Evolutions de la radiothérapie à l'Institut Curie

ENSEMBLE, PRENONS
LE CANCER DE VITESSE

institut Curie

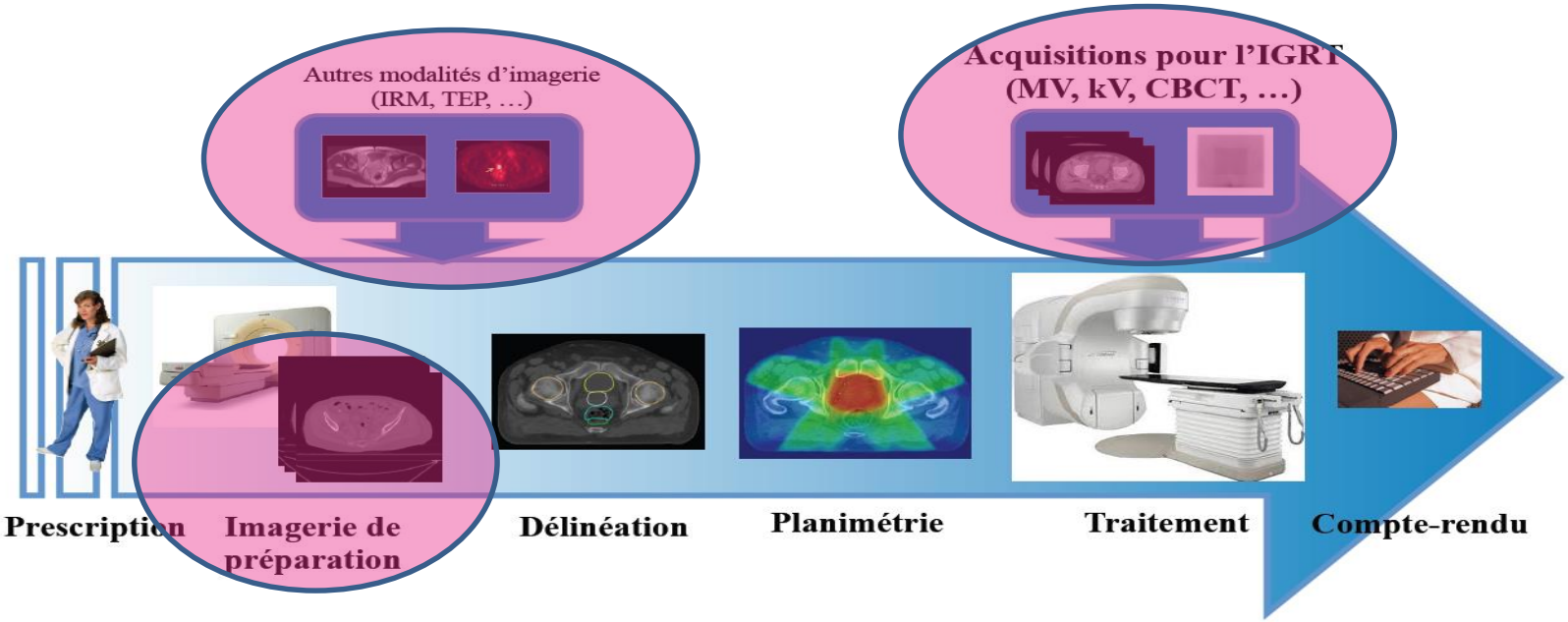
RT Workflow

- « …Délivrer la bonne dose dans le bon volume …»

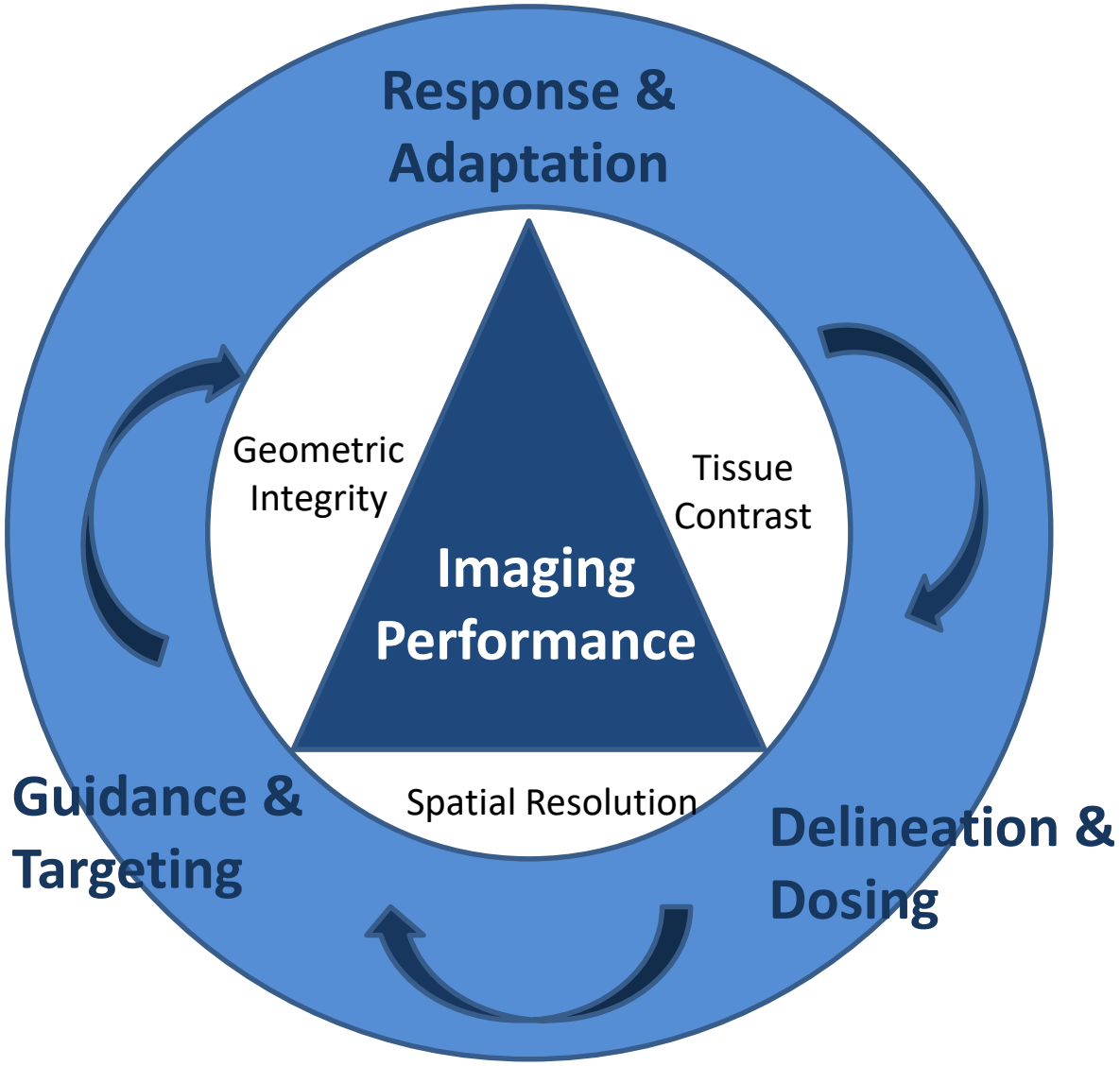
- ☞ Quality assurance of dose delivery
- ☞ 2 measures:

-Geometrical

-Dose metrics (Dosimetry)



Radiothérapie guidée par « l'imagerie multimodale »



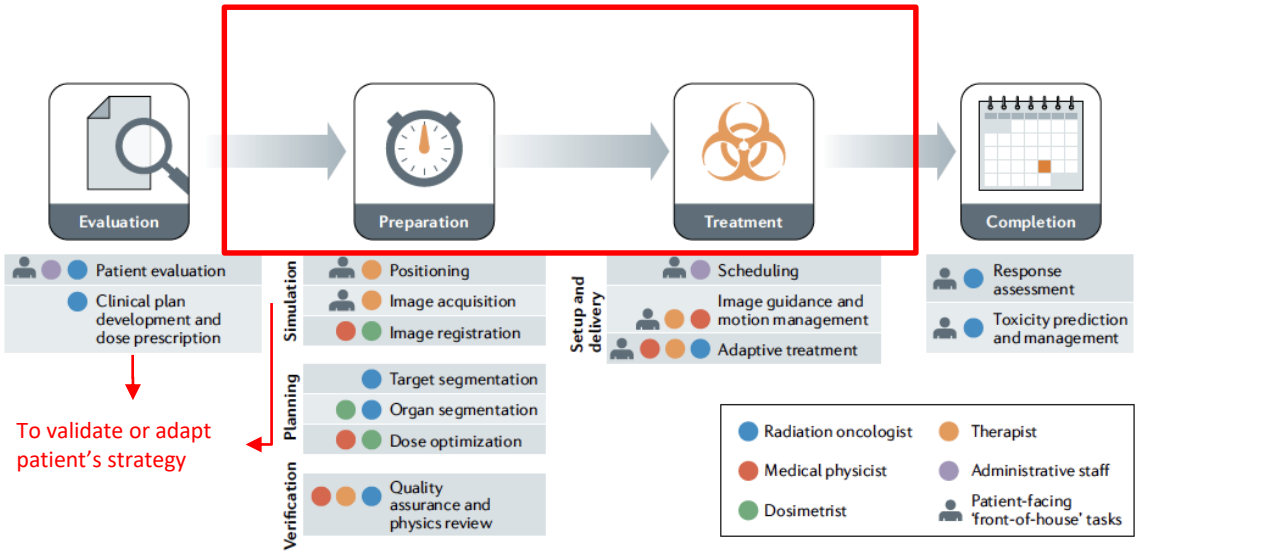
Adapted from Menard C and Dawson L, Oncologist 2010

Place de l'imagerie multimodalité et multiparamétrique en radiothérapie

1. **Delineation & dosing : IA**
2. **Guidance and Targeting : IRM/Linac, TEP Linac**
3. **Response and adaptation : Biomarqueurs de réponse in vivo**
4. **Nouvelles indications : cancer métastatique, réirradiations**
5. **Nouveaux concepts : Fractionnement spatial et temporal**

1. Améliorer workflows contourage et planification : IA

Qualité du traitement et facteur « temps »



✓ To better predict survival
✓ To improve workflows
✓ To increase homogeneity of contours and plans

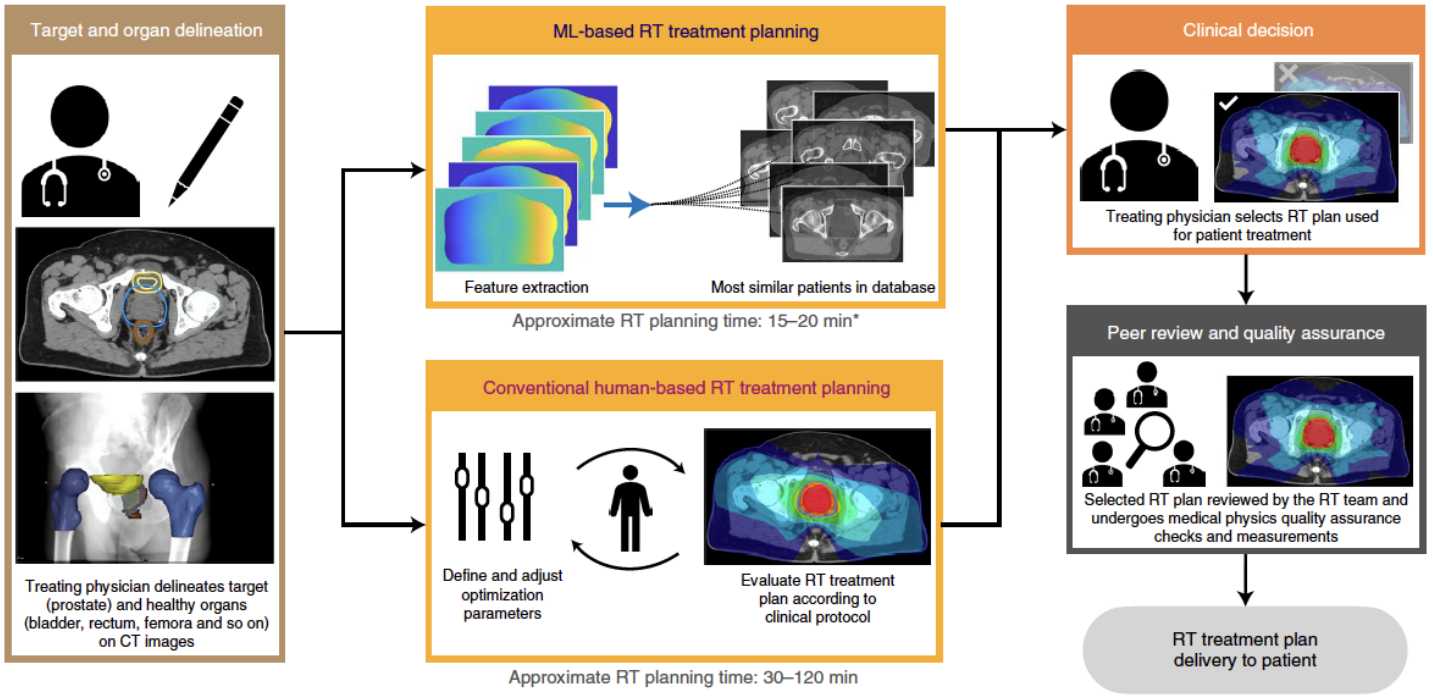
✓ To quickly decide whether adaptive is needed or not
✓ To shorten treatment time and to decrease residual uncertainties in extremely hypofractionated RT

