INSTITUT
JULES BORDET
INSTITUUT

THYROID CANCERS
Dosimetry
Clinical (and practical) Considerations (and implications)

Prof. BOURGEOIS Pierre, MD, PhD,

Service of Nuclear Medicine,

Institut Jules Bordet,

Université Libre de Bruxelles,

Brussels, Belgium

« Dosimetry » for thyroid cancers? ➔ Imagings…At least 2… When?

- **BEFORE?**

The « simple » Thyroid Uptake scan with a « tracer » activity…

➔ Diagnosis of

a) Gross Remnants
b) Loco-Regionall and/or Distant Metas

- **AFTER? But « from 2 to 12… »**

➔ Diagnosis (of Remnants and) of Loco-Regional and/or Distant Metas…

Maxon's Formula and the activity? The controversy about the activities… « Forfaitary » OR « Calculated »?

- **30 mCi? Or 100 mCi?**
- **... Or less? Or more?**
- **Under Thyrogen? (but cost…) or**
- **After THW? (but hypothyroidism…)**
- **« The same results… »**
- **« It is so simple… »**

- ➔ pre-therapeutic dosimetry?
- « It is « complicated », « expansive » (?), « time consuming » (time of the MD, technicians, physicians, cameras-PET),…
- ➔ **« Can we do it simple? »**

THYROID CANCERS
Dosimetry
Clinical (and practical) Considerations (and implications)

Can we perform (simple)

pre-therapeutic and/or post-therapeutic imagings-dosimetric approaches?

And

Can they be usefull in the management of these patients?

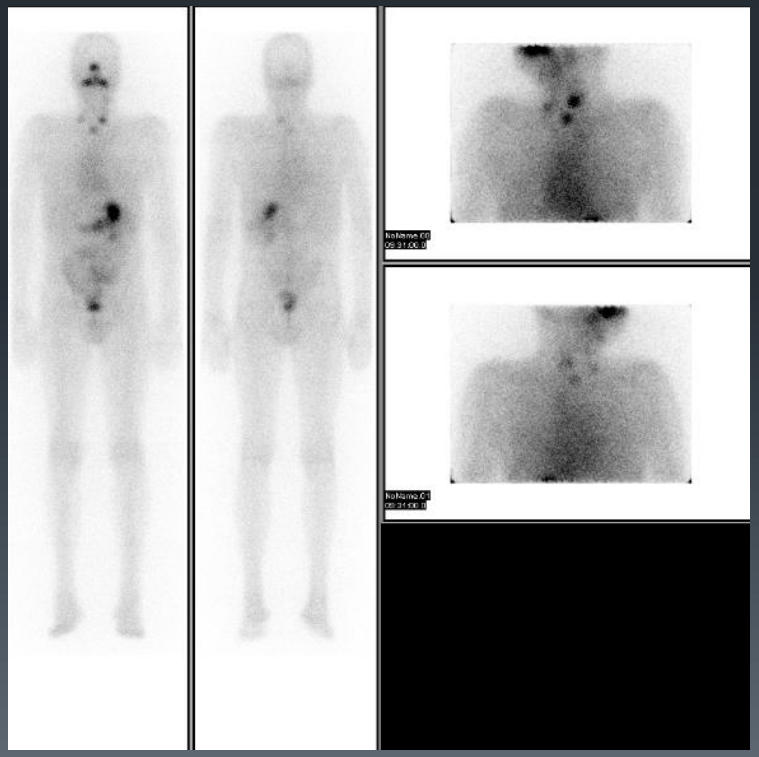
The pre- and post-ther. imagings: what do we perform here and now?

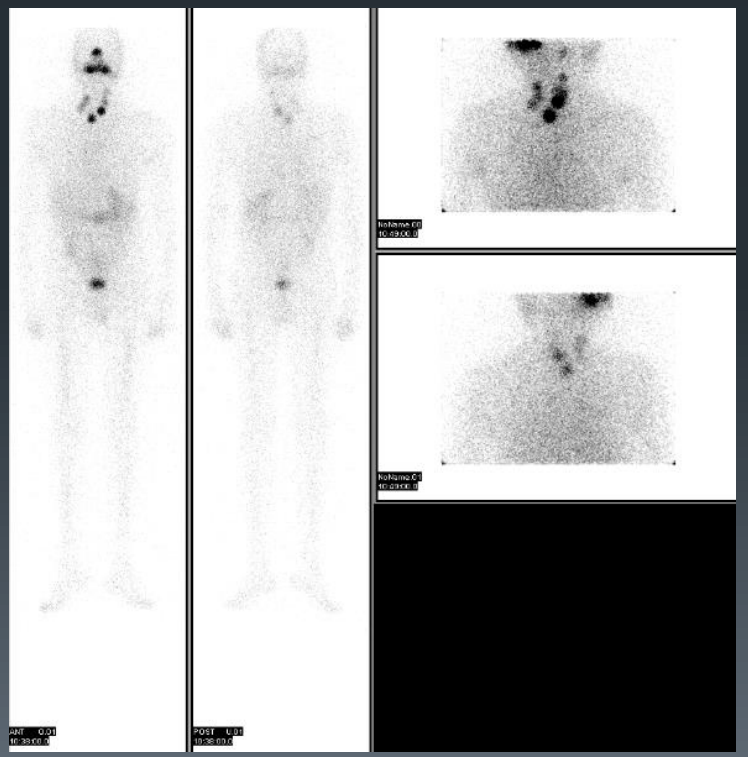
- **One pre-ther static imaging** (20 min long) PLUS Whole Body Scanning and one SPECT (when possible) 24 hours after the intake of 18,5 MBq (500 µCi) of D-131I
- **Two sets of post-ther imagings**: the 1rst at the hospital discharge (usually 2 to 3 days after T-131I Intake) and the 2nd 5 to 7 days after T-131I Intake
- WBS PLUS static imagings centered on neck and thorax (including one reference source of known activity) PLUS (now) Spect-Ct acquisition(s) centered on neck and thorax (and other areas of interest if suspicious…)
- PLUS clinical consultation, measurements of dose rate, blood samplings (Tg, anti Tg and lymphocytes counts…), radio-protection « counsellings »…

