Quelle place pour la dosimétrie interne en routine clinique ?

Session Physique Médicale

2e Journées Francophones de Médecine Nucléaire

19 – 22 mai 2016

Grenoble

Quelle place pour la dosimétrie interne en routine clinique ?

- Quels traitements ?
- Quelles approches ?
- Quels outils ?
- Quel impact dans la prise en charge clinique ?
- …

Quelques questions pour commencer...

Q1 : La dosimétrie interne est…

A. Trop complexe
B. Un joujou pour les physiciens
C. Un outil pour maitriser la balance bénéfice/risque

Q2 : L'implémentation de la dosimétrie interne dépend

A. De la modalité thérapeutique
B. Du niveau de précision souhaité
C. Du temps que l'on veut bien y consacrer
D. De l'impact clinique que l'on en attend

Q3 : L'implémentation de la dosimétrie interne doit être considérée

A. Lorsque la relation dose-effet a déjà été mise en évidence dans le traitement
B. Lorsque sa mise en œuvre peut être simplifiée
C. Pour chaque modalité de traitement

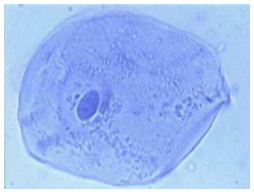
Q4 : L'implémentation clinique de la dosimétrie est limitée par

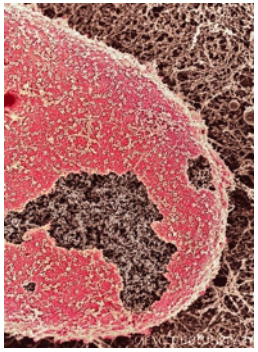
A. Le manque d'outils adaptés
B. Le manque de physiciens impliqués en MN
C. Le manque de recommandations claires
D. Le manque de pertinence clinique
E. L'absence de valorisation (acte CCAM…)

Quelles réponses peut-on apporter ?

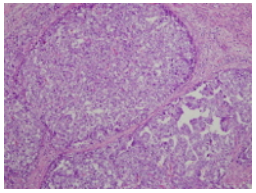
Formalisme du MIRD

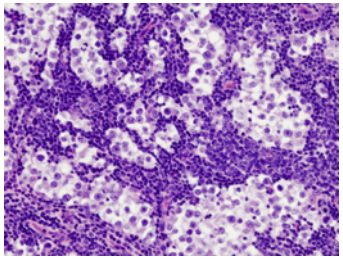
Cells, cell wall, cell nucleus...



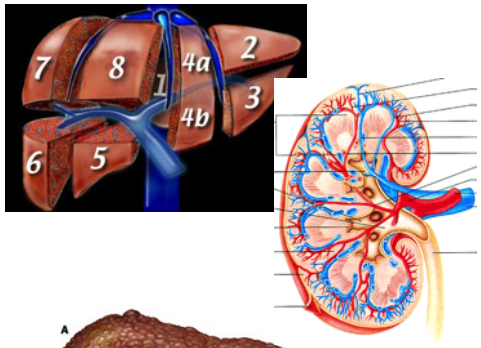


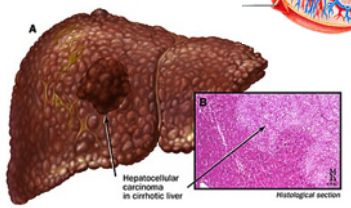
Cluster of cells, metastases



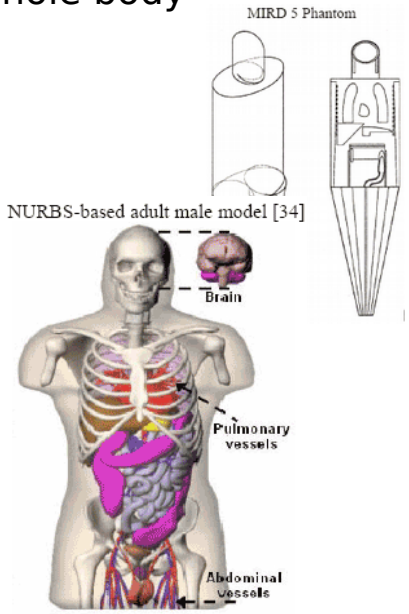


A tissue, solid tumor, sub-organ (liver segment, kidney cortex, medulla...)



