La Physique Médicale demain: Perspectives en Radiothérapie

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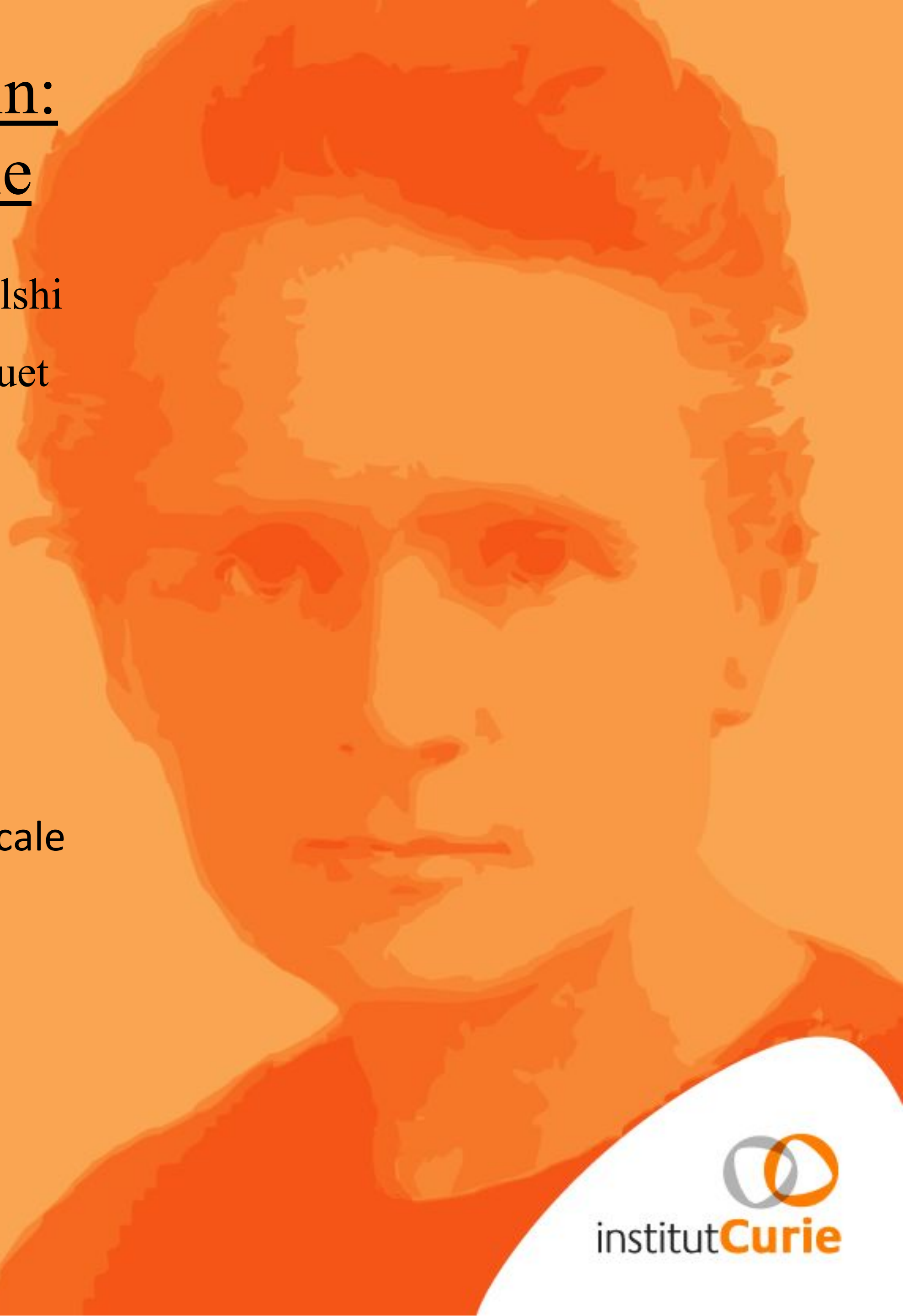
Service de Physique Médicale
Dept de Radiothérapie Oncologique
Institut Curie, France



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Institut Curie, 7 Novembre 2013

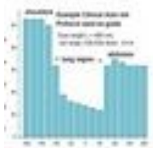
Remerciements: J-C.Rosenwald,
P.Lambin (Maastro), D.Verellen,
T.Lomax, G.Olivera, D.Galmarini
…………
France-Hadron, Areva, Cancéropôle

institutCurie

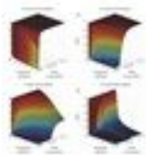
Medical Physics
The International Journal of Medical Physics Research and Practice

EDITOR'S PICKS

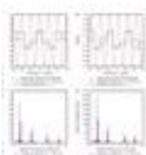
Imagerie



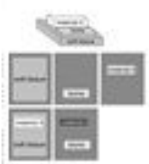
Dose equations for tube current modulation in CT scanning and the interpretation of the associated $CTDI_{vol}$



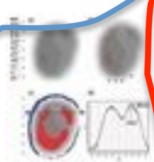
Oblique reconstructions in tomosynthesis. I. Linear systems theory



Oblique reconstructions in tomosynthesis. II. Super-resolution



Dimensionality and noise in energy selective x-ray imaging



Evaluating IMRT and VMAT dose accuracy: Practical examples of failure to detect systematic errors when applying a commonly used metric and action levels

MOST READ THIS MONTH

Increasing dependence on industry-funded research creates higher risk of biased reporting in medical physics

Vision 20/20: Single photon counting x-ray detectors in medical imaging

The more important heavy charged particle radiotherapy of the future is more likely to be with heavy ions rather than protons

MOST CITED THIS MONTH

Dosimetry of interstitial brachytherapy sources: Recommendations of the AAPM Radiation Therapy Committee Task Group No. 43

Dosimetry

BEAM: A Monte Carlo code to simulate radiotherapy treatment units

Evaluation de la dose

A technique for the quantitative evaluation of dose distributions

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In the last 30 days

1. Optical properties of biological tissue

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2. CT : Modelling Iterative reconstruction
3. MRI analysis for brain tumor studies
4. MRI Tracer kinetic modelling
5. X-ray phase-contrast imaging

"Imagerie"

6. Brachytherapy : Monte Carlo calculated doses for permanent implant in lung
7. Out-of-field dose in photon craniospinal irradiation
8. Dosimetry: when ^{60}Co is the reference quality for charged-particle and photon beams

"Dosimétrie"

Comme "Evaluation" en Med Phys…

9. Automatic 3D ultrasound calibration in IGRT
10. Automated segmentation of pulmonary structures in CT

Outils "automatiques"

La Physique Médicale demain:
Perspectives en Radiothérapie Externe

Menu du jour :

1) **Physique et technologie :**
   vers la radiothérapie Adaptative

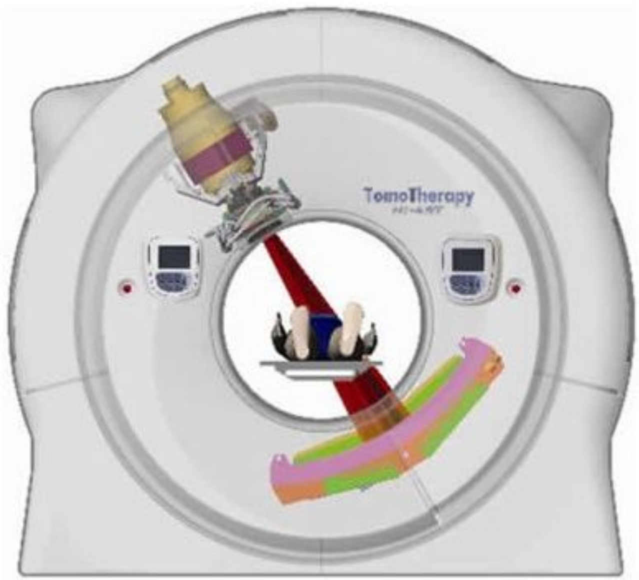
2) **Besoin d'ouverture en R&D :**
   vers la Biologie

3) **Divers, discussion et conclusions**

Physique et technologie : Les systèmes proposés actuellement en RT externe

RapidArc ou equivalentes (wphospitals.org)

www.cyberknife.com

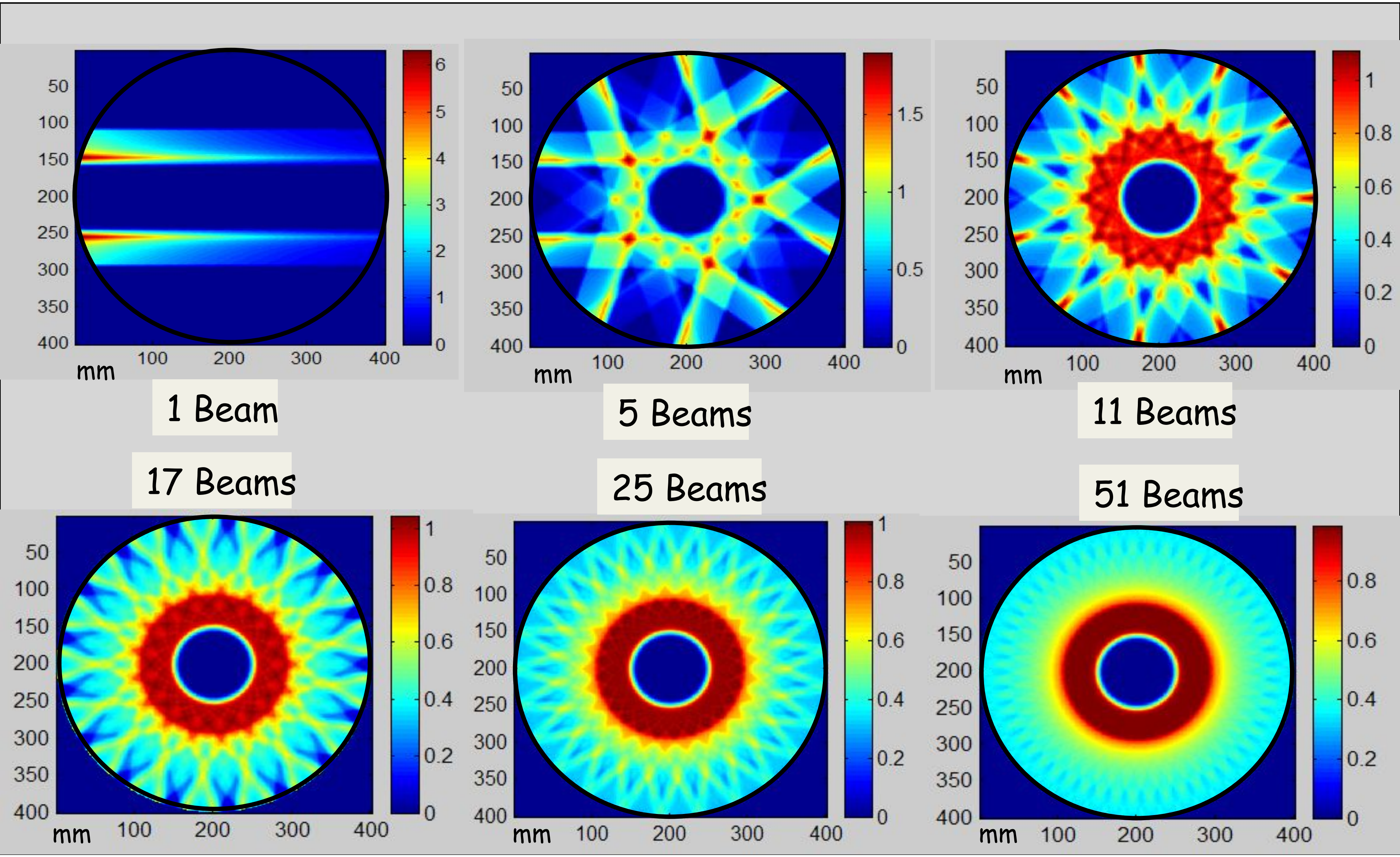


Tomothérapie

Vero

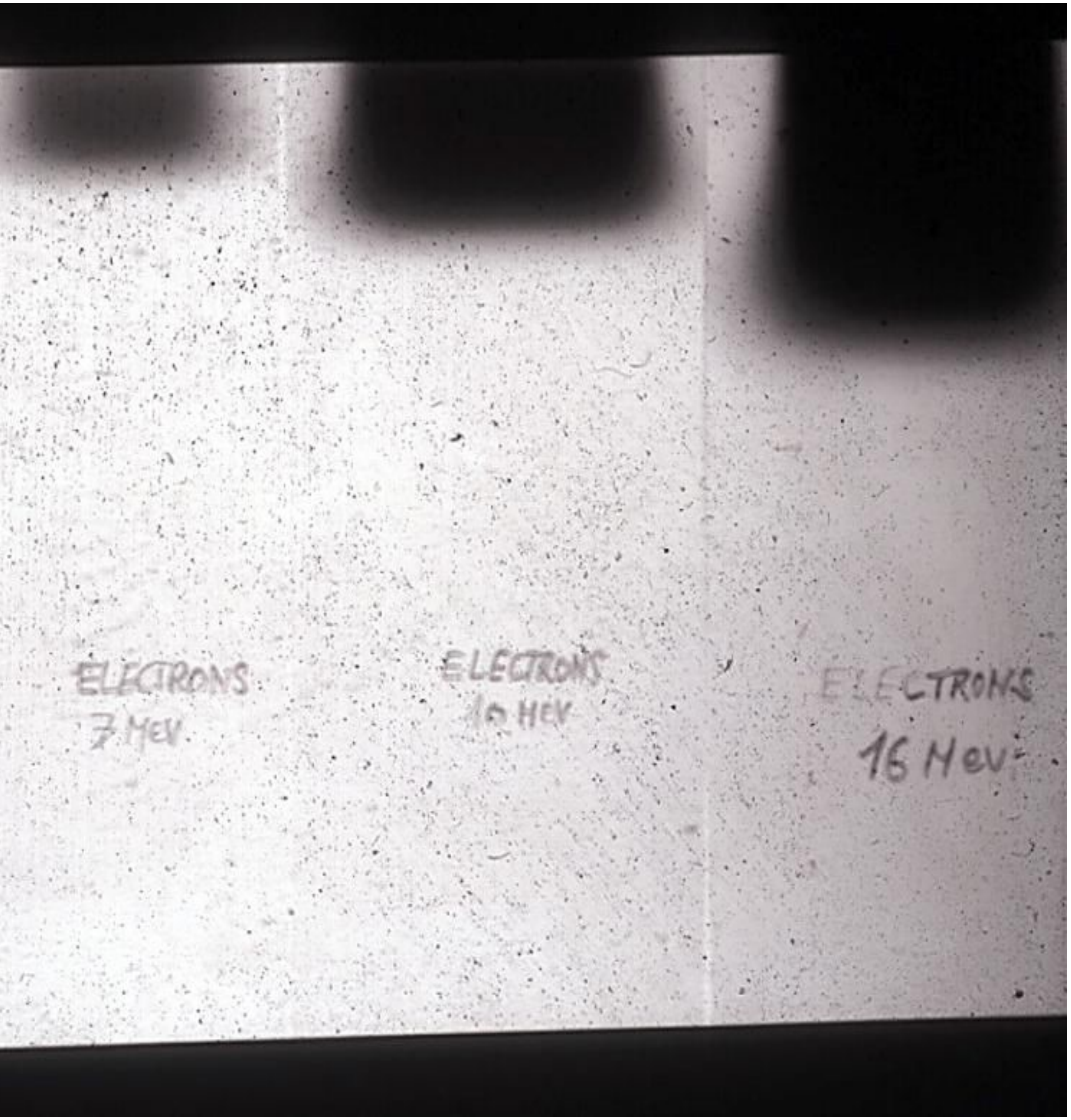
ViewRay (MRI+3Co-60 w/MLC

La multiplicité d'incidences // Le rôle de l'Energie

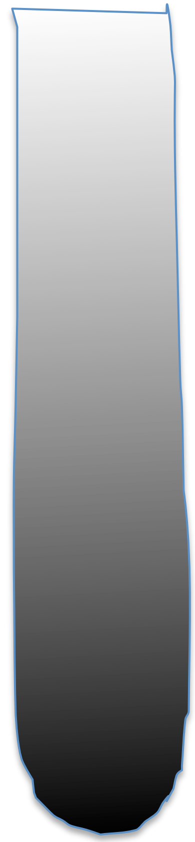


(from Tomotherapy)