✓ To better predict toxicity and local failure on multimodal imaging
✓ To correlate imaging changes with organ functions after RT and delivered doses

Adapted from Huynh E, Nat Rev clin Oncol 2020

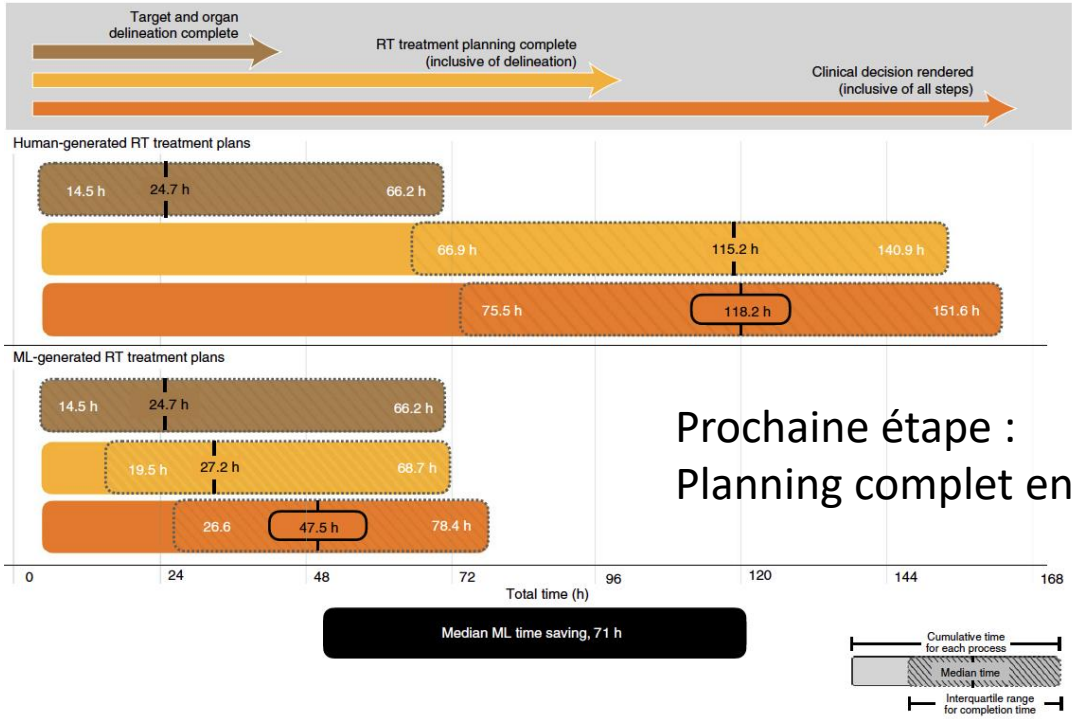
AI-based plans en vie réelle?

- McIntosh C et al., Nat Med 2022



AI-based plan réduit le temps de planification de 60%

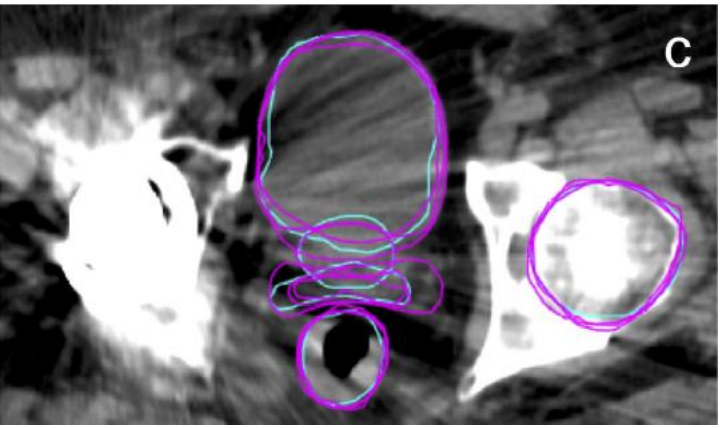
- McIntosh C et al., Nat Med 2022

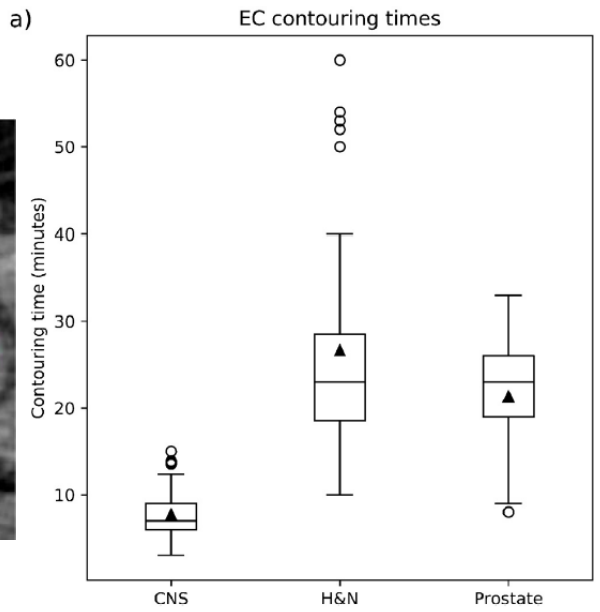


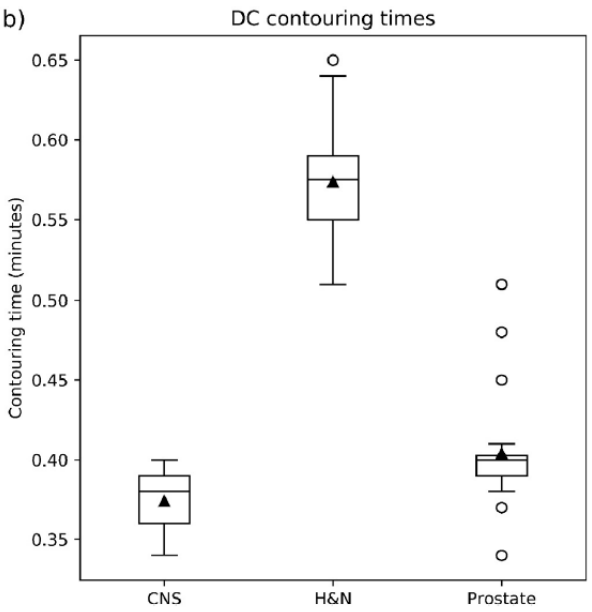
Prochaine étape :
Planning complet en 24h?

Gagner plus de temps au contourage : Améliorer performances IA?

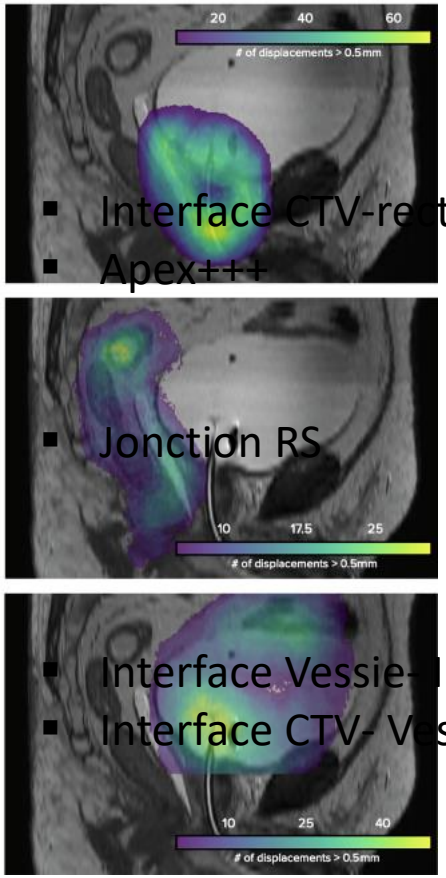
- Wong J et al., Radiother Oncol 2020







Révisions humaines des auto-contours



- Interface CTV-rectum
- Apex+++
- Jonction RS
- Interface Vessie-Intestins
- Interface CTV- Vessie

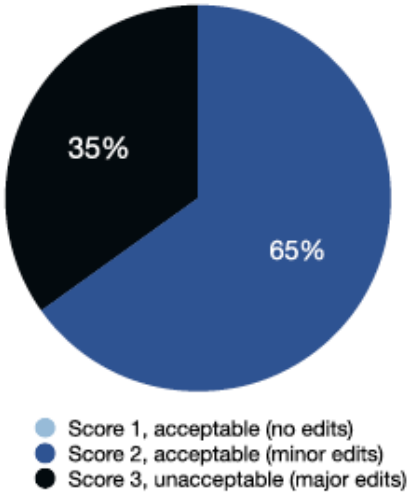


Fig. 2. Physician scoring of automated contours ($n = 43$).

AI-based plans en vie réelle : Etudes prospectives?

- McIntosh C et al., Nat Med 2022

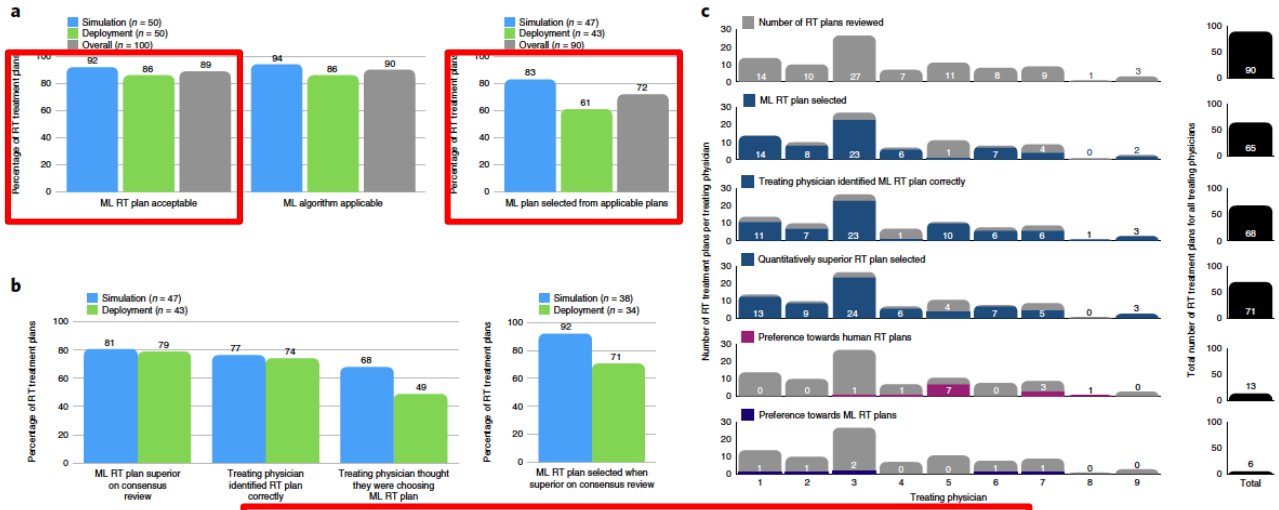


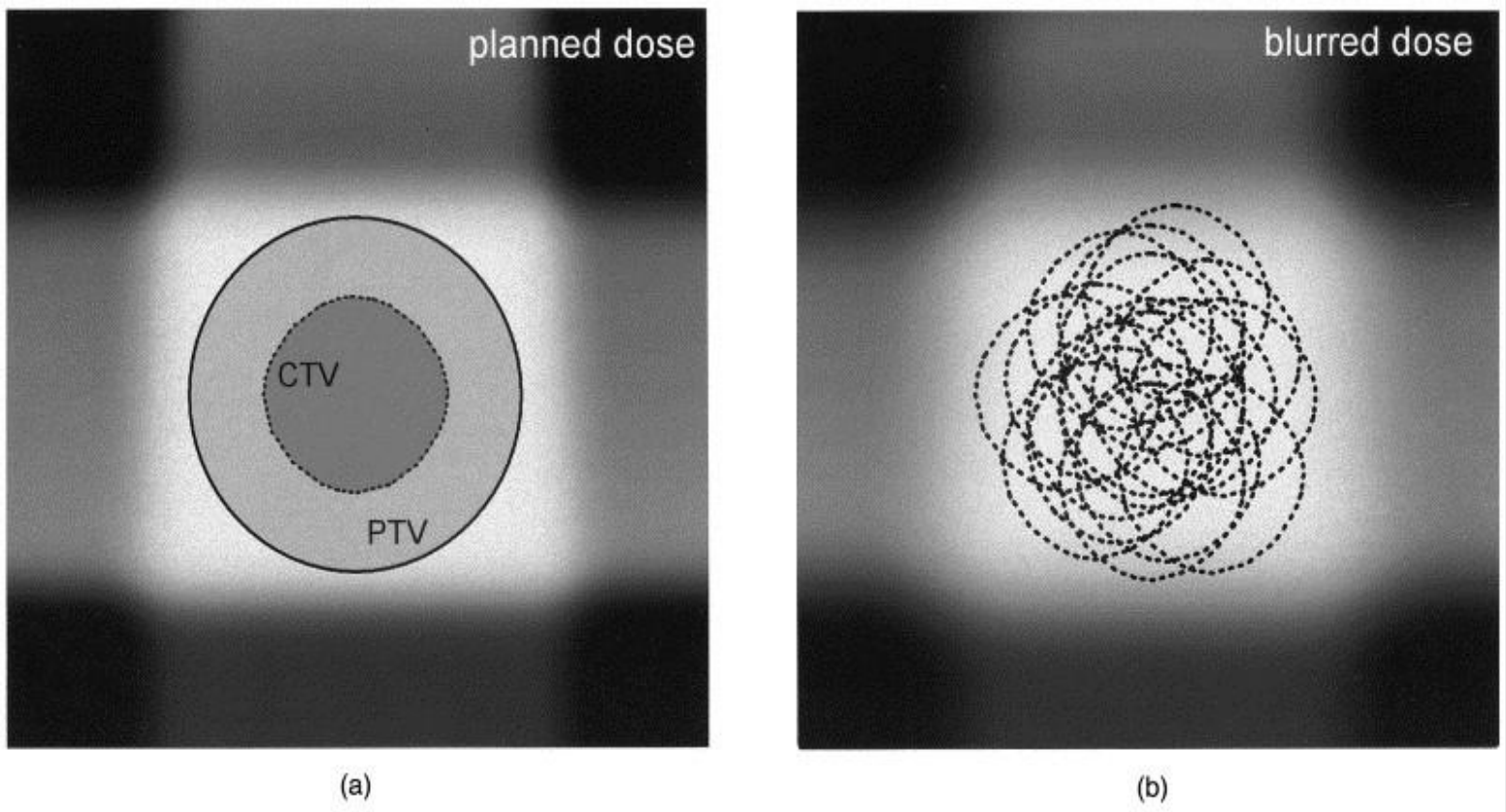
Fig. 3 | Clinical study results deployment phase ($n=50$) a identification and perceived s ($n=9$), where all radiation o treating-physician-selected

enable value-enhancing reallocation of human resources. Our analyses underscore that retrospective or simulated studies cannot recapitulate factors influencing ML–human interaction when patient care is at stake, even with expert and blinded review. Prospective deployment studies validating the impact of ML on real-world clinical settings are necessary to quantify the value of these methods, and to drive acceptance for routine use in patient care.

se ($n=50$), prospective treatment physician lividual treating physician cored by the number of or human) of their selection.

