10^{-8}	0.024×10^{-3}
	15 min	0.149×10^{-7}	0.131×10^{-5}	0.120×10^{-6}	0.340×10^{-3}
555	1 min	3.01×10^{-9}	2.64×10^{-7}	2.43×10^{-8}	0.08×10^{-3}
	15 min	0.448×10^{-7}	0.396×10^{-5}	0.362×10^{-6}	1.022×10^{-3}
1813	1 min	1.007×10^{-7}	7.54×10^{-7}	7.92×10^{-8}	0.24×10^{-3}
	15 min	1.465×10^{-7}	1.112×10^{-5}	1.176×10^{-6}	3.337×10^{-3}
2423	1 min	0.14×10^{-7}	0.11×10^{-5}	0.11×10^{-6}	0.31×10^{-3}
	15 min	1.959×10^{-7}	1.487×10^{-5}	1.572×10^{-6}	4.461×10^{-3}
2516	1 min	0.14×10^{-7}	0.11×10^{-5}	0.12×10^{-6}	0.32×10^{-3}
	15 min	2.033×10^{-7}	1.544×10^{-5}	1.632×10^{-6}	4.631×10^{-3}
3515	1 min	0.21×10^{-7}	0.16×10^{-5}	0.16×10^{-6}	0.46×10^{-3}
	15 min	2.841×10^{-7}	2.157×10^{-5}	2.281×10^{-6}	6.471×10^{-3}
4440	1 min	0.25×10^{-7}	0.19×10^{-5}	0.25×10^{-6}	0.58×10^{-3}
	15 min	3.588×10^{-7}	2.724×10^{-5}	2.880×10^{-6}	8.172×10^{-3}
5476	1 min	0.31×10^{-7}	0.23×10^{-5}	0.24×10^{-6}	0.74×10^{-3}
	15 min	4.385×10^{-7}	3.309×10^{-5}	3.470×10^{-6}	10.079×10^{-3}
6105	1 min	0.34×10^{-7}	0.26×10^{-5}	0.27×10^{-6}	**0.76×10^{-3}**
	15 min	4.934×10^{-7}	3.746×10^{-5}	3.960×10^{-6}	**11.237×10^{-3}**

These values of risk assessment has to be considered in RP protocols.

Sum = $11.27\text{x}10^{-3}$ **Stomach = $11.23\text{x}10^{-3}$**

Risk assessment

Organ	$\bar{H}$[μSv/s]	$\bar{H}$[mSv/1 min]	*E*[μSv]	Risk
Bladder	18.315	1.12	55.08	0.34 x10^{-7}
Colon	14.372	0.87	103.61	0.26 x10^{-5}
Ovary, gonads	4.406	0.27	53.01	0.27 x10^{-6}
Stomach			**8200**	**0.76 x10^{-3}**

E = 8.2 mSv
Risk 0.76 x10^{-3}
for 1 min

E = 122 mSv
Risk 11.23 x10^{-3}
for 15 min

Organ	$\bar{H}$[μSv/s]	*H*[mSv/15min]	*E*[μSv]	Risk
Bladder	18.315	16.418	821.70	4.934 x10^{-7}
Bone surface	1.018	0.918	917.40x10^{-5}	4.587 x10^{-10}
Colon	14.372	12.936	1552.65	3.746 x10^{-5}
Liver	0.211	0.190	0.949	28.545 x10^{-8}
Lungs	0.046	0.042	0.500	33.248 x10^{-8}
Ovary, gonads	4.406	3.960	793.65	3.960 x10^{-6}
Skin	0.243	0.220	0.220	4.373x10^{-8}
Stomach			**122595**	**11.237 x10^{-3}**

A=6105 MBq

The results show that the stomach has the highest risk among the other organs. From statistical analysis the correlation coefficient (r) among the estimated risk was found to be very significant ($p<0,00001$) for stomach-bladder, stomach-colon and stomach-ovary.

- Epidemiological studies report a higher incidence of stomach cancer in patients treated with ^{131}I also increased incidence of leukemia was observed.

- Swedish report from authors Jall P., Holm L.E., studied (834 pt. – 4551 MBq) a dose related increased risk of cancer was observed.

- Cohort study in 3 EU countries (Sweden, France and Italy) was conducted. Mean given activity was 6 GBq. The risk of leukemia was elevated but it didn’t reach statistical significance (RR=1.9).

- Study from Ahmed S. et al. indicates that significant uptake of radioiodine by stomach of thyroid cancer patients carries additional risk of probabilistic fatal occurrences compared with other organs.

- For patients receiving the dose of less than 1850 MBq there was no significantly elevated risk of subsequent malignancy.

- In (25 Institution in US and 1 in UK), prospective study of hyperthyroid patients (70 MBq to 600 MBq) reports were based on follow up of 22000 pts. treated with radioactive iodine ^{131}I and 14000 pts. treated with antithyroid drugs. Small increase in leukemia was noticed in ^{131}I treated patients.

Factors in the studies that might have an effect on the results:

- ✓ The period of following the patients is less than 15 years, which might be not enough to develop a cancer.
- ✓ The absorbed dose calculation were based on a model (ICRP 53) not the individual based biokinetics.
- ✓ The age limit for radioiodine treatment is lowered. More young people, even children are prescribed radioiodine therapy today.

CONCLUSION

- Individual external measurements give information about dose rate at the moment of releasing the patient from hospital. Hyperthyroid patients should continue to be treated ambulatory because it has positive benefit, reduced hospital costs, less exposure of medical personal, and positive psycho socio economical aspects for patient and his family members.

- Internal dosimetry has clinical benefit and is becoming standard practice as requirements for personalized treatment are introduced and regulations regarding treatment planning are brought into force.

- Monte Carlo method is a widely used research tool and has proven to be very useful for solving complex problems when experimental measurements may be impracticable.

CONCLUSION

- The estimation of additional risk for each type of procedure as a part of QA programs for ^{131}I capsule should be implemented during radioiodine treatment. It is very important for radiation protection and to reduce psycho emotional distress for a patient.

- Radioactive iodine ^{131}I still remains nuclide of choice in treatment of thyroid diseases. It has proven to be a safe, and a relatively inexpensive treatment modality.


Thank you for your attention!