Medical Physics, High Energy Physics and Hadrontherapy

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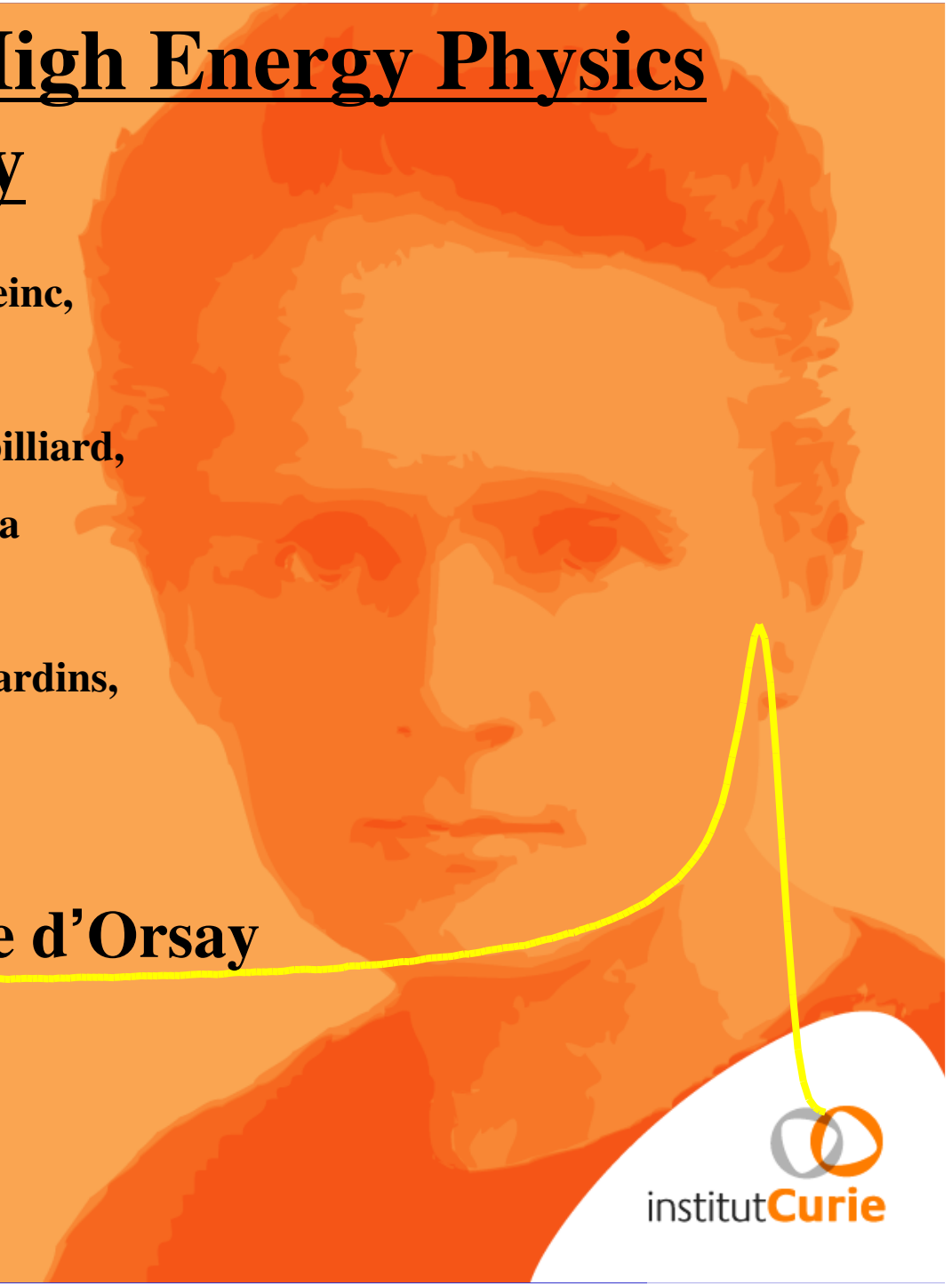
A.Fourquet

Institut Curie
Centre de Protonthérapie d'Orsay
France



Sarajevo
24th mai 2014

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The goal :

- **Not to teach you "hadrontherapy" in 1 hour**
- **But to give you a "fast movie" of this passionnating world …**

…and give you the wish to know more !

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Menu :

I. Medical Physics in RT : past, present

I. Hadrontherapy :
   1. Types of particles
   2. Interactions with electric (E) and magnetic fields (B)
   3. Interaction with matter (eg: beam line, patient)
   4. Planning and treating with particles
   5. Moving towards heavier ions