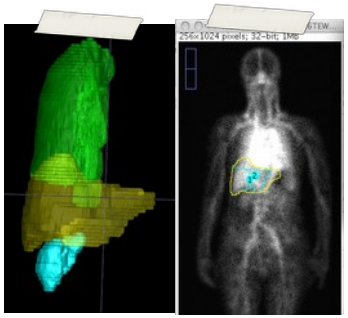


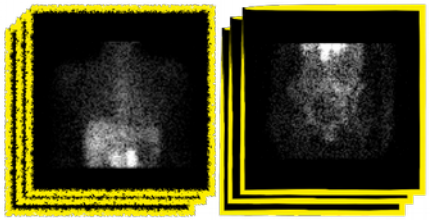
An organ, body part or whole body

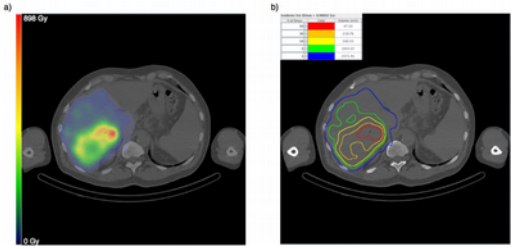


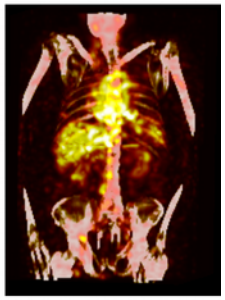
1-10 µm | 0.1-1 mm | 1-5 cm | 0.01-1 m

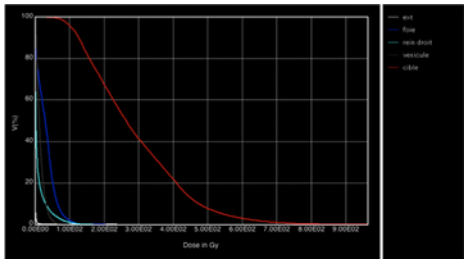
Dosimétrie par imagerie : vers une dosimétrie personnalisée

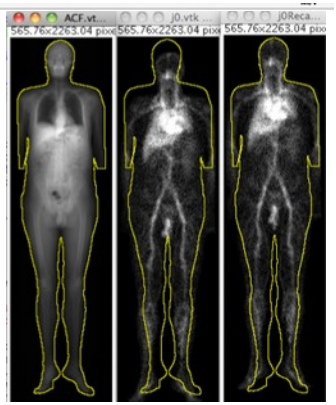


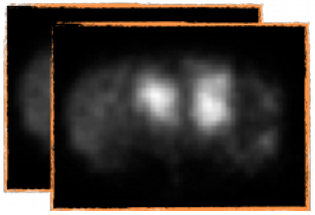






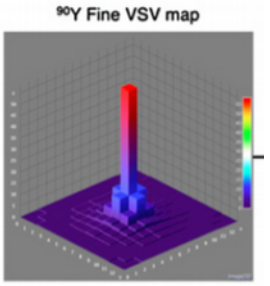




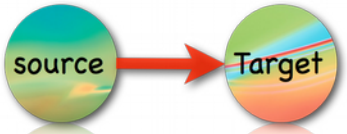


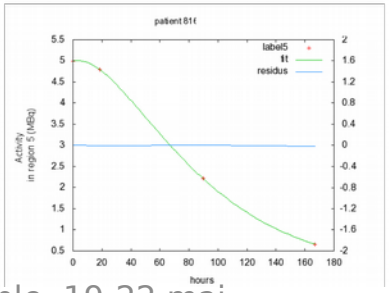
$$\bar{D}_{(t \leftarrow s)} = \tilde{A}_s \times S_{(t \leftarrow s)}$$