2. Guidance and targeting : Gating, Tracking on MRI

Mouvements inter et intrafractions



- Gating respiratoire ou Tracking tumoral

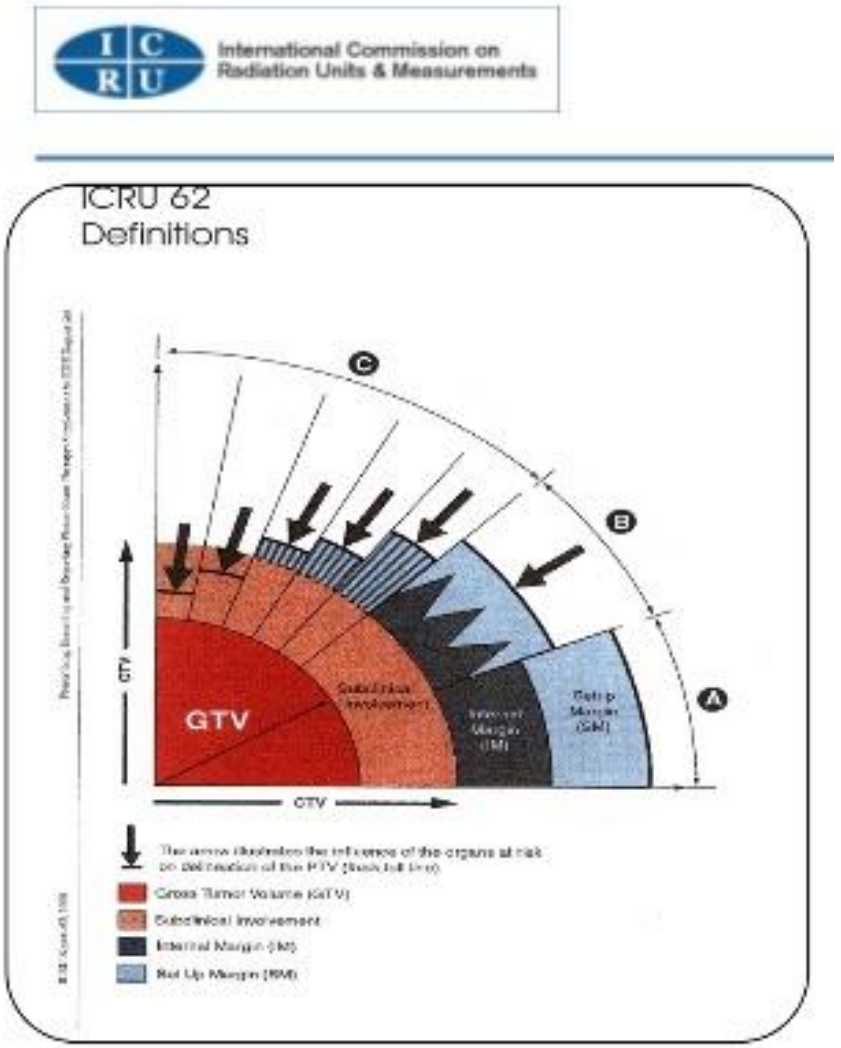
ICRU report 62

- **1- INTERNAL MARGIN :**

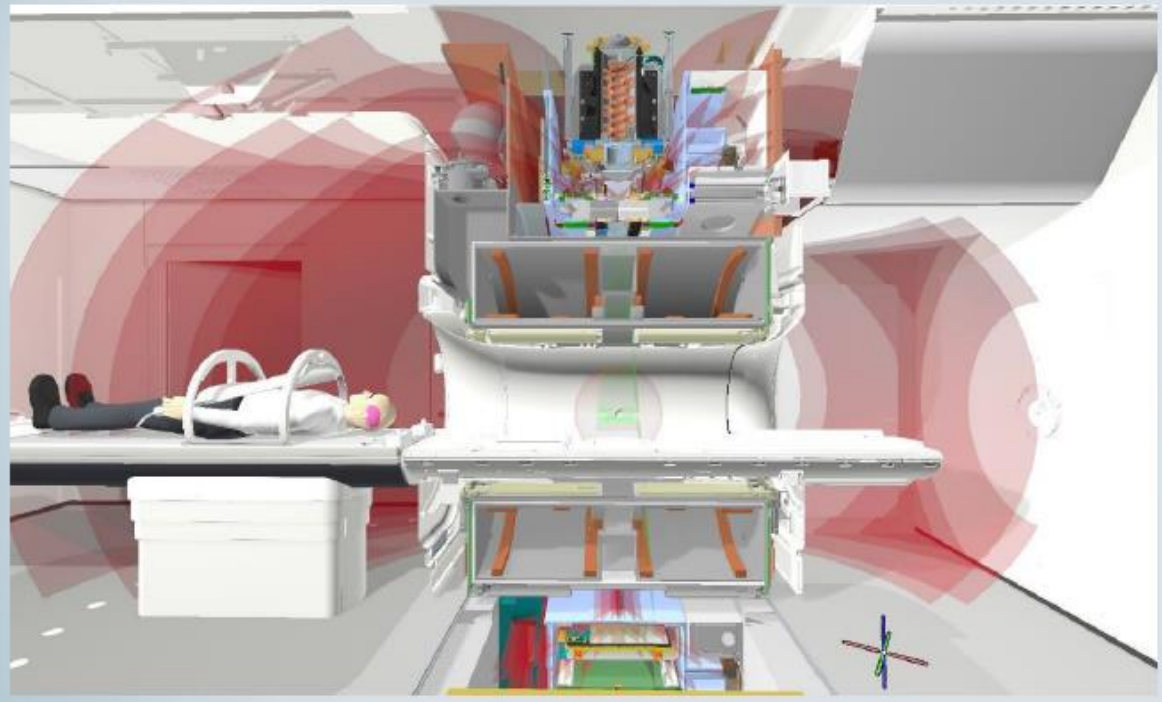
  added to compensate for expected movements and variation in shape, size and position of the CTV.

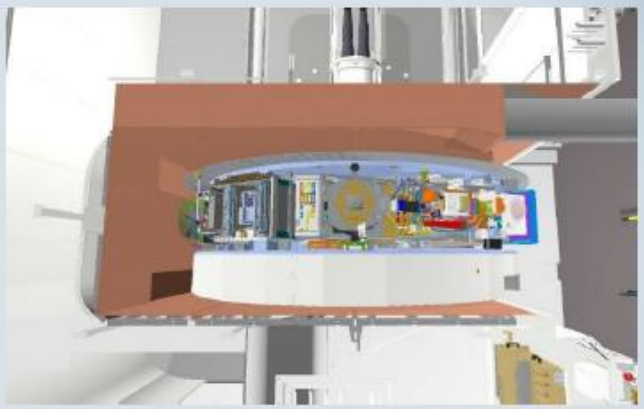
- **2- SET-UP MARGIN :**

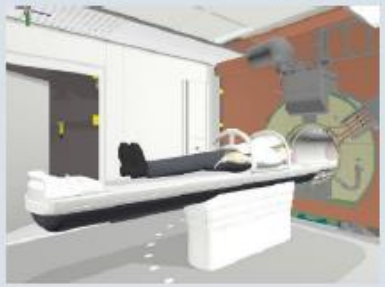
  to account specifically for uncertainties in patient positioning and alignement of the beams during treatment planning and through all sessions.