The post-therapeutic imagings and Their interests…

D… Robert 236537 Pap. Ca. Foll. Pres. pT4N1b
15-19/04/2005 WBS at D+3 (Tg=14) and D+7 (Tg=130) after 156 mCies of 131-I given the 12/04/2005 (Tg=5,5)
Planar D+7 better planar D+3 but versus SPECT at D+3 ?

Activities in the cervical foci is estimated to 6 to 20 µCies





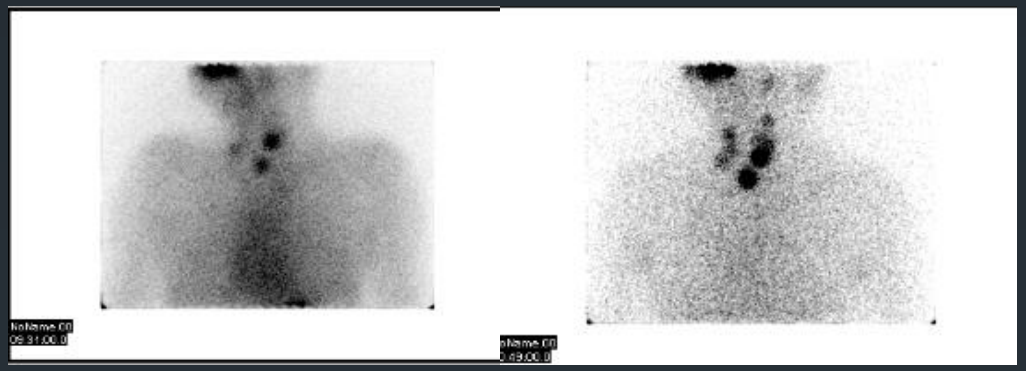
The (2) post-therapeutic imagings and their interests…

- 10% to 15% of the thyroid remnants and/or of the loco-regional extra-thyroidal localisation are better seen on early (planar) imagings than on delayed (planar) imagings and, on the opposite, 10% to 20% better on delayed (planar) imagings than on early (planar) imagings

- The tumor to background ratios (TBR) of the distant metas (lung, mediastinum, bones, liver,…) (their « contrast ») is higher on delayed (planar) imagings than on early (planar) imagings and these lesions are better identified and diagnosed on delayed (planar) imagings than on early (planar) imagings but… SPECT-CT?

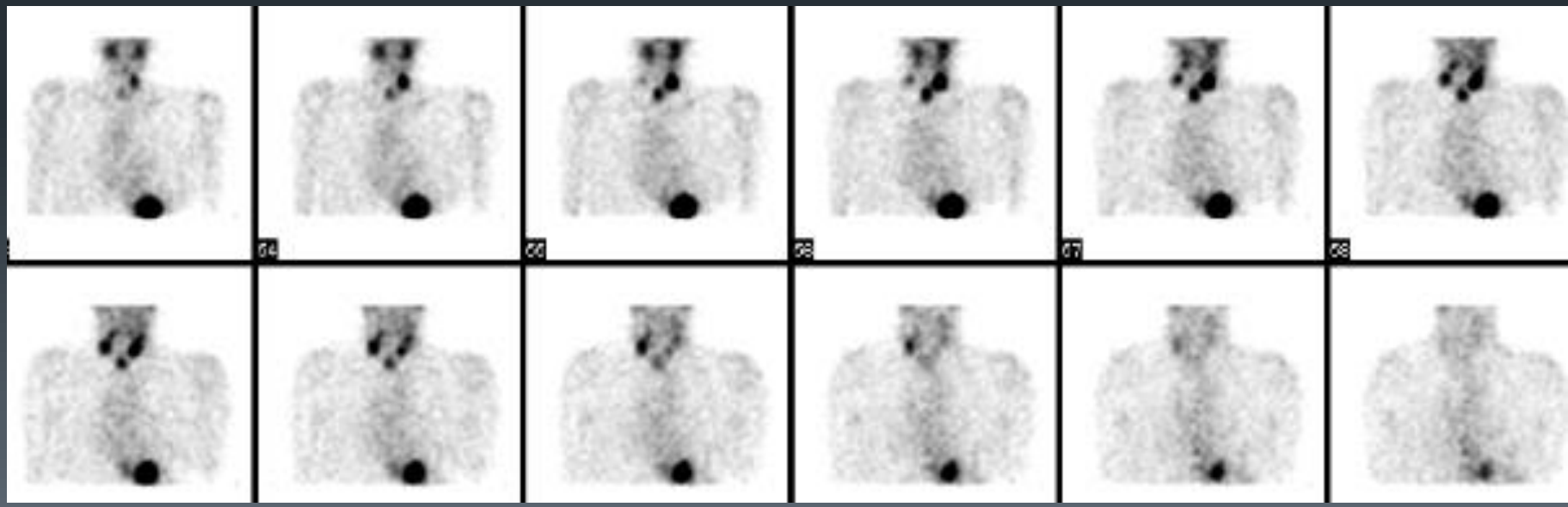
- « 7,5 % of early scans provided more information than the late scans and 12,0 % of the late scans more information than the early scans » (Salvatori… Nucl Med Commun 2013;34:900-908)