Electrons

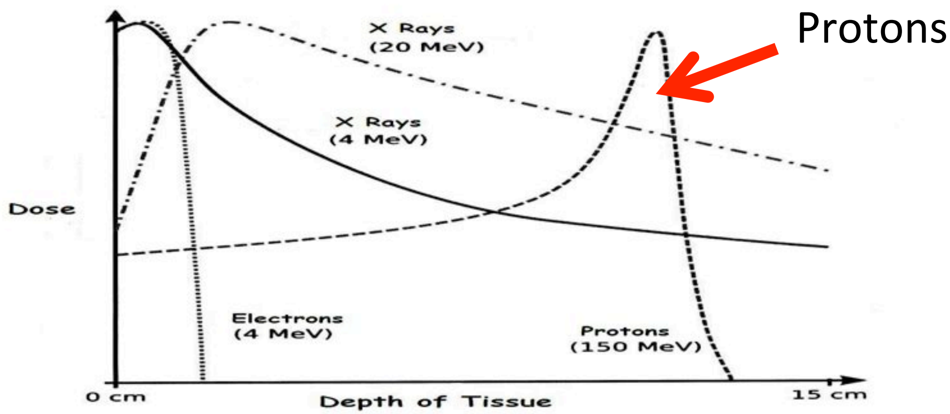


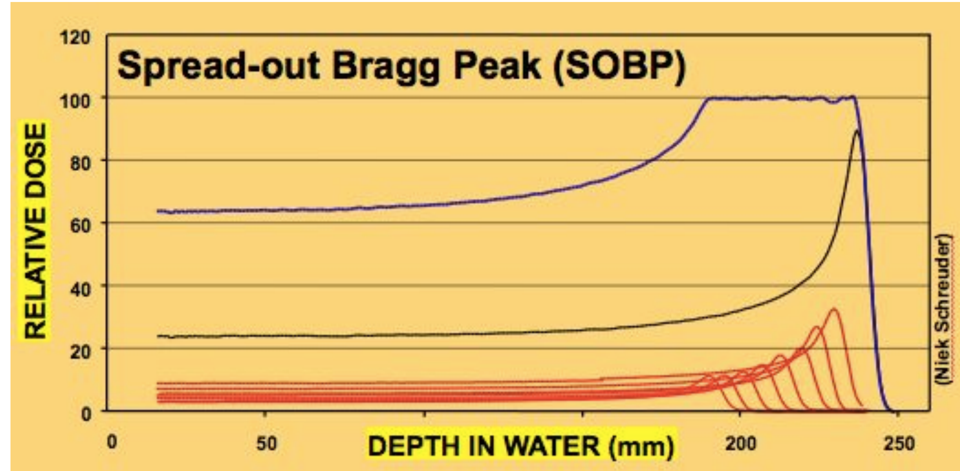
Protons/Ions

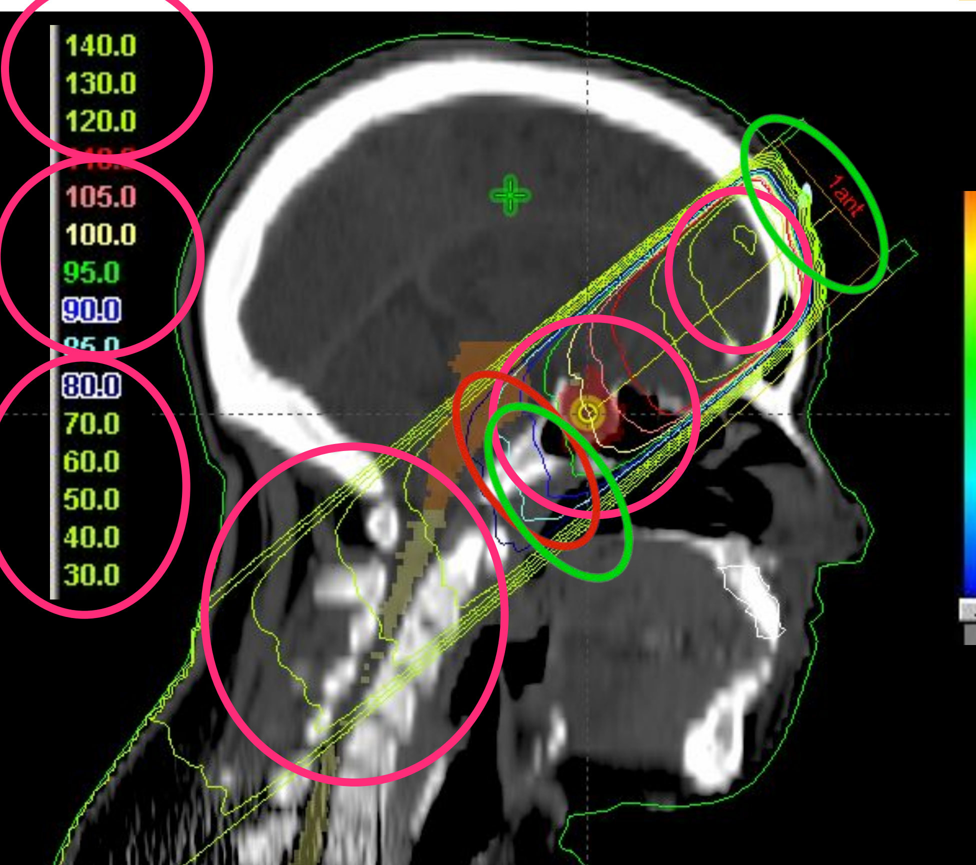


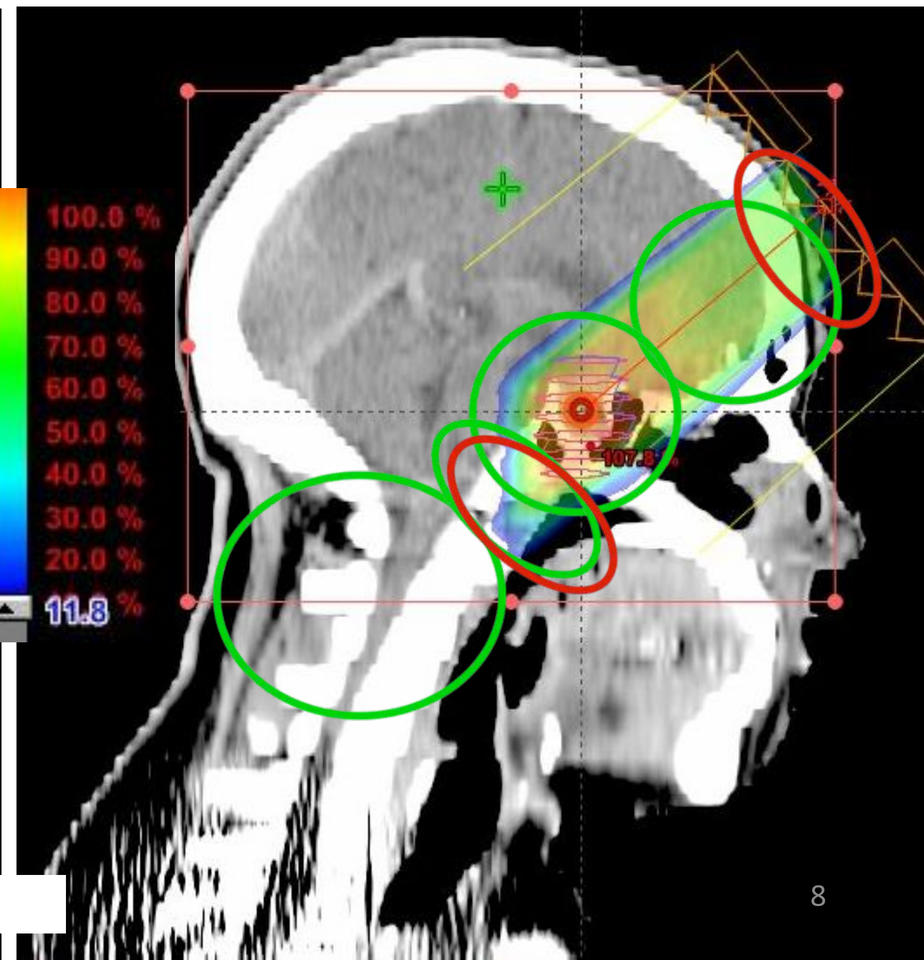
Photons

J-C.Rosenwald





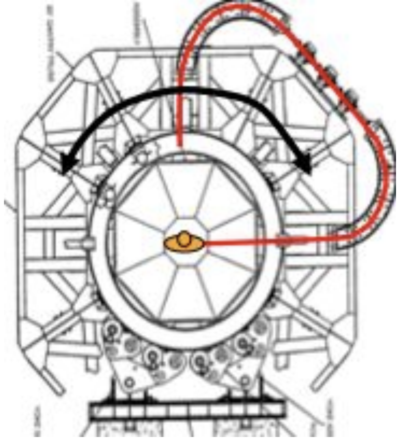




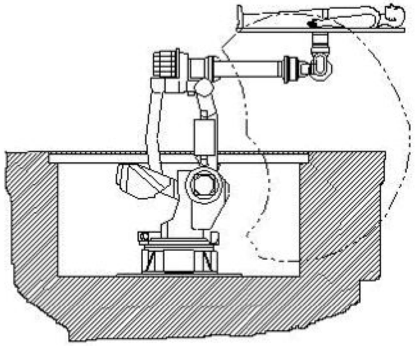
Software: Varian´s Eclipse // Beam Data : IBA // Calcs : A.Mazal- I.Curie

L’évolution technologique en hadronthérapie

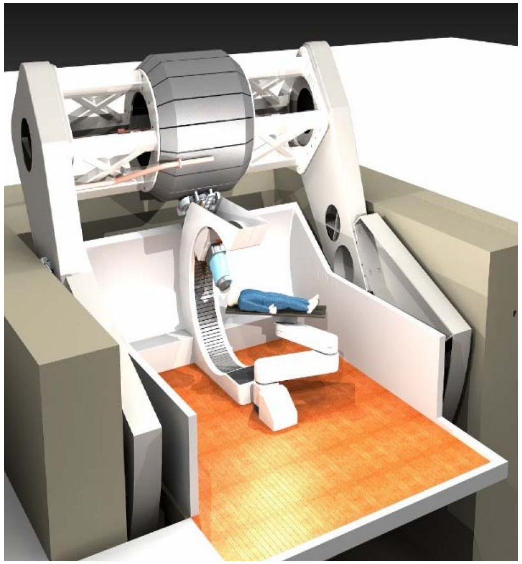
Machines plus compactes



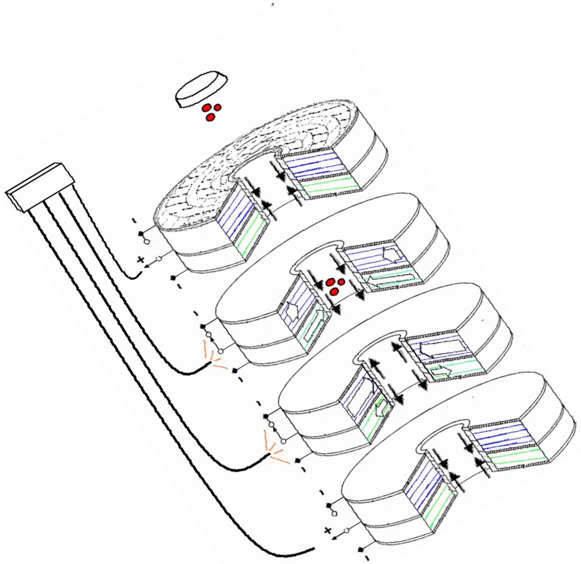
Bras isocentriques



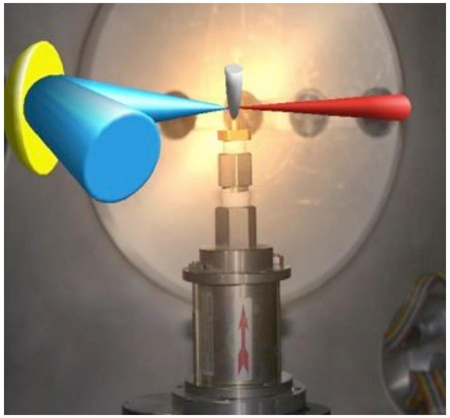
Robotique de positionnement



Cryogénie



Accélerateur a paroi dielectrique

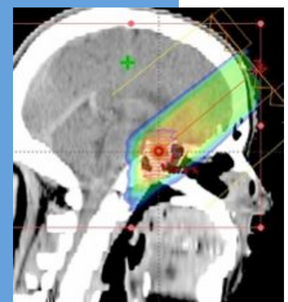


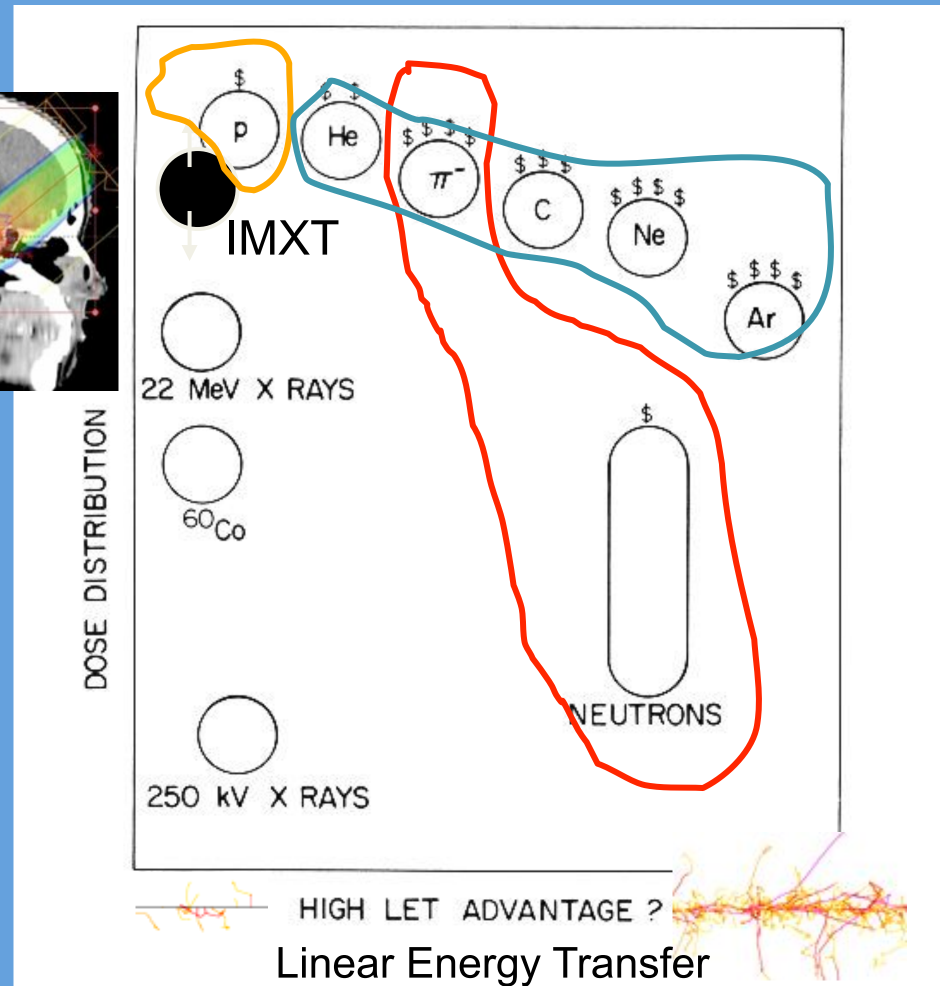
Accélération Laser

Hadrontherapy : Physical selectivity and/or Radiobiological effects

* pions
* fast
& slow neutrons

(Past)





* protons

(Present)

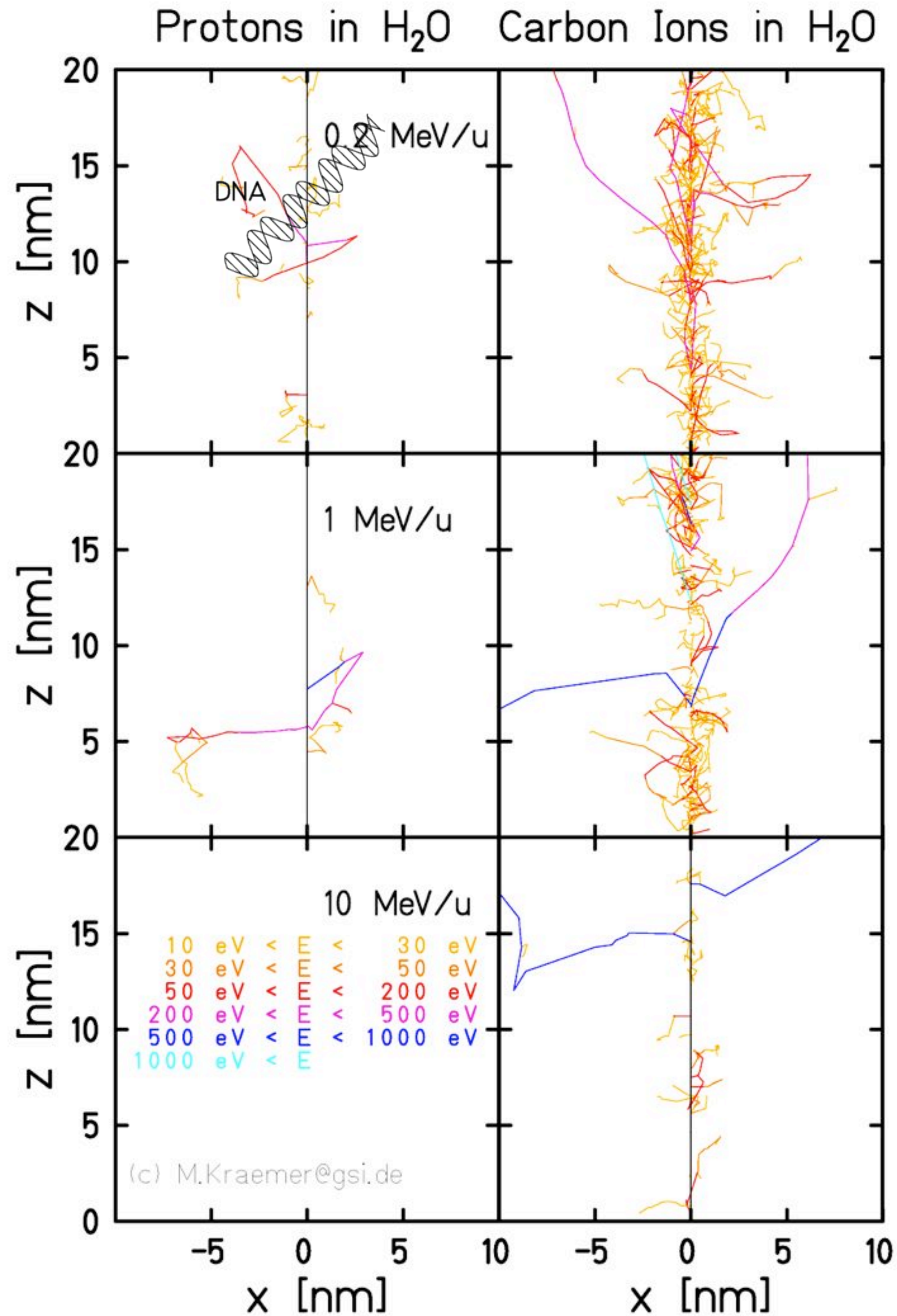
* light and heavy ions

(Future ?)