III. The future : revisiting radiation biology

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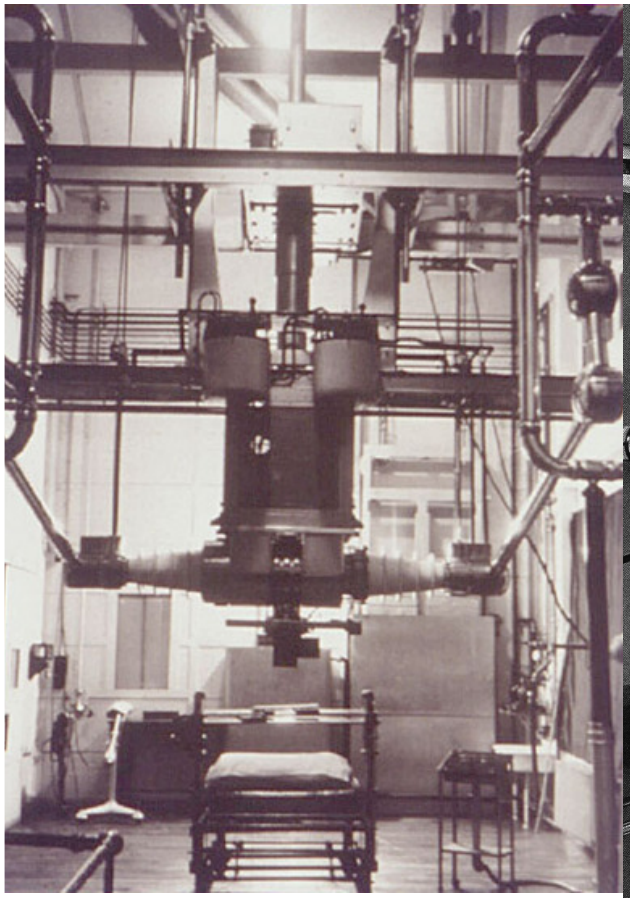
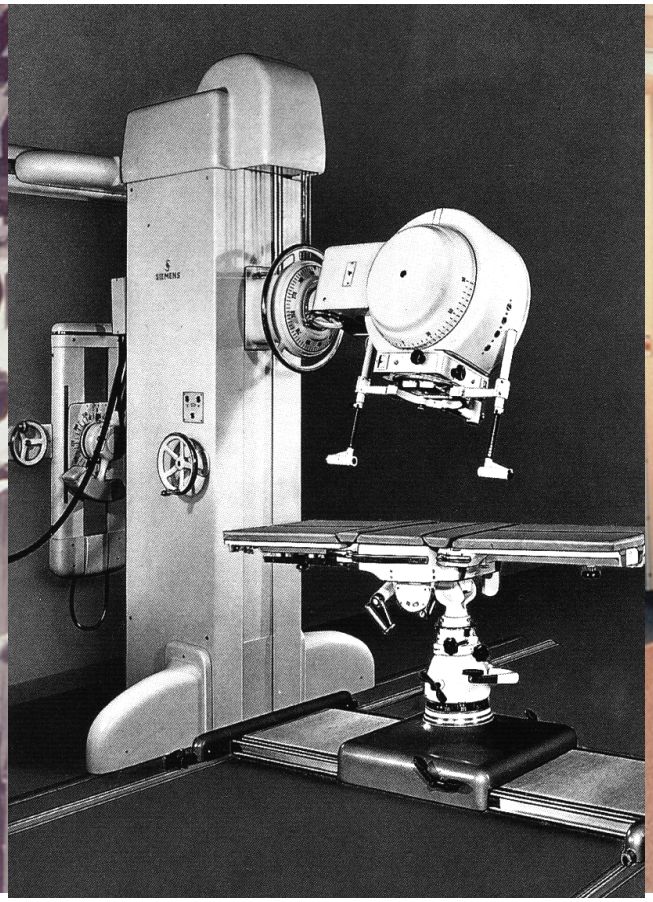
The technological evolution of external radiation therapy : 100 years of history



600 kV- 1930'



Gammatron Siemens 1956 Co-60 et Cs-137

Linacs

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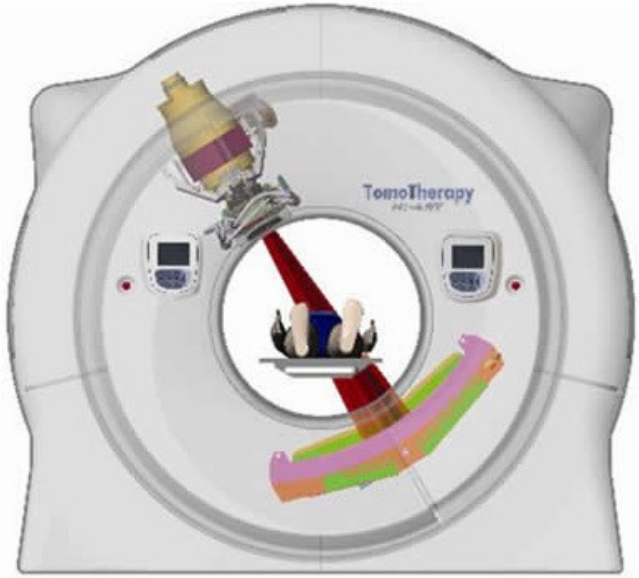
Physics and technology: delivery systems in external radiation therapy

RapidArc or equivalents (wphospitals.org)

www.cyberknife.com



Tomotherapy

Vero

ViewRay (MRI+Co)