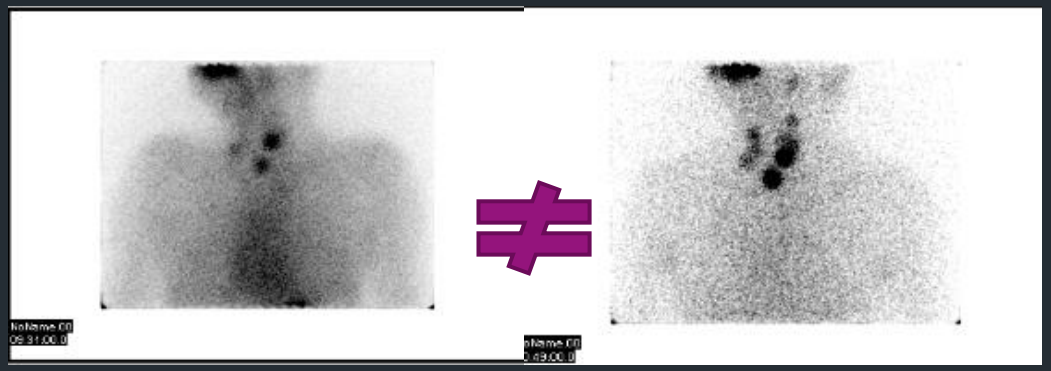
The (2) post-therapeutic imagings and their interests… Planar and/or SPECT-CT?



Activities in the cervical foci is estimated to 6 to 20 µCies

Devr… Robert 236537
15-19/04/2005 WBS at D+3 and D+7 after 156 mCies of 131-I
Planar versus SPECT at D+3 ?





The Effective Half-Lives of 131I in the iodine positive lesions versus the whole-body clearance of the 131I

EANM Congress 2005, Istanbul, Turkey
Oral Presentation
EJNMMI Vol 32, Supplement 1 (09/2005), S111
“Effective Half-Lives (Eff T1/2) of I-131 In Cervical (CL) and Distant (DL) Localisations of Patients Treated for DTC?”

BOURGEOIS Pierre, MD, PhD,

Service of Nuclear Medicine,

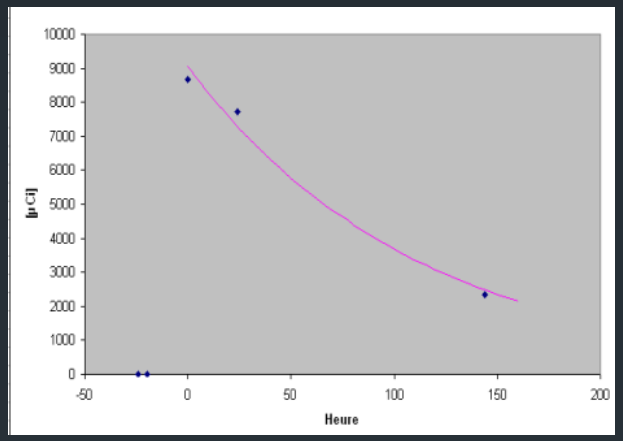
Institute Jules Bordet, Université Libre de Bruxelles,

Brussels, Belgium

D… Rita 168543 (1965) : 1994 left lobectomy but AP benign
1999 right lobectomy Pap. Ca. 4 mm
2004 Right LN 1/8 pN+ ➔ decision to treat
Uptake, absorbed dose, radio-thyroiditis and Tg…

Pre-Ther Uptake after 24 hrs = 30% !