Raju & Koehler, 1980

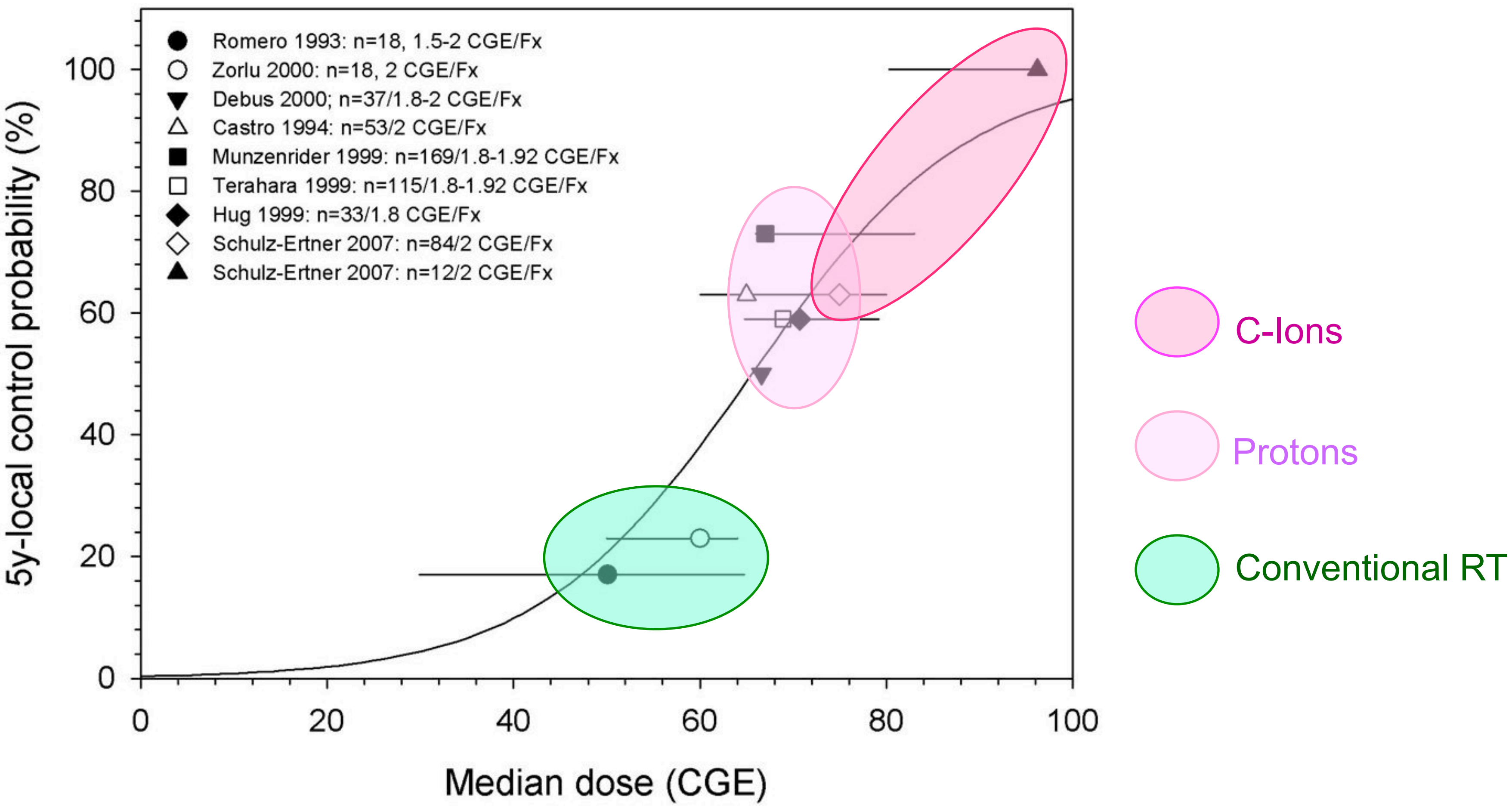
Radiation Biology:

Dose distribution
in
nanometer scale



M. Kraemer

Au top de la sygmoide de contrôle local ??



Ex sarcomes de la base du crâne

Darmstadt & Heidelberg

Dosimetric comparisons:
systems available at Institut Curie

PHOTONS | **HADRONS**

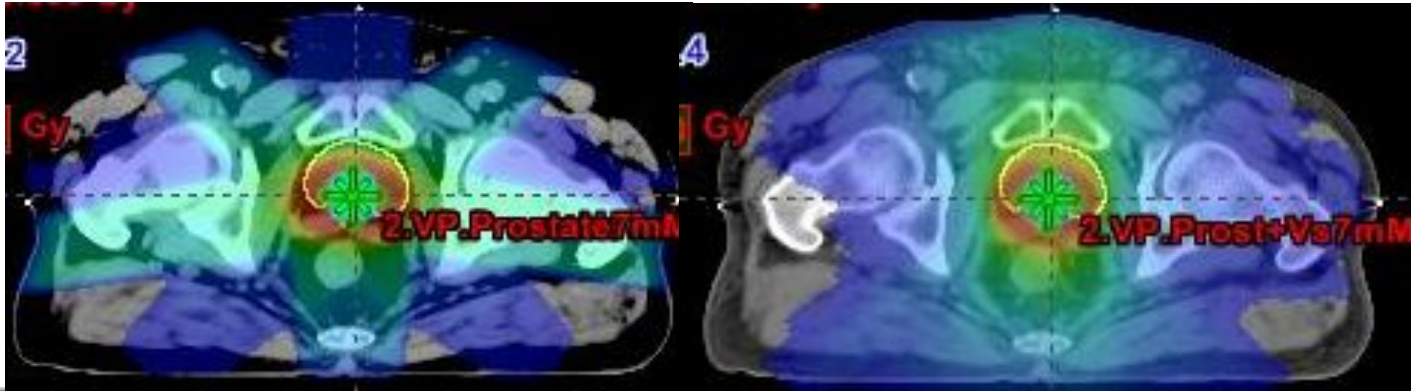
1 Brachy	2 Conform	3 IMRT	4 Rapid Arc	5 Tomo	6 Prot2	7 Prot4	8 Prot5	9 Prot Patch	10 O

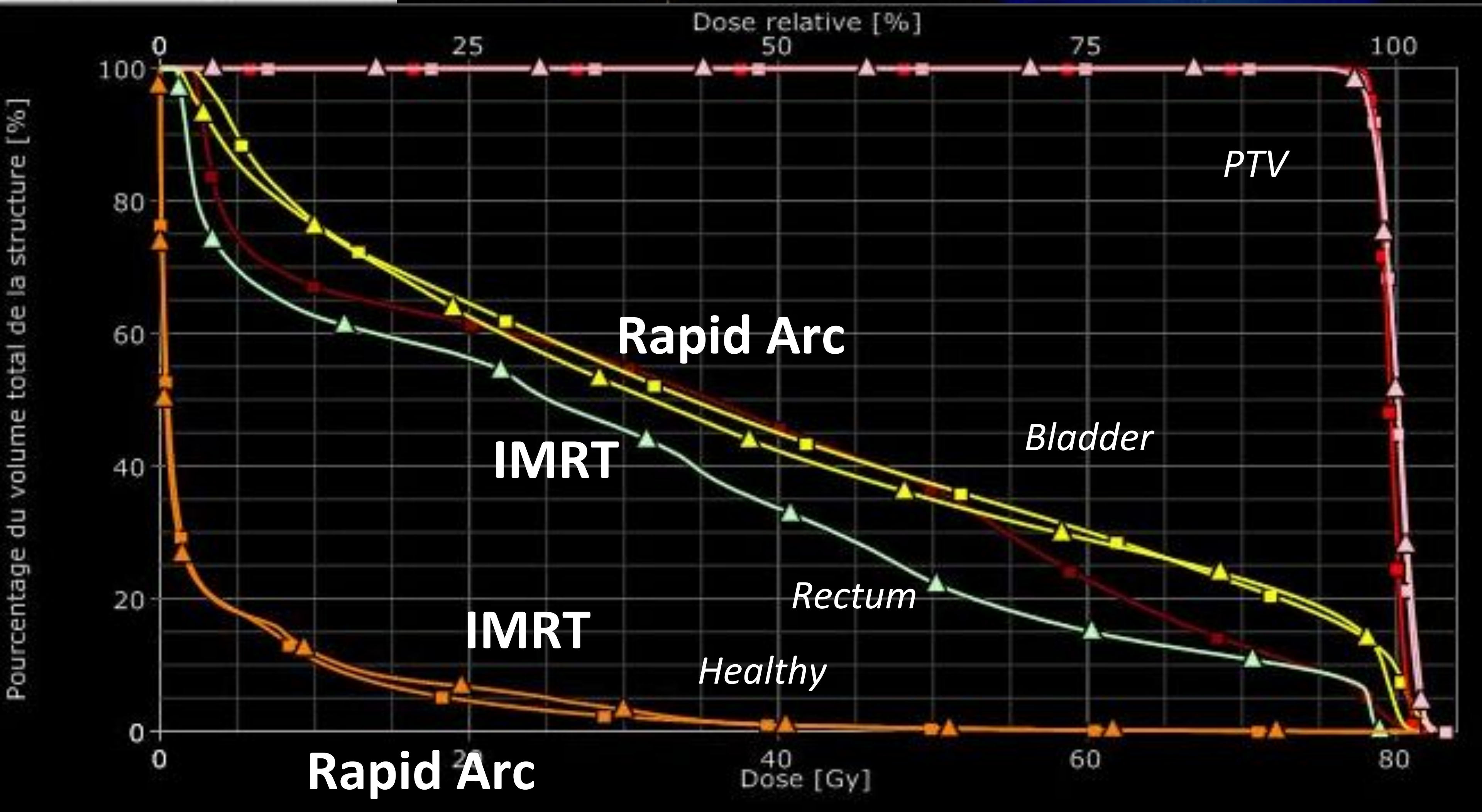

LinacVarian 2100CSE

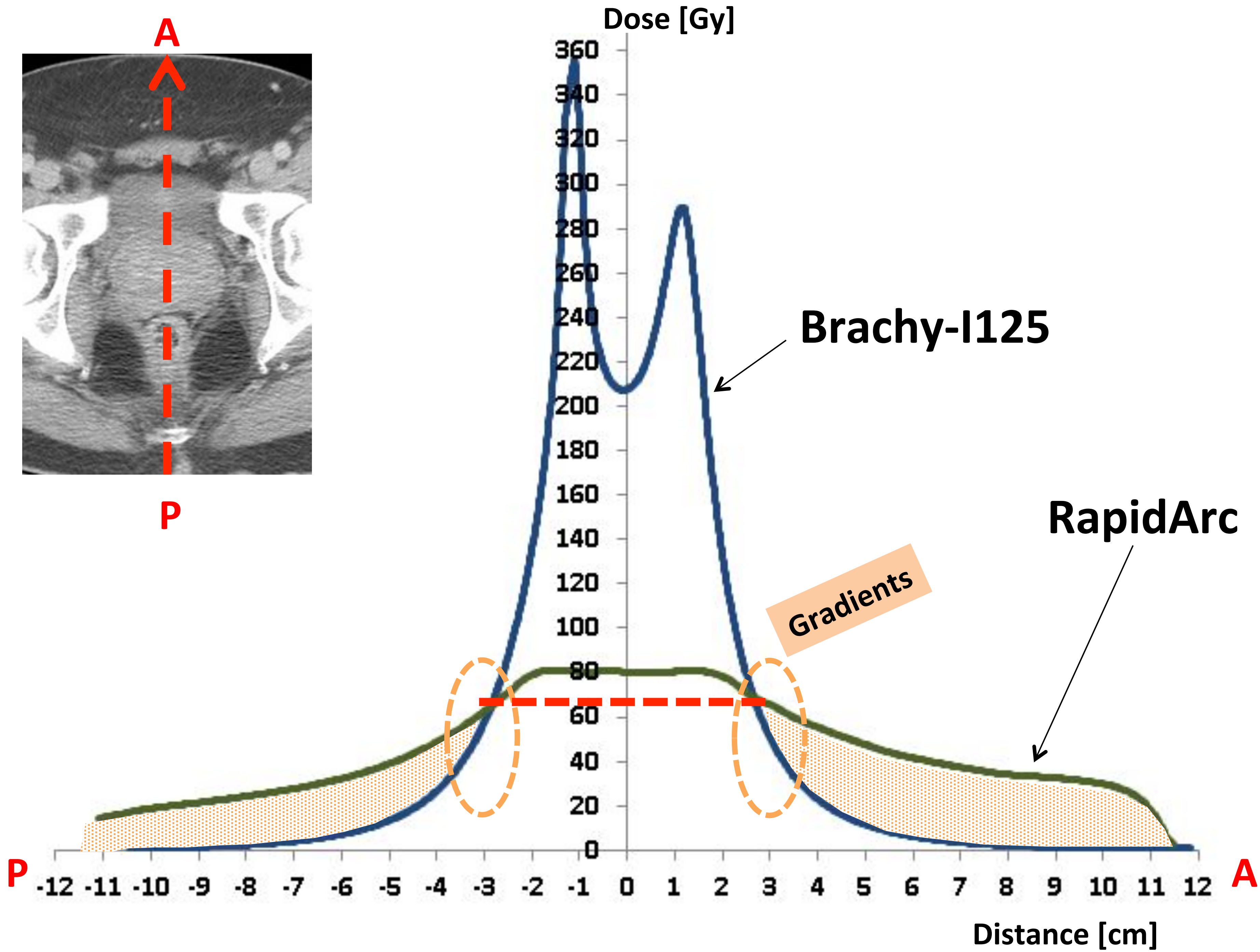
Tomotherapy HD


IBA protontherapy system

IMRT fixed vs RapidArc

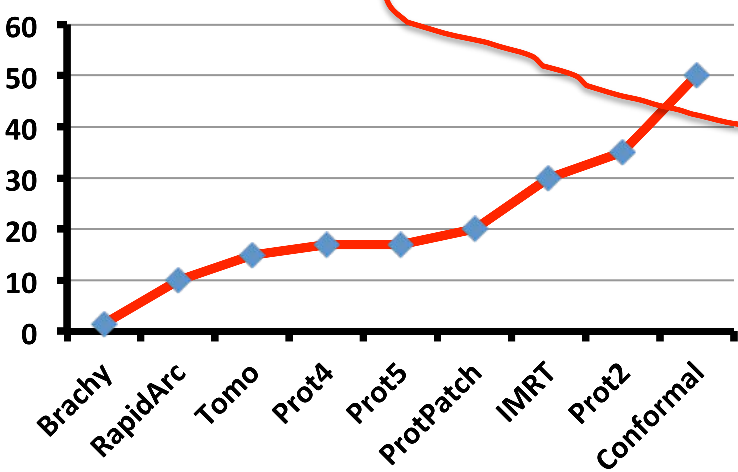


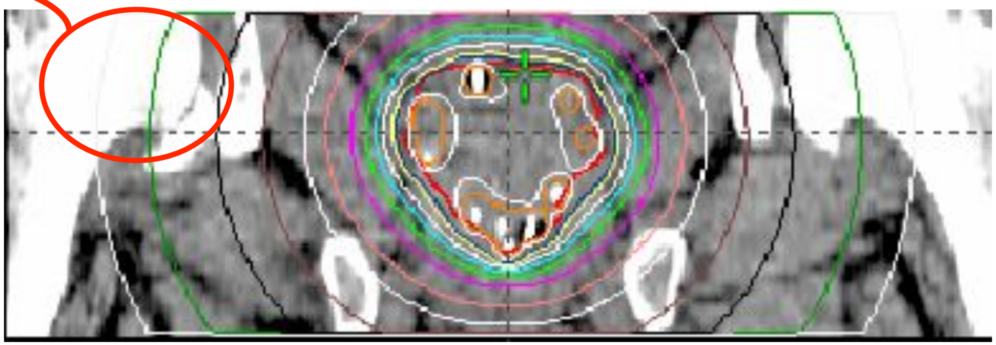


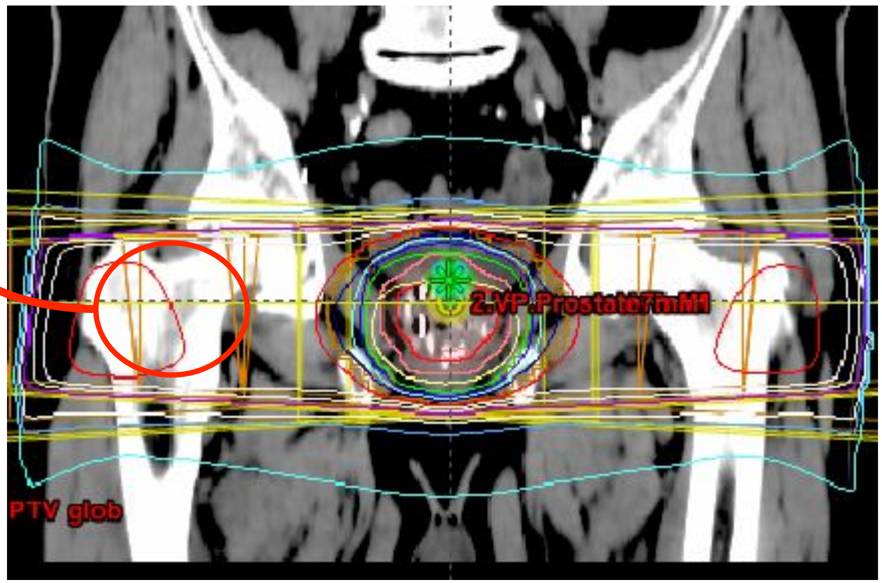

A
P
Dose [Gy]
360
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
Brachy-I125
RapidArc
Gradients
P
-12 -11 -10 -9 -8 -7 -6 -5 -4 -3 -2 -1 0 1 2 3 4 5 6 7 8 9 10 11 12
A
Distance [cm]