Tabulated S value **adjusted** for organ masses

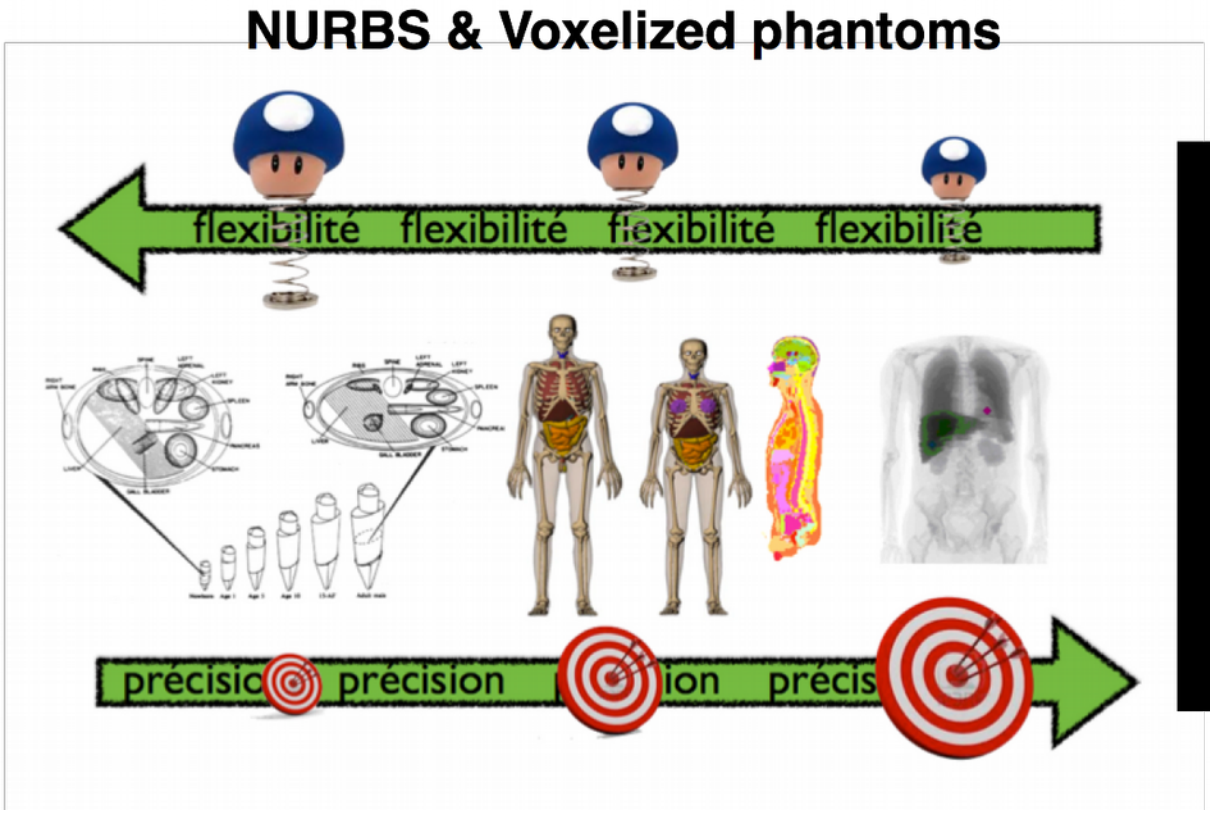


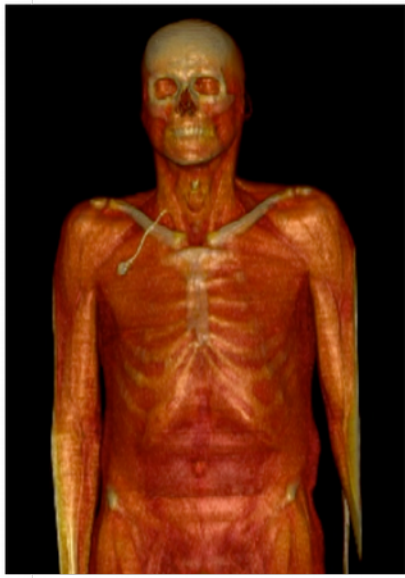
MIRD committee schema





Dosimétrie par imagerie : vers une dosimétrie personnalisée





Mise en œuvre imagerie

- Imagerie 2D
  - mise en œuvre ++
  - quantification –
  - dosimétrie corps-entier, MO
- Imagerie 3D
  - mise en œuvre +
  - quantification ++
  - Personnalisation ++
  - dosimétrie OAR, tumeurs

Mise en œuvre imagerie

- Thérapie systémique (RIV mol, pept, imuno…)
  - Modélisation de la cinétique d'élimination nécessaire
  - Imagerie multi-temps

- Thérapie sélective (RIV sélective ou radio-embolisation)
  - Pas d'élimination biologique
  - Un seul point temps
  - Mise en œuvre ++

Quelques illustrations de l’apport de la dosimétrie personnalisée

^{131}I - K Thyroidien

- Approche empirique :
  - activité fixe ou modulée en fonction d'un risque estimé par le médecin pour éviter les complications
    - Adjuvant :
      - Risque faible ~ 1GBq
      - Risque modéré ~ 4 GBq
    - Non opérable ou métastatique ~ n x 4 GBq

Table 2 Differentiated thyroid cancer (DTC): risk classification, adapted from Reiners et al. (2008a)

Organization	Risk classification characteristics		
UICC, AJCC, ATA Stage I: Stage II: Stage III: Stage IV:	*Pts. <45 years* Any T or N, M0 Any T or N, M1 Not applicable Not applicable		*Pts. ≥45 years* T1, N0, M0 T2, N0, M0 T3N0M0 or T1/T2N1M0 all other TNM categories
ETA	*Very low risk* T1(≤ 1 cm)N0M0	*Low risk* T1(>1 cm)N0M0 T1mN0M0 T2N0M0	*High risk* T3 and T4 N1 M1