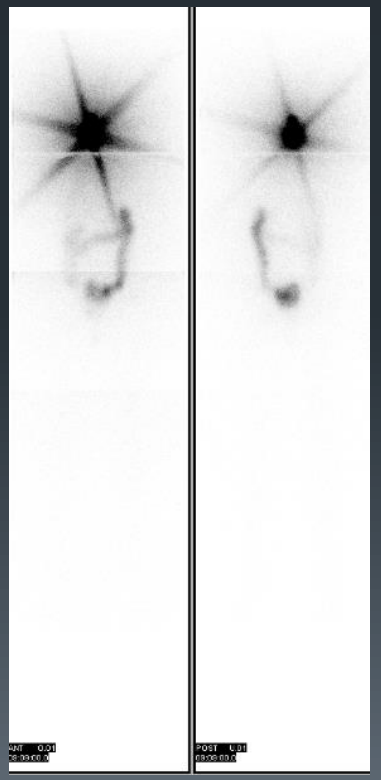
➔ Decision to treat with 28.9 mCies



Eff T1/2 = 77 hrs

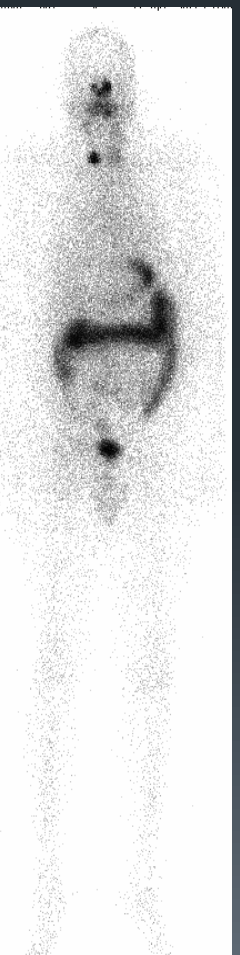
➔Absorbed dose = 4157 mJ! ➔ Thyroiditis
Tg at D0 = 19 ➔ 31 at D+2
but under DXM 4x4mg…
➔ Tg = 5700 at D+7 (when DXM stopped)
Clinically obvious thyroiditis…

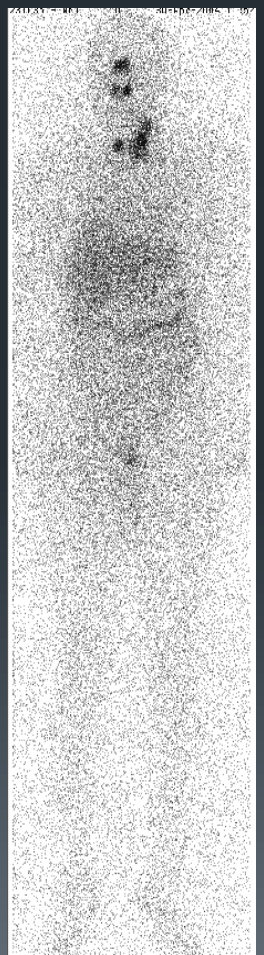
WBS at D+2…



The post-therapeutic imagings: Diagnosis and caracterisation of the thyroid tissues…

B… Jean 231053 LN relapse
26-30/04/2004 WBS J+3 and J+7 Post-Ther (205 mCies)



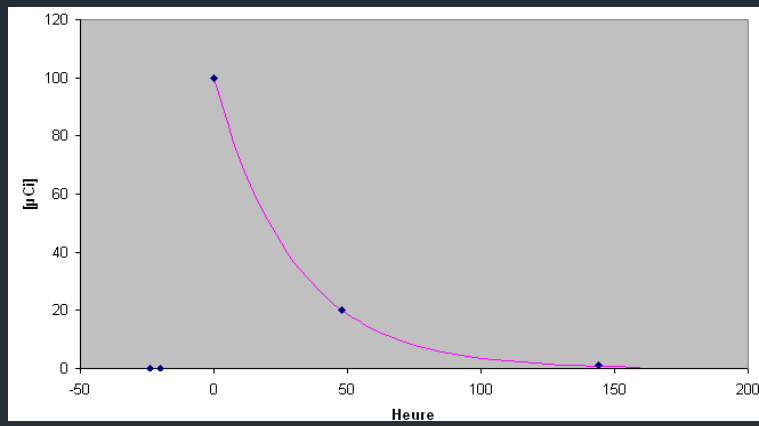


Cervical Inf Right:

J+1 = 5 10e-4 = 100 microCies
J+3 = 20 microCies = 1 10e-4
J+7 = 1 microCie = 0.5 10e-5

T1/2Eff = 21 hours

➔ 13,2 mJ

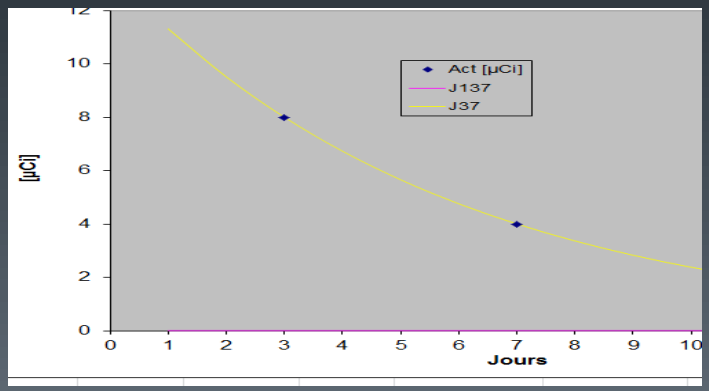


All Cervical Left:

J+1 = Not detected (est = 11,3)
J+3 = 8 microCies = 0.4 10e-4
J+7 = 4 microCies = 0.2 10e-4