Dose to femoral head [Gy] : Ratios vs Brachytherapy

Point dose to femoral head		
[Gy]	D femur	Ratio
Brachy	1.5	1
RapidArc	10	7
Tomo	15	10
Prot4	17	11
Prot5	17	11
ProtPatch	20	13
IMRT	30	20
Prot2	35	23
Conformal	50	33





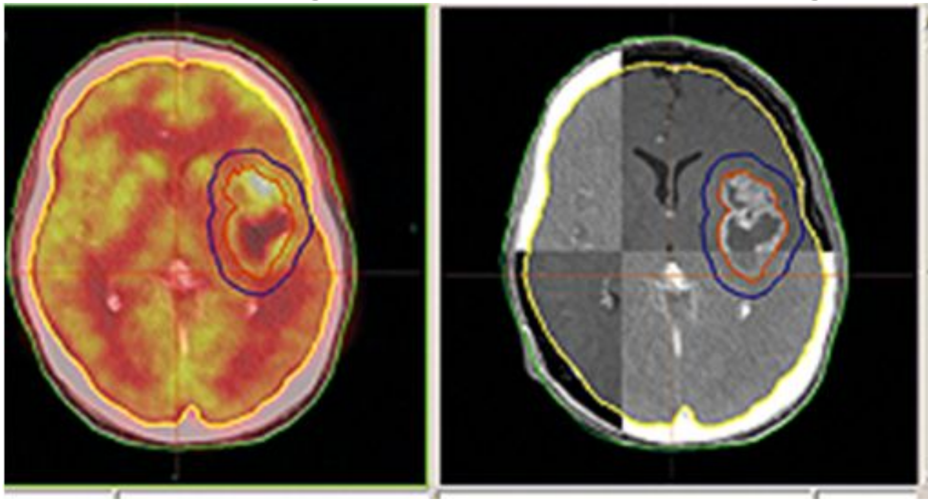


For 1.5 Gy (max) given by Brachy to the femoral heads,
all the others techniques deliver 10 to 50 Gy, so a ratio of 7 to 30 times higher

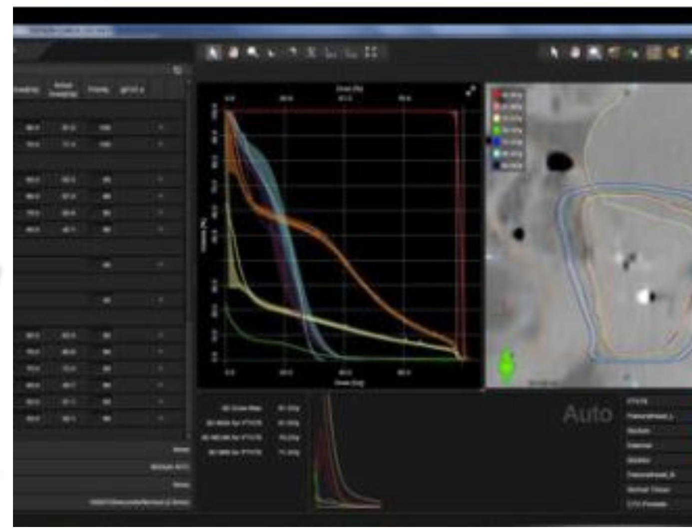
L’évolution des outils logistiques :

Imagerie multimodalité :

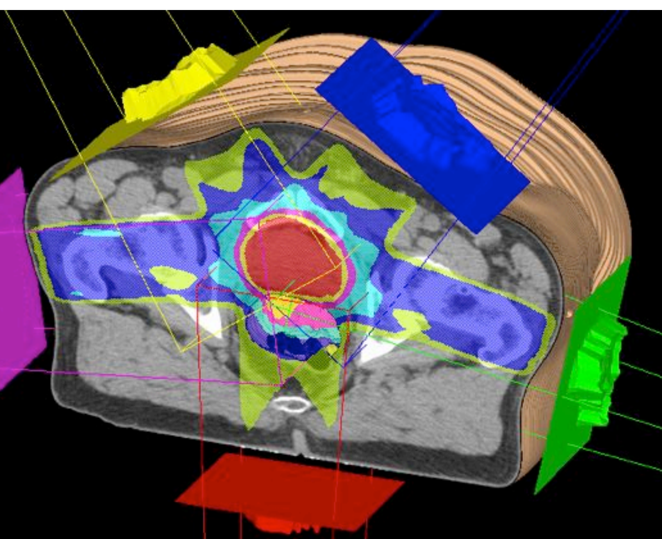
Correlation d’images, Outils de contourage

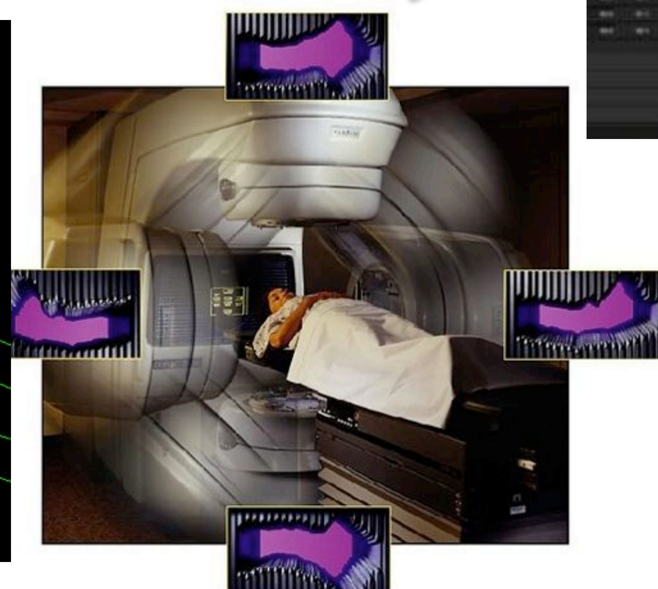


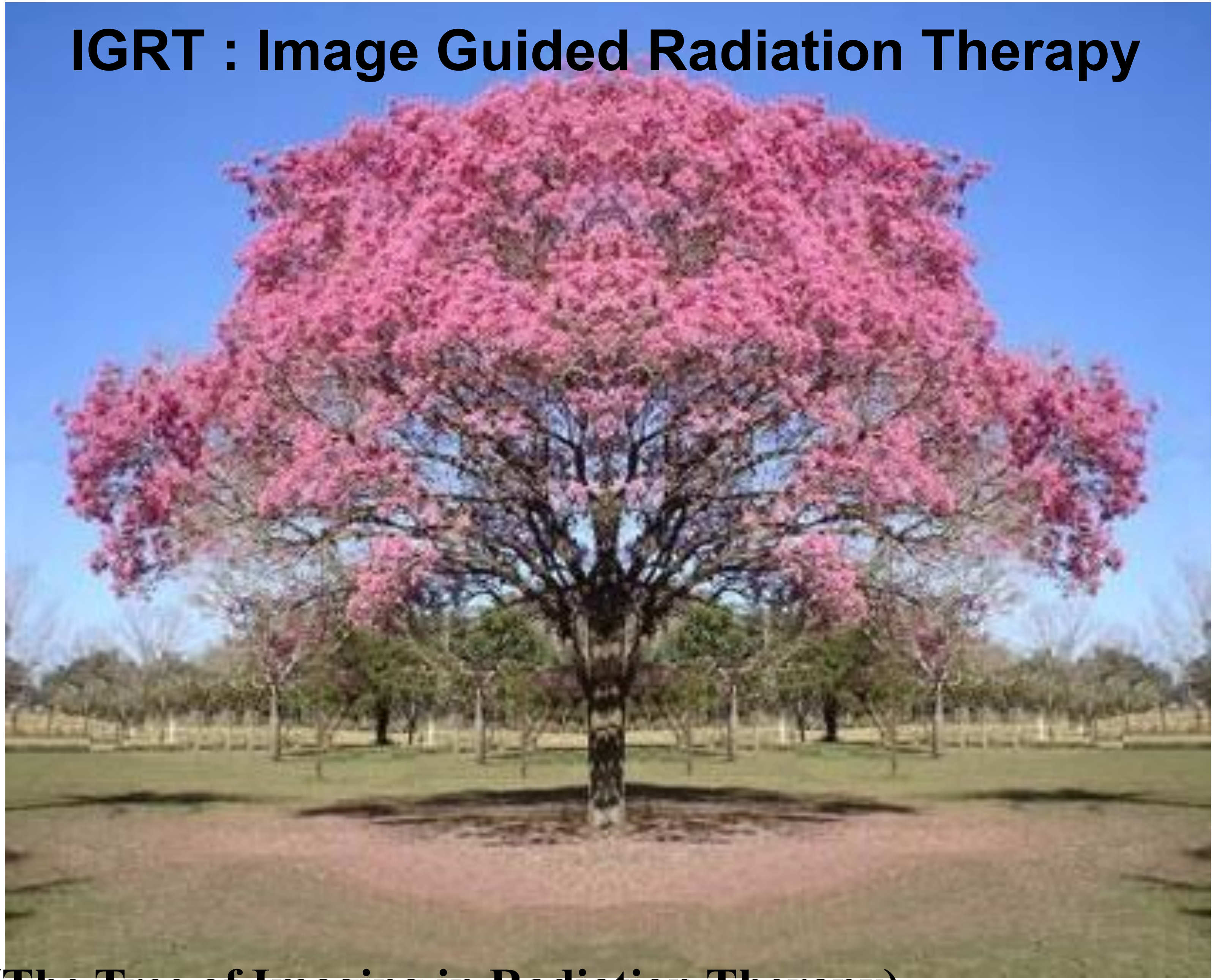
En cours d’introduction:
“Fast
Knowledge based
Planning”



Systèmes de planification : IMRT, 4D

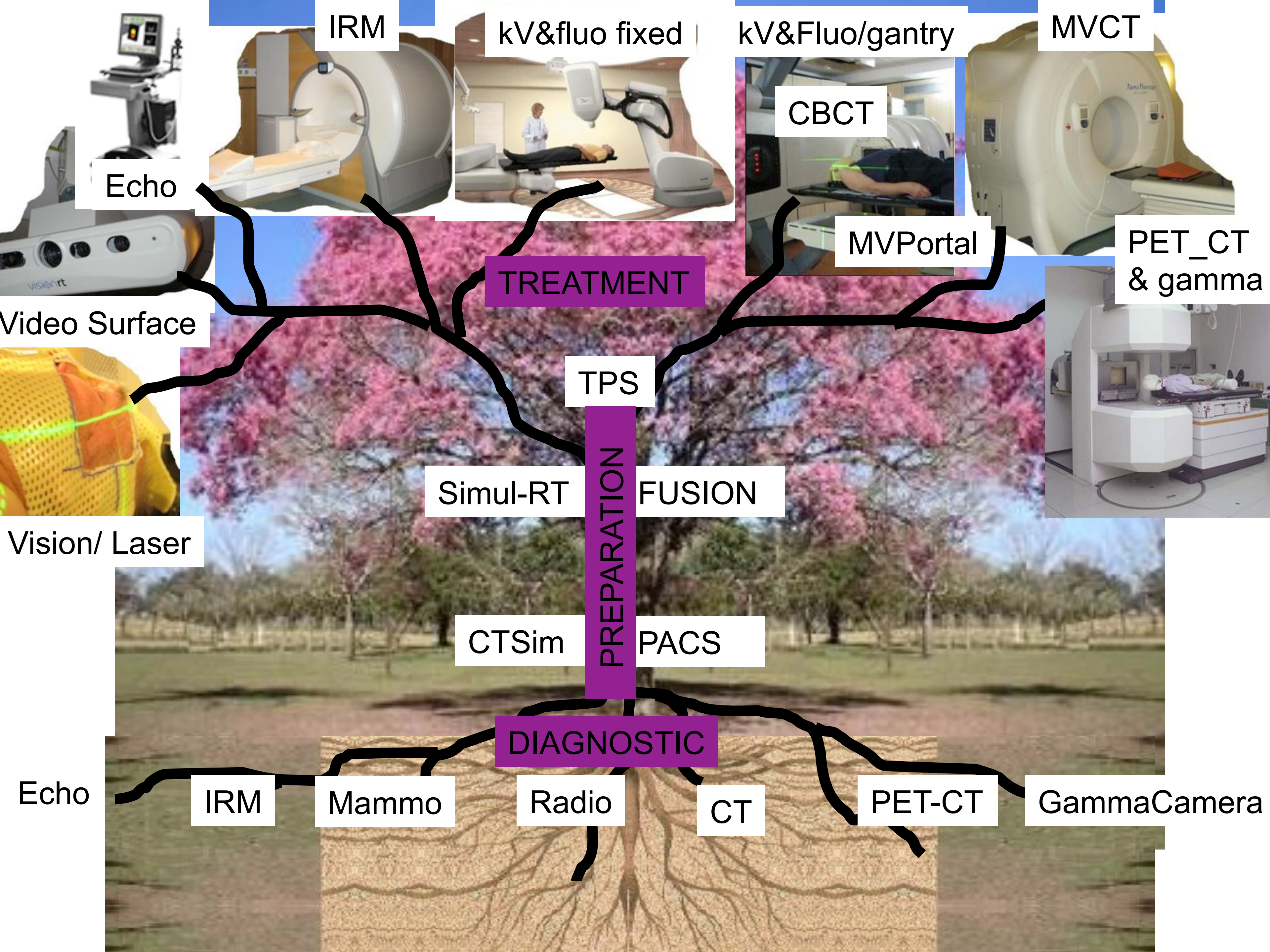




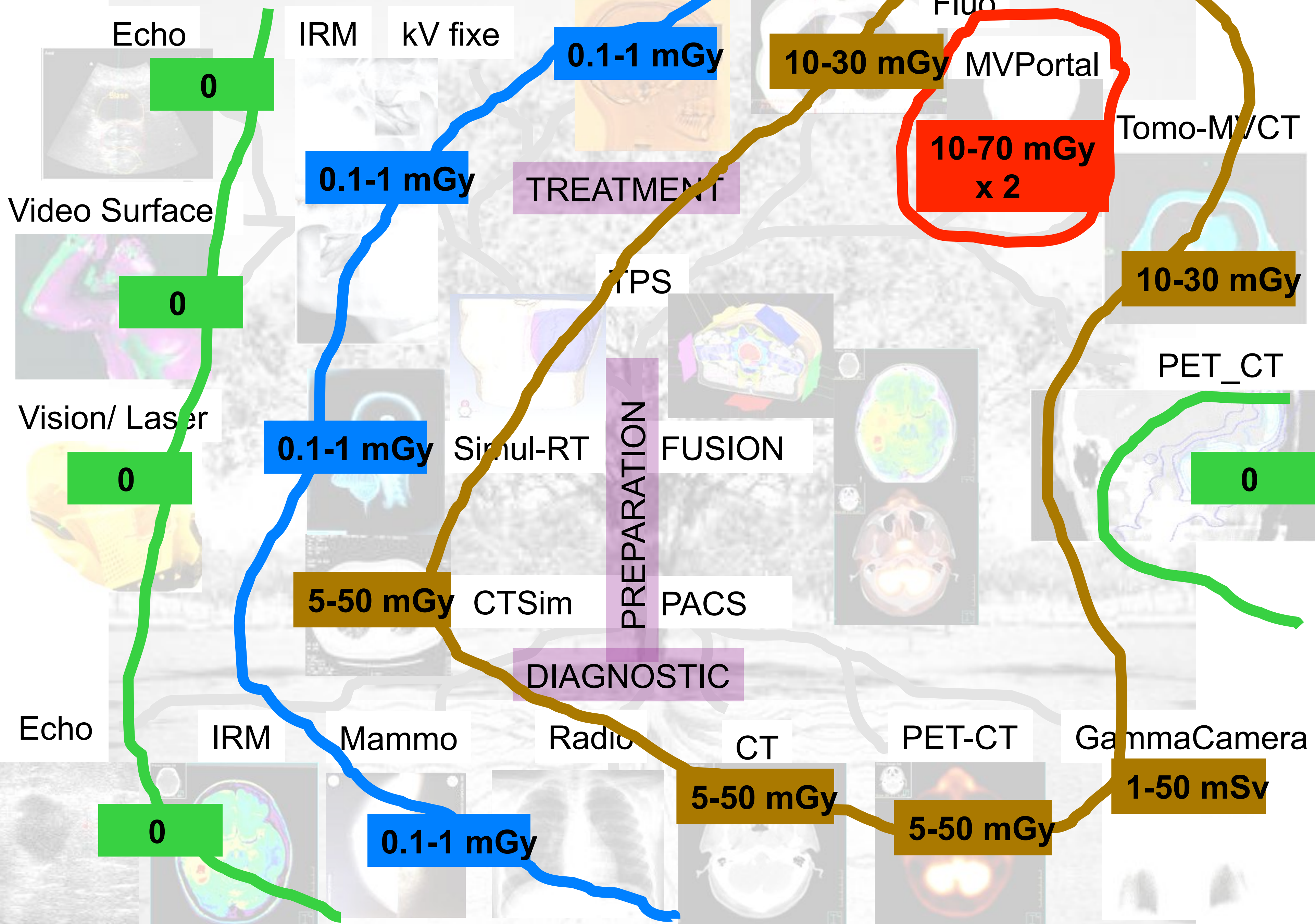


(The Tree of Imaging in Radiation Therapy)
Creteil, EPU G.Marinello

Lapacho (Tecoma curialis)