AJCC American Joint Committee against Cancer, *ATA* American Thyroid Association, *ETA* European Thyroid Association, *UICC* Union Internationale contre le Cancer

D'après C. Reiners in Therapeutic nuclear medicine 20

^{131}I - K Thyroidien

- Approche dosimétrique :
  - Activité pré-thérapeutique : A_0 [10-40 MBq]
  - Benua *AJR 1962* : MO < 2Gy, reliquats ≥ 300 Gy, Meta > 80 Gy
  - EANM Guidelines *EJNMMI 2008*:
    - Dosimétrie reliquats/métas

$$\bar{D}_t = \tilde{A} \times S \times \frac{m_r}{m_t}$$

      - plusieurs acquisitions scintigraphiques (CE, SPECT)
      - Intégration temporelle bi-exponentielle
      - MIRD pamphlet 11 : $5.652 \times 10{-}3$ Gy MBq^{-1} h^{-1}
      - Masses des reliquats : CT, US .... difficile en pratique

    - Dosimétrie moelle (sang): MO ≤ 2Gy
      - Activité sanguine : prélèvements sanguins -> temps de résidence
      - Activité CE : sonde, scintigraphie CE A/P -> temps de résidence

$$\frac{\bar{D}_{sang}}{A_0}\left[\frac{Gy}{GBq}\right] = 108 \times \tau_{\text{ml de sang}[h]} + \frac{0.0188}{poids[kg]^{2/3}} \times \tau_{\text{CE}}[h]$$

K Thyroidien

Eur J Nucl Med Mol Imaging (2011) 38:673–680
DOI 10.1007/s00259-010-1689-5

ORIGINAL ARTICLE

The absorbed dose to the blood is a better predictor of ablation success than the administered ^{131}I activity in thyroid cancer patients

Frederik A. Verburg · Michael Lassmann · Uwe Mäder · Markus Luster · Christoph Reiners · Heribert Hänscheid

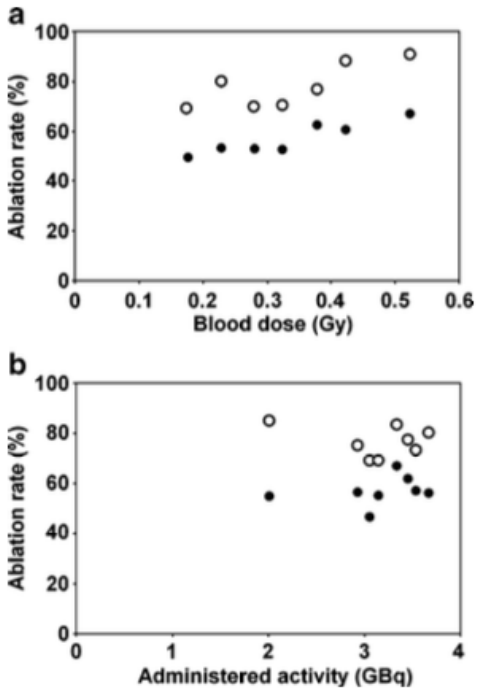


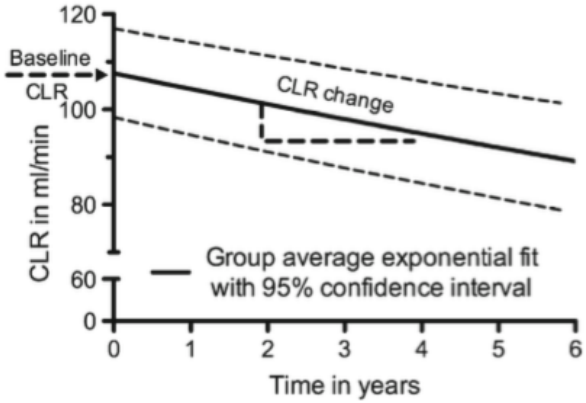
Fig. 1 Rates of successful ablation in subgroups of patients after stratification to intervals of absorbed dose to the blood (**a**) and administered activity (**b**). Criterion 1 (*filled dots*) was matched if in addition to visually negative diagnostic whole-body scintigraphy the concurrent TSH-stimulated serum TG level was undetectable. Successful ablation according to criterion 2 (*open circles*) was assumed in cases of visually negative diagnostic whole-body scintigraphy only. Values are drawn at the median of the correspondent interval

Etude rétrospective sur 449 patients montrant une corrélation entre l'effet thérapeutique et la dose absorbée

^{177}Lu-PRRT

Nephrotoxicity after PRRT with ^{177}Lu-DOTA-octreotate

Hendrik Bergsma[1] · Mark W. Konijnenberg[1] · Wouter A. van der Zwan[1] · Boen L. R. Kam[1] · Jaap J. M. Teunissen[1] · Peter P. Kooij[1] · Katya A. L. Mauff[2] · Eric P. Krenning[1] · Dik J. Kwekkeboom[1]



No risk factors for renal toxicity could be identified. Our data support the idea that the radiation dose threshold, adopted from external beam radiotherapy and PRRT with ^{90}Y-labelled somatostatin analogues, does not seem valid for PRRT with ^{177}Lu-octreotate.