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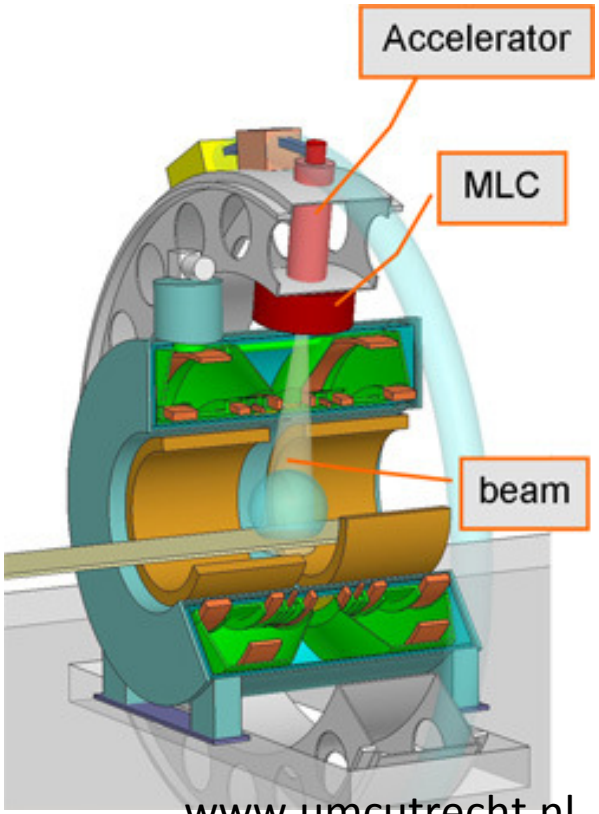
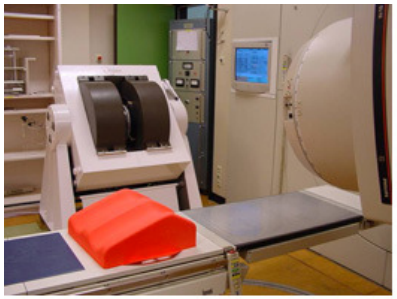
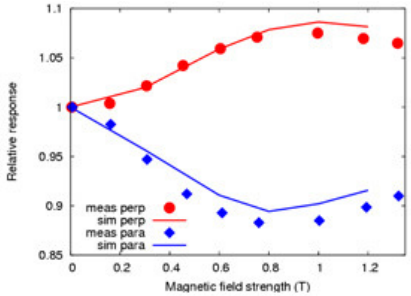
Integrating 1.5T MRI functionality with a radiotherapy accelerator Lagendijk et al, Utrech

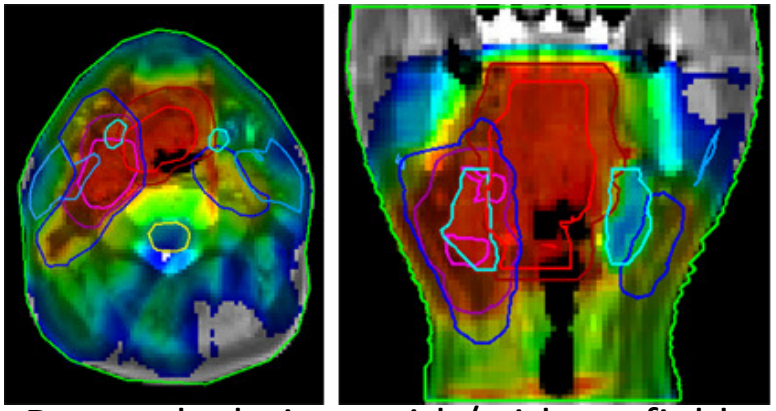


www.umcutrecht.nl

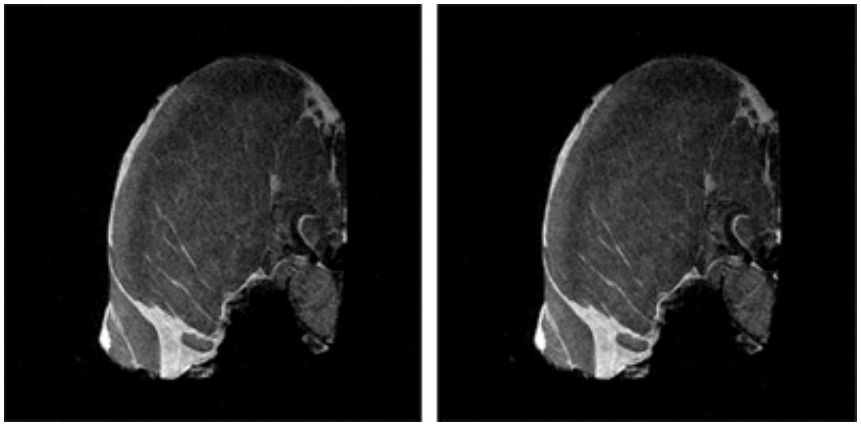




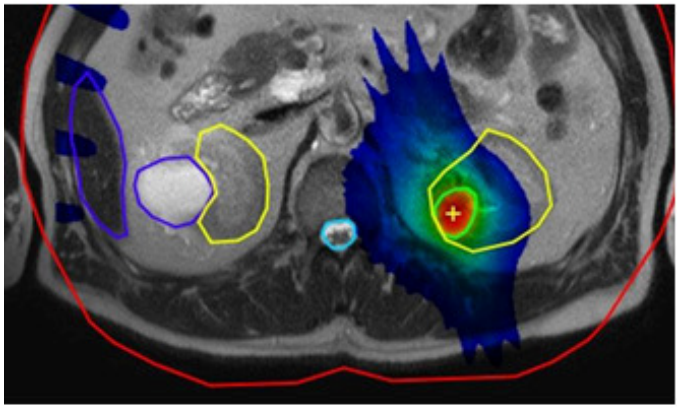
Ion chamber response vs orientation in magnetic field