IRM
kV&fluo fixed
kV&Fluo/gantry
MVCT
CBCT
Echo
MVPortal
PET_CT
& gamma
TREATMENT
Video Surface
TPS
Simul-RT
PREPARATION
FUSION
Vision/ Laser
CTSim
PACS
DIAGNOSTIC
Echo
IRM
Mammo
Radio
CT
PET-CT
GammaCamera

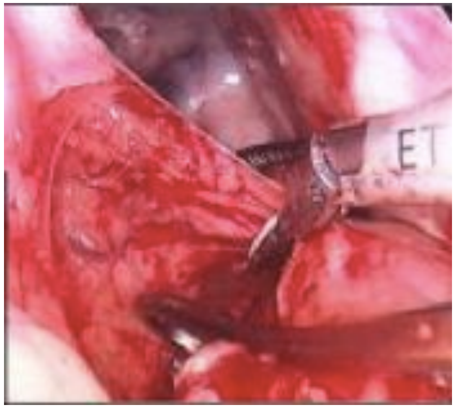
7. Dose delivered per image



Physique médicale demain: Perspectives en Radiothérapie

Dirk Verellen. Brussels. Belgium

- ***Poor quality RT will produce poor quality clinical outcome***



- We need to "see" the tumor, the micro-environment and to ***"see our scalpel"***

- We ***need to redesign the QA process,*** and to perform a ***process oriented risk analysis***.

Physique médicale demain: Perspectives en Radiothérapie

Dirk Verellen. Brussels. Belgium
(2/2)

- Our priority is ***NOT the development of new beams and new fancy machines***

- We need accurate reports of the ***actual delivered dose*** at each fraction …,

- We need good ***data mining tools*** from different hospitals

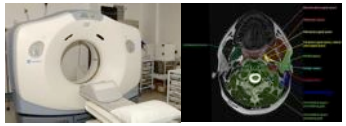
- Then we might start to understand the ***radiobiology of the tumor and healthy tissues***, …

Ideas for Medical Physics in the future
Tony Lomax, Switzerland

- Automated, risk minimised and time efficient QA
- Daily Adapted Treatments (real-time)
  In-vivo dose/range verifications/reconstructions
- Biological assessment based on accurate treatment dose distributions/reconstructions
- From Macro to micro : cellular level

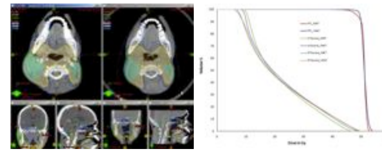
Adaptive : the workflow

Planning Imaging



Electronic Prescription

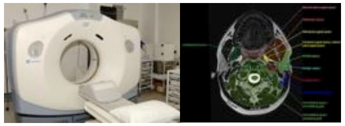
Treatment Planning



G. Olivera D.Galmarini
USA

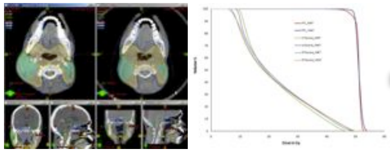
The workflow

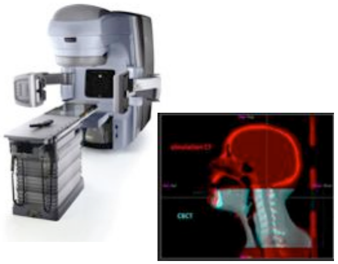
Planning Imaging



Electronic Prescription

Treatment Planning

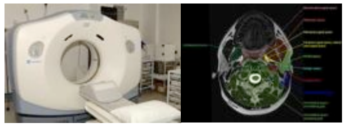




2D – 3D In room Imaging

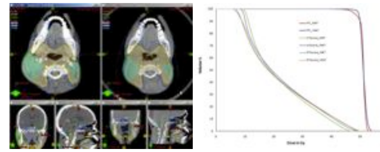
The workflow

Planning Imaging



Electronic Prescription

Treatment Planning



In room Imaging

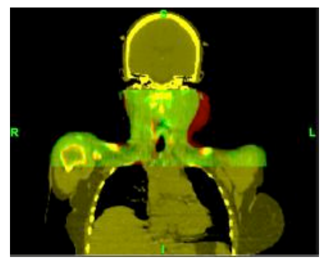
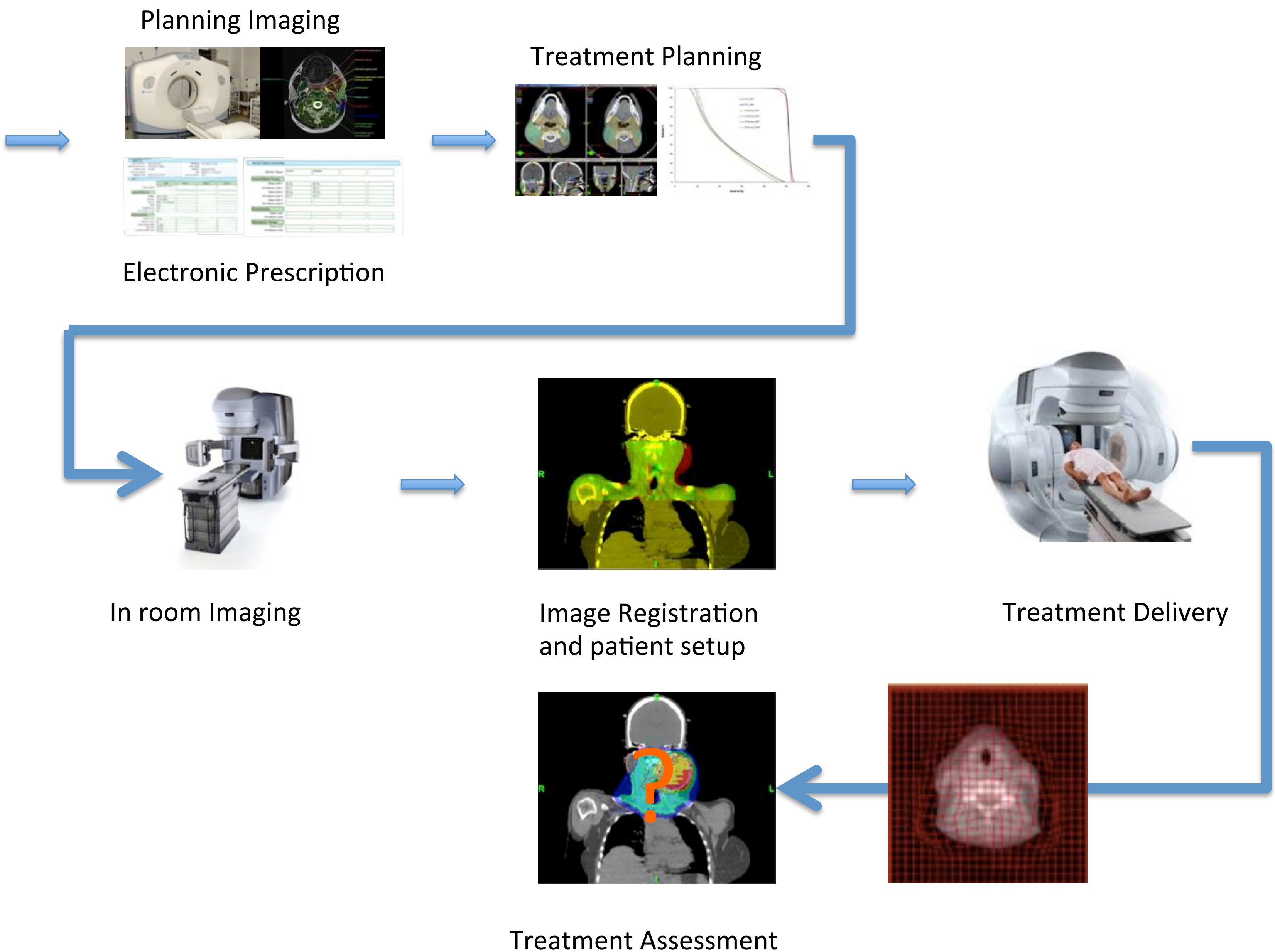


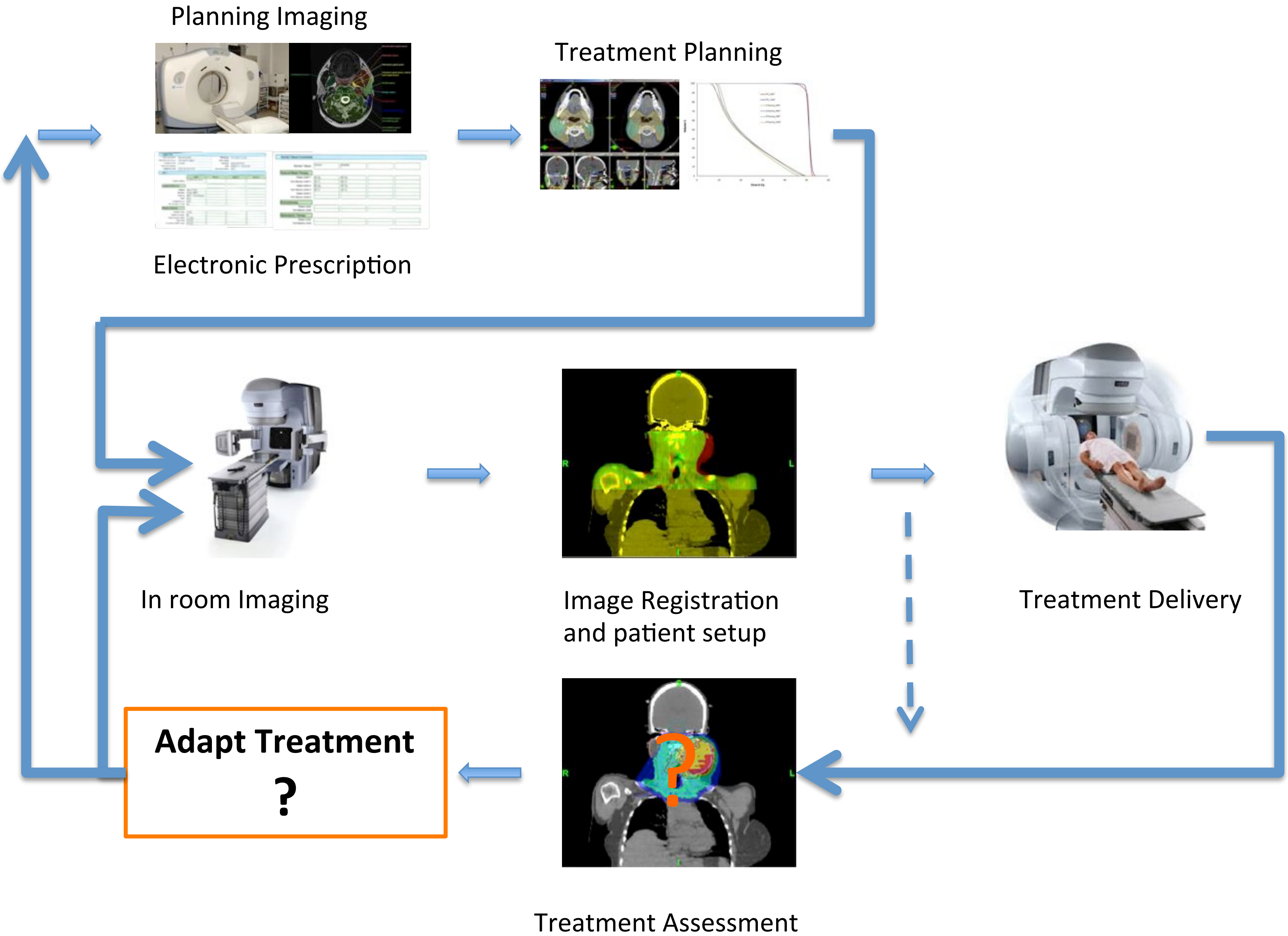
Image Registration
and patient setup

Treatment Delivery

The workflow

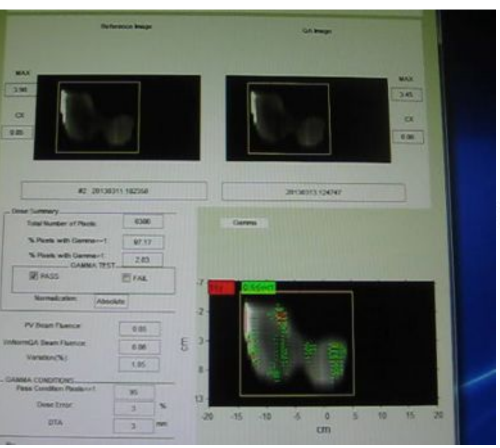


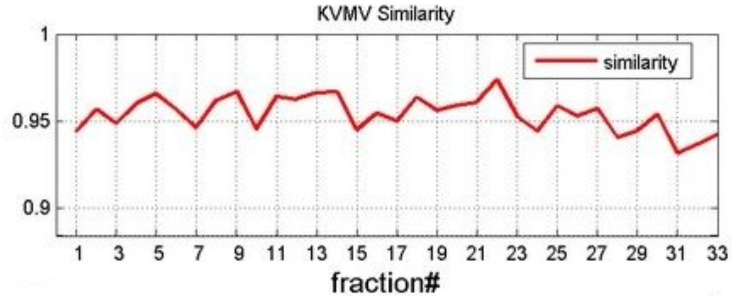
The workflow

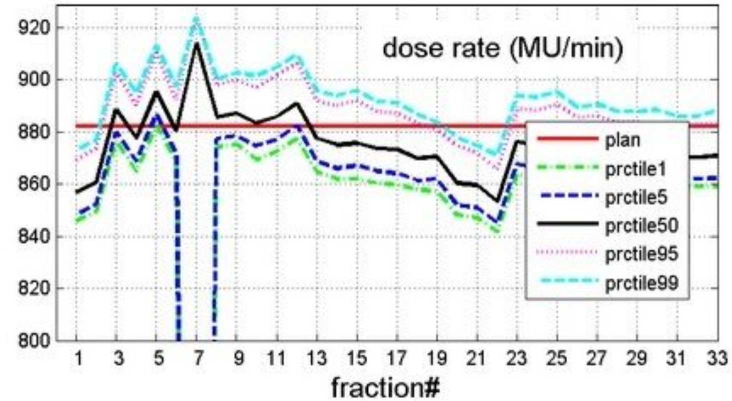


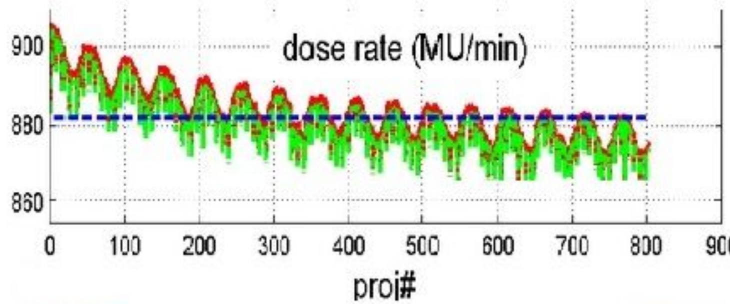
Claas Wessels,
PhD student, I.Curie

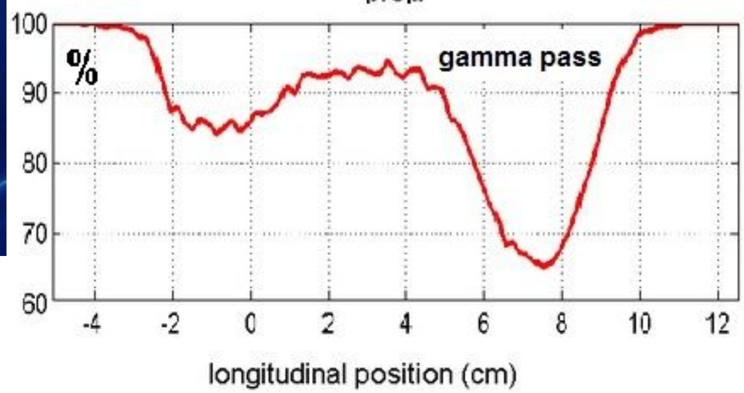
Incertitudes
en nlles techniques:
rotationnelles
et protons