Peptide receptor radionuclide therapy with ^{177}Lu-DOTATATE: the IEO phase I-II study

Lisa Bodei ✉ , Marta Cremonesi, Chiara M. Grana, Nicola Fazio, Simona Iodice, Silvia M. Baio, Mirco Bartolomei, Dario Lombardo, Mahila E. Ferrari and 3 more

^{177}Lu-DOTATATE was well tolerated up to 29 GBq cumulative activity (up to 7.4 GBq/cycle). The maximum tolerated dose/cycle was not reached. However, considering the individual bone marrow function and the presence of risk factors for kidney toxicity, it seems safer to divide cumulative activities into lower activity cycles.

Long-term tolerability of PRRT in 807 patients with neuroendocrine tumours: the value and limitations of clinical factors

Lisa Bodei · Mark Kidd · Giovanni Paganelli · Chiara M. Grana · Ignat Drozdov · Marta Cremonesi · Christopher Lepensky · Dik J. Kwekkeboom · Richard P. Baum · Eric P. Krenning · Irvin M. Modlin

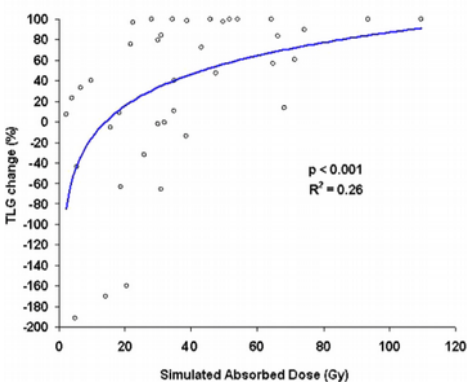
Conclusion Identified risk factors provide a limited (<30 %) risk estimate even with target tissue dosimetry. These data strongly suggest the existence of unidentified individual susceptibilities to radiation-associated disease.

^{90}Y-RTIS

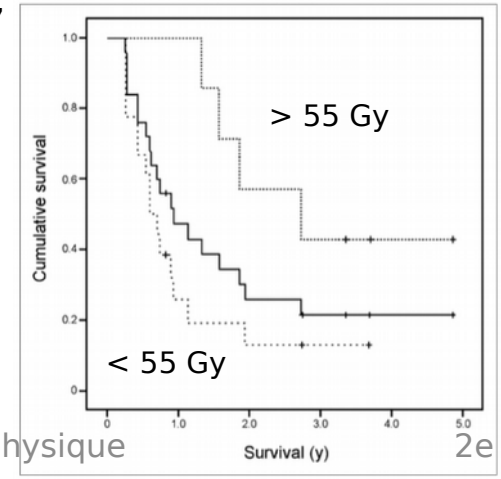
	Glass-microspheres	**Resin-microspheres** for diffuse lesions	**Resin-microspheres** for lesions with clearly definable regions
Prescription	Dose to targeted liver (segment ou lobe): 120±20 Gy	Activity	Dose to tumor: 120 Gy Dose to normal liver < 70 Gy Dose to cirrhotic liver < 50 Gy
Lung dose	L = lung / (lung + liver) / Dose to lung < 30 Gy		
Method	Simplified MIRD	BSA	Partition Model / MIRD
Activity calculation	$A[\mathrm{GBq}] = \frac{D_{\text{prescrite}}[\mathrm{Gy}] \times m_{\text{foie ciblé}}[\mathrm{kg}]}{50}$	$\text{Activity of SIR-Spheres in GBq} = (BSA - 0.2) + \left(\frac{\text{volume of tumour}}{\text{volume of tumour + volume of normal liver}}\right)$	$\overline{D}_{TL/NTL}\ [\mathrm{Gy}] = \frac{49.67 \times A_{TL/NTL\_0}[\mathrm{GBq}]}{m_{TL/NTL}\ [\mathrm{kg}]}$

^{90}Y-RTIS - metastases colorectales

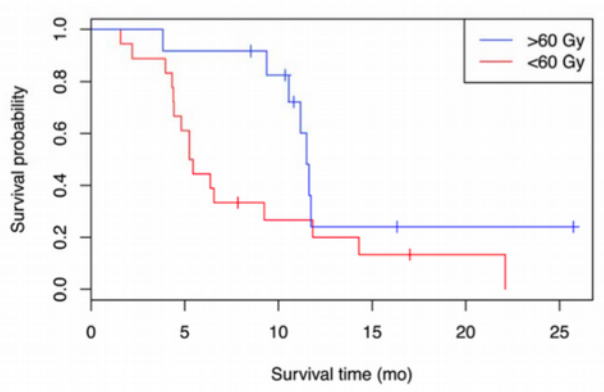
- Flamen P *et al.* Phys Med Biol. 2008 Nov.21;53(22):6591–603.