T1/2Eff = 96 hours

➔ 6,85 mJ

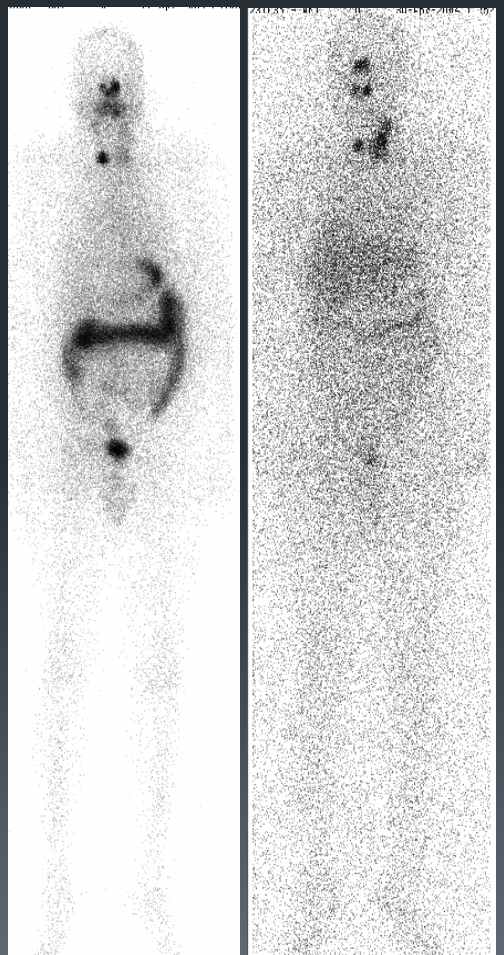


The post-therapeutic imagings: Diagnosis and caracterisation of the thyroid tissues…

B… Jean 231053 LN relapse

26-30/04/2004 WBS J+3 and J+7 Post-Ther (205 mCies)

➔ 13/04/2005 (Tg = 29,5 and) after 147 mCi (under THW) (➔ no ab)



Cervical Inf Right:

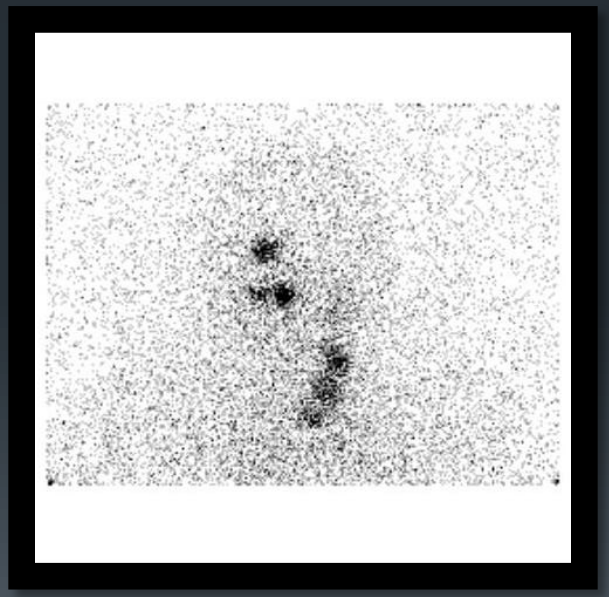
J+1 = 5 10e-4 = 100 microCies

J+3 = 20 microCies = 1 10e-4

J+7 = 1 microCie = 0.5 10e-5

T1/2Eff = 21 hours

➔ 13,2 mJ



All Cervical Left:

J+1 = Not detected (est = 11,3)