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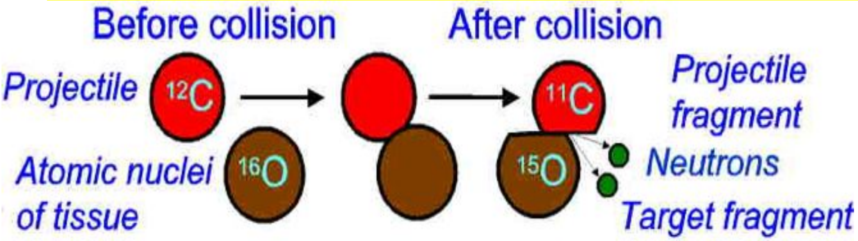
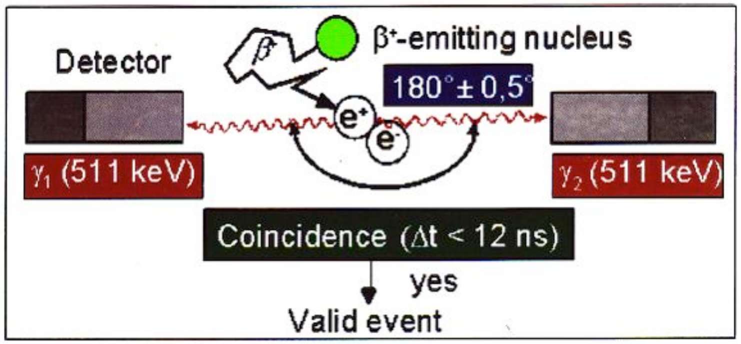
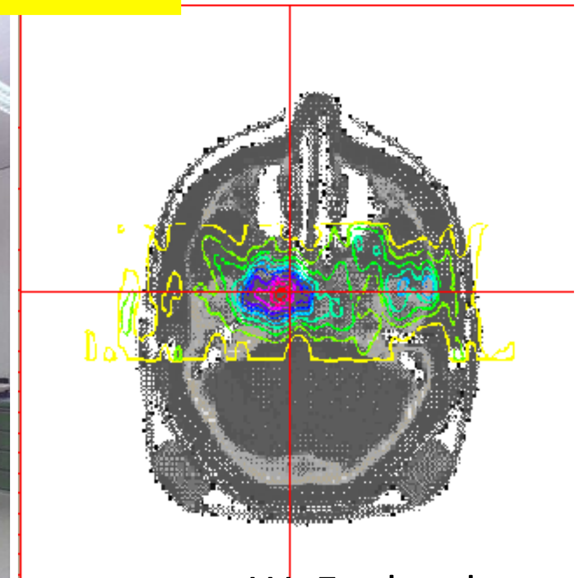
2	20130827.	Green	Yellow	Green	
3	20130828.	Yellow	Green	Yellow	
4	20130829.	Green	Green	Green	
5	20130830.	Green	Yellow	Yellow	
6	20130902.	Green	Green	Green	
7	20130903.	Yellow	Red	Red	Interr
8	20130904.	Green	Green	Green	
9	20130905.	Green	Green	Green	
10	20130906.	Yellow	Green	Green	
11	20130909.	Green	Green	Green	
12	20130910.	Green	Green	Green	
13	20130911.	Green	Green	Green	
14	20130912.	Green	Green	Green	
15	20130913.	Yellow	Green	Green	
16	20130916.	Green	Green	Green	
17	20130917.	Yellow	Green	Green	
18	20130918.	Green	Green	Green	
19	20130919.	Green	Green	Green	
20	20130920.	Green	Yellow	Green	
21	20130923.	Green	Yellow	Red	Interr
22	20130924.	Green	Red	Green	
23	20130925.	Green	Green	Green	
24	20130926.	Yellow	Green	Green	
25	20130927.	Green	Green	Green	
26	20130930.	Green	Green	Yellow	
27	20131001.	Green	Green	Green	
28	20131002.	Yellow	Green	Yellow	
29	20131003.	Yellow	Green	Green	
30	20131004.	Green	Green	Green	
31	20131007.	Yellow	Green	Green	
32	20131008.	Yellow	Green	Green	
33	20131009.	Yellow	Green	Yellow	

Positron Emission Tomography from patient activation with the beam



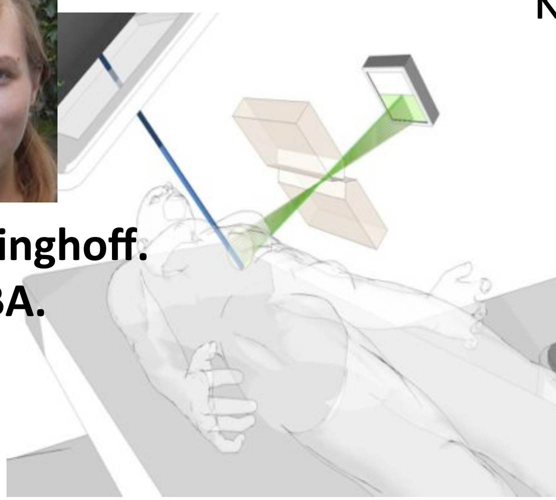




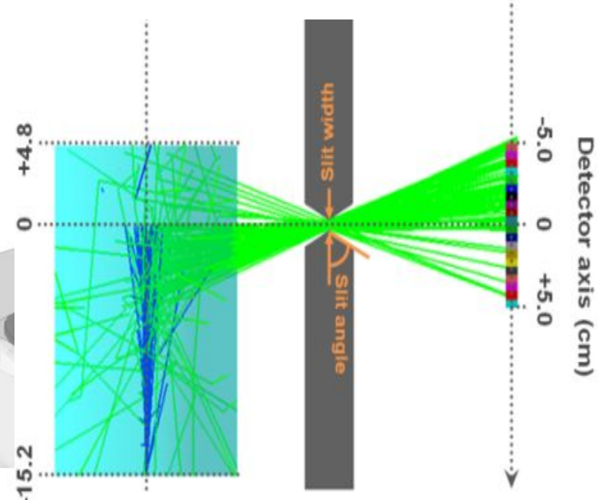
W. Enghardt et al

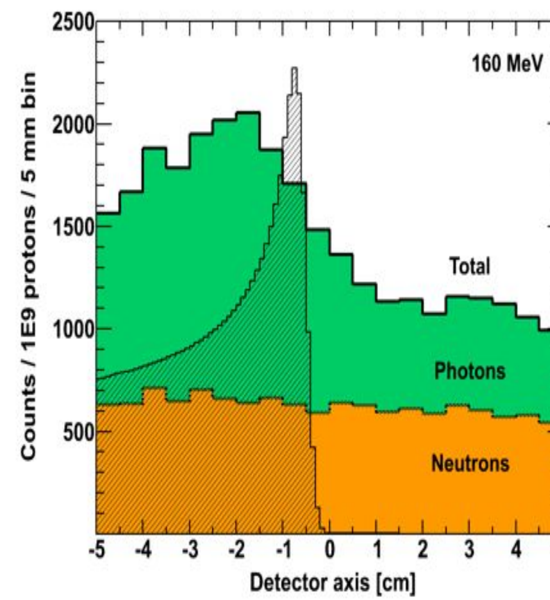
Prompt Gamma

F.Roellinghoff.
PhD, IBA.



Knife-edge slit camera





One idea/vision on physics in radiation therapy tomorrow?

Thomas Bortfeld, Boston, USA

1. We have almost plateaued out in the dose conformation problem (100 years)

2. Optimization of dose delivery over time (hypo-fractionation,…), biological targeting, combined modalities (chemo-RT),….

3. Cost-effectiveness in healthcare (cheaper treatments)

➔ research in Medical Physics!

M.D.Anderson, Houston, USA

LUNG

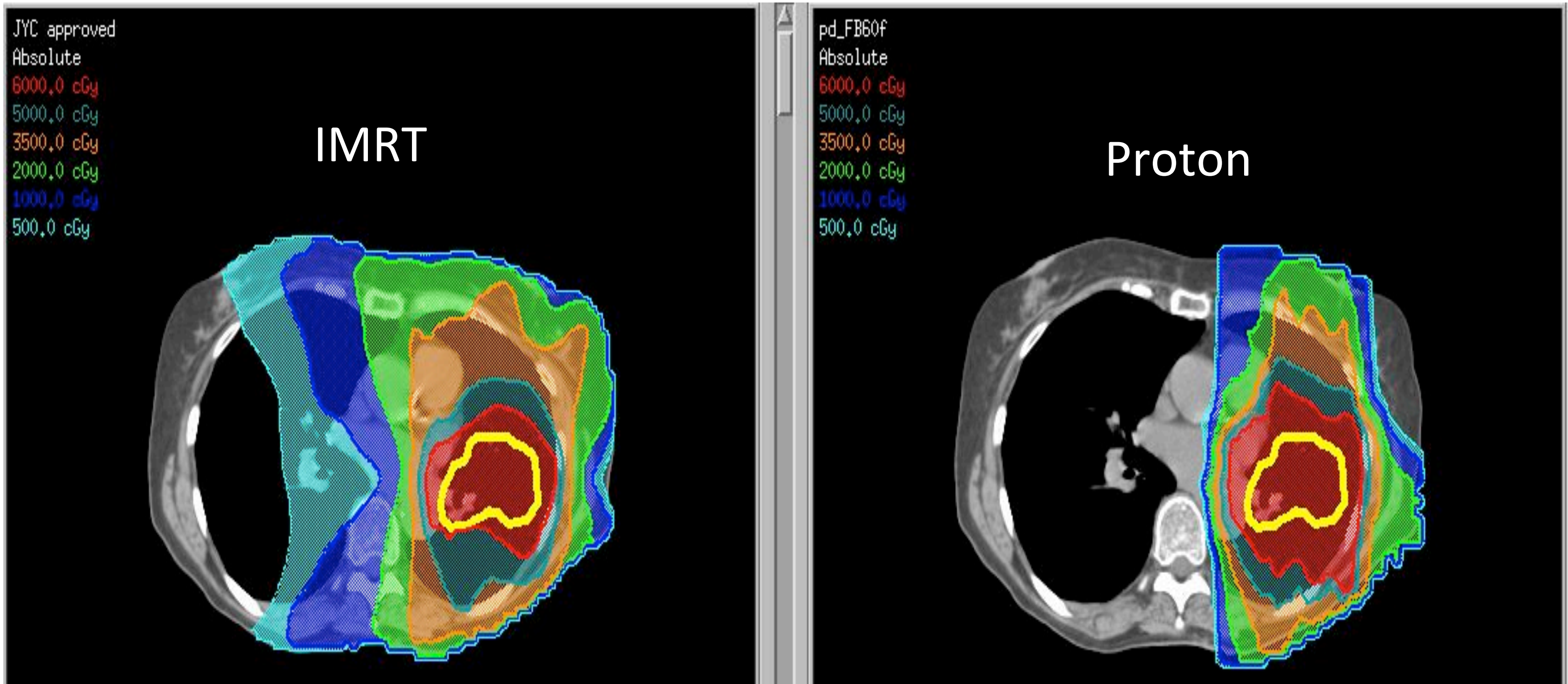
Proton dose escalation still spares more normal tissues

Proton 87.5 GY vs photon 60 GY in stage I

Proton 74 GY vs photon 60 Gy in stage III

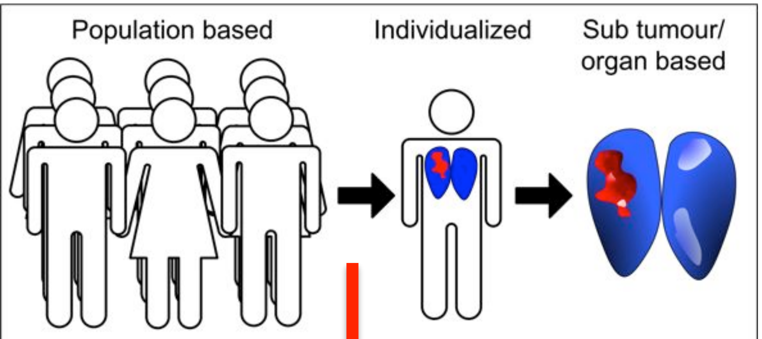
(Chang et al: Int J Rad Onc Bio Phys 65:1087-96, 2006)

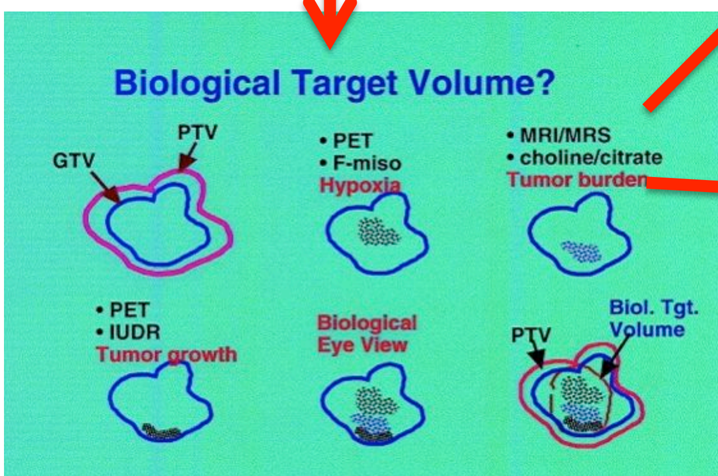
Stage III



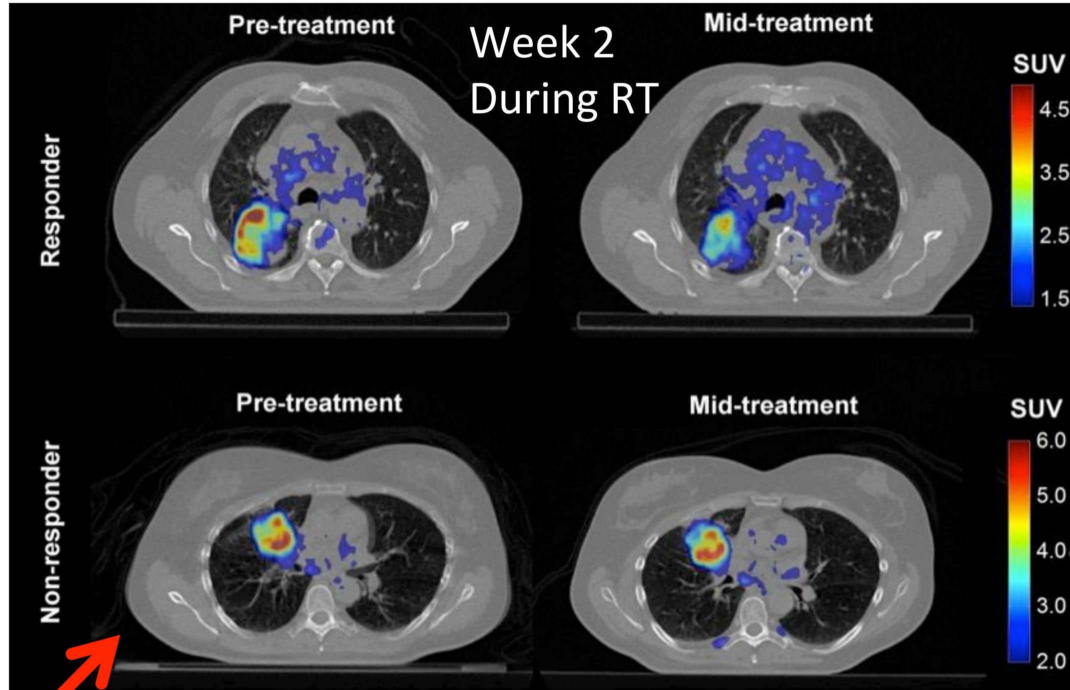
PET Guided Radiotherapy

Philippe Lambin,
Maastro, Belgium



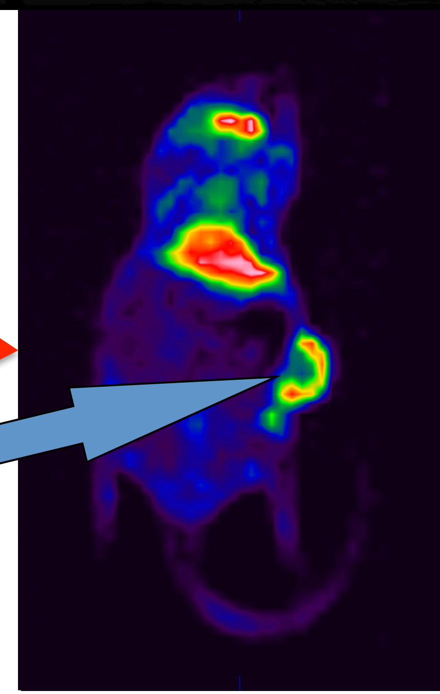


Ling et al



Van Elmpt et al

Drug Uptake
89Zirconium – Cetuximab



Aerts et al

« Cold spot »:

Less Drug Uptake

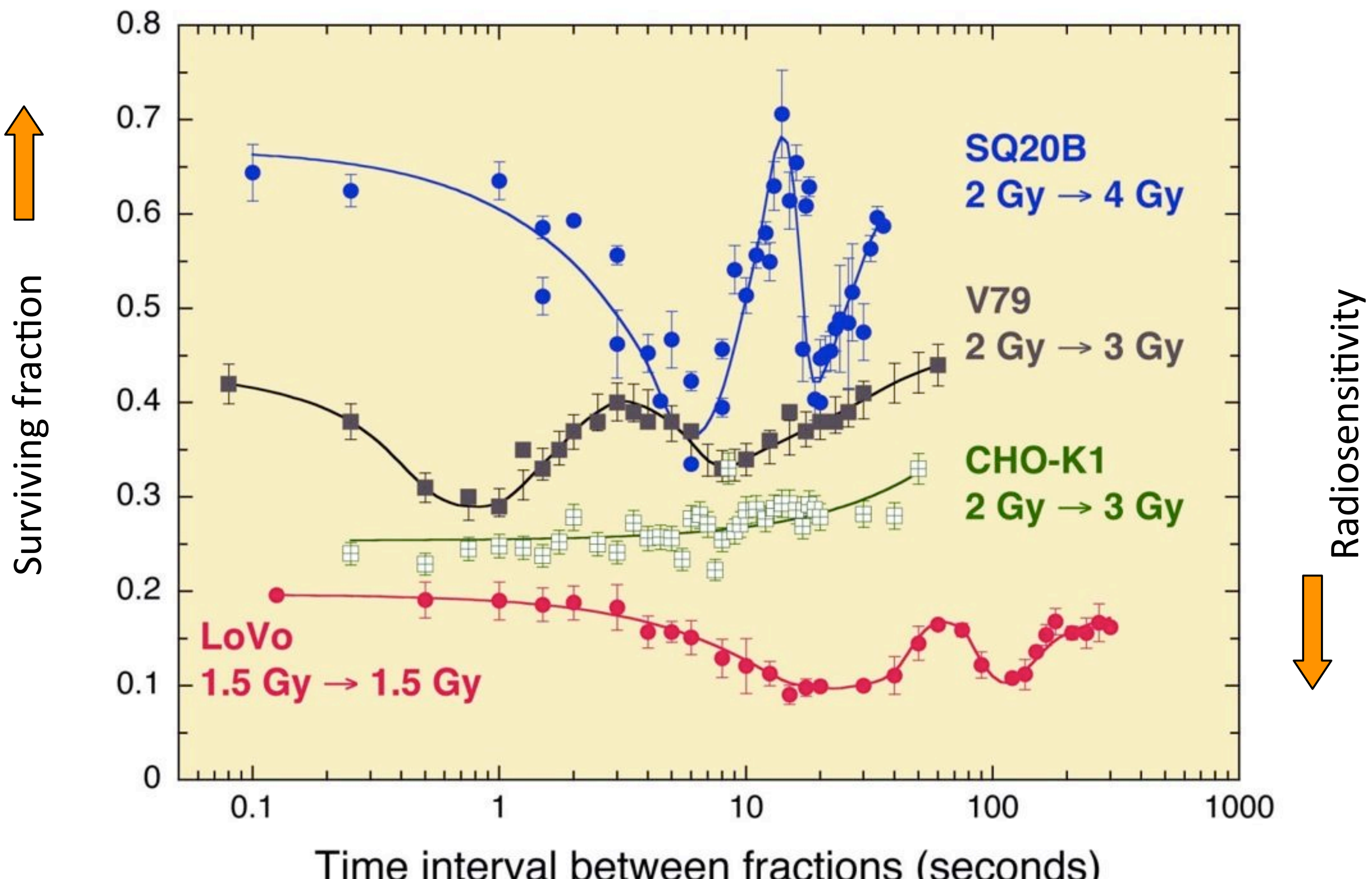
(GTV_{LDU})

R&D Early cell response to split-dose irradiation

"W-Effect"

Ponette et al. (2000) Int J Radiat Biol 76: 1233-43 - Fernet et al. Int J Radiat Biol 76: 1621-29

Vincent Favaudon



Effet dans le temps…

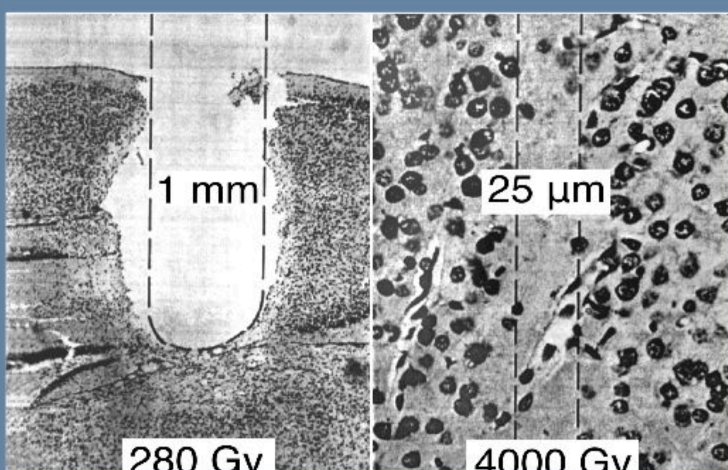
Yolanda Prezado, France : effet dans l'espace

Novel RT techniques based on ''different'' dose delivery methods

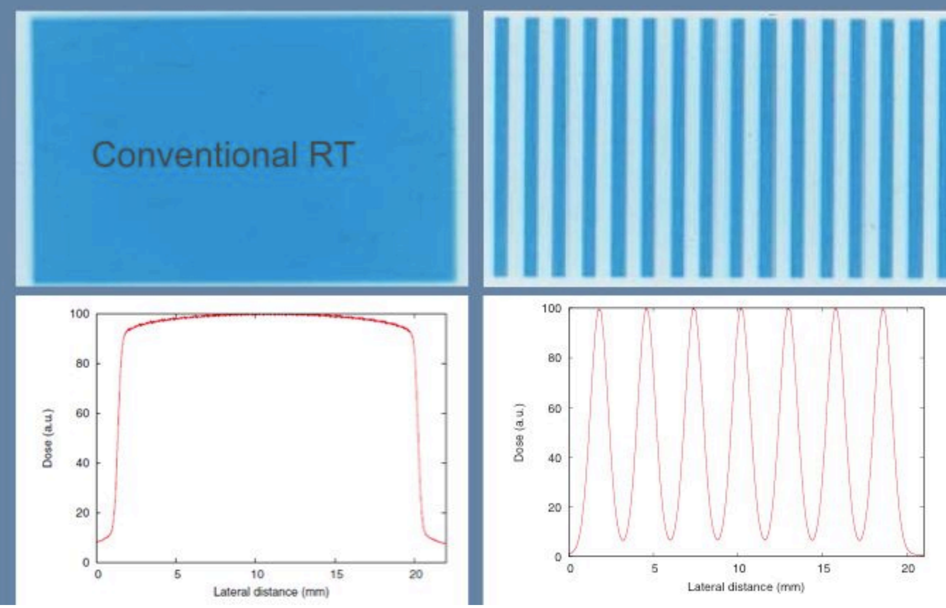
Combination

Very small field sizes (< 1mm²) + **spatial fractionation of the dose**

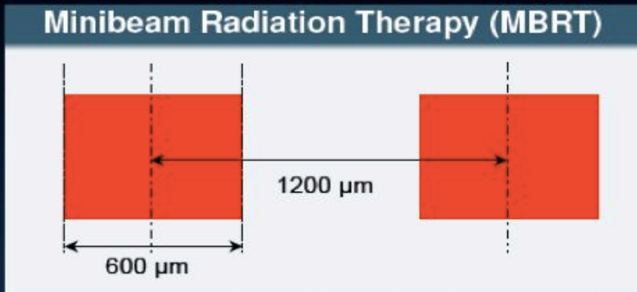
Dose-volume effects



Zeman et al., Science (1959)



X-rays minibeam radiation therapy

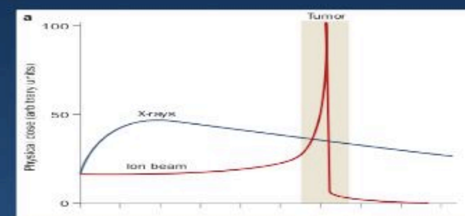


Extremely high resistance (> 100 Gy in one fraction) of healthy rat brain & increase of lifespan of glioma bearing rats

Prezado et al., J. Synchr. Radiat. 2012

Proton-minibeam radiation therapy

+



Proof of concept: promising dose distributions *(Prezado et al., Med. Phys. 2013)*

Biological experiments warranted

Perspectives: technical implementation at CPO (Orsay), development of dosimetry tools & radiobiological studies

Review Article

Transl Cancer Res 2013;2(4):269-279

Radiosensitization by gold nanoparticles: effective at megavoltage energies and potential role of oxidative stress

Karl T. Butterworth, Stephen J. McMahon, Laura E. Taggart, Kevin M. Prise

Centre for Cancer Research and Cell Biology, Queen's University Belfast, Belfast, Northern Ireland, UK

Corresponding to: Karl T. Butterworth, Ph.D. Centre for Cancer Research & Cell Biology, 97 Lisburn Road, Belfast, BT9 7BL, Northern Ireland, UK. Email: k.butterworth@qub.ac.uk.

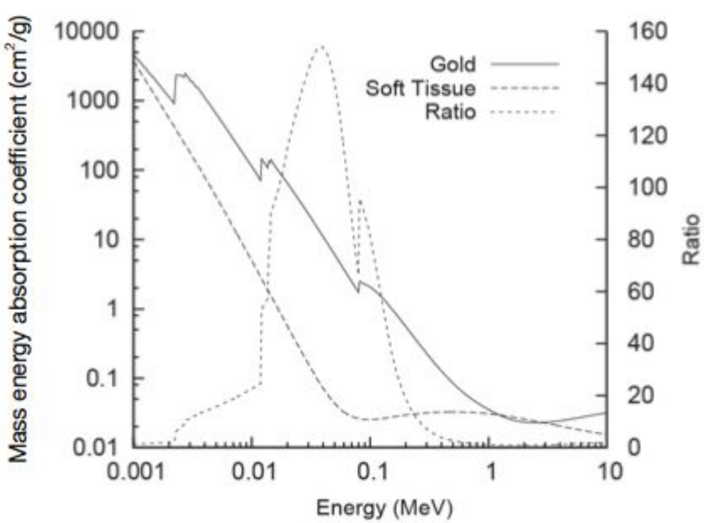


Figure 1 Comparison of the photon mass energy absorption coefficients for gold and soft tissue. The ratio of the mass energy absorption coefficients is shown as a function of photon energy. Data taken from Hubbell and Seltzer (1)

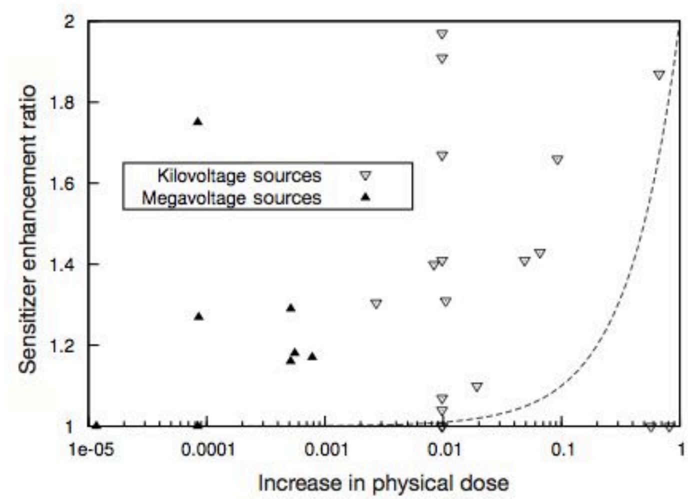


Figure 3 Comparison of predicted and observed experimental dose enhancement for gold nanoparticle studies conducted using kilovoltage (▽) and megavoltage (▲) energy sources. "Increase in physical dose" here refers to the ratio of the additional dose deposited by X-rays in the system due to the addition of GNPs to that which would be deposited in the absence of gold. The dashed line shows the trend which would be followed if the sensitizer enhancement ratio directly followed predicted increases in physical dose

Gold nanoparticles
Butterworth et al
Translat Cancer Res, 2013

In vitro

Table 1 Summary of experimental parameters for investigations demonstrating the radiosensitizing properties of GNPs *in vitro*

Author	Size (nm)	Concentration	Surface coating	Cell model	Source energy	Observed SE˜
Butterworth *et al*. (30)	1.9	2.4 μM	Thiol	DU-145	160 kVp	<1
		0.24 μM		MDA231MB		<1.67
				AG0-1522		<1.97
				Astro		<1.04
				L132		<1
				T98G		<1.91
				MCF-7		<1.41
				PC-3		<1.07
Chang *et al*. (31)	13	11 μM	Citrate	B16F10	6 MV e^-	1
Chien *et al*. (32)	20	<2 mM	Citrate	CT-26	6 MV	1.19
Chithrani *et al*. (33)	14	1 μM	Citrate	HeLa	220 kVp	1.17-1.6
	74				6 MV e^-	
	50				662 keV	
Coulter *et al*. (34)	1.9	12 μM	Thiol	DU-145	160 kVp	<1.8
				MDA-231MB		
				L132		
Geng *et al*. (35)	14	5 μM	Glu*	SK-OV-3	90 kVp	1.3
					6 MV	1.2
Jain *et al*. (36)	1.9	12 μM	Thiol	DU-145	160 kVp	<1.41
				MDA-231MB	6 MV	<1.29
				L132	15 MV	1.16
					6 MeV e^-	<1.12
					16 MeV e^-	1.35
Kong *et al*. (37)	10.8	15 nM	Glu*	MCF-7	200 kVp	1.3
			AET^	MCF-10A	662 keV	1.6
					1.2 MV	
Lui *et al*. (38)	6.1	>1 mM	PEGˇ	CT-26	6 keV	2
				EMT-6	160 kVp	1.1
					6 MV	1
Rahman *et al*. (39)	1.9	<1 mM	Thiol	BAEC	80 kV	20
					150 kV	1.4
					6 MV e^-	2.9
					12 MV e^-	3.7
Roa *et al*. (40)	10.8	15 nM	Glu*	DU-145	662 keV	>1.5
Zhang *et al*. (41)	30	15 nM	Glu*	DU-145	200 kVp	>1.3

*thioglucose; ^cysteamine; ˇpolyethyleneglycol; ˜Sensitizer enhancement defined as the level of radiosensitization observed when

In vivo

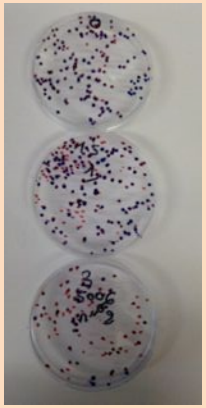
Table 2 Summary of experimental parameters for investigations demonstrating the radiosensitizing properties of *in vivo*

Author	Size (nm)	Surface coating	Dose (g/kg^{-1})	Tumour conc (mg/g^{-1})	Cell model	Source energy	Outcome
Chang *et al*. (31)	13	Citrate	0-0.036	74	B16F10	6 MeV e^-	MS
Hainfeld *et al*. (42)	1.9	Thiol	0-2.7	7	EMT-6	250 kVp	1 year OS
Hainfeld *et al*. (43)	1.9	Thiol	0-2.7	7	SCCVII	68 keV	OS
						157 keV	
Hainfeld *et al*. (44)	11	Thiol	0-4	1.5	Tu-2449	100 kVp	1 year OS
Hebert *et al*. (45)	5	DTDTPA-Gd	0-0.675	0.1	MCF7-L1	150 kVp	MS