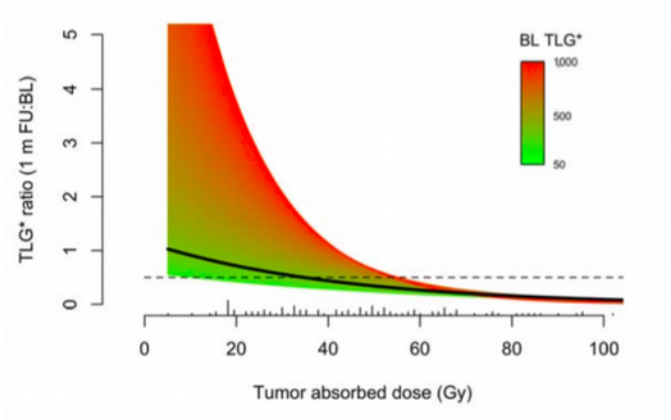


- Lam M. et al. J Nucl Dec. 2013. 54(12), 2055–2061



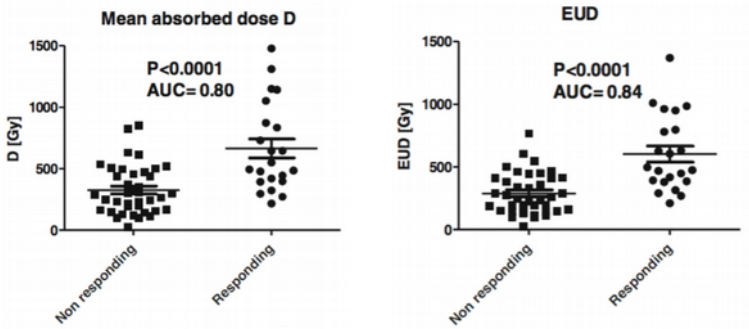
- Van den Hoven A. F. *et al.* J Nucl Med. 2016 Feb.21;*in press*.



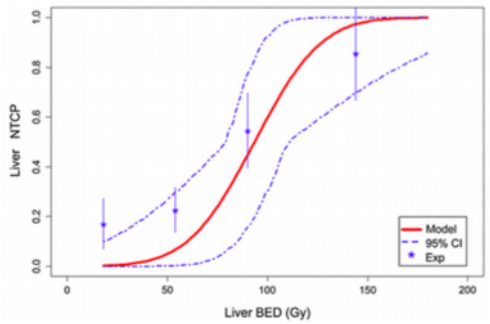


^{90}Y-RTIS - hépatocarcinome

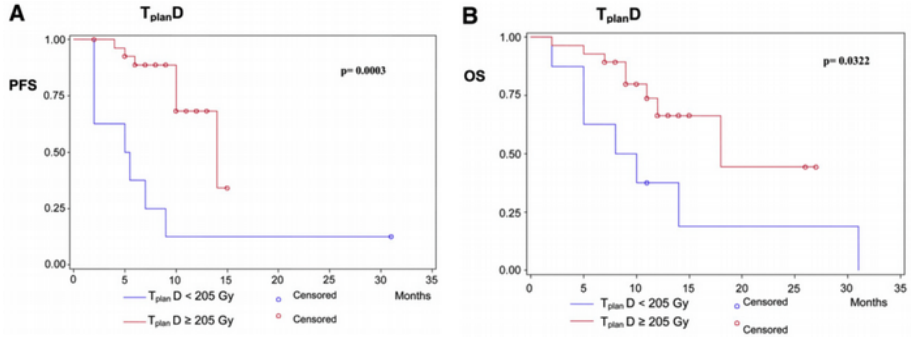
- Chiesa C et al. Eur J Nucl Med Mol Im. 2015 Jun;42(11):1718-38