Dose calculations with/without field

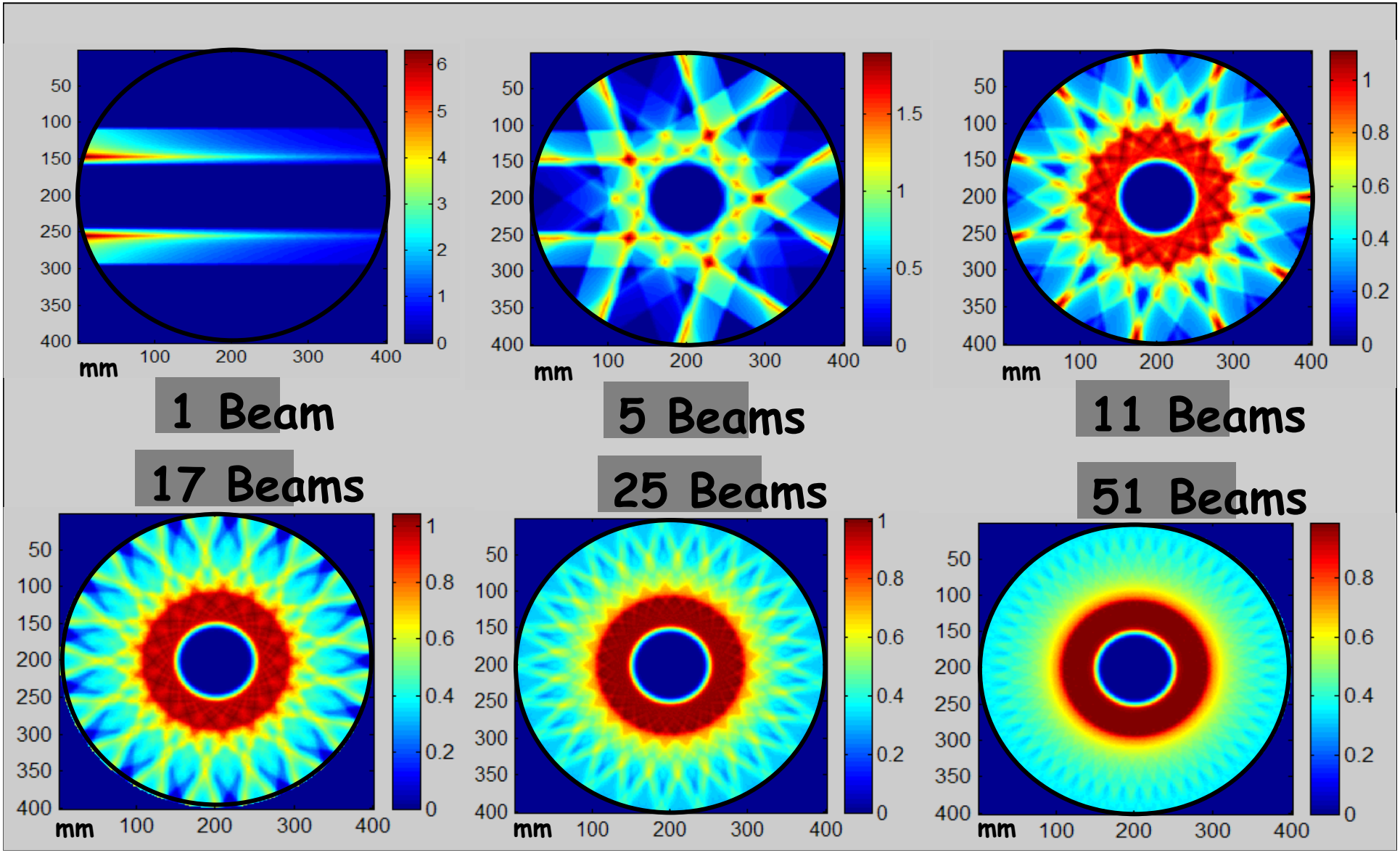


T2 pork chop with/without radiation beam



Renal carcinoma MRI & breath hold IMRT

Multiplicity of incidences// changing the role of the energy



(from Tomotherapy)

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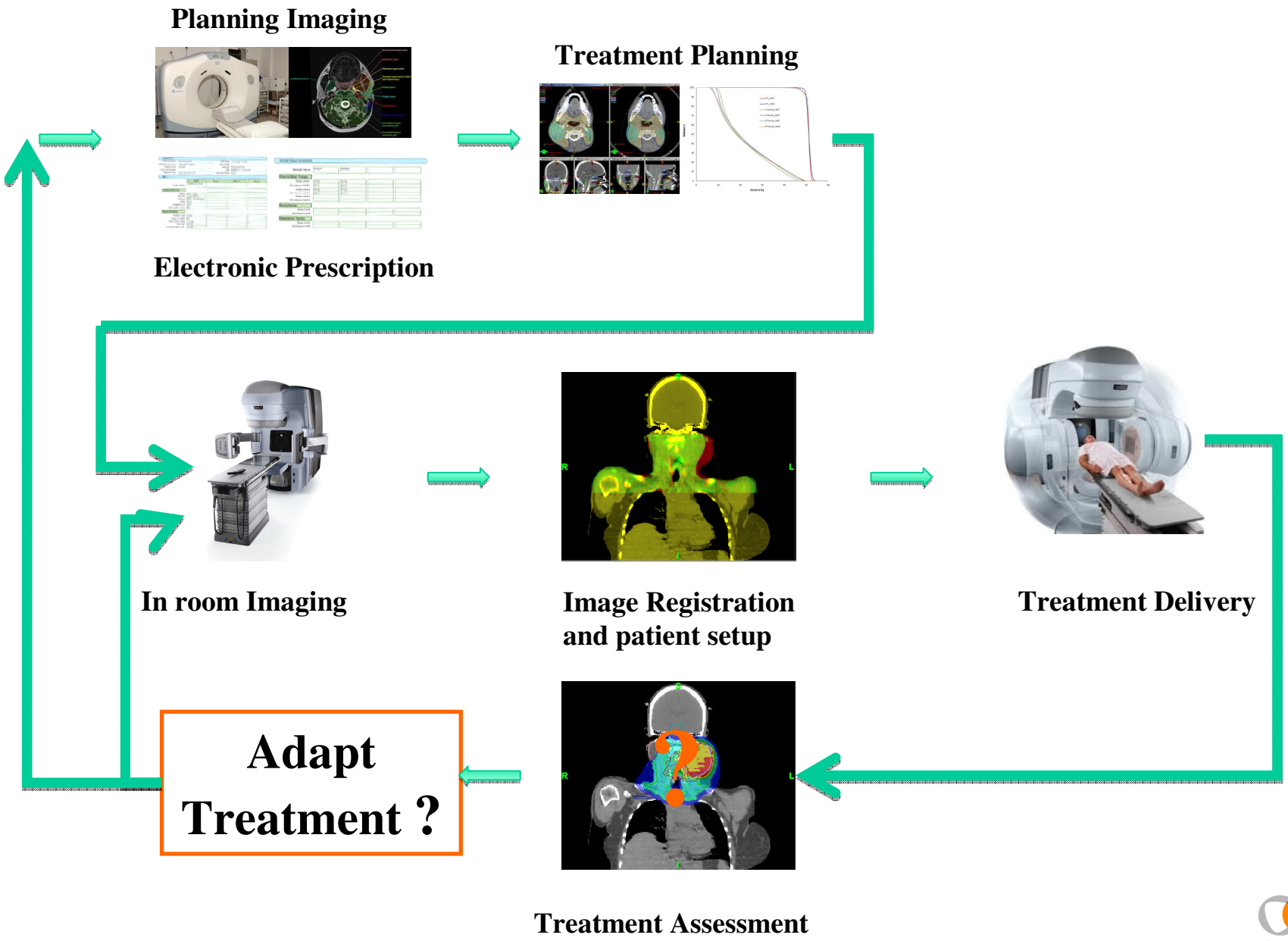
The workflow: towards “Adaptive therapy”