Intégration sans compromis de deux systèmes performants



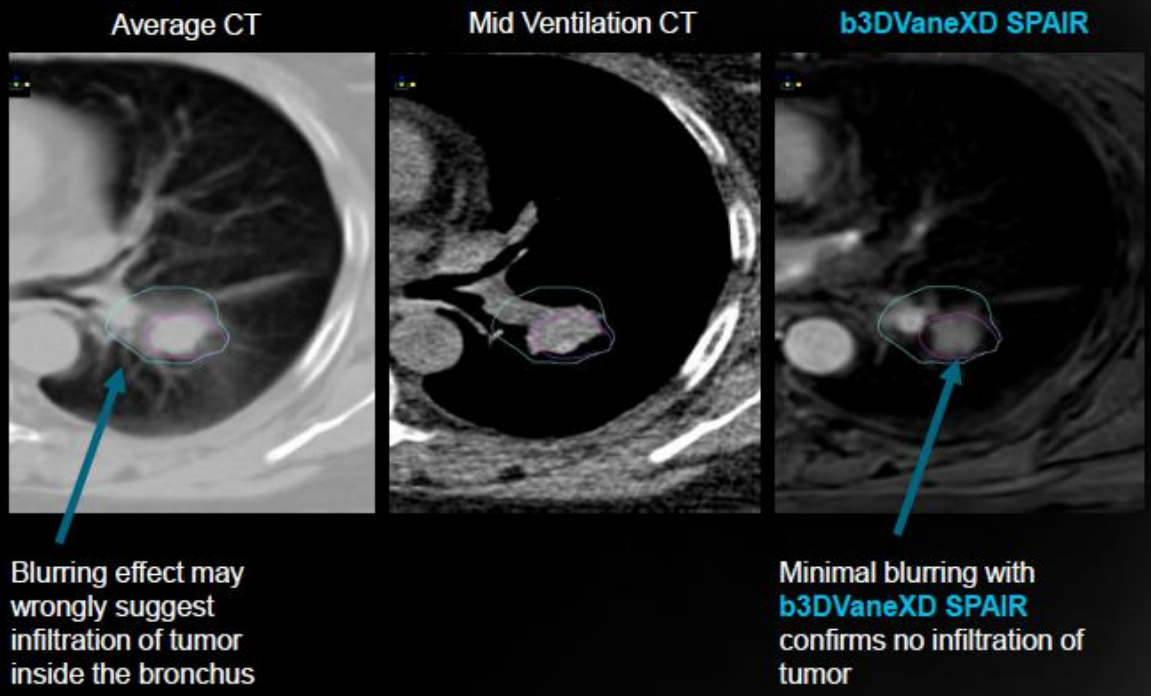




Techniques de gestion du mouvement: intérêt clinique

Femme de 55 ans avec adénocarcinome pulmonaire

Oligoprogression d'une lésion de 24 mm x 21mm, très proche de la bronche

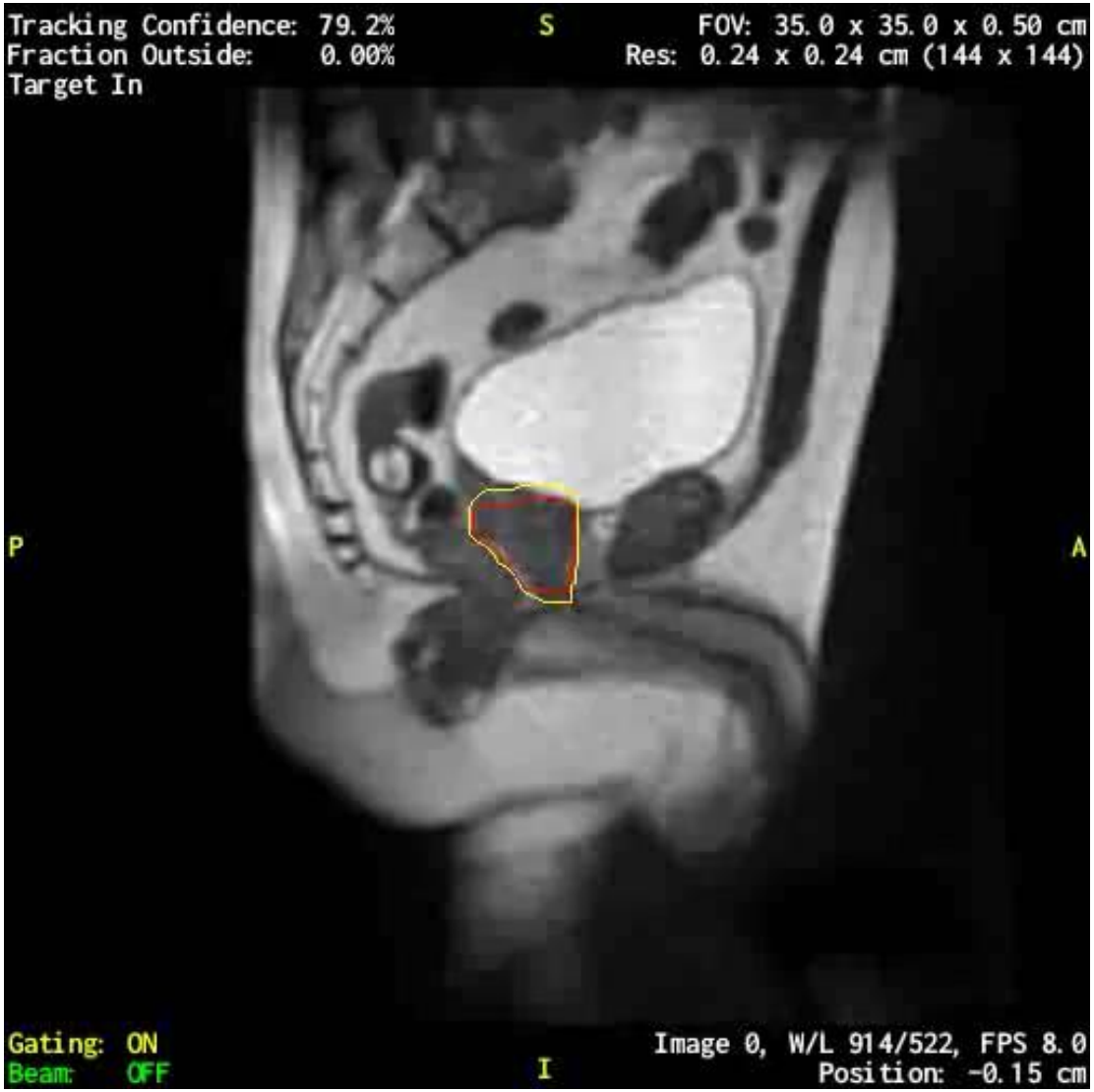


Elekta

SACRO CUORE DON CALABRIA I R C C S

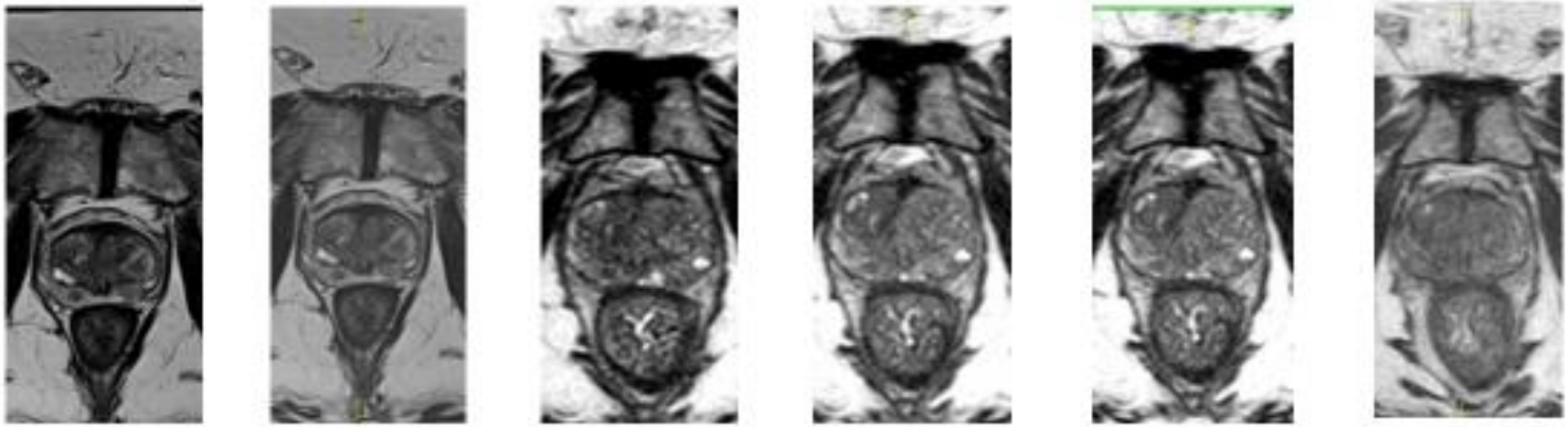
ARO ADVANCED RADIATION ONCOLOGY DEPARTMENT

Contraction des fessiers : Beam off en temps réel sous IRM (0.35T)

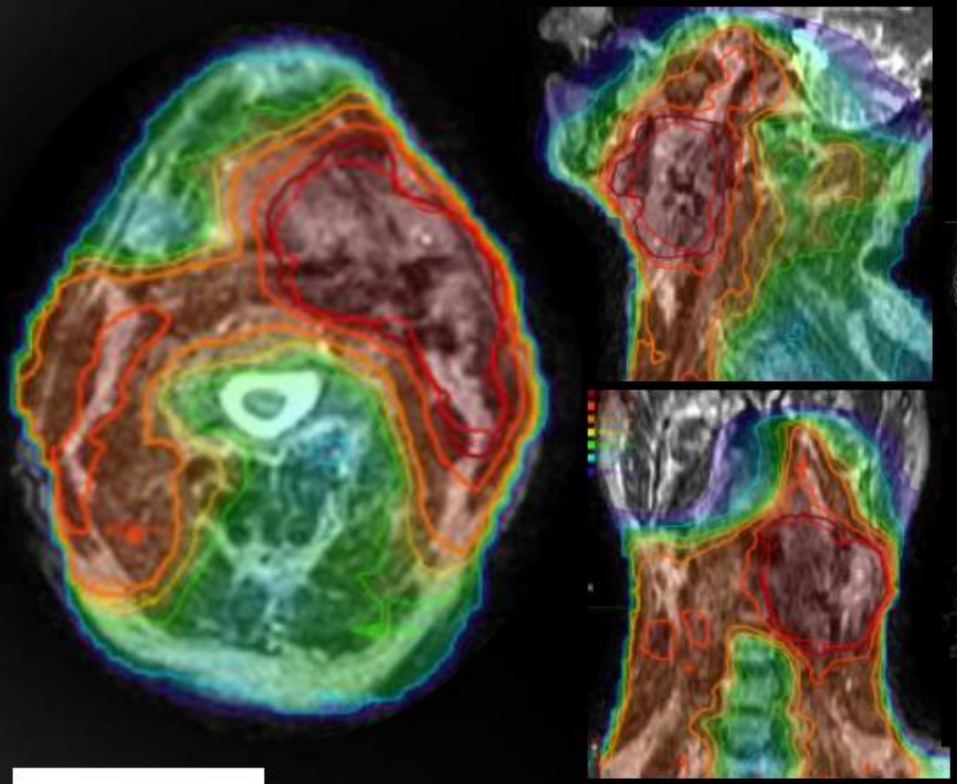


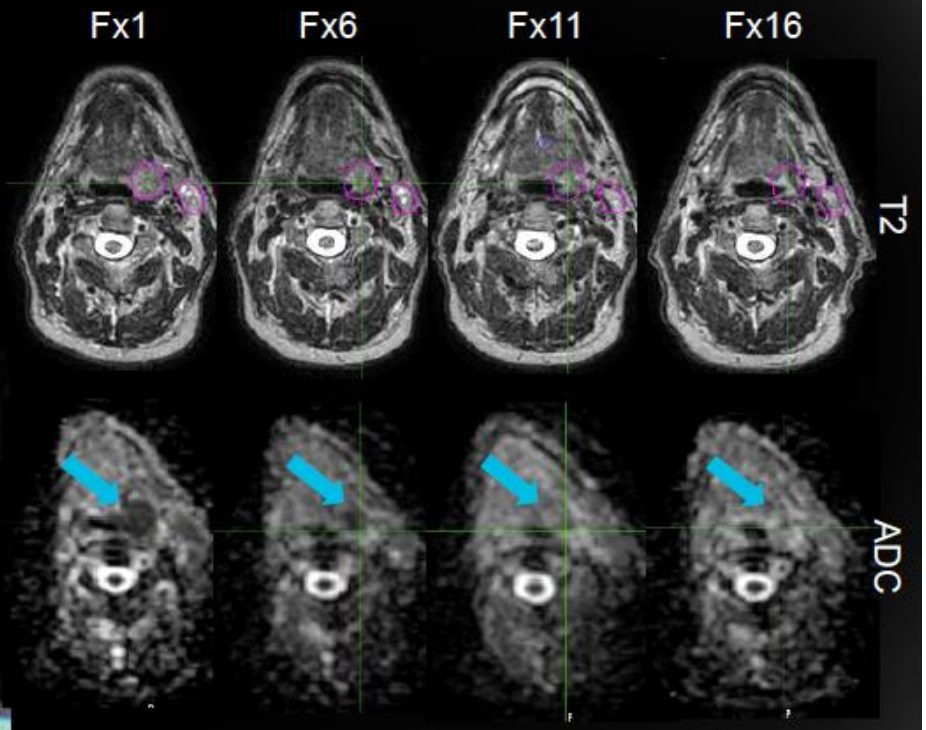
3. Response and adaptation

Biomarqueurs IRM in vivo de radiosensibilité?



Cancer de la sphère ORL: suivi de la réponse et BgRT (1)





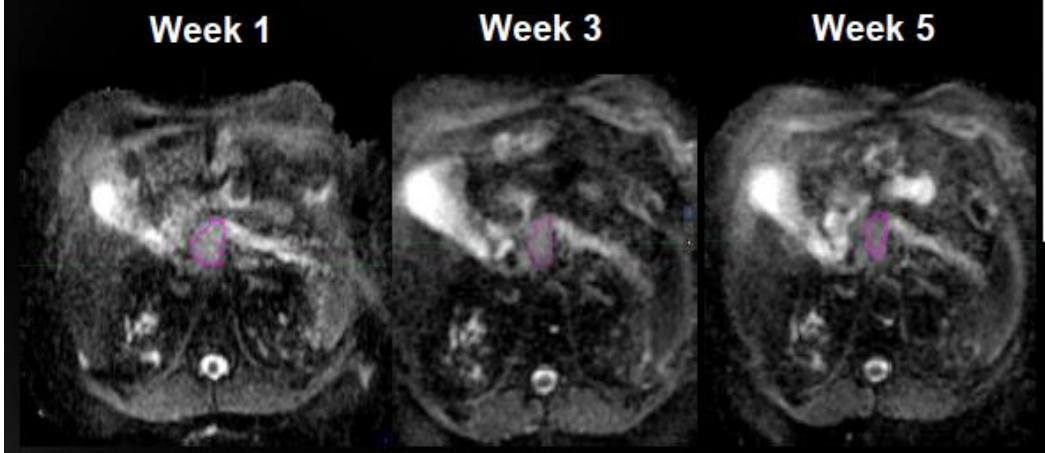
Elekta

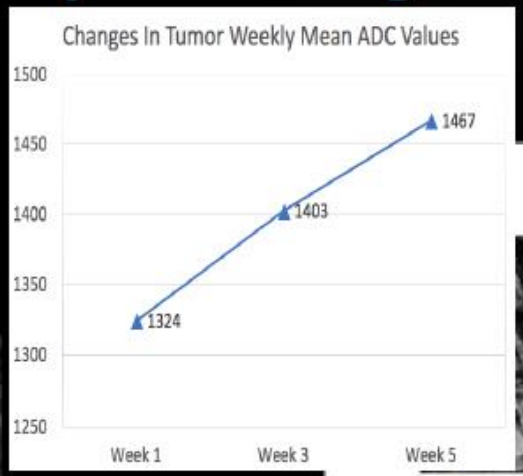
Courtesy of Froedtert Hospital / Medical College of Wisconsin.

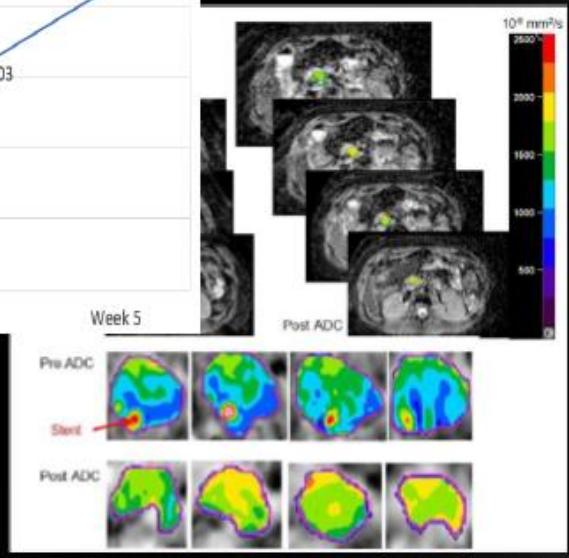
66 Gy / 30 fx; Adapt to position

Cancer du pancréas : suivi de la réponse et BgRT

ADC utilisé pour prédir la réponse tumorale







*ADC values following RT could be used to predict tumour pathological response and aid dose escalation

Courtesy of Froedtert Hospital / Medical College of Wisconsin

*Dalah E, Erickson B, Oshima K, et al. Correlation of ADC With Pathological Treatment Response for Radiation Therapy of Pancreatic Cancer. *Translational Oncology*. 2018;11(2):391-398.