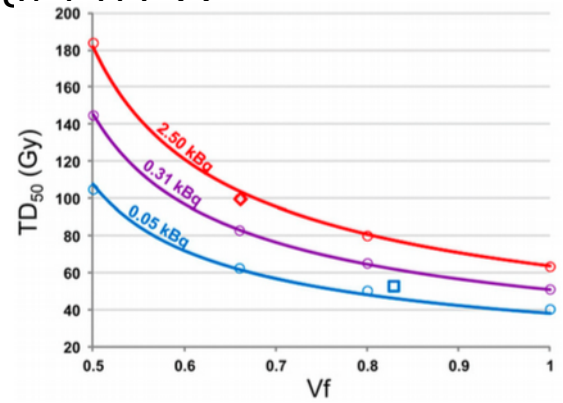
- Strigari L et al. J Nucl Med, 2010 Sep; 51(9):1377–85



- Garin E *et al.* J Nucl Med. 2012Feb.;53(2):255–63



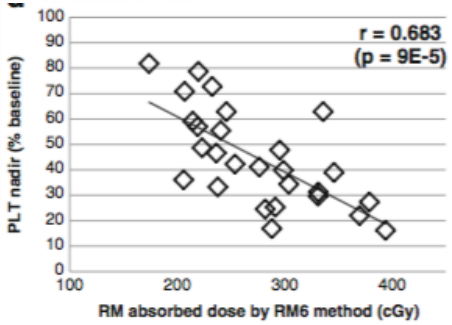
- Walrand S et al. J Nucl Med, 2014 Jun; 55(8):1317-22

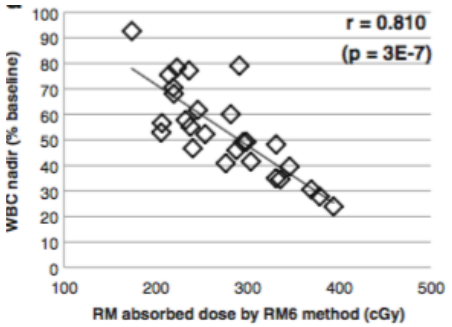


^{153}Sm-RM – métas Os

Improving the dose–myelotoxicity correlation in radiometabolic therapy of bone metastases with ^{153}Sm-EDTMP

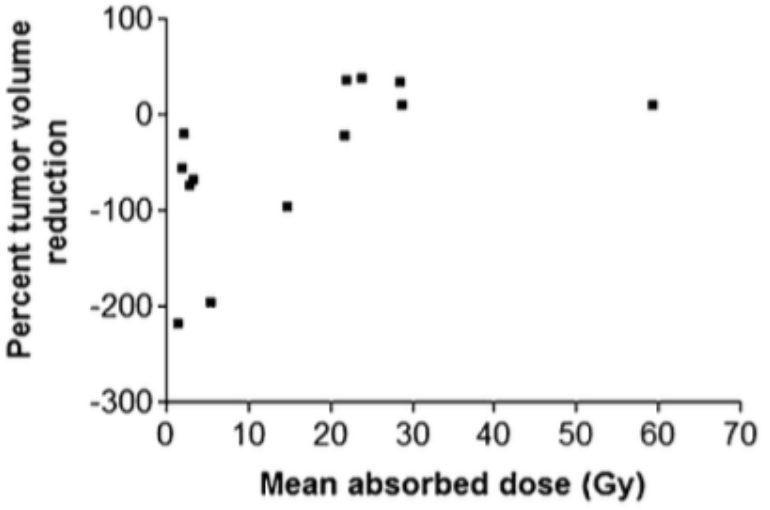
Massimiliano Pacilio · Guido Ventroni · Chiara Basile · Pasquale Ialongo · Domenico Becci · Lucio Mango



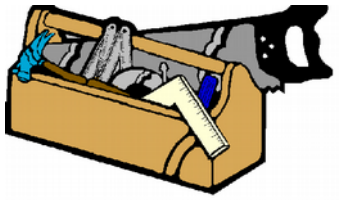


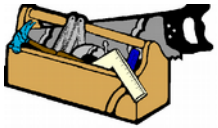
Tumor Dosimetry and Response for ^{153}Sm-Ethylenediamine Tetramethylene Phosphonic Acid Therapy of High-Risk Osteosarcoma

Srinivasan Senthamizhchelvan[1], Robert F. Hobbs[1,2], Hong Song[1], Eric C. Frey[1], Zhe Zhang[3], Elwood Armour[2], Richard L. Wahl[1,4], David M. Loeb[5], and George Sgouros[1]



Quels outils, quelle méthodologie ?