Courtoisy : G. Olivera et al

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Medical Physics

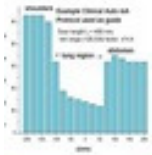
The International Journal of Medical Physics Research and Practice

(Similar for PMB)

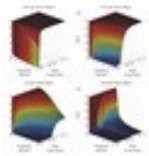
Research funded by Industry ?

Imaging

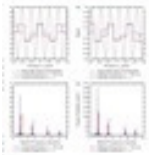
EDITOR'S PICKS



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

MOST READ

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

Charged particles

The more important heavy [illegible] radiotherapy of the future is more likely to be with heavy ions rather than protons

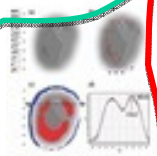
MOST CITED THIS MONTH

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

A technique for the quantitative evaluation of dose distributions



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

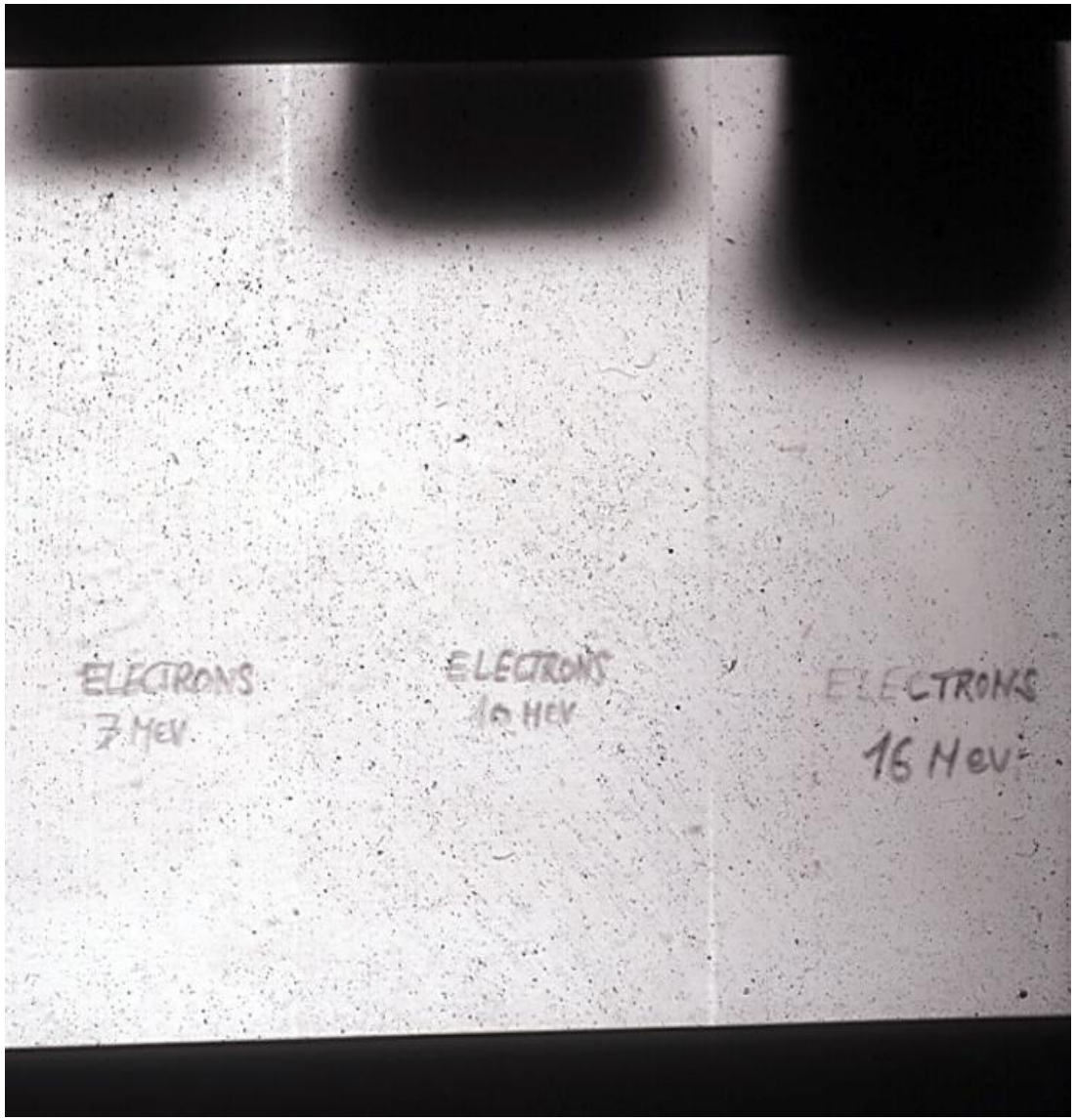
Dose Accuracy and Evaluations

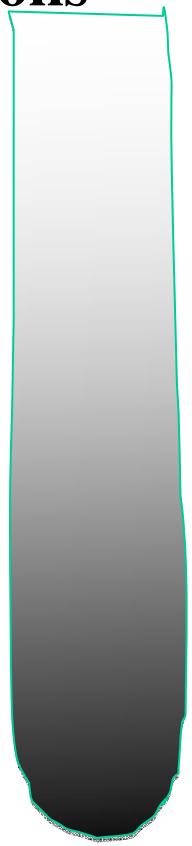
irie

Electrons

Protons/ Ions

Photons





J-C.Rosenwald & A. Mazal

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II. « Hadrons » in therapy

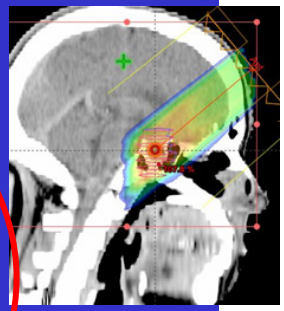
Physical selectivity and/or Radiobiological effects