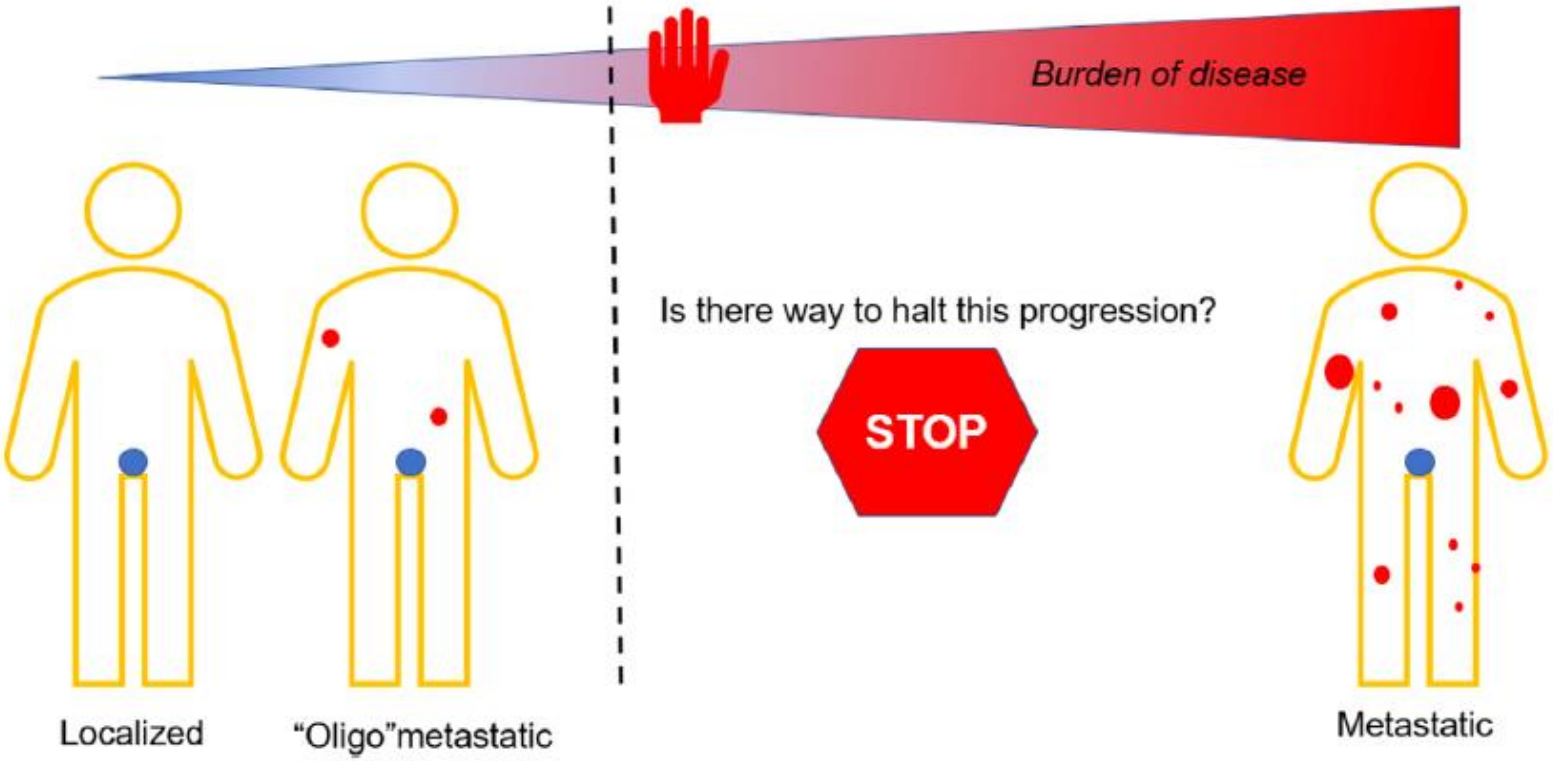
4. Radiothérapie ablative et métastases

ELSEVIER

Seminars in
RADIATION
ONCOLOGY

Technical Giants But Biologic Infants: Defining a More Sophisticated Role for Local Therapy in Metastatic Disease

Sophia C. Kamran, MD,* David Palma, MD PhD,† Matthew S. Katz, MD,‡ and Anthony L. Zietman, MD*

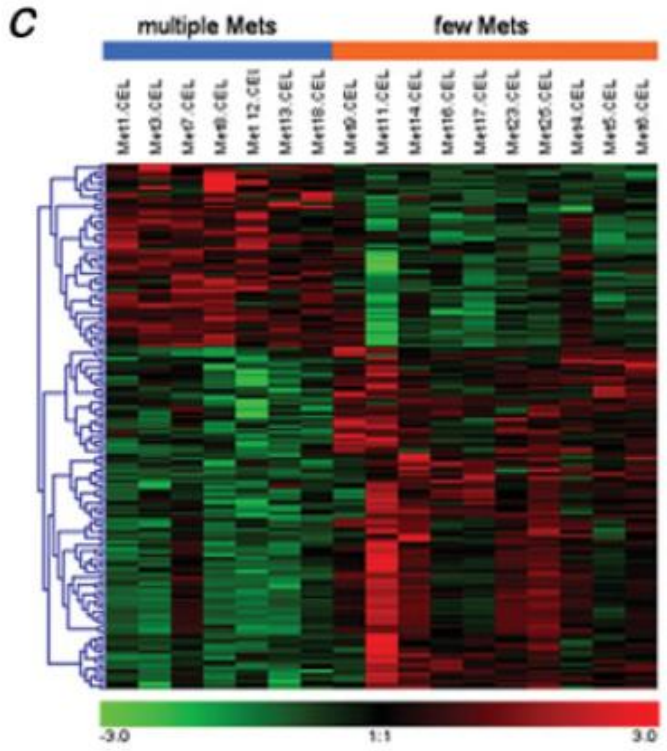


Progression métastatique et signatures génétiques

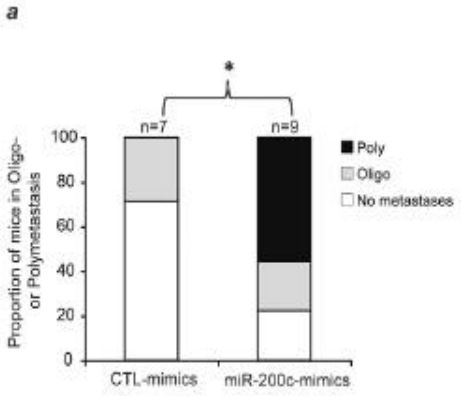
- 20 mets pulm de 18 cancers du rein

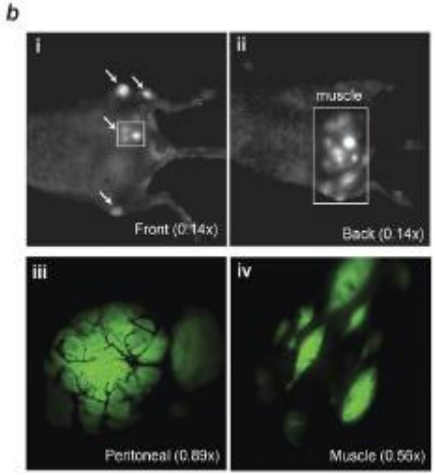
- Transcriptome (Oligonucleotides microarrays)
- 135 genes différemment exprimés

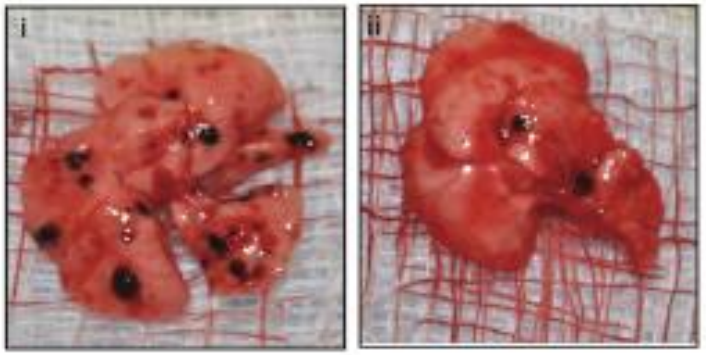
- Patients <8mets vs >16 mets
- IL <9 mois vs IL >5 ans
- Signatures des gènes différentes

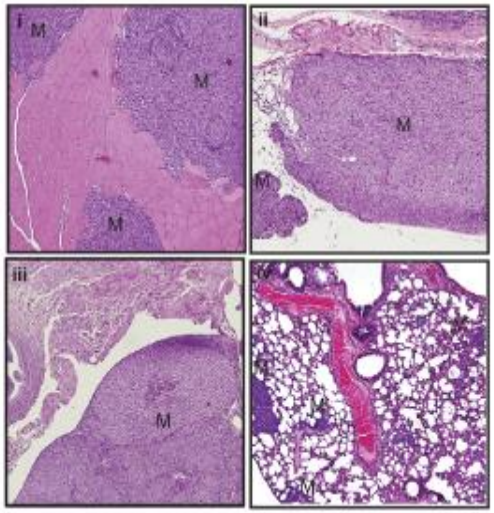


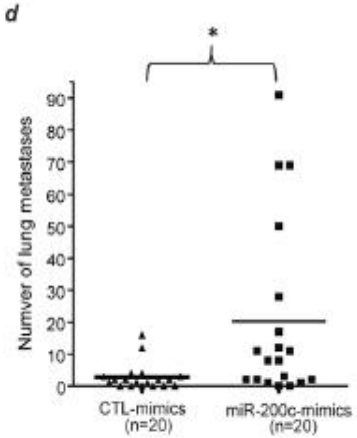
Oligomets : Expression des microARN











Imagerie ou biologie?

Métastases multiples

- Médecine personnalisée
- Guidée par la biologie
- Ciblage de voies moléculaires
- Cytotoxiques

Oligométastases

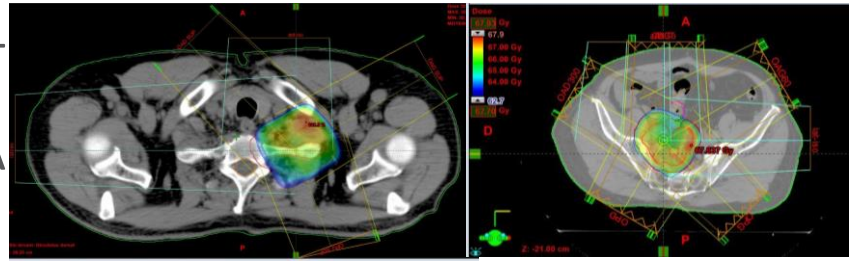
- Médecine de précision
- Guidée par l'imagerie
- Traitements ablatifs

- **Médecine personnalisée**
- **De précision**
- **Guidée par la biologie et l'imagerie**

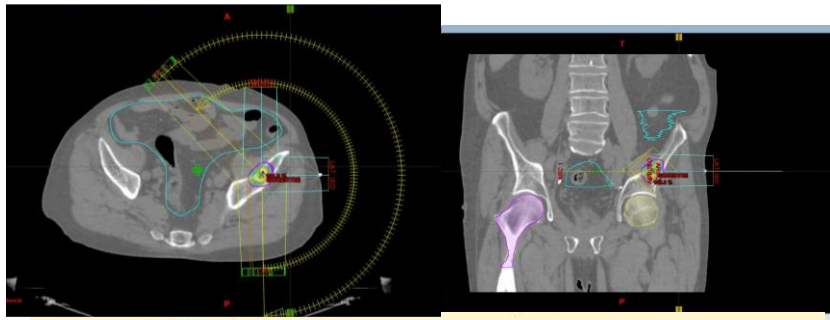
Oligoprogression : Le « BON »…

- 2007: 69 ans pT3a R1, GS3+3, PSA 2.93, 1.4 postop

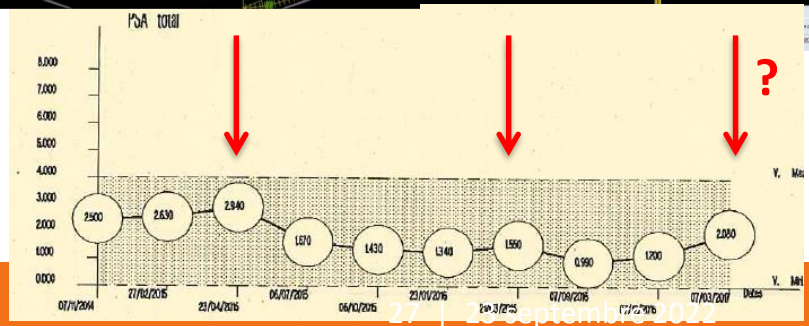
- 2008 : TEP choline Apophyse transverse C1 +
- Loge + C1 + ADP 66Gy/33fx (IDL 95% 4fx) + A
- 2009 : Rechute : Hormones