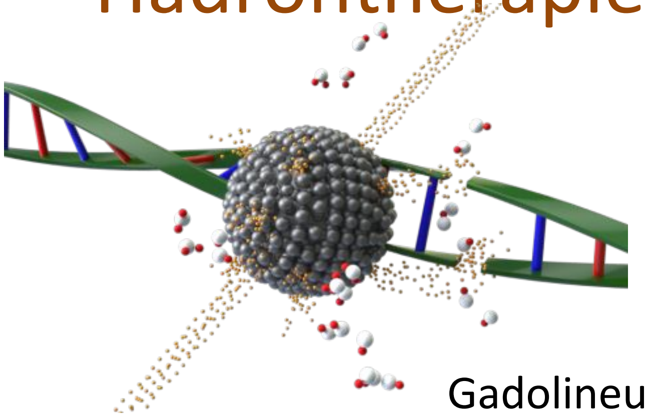

Erika PORCEL
Institut des Sciences Moléculaires d'Orsay

Soutenance de thèse

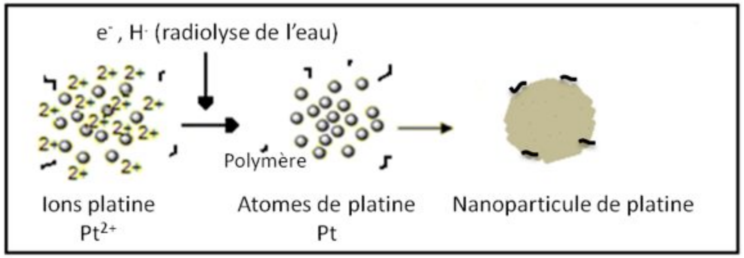
Direction : S. LACOMBE


Utilisation des Nanoparticules pour améliorer les performances de la Hadronthérapie

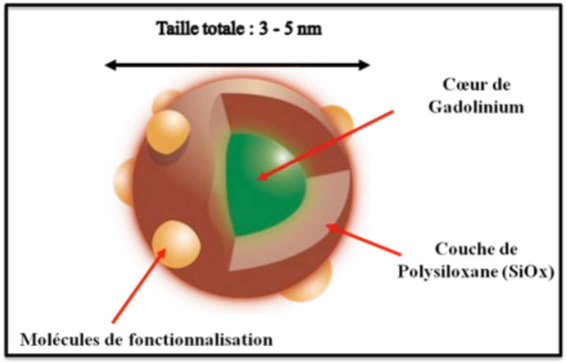


Platine



Remita et al

Gadolineum

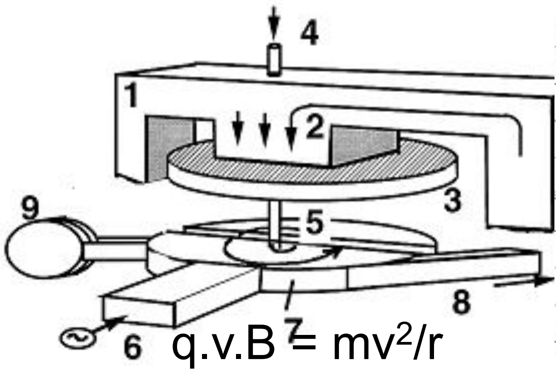


Mowat et al

Multidisciplinarité : besoin d'un langage commun

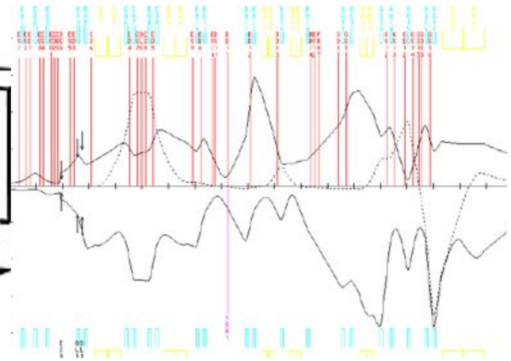
« Hadrontherapy » for a physicist?

Accelerators

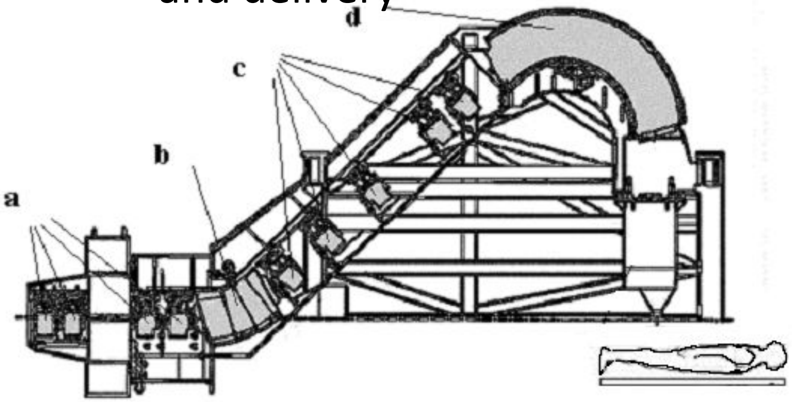


$q.v.B = mv^2/r$

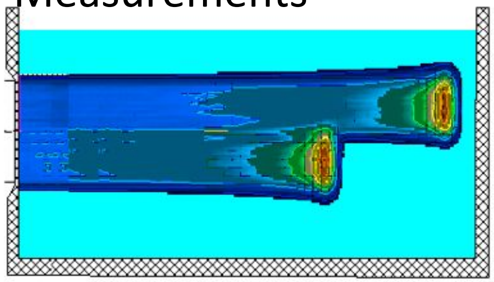
Beam transport

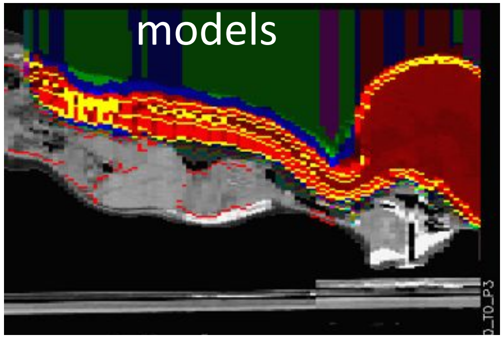


and delivery



Measurements





$$(dE/dx)= 4 \pi z_{eff}^2 e^4 N_A Z/A\, m_e v^2 \{ \ln (2mv^2/ I (1-\beta^2)) - \beta^2 - \Sigma(Ci/Z) \}$$

$$\theta_0 = 14.1 \; z / p v \; \{ \mathrm{sqrt} (L / L_R) \; (1+ \log(L /L_R) / 9) \}$$

« Hadrontherapy » for the physician

2．筑波大学の陽子線治療成績

筑波大学の陽子線治療は、１９８３年以来色々な部位を対象に行われていますが、なかでも日本人に多い深部臓器がんに主体を置いているという特徴があります。表５に治療部位と治療成績を揚げました。これまでの経験で、皮膚、頭頸部、肺、食道、肝臓、子宮、膀胱、前立線などで満足すべき結果が得られています。

第６図から第14図までは、実際に陽子線で治療した患者さんの写真です。

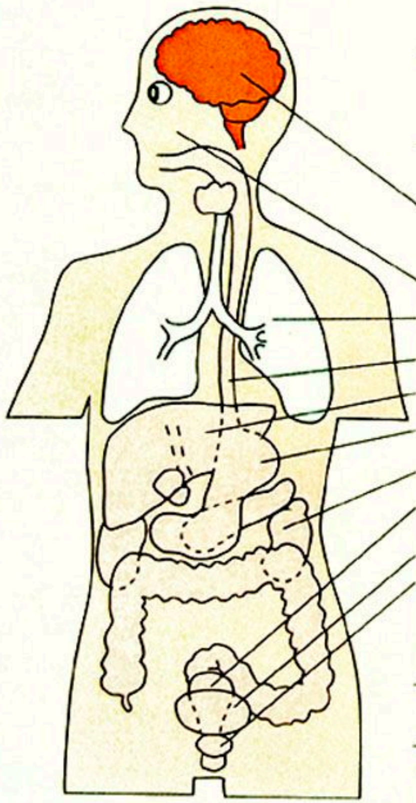


表５　筑波大学の陽子線治療結果

部位	患者数	局所治癒率推定(%)	3年生存率	後遺症
皮膚	8	7 (87.5)	87.5	0
脳 ｸﾞﾘｵｰﾑ	13	3 (23.1)	18.5	3
髄膜腫など	9	8 (88.9)	75.0	0
頭頸部	15	11 (73.3)	81.5	0
肺	19	14 (73.7)	54.1	1
食道	23	18 (78.3)	51.6	3
肝臓	30	26 (86.7)	25.5*	0
胃	5	3 (60.0)	61.0	0
腎臓	5	2 (40.0)	60.0	0
子宮	24	21 (87.5)	72.7	3
膀胱	12	8 (66.7)	62.5	2
前立腺	7	7 (100.0)	68.6	0
小児腫瘍	4	4 (100.0)	75.0	0
その他	4	3 (75.0)	100.0	1
合計	178	135 (75.8)		13(7.1%)

*肝機能良好例の3年生存率75.0%

« La physique médicale demain: perspectives en radiothérapie »
Vue de la Biologie

Marie Dutreix

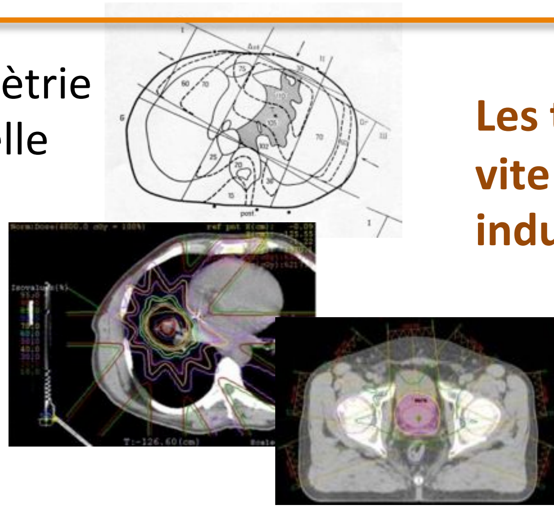
1950

Une dosimètrie
Multi-échelle

2D

3D

4D



Les techniques et les instruments ont progressé plus vite que notre connaissance des effets que ces rayons induisent sur le vivant

Radiothérapie conformationelle
Radiation avec modulation d'intensité (IMRT) et arc thérapie volumétrique (VMAT)

2013

TISSU SAIN &TISSU TUMORAL , QUELLE DOSE?

?

Plusieurschallenges liés aux nouveaux faisceaux

- les micro- et mini-faisceaux
- les ultrahauts débits de dose (irradiations pulsées)
- l'hadronthérapie
- les plasmas….

Plusieurs challenges liés aux combinaisons

- nanoparticules à effet amplificateur des rayons
- thérapies ciblées (inhibiteurs de l'angiogénèse, de la réparation, du cycle…)

DOSE relative?

DOSE cumulée?

DOSE apparente?

DOSE biologique?

L'intégration de la Physique et de la Biologie: une révolution à venir!

EXPERIMENTAL RADIOTHERAPY FACILITY

institutCurie
Ensemble, prenons le cancer de vitesse.

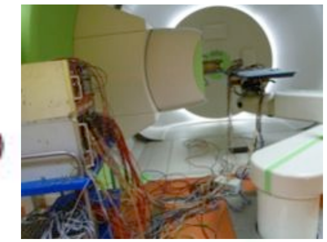
Radiations sources:

- Name : KINETRON
- Source: Linear Accelerator
- Energy: 4,5 MeV electrons
- *Dose rate: from 4 Gy/min to $4 X 10^3$ Gy/s (mean dose rate)*
- Applications:
  - *Pulsed Radiolysis*
  - *Cells irradiations*
  - *Mice irradiations (total body, localized)*

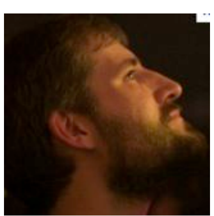
- Name: IBL 637
- Source: Cesium 137
- Energy: 662 keV photons
- *Dose rate: 1 Gy/h to 10 Gy/min*
- Applications:
  - *Cells irradiations*
  - *Mice irradiations (total body)*

- Name: Xrad320Dx
- Source: 320 kV X-rays generator
- Mean energy: from 30 keV to 160 keV
- *Dose rate: from 0.05 Gy/min to 4 Gy/min*
- Applications:
  - *Cells irradiations*
  - *Mice irradiations (total body, localized)*

Access to proton beams of Protontherapy Center of Orsay (as part of France Hadron)
- Source: Cyclotron (IBA)
- Energy: 76-201 MeV
- Raw or Spread Out Bragg Peak
- *Dose rate: 0.1 to 20 Gy/min*
- Applications:
  - *Cells irradiations*
  - *Mice irradiations (total body, localized)*



Coming Soon (available in 2014): irradiator/CT
- Source: 225 kV X-rays generator
- Mean Energy: 30-100 keV
- *Dose rate: 0.05 to 1 Gy/min*
- Applications:
  - *Small fields irradiations (diameter:1 mm)*
  - *Image guided radiotherapy*



Frederic Pouzoulet

Sophie Heinrich

La Physique Médicale demain: Perspectives en Radiothérapie Externe

Conclusions

1) Physique et technologie :
   vers la radiothérapie Adaptative
   avec optimisation du flux

2) Besoin d'ouverture en R&D :
   par ex vers la Biologie

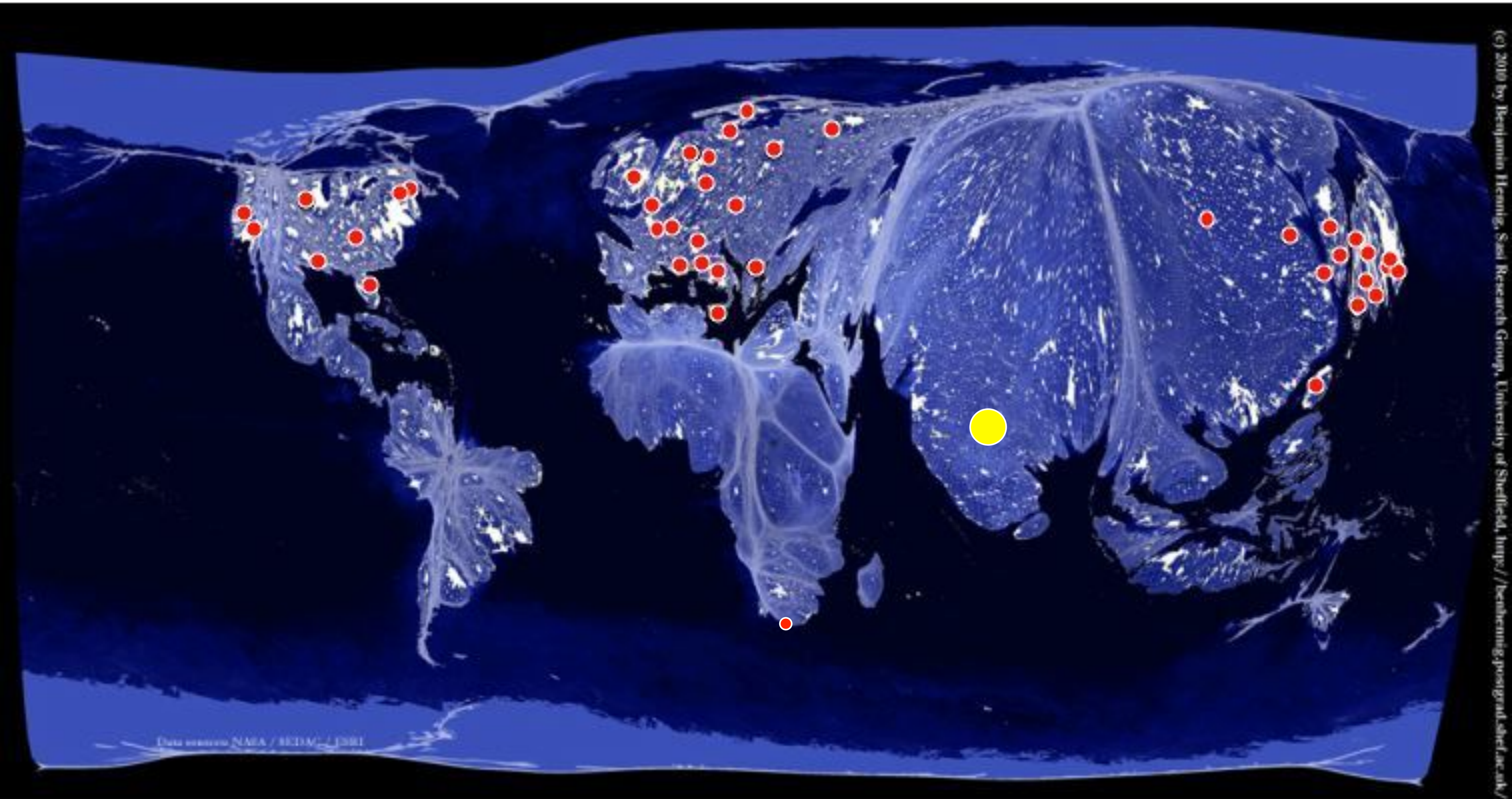
Image	IGRT
Physics	PGRT
Biology	BGRT
Economical	ECRT
……..	

Clinical	CGRT

Social	SGRT

Proton and Carbon-Ion Therapy Facilities Around the World

Area resized according to the nation's **population** (2010)



From Bill Chu, PTCOG 50, USA

Merci !