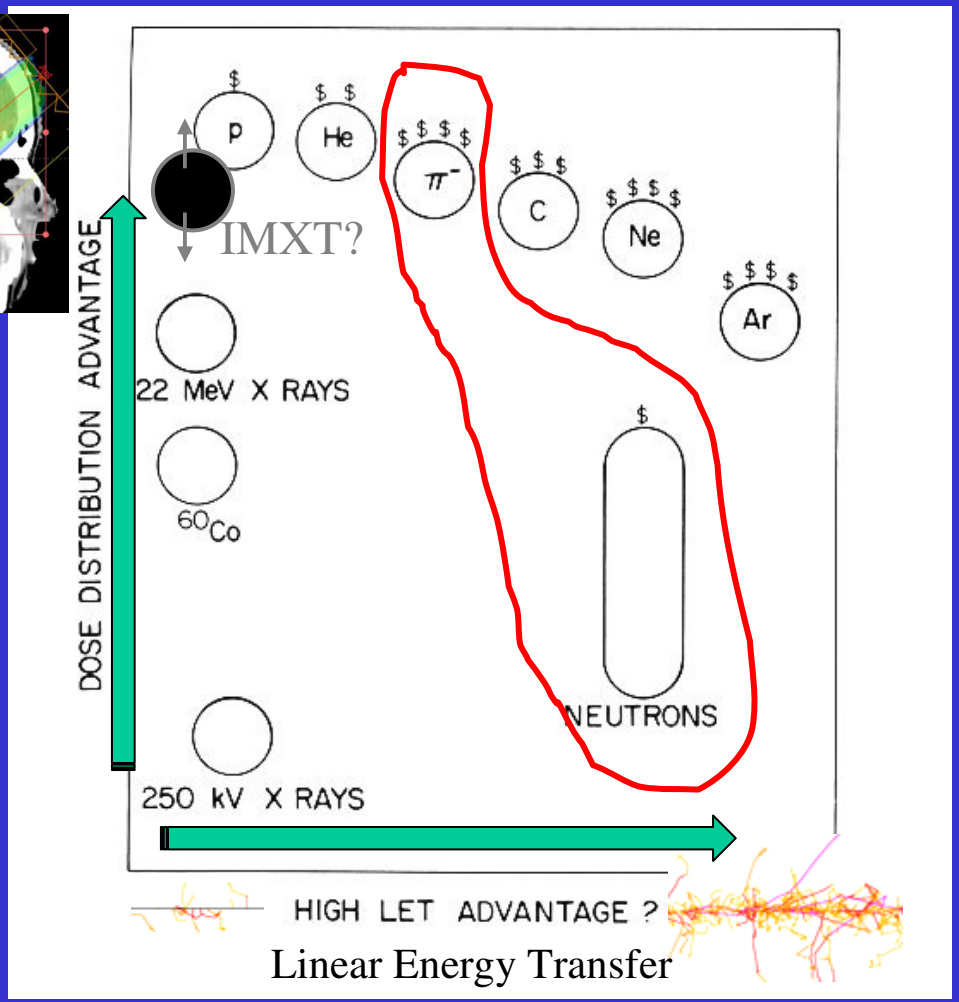
* pions

* fast & slow neutrons

* protons

* light and heavy ions





Raju & Koehler, 1980

« Hadrons » in therapy

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* pions

* fast
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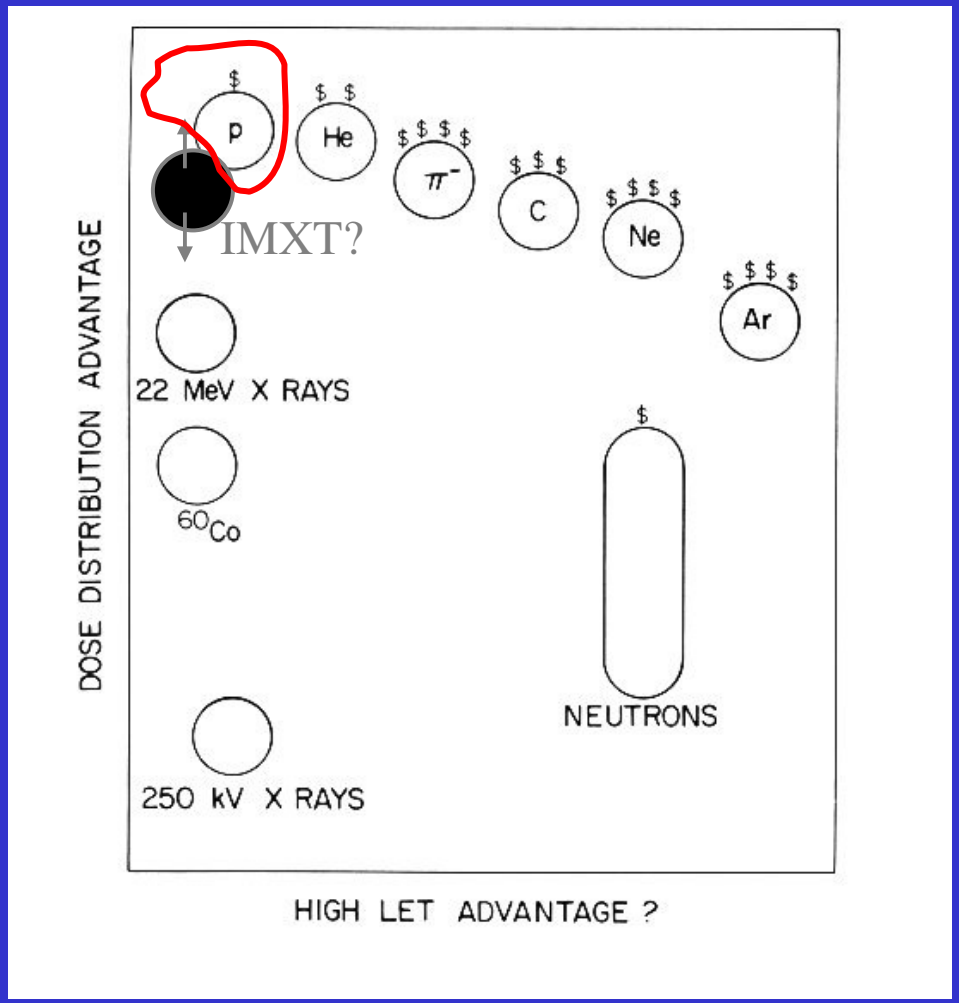