- 09/2014 : PSA 1.91 TEP choline Aile iliaque G
-

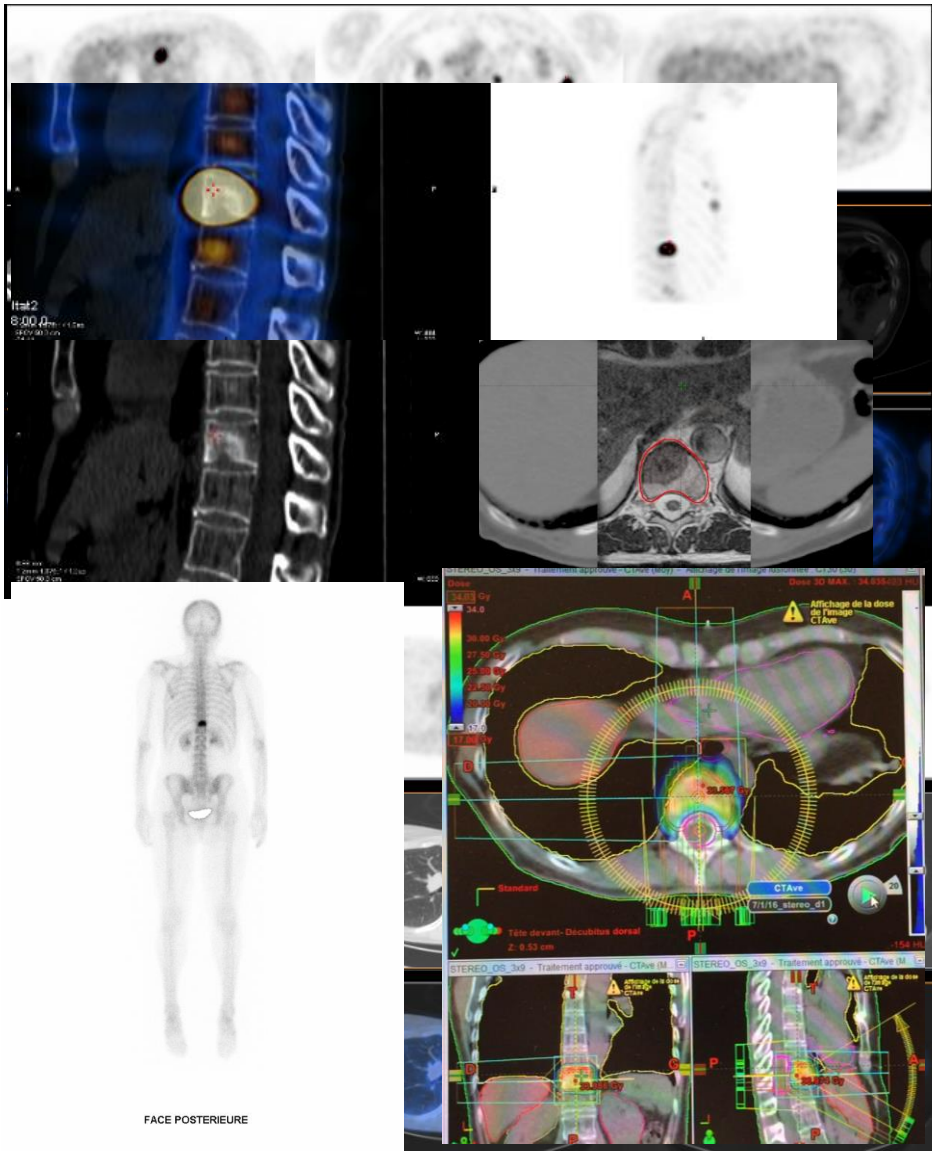


- 2016 : PSA 1.55 L5 (30Gy/3fx IDL 80% VMAT)
- TEP choline + FNa : Doute L1?
- 2017 : 79 ans, PSA 2.2



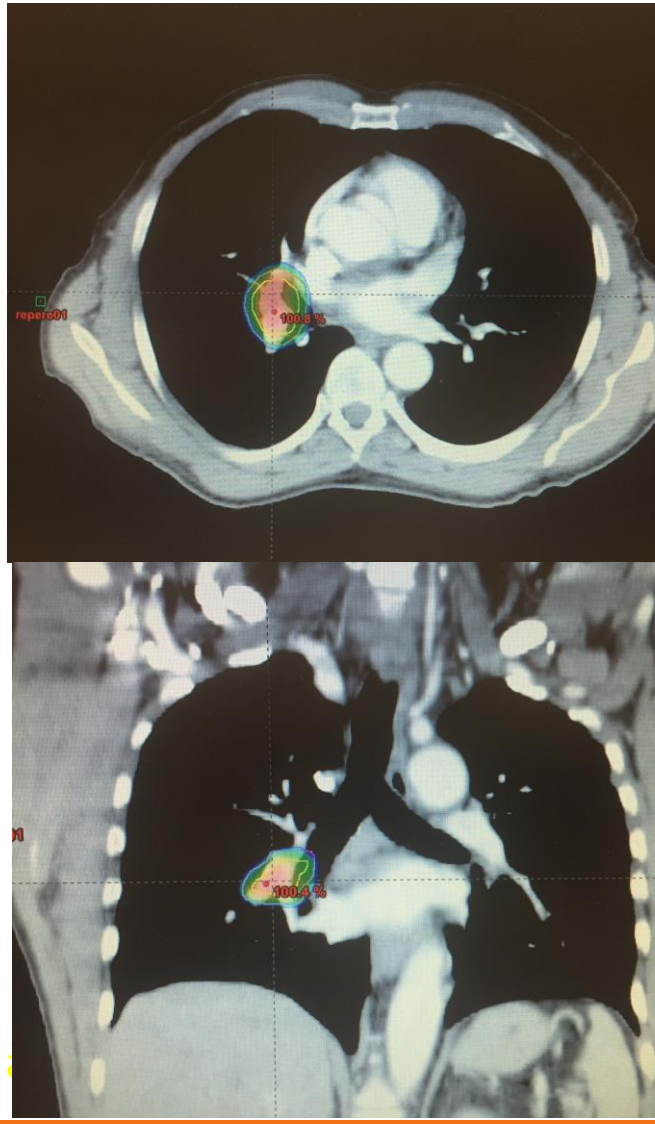
Oligoprogression : La « BRUTE »…

- Femme de 55 ans
- 2013 : CBNPC LIG Her2-, EGFR, KRAS, BRAF, ROS et MET
- Métastatique poumons, plèvre d'emblée
- CT: CDDP-Alimta puis Taxol
- 2015 : T11 : cimentoplastie +RT
  - Avril 2016 : Nivolumab 4 cycles
  - **Juin 2016 : Mets poumons, os, cerveau**
  - Carbo Gemzar 6 cycles
  - Olaparib
  - Janv 2017 : Carbo taxol



Oligoprogression : Le « TRUAND »…

- Mr V… Pascal, 57 ans
- carcinome urothélial de l'uretère
- 1N+ médiastin hilaire D lentement évolutive

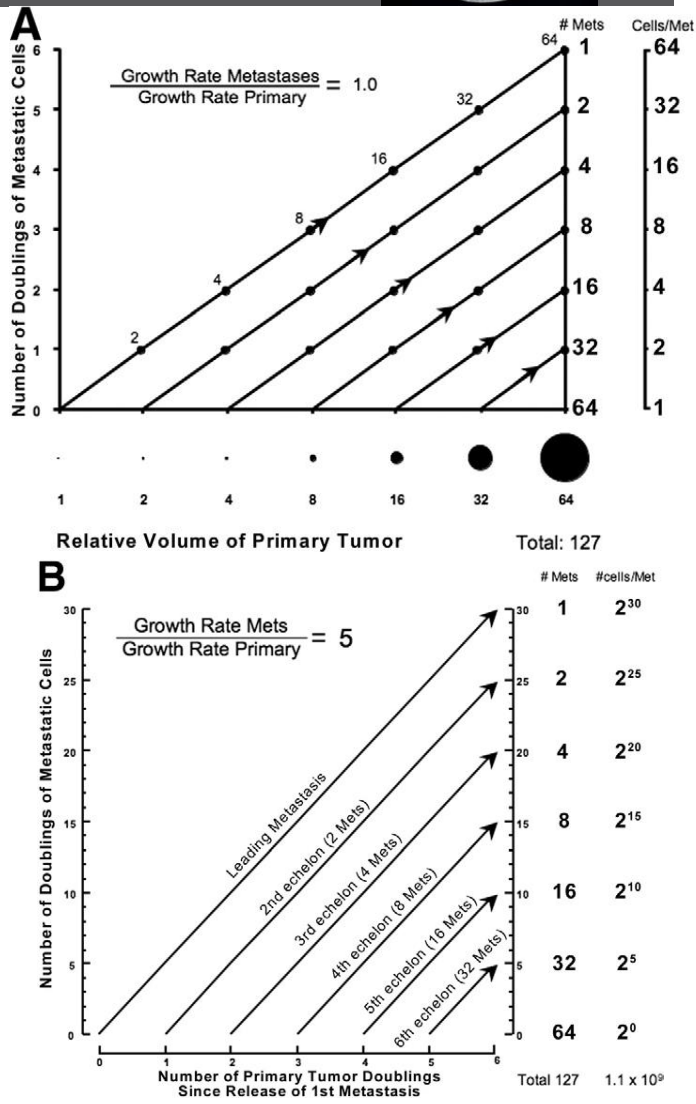


- Stéréo en juillet 2012 : 48 Gy en 8fr (IDL 80%)
- poumon : V20 à 3%, V10 à 12% et dose moyenne à 3.3 Gy
- moelle épinière : dmax à 8.7 Gy
- œsophage : Dmax à 22.5 Gy
- trachée : Dmax à 27.2 Gy
- Evolution méta hépatique 2 mois après
- Décédé d'une hémoptysie massive sur nécrose bronchique

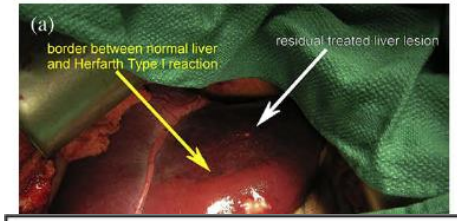
Projet Master 2 LITO :
Signature métabolique d'une oligométastase PSMA+

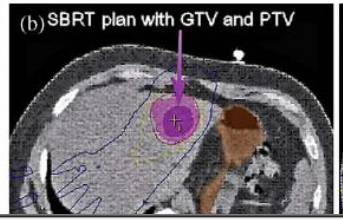
- **Objectifs / Questions :**

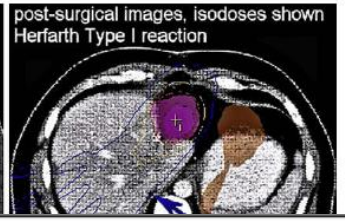
1. **Signature radiomique pour prédire le métabolisme d'une « vraie » oligométastase (…ou d'une métastase parmi d'autres?)**
2. **Différences de métabolismes en fonction du nombre de métastases**
3. **Signature radiomique pour prédire l'absence de progression dans les champs et en dehors des champs**
4. **Métabolisme du rachis et du bassin différents chez un oligométastatique et un polymétastatique (trace de la maladie micrométastatique diffuse non encore visualisée)**

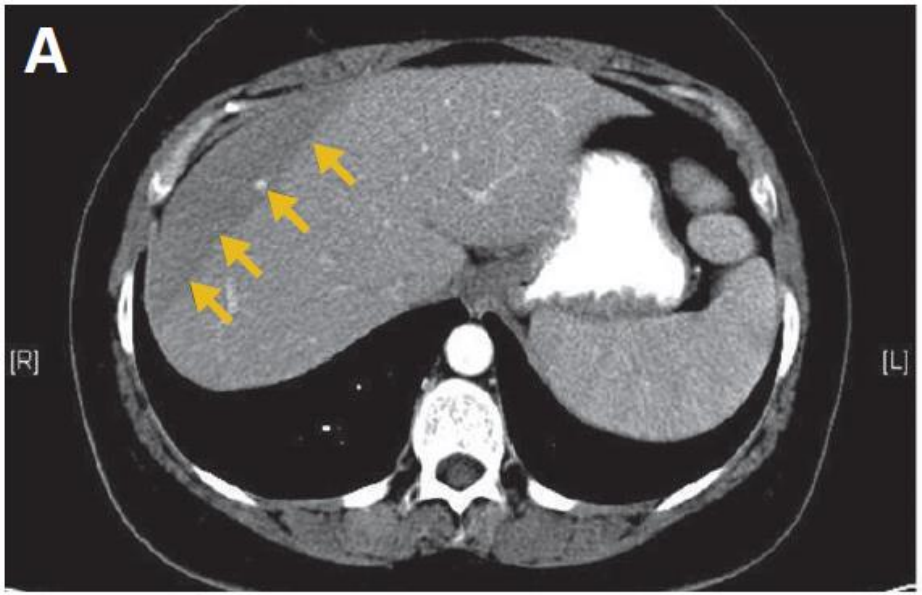


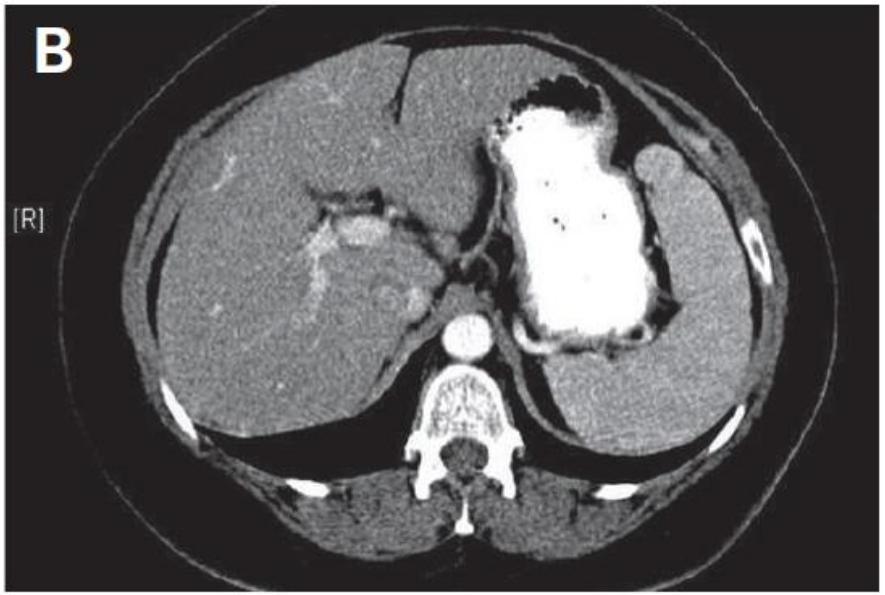
5. Réirradiations : Réponse des tissus sains et optimisation de la balistique