J+3 = 8 microCies = 0.4 10e-4

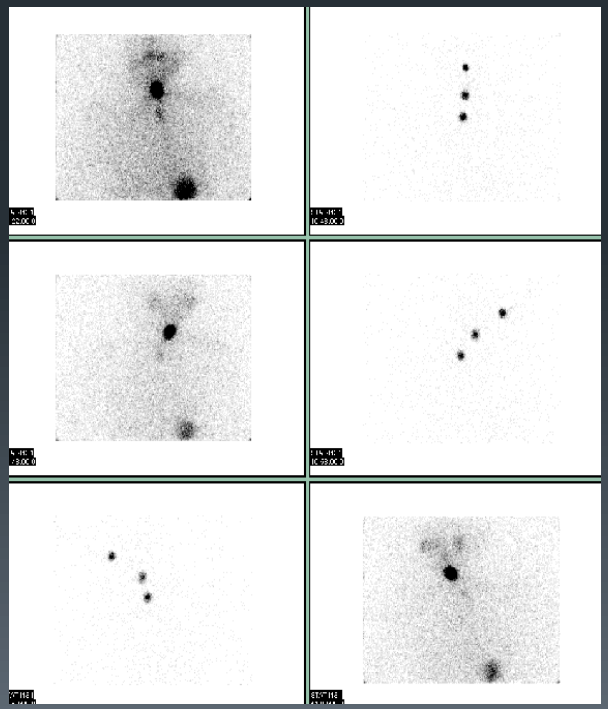
J+7 = 4 microCies = 0.2 10e-4

T1/2Eff = 96 hours

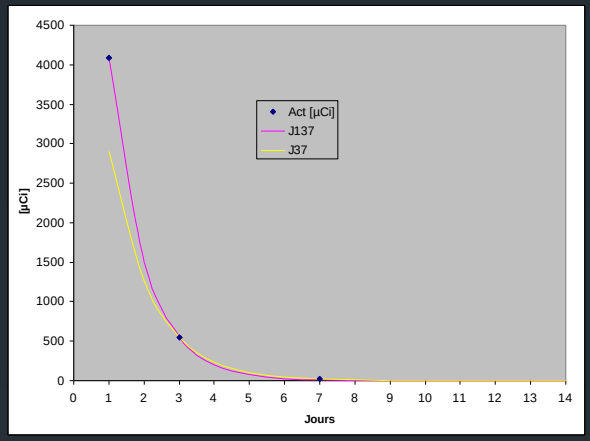
➔ 6,85 mJ

M… Geneviève 221632
Ca. Pap. pT4N1a (3 LN pN+ R+ / 4)
5/07/2005 « Uptake » 3, 6 and 24 hours after 500 µCies
(8-)11-15/07/2005 WBS D+3 and D+7 after 148 mCies 131-I
Tg = 3,7 ➔ 282,0 ➔ 126,0 (➔ Fup Ablation!)

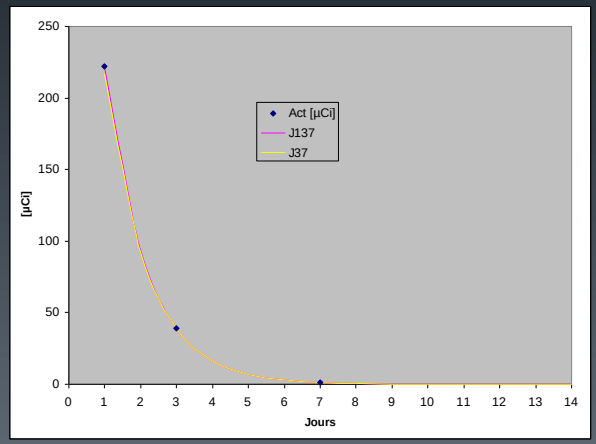
Upper foci: 2.74 % (24h)
Lower foci: 0.15% (24h)



Upper foci
WBS D+3 ➔ A eff = 550 µCies
or 0.37% or 37 10e-4
WBS D+7 ➔ A eff = 19.8 µCies
or 0.013% or 1.3 10e-4
➔ T1/2 eff = 16.6 hours
➔ 359 mJ



Lower foci
WBS D+3 ➔ A eff = 38.8 µCies
or 0.026% or 2.6 10e-4
WBS D+7 ➔ A eff = «1.24» µCies
or 0.0008% or 8.3 10e-6
➔ T1/2 eff = 19.1 hours
➔ 26,2 mJ



Maxon's Formula… in practice

- The Activity… what we gave
- The Uptake… what we measured before
- The Effective Half-Life… what we measured after (post-therapeutic imagings-dosimetry)
- ➔ Energy in the lesions in mJ…

- **BUT ….**
- **The Mass of the « targeted » thyroid tissue?**
- **The Energy (the Grays) (necessary…) to destroy the tissues?**

The « unknown » variables in the Maxon's Formula

Dosimetry in thyroid cancers: How are defined the «mass» of the targeted tissues?

- Maxon's ways (JNM 1992): « The mass of residual thyroid tissue was calculated using estimates of thickness (determined from the surgeon's operative notes and from discussions with the surgeon) and actual determinations of surface area (based on anterior 1:1 rectilinear scans of the neck). The masses of nodal metastases were calculated from anterior 1:1 rectilinear scans of the neck, assuming spherical or effipsoidal configurations. »
- Echography? (only what is morphologically detectable…)
- SPECT-CT (with tracer Act. of 131-I) and/or PET-CT (with a tracer Act. of 124-I) ➔ the « volume » (➔ the « mass ») of iodine positive lesions… but detectable by these ways (« What about small lesions and/or lesions with low uptake-signal and/or lesions without iodine uptake? »)

“Our Approach…”

- **« Circulating Thyroglobulin is proportional to and representative of the mass of all the thyroid tissues(-cells) present in the patient… irrespective of their sizes, of their localisation and of their iodine uptake »**

- **“The serum levels of Tg are proportional to the volume of thyroid tissue at a rate 1 ng/mL per 1 g of thyroid mass in euthyroid state and to 0,5 ng/mL in TSH=0.”** (World J biol Chem 2017;8(1):81-85)

➔ From mJ/g to mJ/ngTg…

EANM Congress 2007, Copenhague, Danemark Oral Presentation EJNMMI Vol 34, Supplement 2 (09/2007), S231 "Can We Predict the Ablation of Thyroid Tissues After 131-Iodine Treatment For Differentiated Thyroid Carcinoma (DTC)?"

P. BOURGEOIS,

B. Vanderlinden, K. Muylle, C. Garcia and P. Flamen

Service of Nuclear Medicine, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium

Aim of the work: To study the value of the calculated absorbed doses (AbD) and of the Thyroglobulin (Tg) changes after 131-I treatment to predict successful ablation of thyroid tissues in patients operated for DTC.