* protons

* light and heavy ions



Raju & Koehler, 1980

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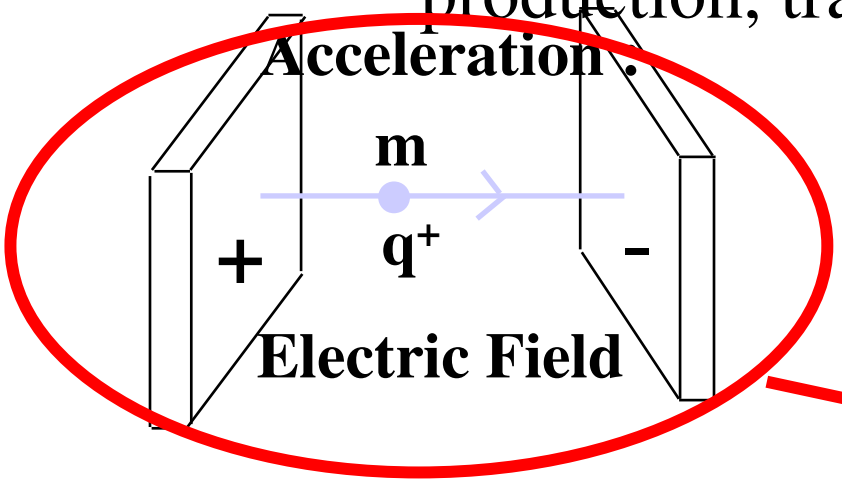
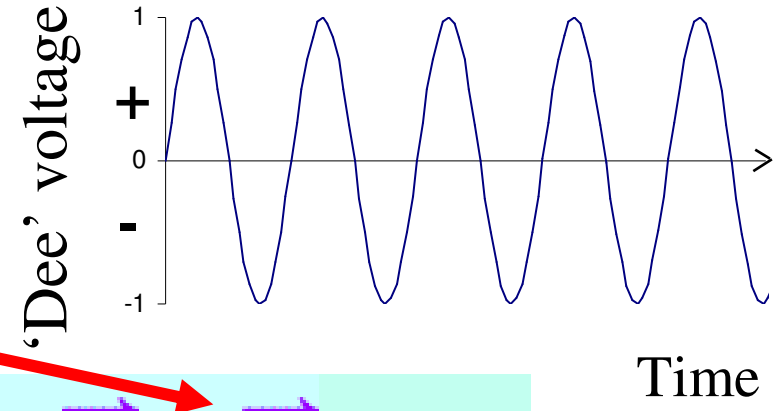
Interaction with electric and magnetic fields : Beam production, transport & delivery