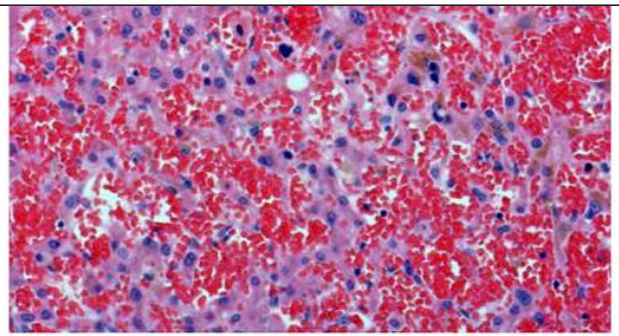












Herfarth Type I reaction, in vivo

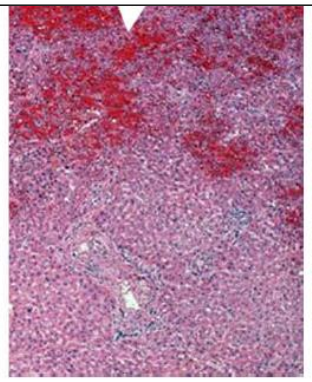
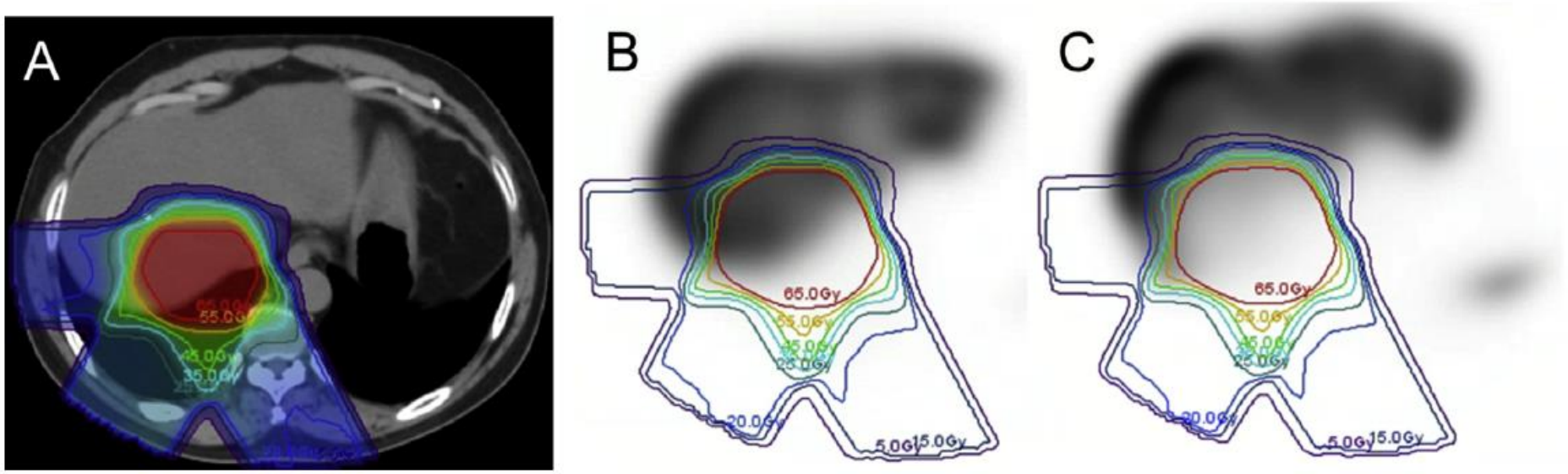


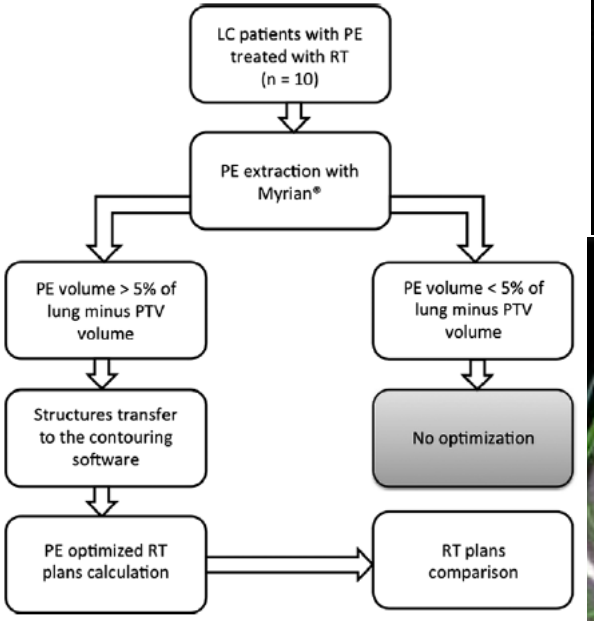
Fig. 6. Histopathologic zones of injury. See text for details. VOD = veno-occlusive disease; SBRT = stereotactic body radiotherapy.

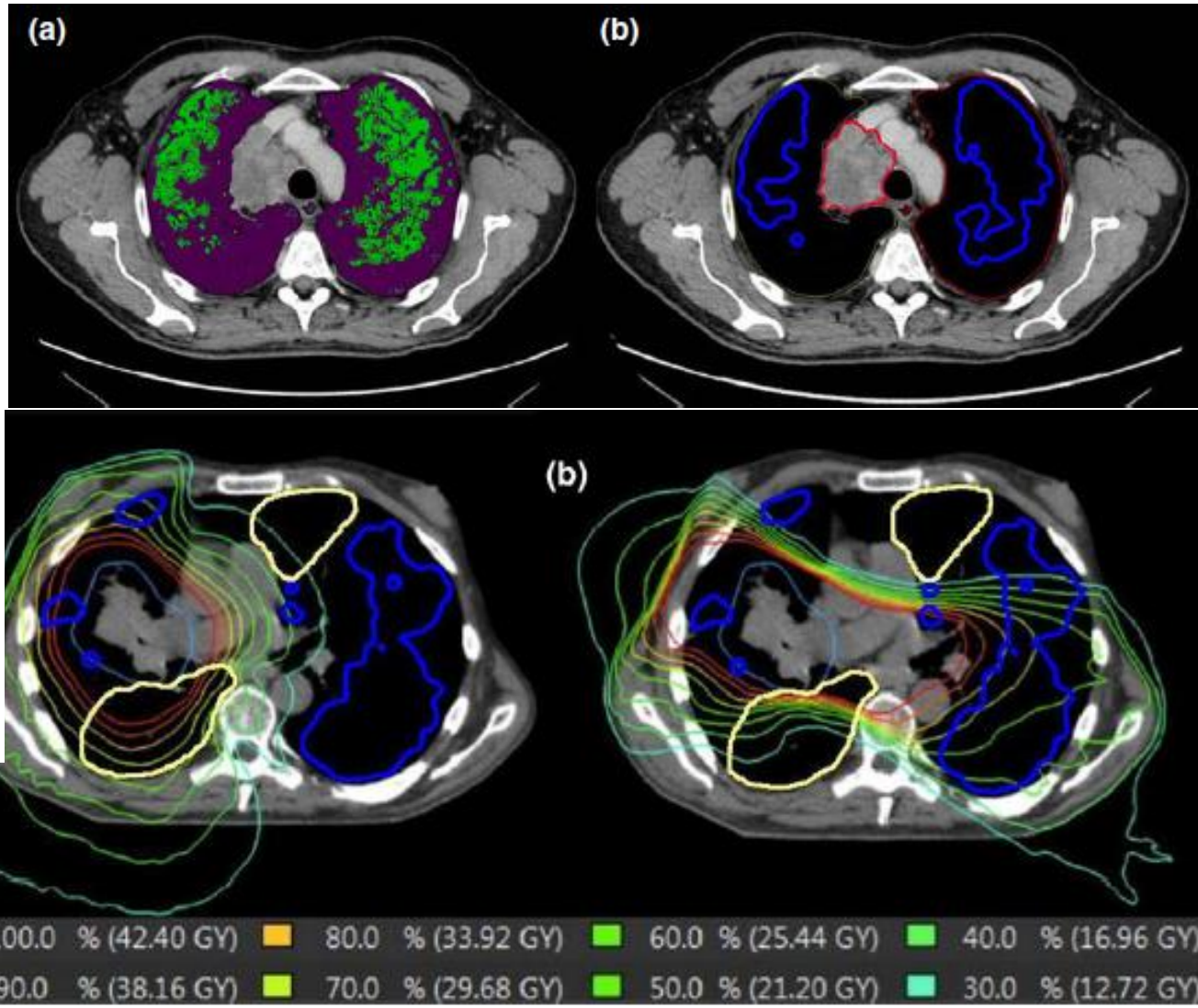
Functional Liver in Hepatocellular Carcinoma Patients With Longitudinal Sulfur Colloid



Longitudinal SC SPECT/CT imaging can noninvasively characterize hepatic radiation dose-response relationships at the individual patient level with the clinical potential to inform HCC treatment regimens, liver dose tolerances, and functional tissue avoidance planning constraints.

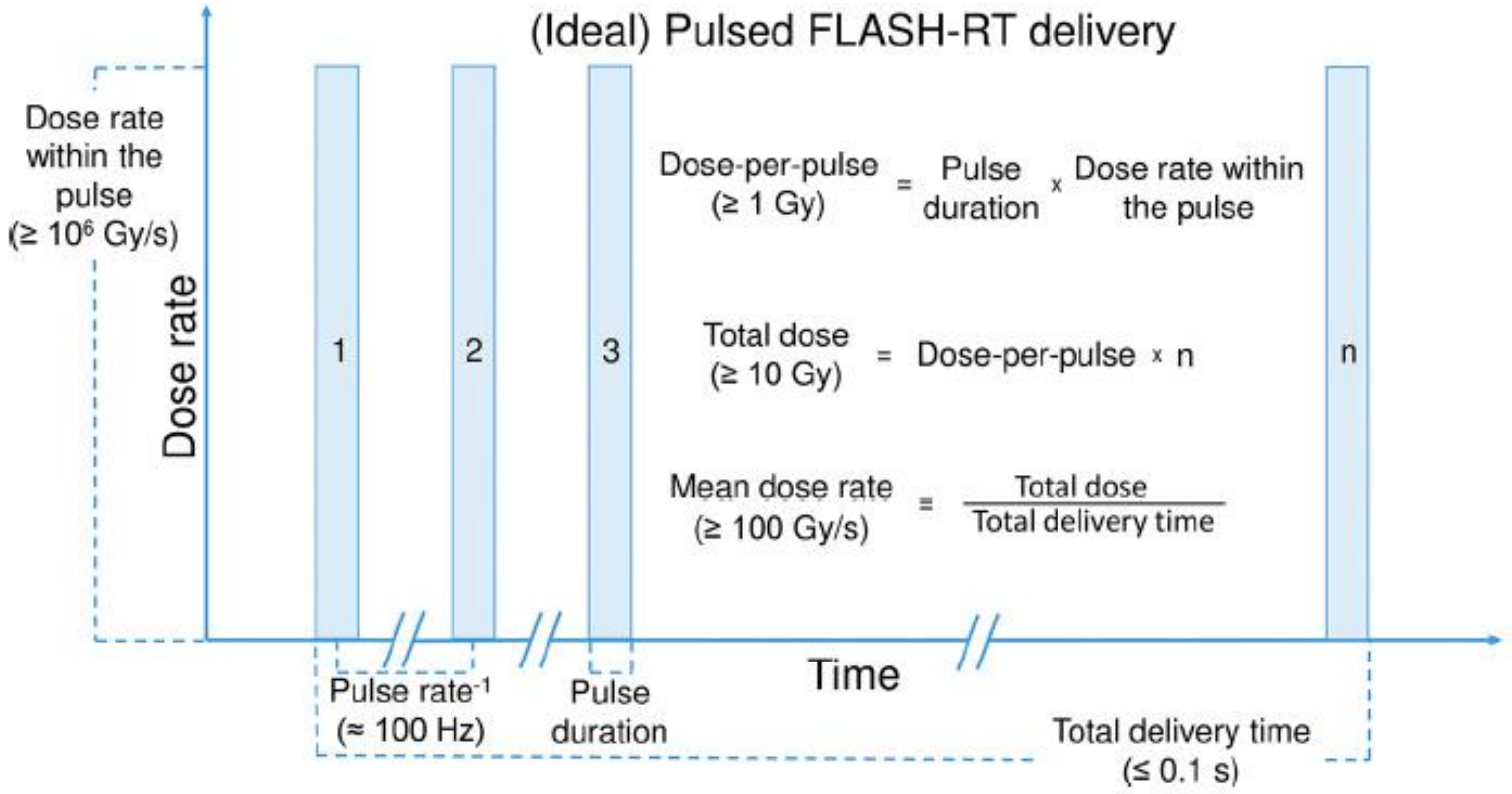
Balistique pour protéger les tissus fonctionnels





6. Nouveaux concepts : Fractionnements spatio-temporels

FLASH : Technical parameters for delivery



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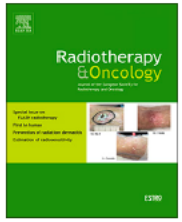


Review Article

Clinical translation of FLASH radiotherapy: Why and how?