- Ablation = 31/39 or 79.5%
- Cut-off level for **AbD = 20 mJ/ng-Tg-ml**

➔ **PPV = 27/31 = 87%**

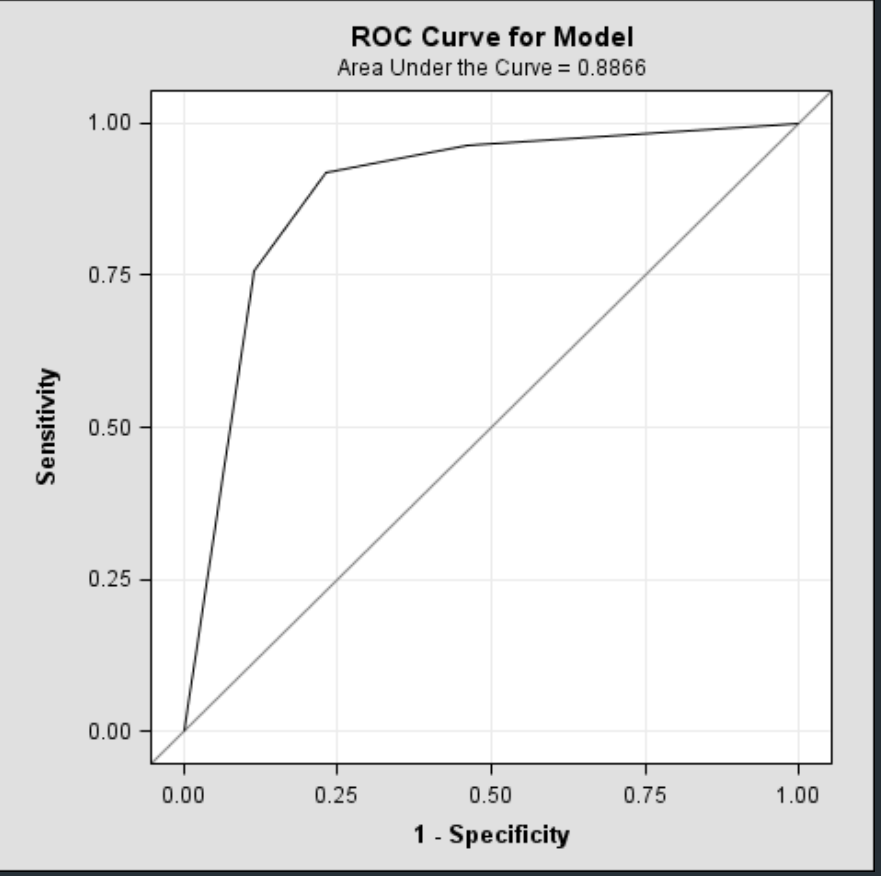
	Ablation		
	Yes N = 31	**No** N = 8	Level of Significance
AbD mJ/ng-ml Tg	**58.0** 5.2-811.0	**6.1** 0.2-16.3	**p < 0.001**
TgD3D0	**11.8** 1.9-83.0	**2.4** 0.7-8.7	**p < 0.001**
TgD7D0	**11.5** 0.7-78.7	**1.85** 0.7-7.9	**P = 0.009**

n=123 from 03/2005 to 06/2009
26 without ablation at 1 year
statistical analysis of the differences- predictive factors for ablation

	No ablation (N=26)	Ablation (N=97)	Odds ratio (95% CI)	P Value
Sexe – no. (%)				
Male	12 (30.0)	28 (70.0)	0.47 (0.19 to 1.15)	**0.09**
Female	14 (16.9)	69 (83.1)		
Age				
Median	49	50		**0.33**
Interquartile range	31-57	38-61		
<45 – no. (%)	12 (24.5)	37 (75.5)	0.72 (0.30 to 1.72)	**0.46**
≥ 45	14 (18.9)	60 (81.1)		
TNM				
N0 or Nx, and T0, Tx, T1 or T2	6 (7.8)	71 (92.2)	10.59 (3.67 to 30.58)	**<0.001**
N0 or Nx, and T3 or T4	3 (30.0)	7 (70.0)	2.09 (0.46 to 9.38)	
N1	17 (47.2)	19 (52.8)		
Anti Tg antibodies – no. (%)				
≥60 UI/mL	3 (13.4)	19 (86.6)	1.87 (0.51 to 6.88)	**0.40**
<60 UI/mL	23 (22.8)	78 (77.2)		
Normalized Absorbed dosis (mJ per ng-mL Tg at day 0)				
Median†	15	91		**<0.001**
Interquartile range†	6 – 19	48 – 189		
≥20 – no. (%)‡	6 (6.3)	89 (93.7)	37.08 (11.57 to 118.81)	**<0.001**
<20	20 (71.4)	8 (28.6)		

"Prediction of Ablation Using a Simplified Dosimetric Approach After ^{131}I Administration for DTC" (n=123 from 03/2005 to 06/2009)