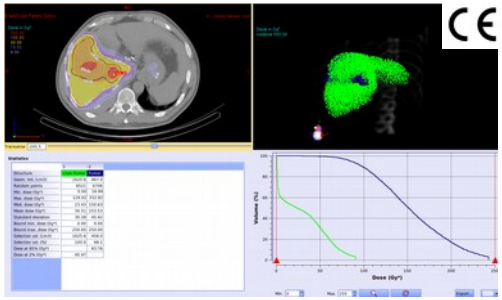




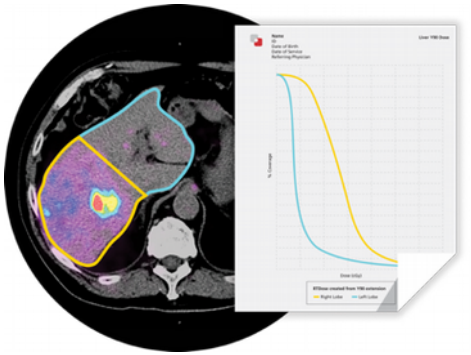
Outils

Solutions commerciales

RT sélective

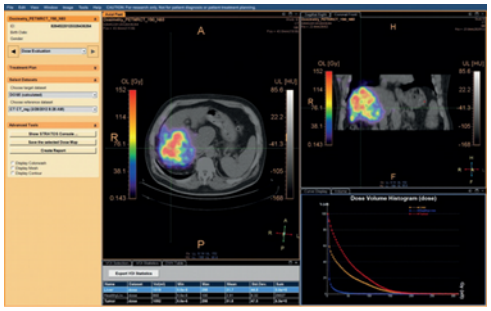


Planet Dose (DOSISOFT)

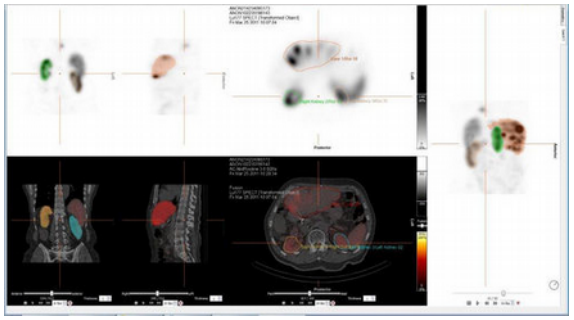


SurePlan Liver Y90 (MIM)

RT sélective + systémique



STRATOS (Philips)



Hybrid Dosimetry (HERMES)

Solutions gratuites

3DSlicer

python

ImageJ
Image Processing and Analysis in Java

MITK

itk-SNAP

Etc.

Méthodologie

MIRD Pamphlet No. 21: A Generalized Schema for Radiopharmaceutical Dosimetry—Standardization of Nomenclature

Wesley E. Bolch[1], Keith F. Eckerman[2], George Sgouros[3], and Stephen R. Thomas[4]

MIRD Pamphlet No. 23: Quantitative SPECT for Patient-Specific 3-Dimensional Dosimetry in Internal Radionuclide Therapy

Yuni K. Dewaraja[1], Eric C. Frey[2], George Sgouros[2], A. Bertrand Brill[3], Peter Roberson[4], Pat B. Zanzonico[5], and Michael Ljungberg[6]

MIRD Pamphlet No. 24: Guidelines for Quantitative ^{131}I SPECT in Dosimetry Applications

Yuni K. Dewaraja[1], Michael Ljungberg[2], Alan J. Green[3], Pat B. Zanzonico[4], and Eric C. Frey[5]

MIRD Pamphlet No. 26: Joint EANM/MIRD Guidelines for Quantitative ^{177}Lu SPECT Applied for Dosimetry of Radiopharmaceutical Therapy

Michael Ljungberg[1], Anna Celler[2], Mark W. Konijnenberg[3], Keith F. Eckerman[4], Yuni K. Dewaraja[5], and Katarina Sjögreen-Gleisner[1]

EANM Dosimetry Committee guidelines for bone marrow and whole-body dosimetry

Cecilia Hindorf · Gerhard Glatting · Carlo Chiesa · Ola Lindén · Glenn Flux

Recommendations of the American Association of Physicists in Medicine on dosimetry, imaging, and quality assurance procedures for ^{90}Y microsphere brachytherapy in the treatment of hepatic malignancies

<u>En projet :</u> Guide pratique SFPM pour la mise en place de la dosimétrie interne

Pour aller plus loin...

Le Gy peut-il devenir le SUV de la MN thérapeutique ?

- Un outil quantitatif reconnu et utilisé dans la prise en charge de routine mais perfectible
- Un indicateur permettant d’échanger avec les cliniciens
- Un outil à la mode… bientôt tout le monde en demandera

Le Gy de la MN thérapeutique peut-il avoir le même rôle que le Gy de la thérapie externe ?

- Un outil robuste, standardisé et reproductible
- Un outil de prescription
- Un outil de prédiction des effets secondaires
- Un outil de suivi du déroulement du traitement