Jean Bourhis [a,b,*], Pierre Montay-Gruel [a,b], Patrik Gonçalves Jorge [a,b,c], Claude Bailat [c],

Effet différentiel en radiothérapie

1. ~~Fractionner la dose~~

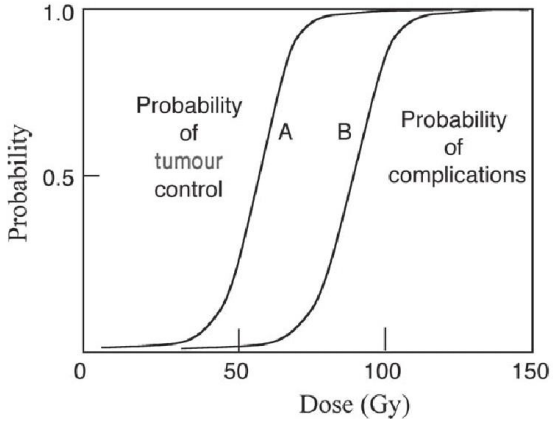
2. ~~Limiter le volume traité (IMRT, IGRT, SBRT, protons)~~

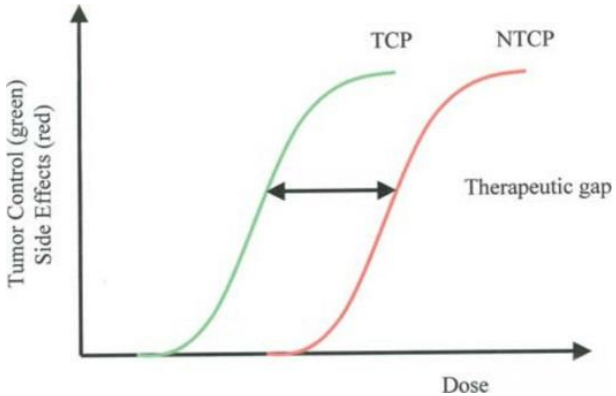
3. FLASH : Réduire la durée d'irradiation (>40Gy/s), séance unique

Isoefficacité = >

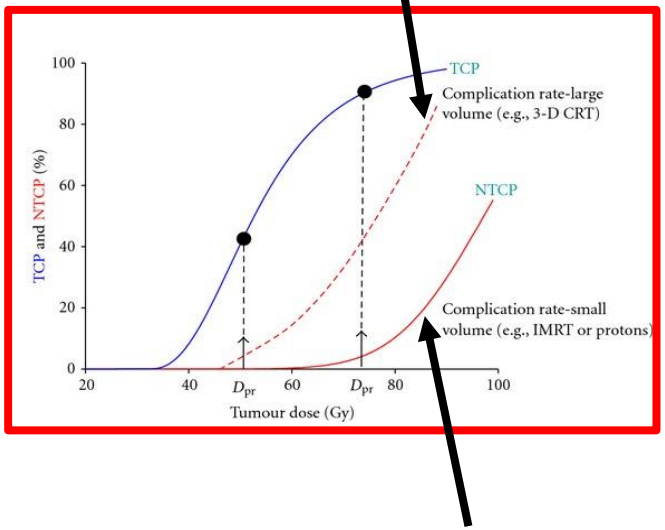
- ✓ stériliser les marges opératoires
- ✓ Diminuer le risque de rechute locale
- ✓ Diminuer le risque de rechute métastatique (R1/R2
- ✓ Réduire la toxicité digestive de la radiochimiothérapie

Radiation Oncology in 2022 : FLASH is the step forward





FLASH protons, VHEE



FLASH electrons

FLASH program

TB eFlash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ELSEVIER

First in Human

Treatment of a first patient with FLASH-radiotherapy

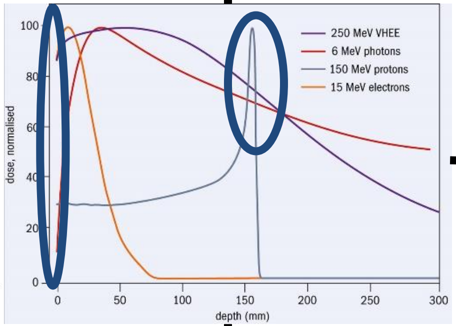
Jean Bourhis[a,b,*], Wendy Jeanneret Sozzi[a], Patrik Gonçalves Jorge[a,b,c], Olivier Gaide[d],

Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice

Vincent Favaudon,[1,2*] Laura Caplier,[3†] Virginie Monceau,[4,5‡] Frédéric Pouzoulet,[1,2§] Mano Sayarath,[1,2¶] Charles Fouillade,[1,2] Marie-France Poupon,[1,2||] Isabel Brito,[6,7] Philippe Hupé,[6,7,8,9] Jean Bourhis,[4,5,10] Janet Hall,[1,2] Jean-Jacques Fontaine,[3] Marie-Catherine Vozenin[4,5,10,11]

institut Curie

Fig. 1. Temporal evolution of the treated lesion: (a) before treatment; the limits of th PTV are delineated in black; (b) at 3 weeks, at the peak of skin reactions (grade 1 epithelitis NCI-CTCAE v 5.0); (c) at 5 months.



VHEE

T superficielles

T profondes

1X15Gy (10 pulses of 1ms)

CdR

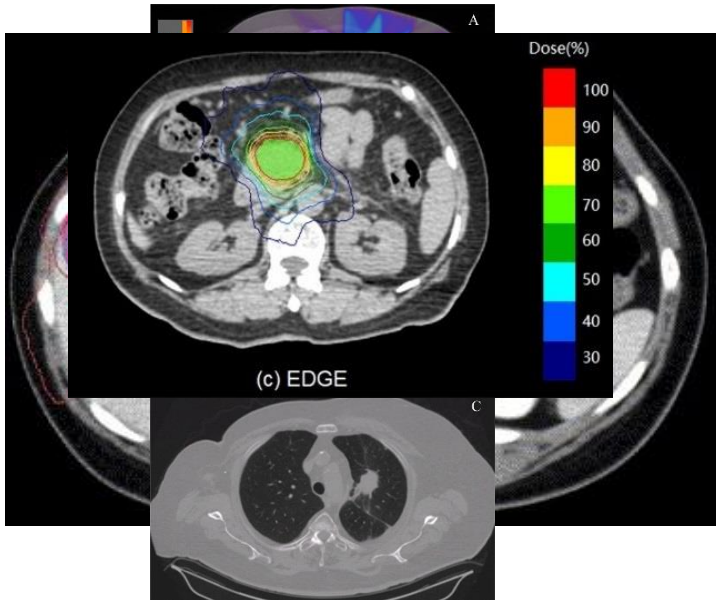
DOR

2014 | 2018-2020 | 2022 | 2023-2024

FLASH protons/VHEE : A changing paradigm

>90% Local control
<10% severe toxicity

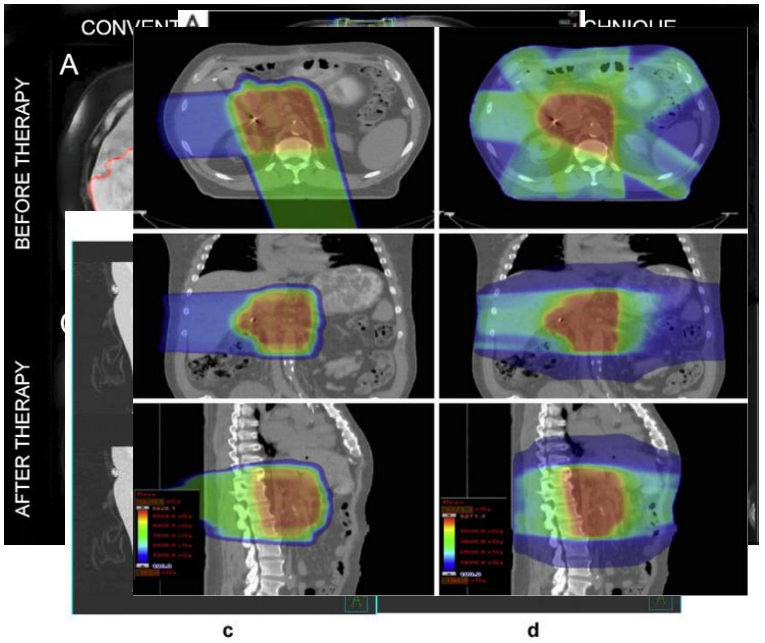
<70% Local control
>20% severe toxicity



LIVER

LUNG

PANCREAS



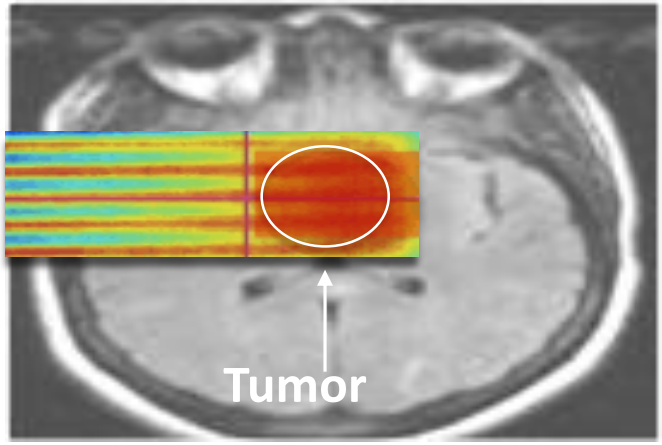
Stage I/II

Stage III

Minibeam radiation therapy + Protons and their specific physics and biology

Proton minibeam radiation therapy

Prezado et al. Med. Phys.2013

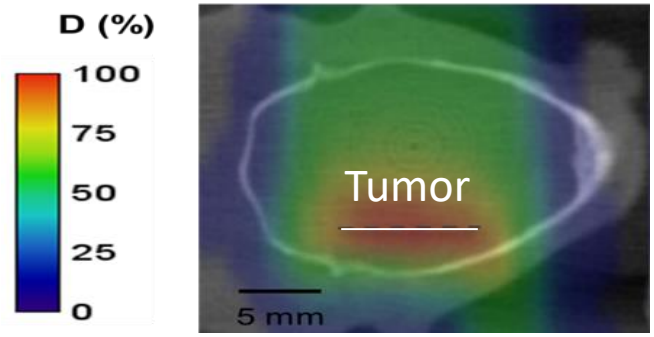


First implementation worldwide at a Orsay proton therapy centre (I. Curie)

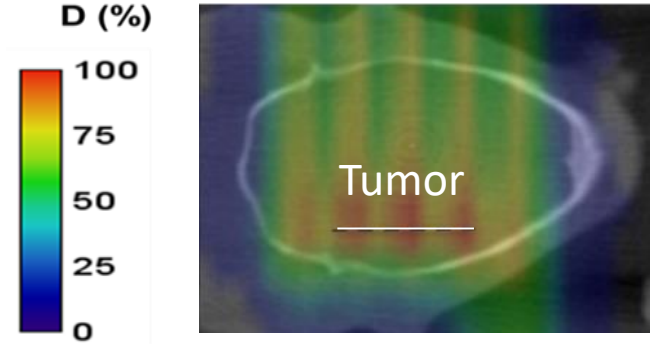
(Peucelle et al., Med. Phys. 2015)

Tumor control effectiveness in glioma (RG2) bearing rats

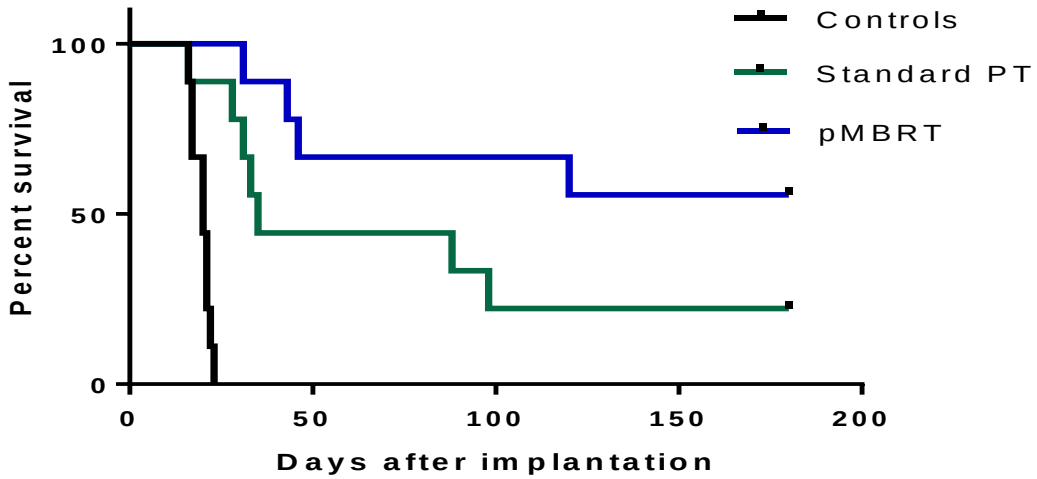
Standard PT



pMBRT



25 Gy/one fraction



pMBRT → 67 % of long-term survivals (free of tumor).

Among the best results ever obtained with radiotherapy alone

Prezado et al., Red Journal 2019

« Les médecins administrent des médicaments dont ils savent très peu, à des malades dont ils savent moins, pour guérir des maladies dont ils ne savent rien. »

Voltaire (1694-1778)