	No ablation (N=26)	Ablation (N=97)	Odds ratio (95% CI)	P Value
Sexe – no. (%)				
Male	**12 (30.0)**	**28 (70.0)**	0.47 (0.19 to 1.15)	**0.09**
Female	**14 (16.9)**	**69 (83.1)**		
TNM				
N0 or Nx, and T0, Tx, T1 or T2	**6 (7.8)**	**71 (92.2)**	10.59 (3.67 to 30.58)	**<0.001**
N0 or Nx, and T3 or T4	**3 (30.0)**	**7 (70.0)**	2.09 (0.46 to 9.38)	
N1	**17 (47.2)**	**19 (52.8)**		
Normalized Absorbed dosis (mJ per ng-mL Tg at day 0)				
Median†	15	91		**<0.001**
Interquartile range†	6 – 19	48 – 189		
≥20 – no. (%)‡	**6 (6.3)**	**89 (93.7)**	37.08 (11.57 to 118.81)	**<0.001**
<20	**20 (71.4)**	**8 (28.6)**		



"Prediction of Ablation Using a Simplified Dosimetric Approach After ^{131}I Administration for Differentiated Thyroid Carcinomas"

Multivariate Logistic Regression models to predict ablation (N=123)

	Odd ratio (95% CI)	P Value
Normalized Abs. dosis ≥20 Gy per ng-mLTgD0	23.24 (6.87 to 78.66) 25.67 (7.69 to 85.73)	**<0.001**
TNM Stage	**0.50 (0.26 to 0.97)**	**0.04**
Sex Male	**0.22 (0.05 to 0.87**	**0,02**

“Prediction of Ablation Using a Simplified Dosimetric Approach After ^{131}I Administration for DTC”

Retrospective analysis of data…

a) between 03/2005 and 06/2009:
n= 123 (ablation rate = 78,8% with 30% N1)

b) between 07/2009 and 11/2016:
n = 109 (ablation rate = 77% with 46,7% N1)

c) Total
n=232… (ablation rate= 76,2% with 37,1% N1)

NEJM may 2012 1663-1685
Schlumberger: 684 pat: Ab 92% but 20% N1
Mallick: 421 pat: Ab 85-89% but 15,7% N1

POSITIVE PREDICTIVE VALUE OF NAbsDTgD0

a)
FOR ABLATION IF > 20 mJ/nG-mL Tg = 93,7%
FOR NON ABLATION IF < 20 mJ/nG-mL Tg = 71,4%

OVERALL ACCURACY = 88,6%

b)
FOR ABLATION IF > 20 mJ/nG-mL Tg = 92,5%
FOR NON ABLATION IF < 20 mJ/nG-mL Tg = 79,3%

OVERALL ACCURACY = 89,0%

c)
FOR ABLATION IF > 20 mJ/nG-mL Tg = 93,1%
FOR NON ABLATION IF < 20 mJ/nG-mL Tg = 75,4%

OVERALL ACCURACY = 88,8%

Conclusions and implications (1) Why pre-therapeutic imagings with 131I?

a) To diagnose unsuspected loco-regional and distant metas → change in activity to be given and/or shift to surgery (even radio-guided) after 131I treatment and/or…?

b) If the pre-therapeutic Tg value and the Upt value are « discording », plan (confirm or not one « optional ») 18F-DG PET-CT imaging the same day as the admission of your patient?

Conclusions and implications (2) Why (2) post-ther. imagings (and dosimetry) with 131I?

- **To diagnose unsuspected lesions and to characterize these lesions by their uptake of Iodine and by their effective half life**

a) By reference to 18F-DG PET-CT… systematically performed (Cost? Availability?) OR only in specific situations, among others, if decreasing uptake and modification of the Eff T1/2 of one or more lesions in patients with x treatments

b) ➔ de-differentiation? ➔ Trial for re-differentiation? (Sumetinib but availability? ➔ retinoic acids….?)

c) ➔ « targeted » radio-guided surgery-ies if possible?

d) ➔ « targeted » radiotherapies?

e) ➔ …?

Conclusions and implications (3) Why post-therapeutic imagings and dosimetry with 131-I?

- **To adapt the follow-up of the patients…**

- If the NAbsD is > 20
  - ➔ FUp = biological and echographic control and Thyrogen test (but cost?) after (6 or) 12 months (good message for the patient…)
- If the NAbsD is < 20
  - ➔ Additional investigations?
  - ➔ Thyrogen test has to be questioned (cost!) and THW seems us to have to be proposed with Tg control after 3 weeks defining the need to treat or not..
  - ➔ with or without pre-therapeutic imagings-dosimetry?

Conclusions and implication (4) Why pre-therapeutic imagings (and dosimetry) with 131-I?

- If the « usefull » NAbsD is 20 mJ/ng-mL TgD0 (at least), the activity to be given can be calculated
  - 1° taking into account the Tg value before treatment,
  - 2° taking into account the Upt value before treatment and
  - 3° assuming that the Eff T1/2 is at least 24 hours

It is not « perfect » but…

It is more rationale than « HEADS OR TAILS »

➔ Some practical exercises with our « magic » program


To « Treat » Or Not To « Treat » ?
To « Dose » Or Not To « Dose » ?
« That's the question »…
« but finally one question of image(s) »…
I thank you for your attention!