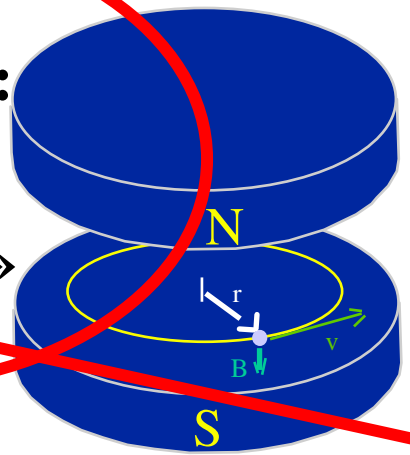




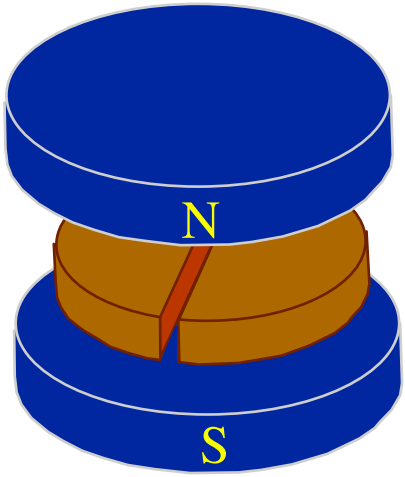
Acceleration of a Charged Particle : $\vec{ma} = q(\vec{E}$

Bended Trajectory:

Magnetic Field « B »



'Dee' Electrodes in Magnet

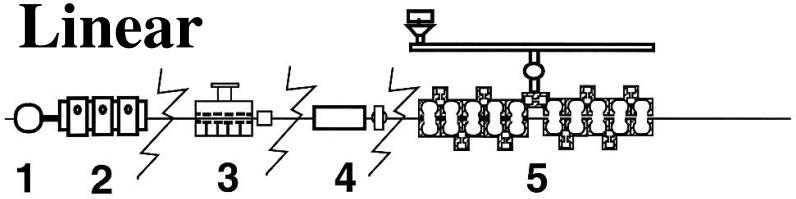


Particle Motion in Magnetic Field

$\vec{ma} = q(\quad \vec{V} \wedge \vec{B})$

$\vec{ma} = q(\vec{E} + \vec{V} \wedge \vec{B})$

a) **Linear**

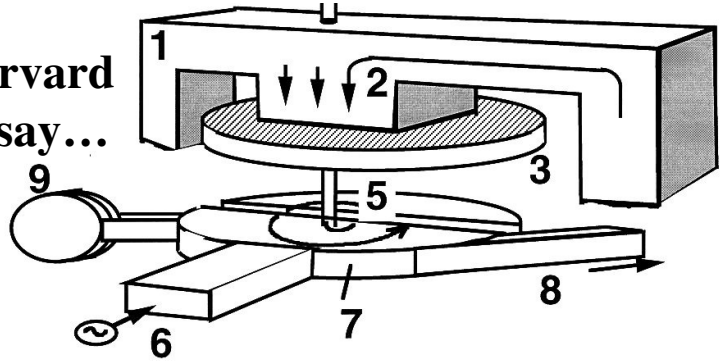


Synchrocyclotron

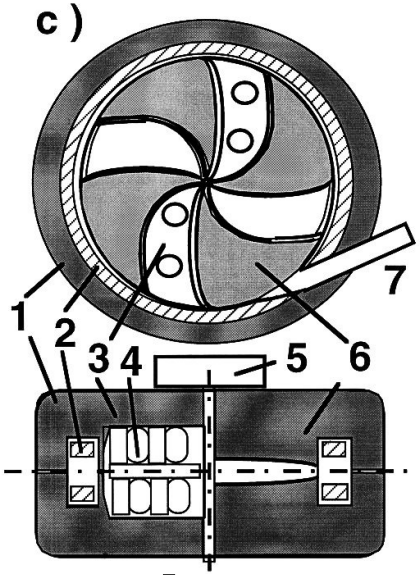
b)

Harvard

Orsay…

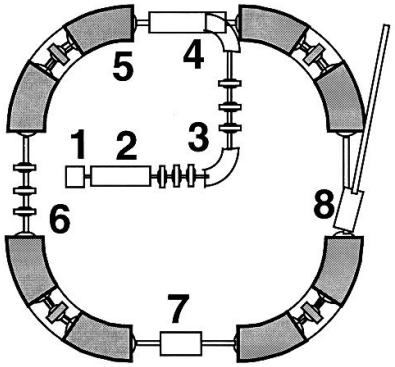


c)



cyclotron

d)



synchrotron

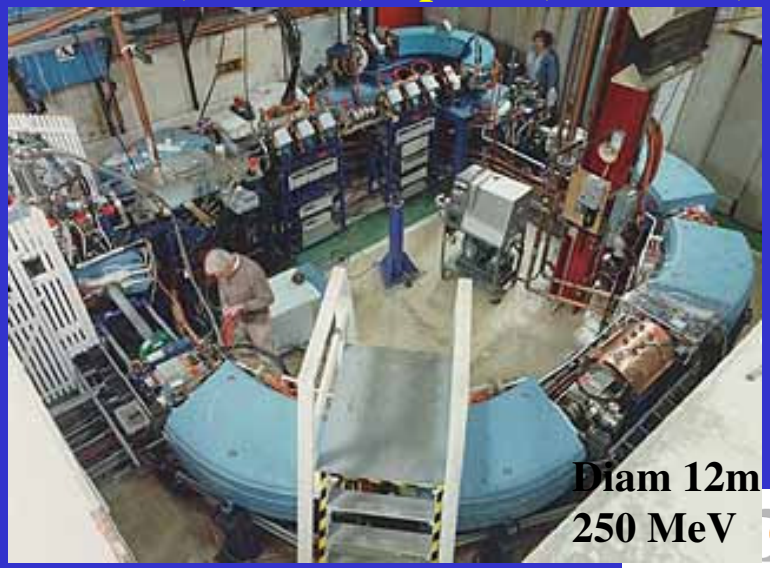
b) Synchrocyclotron (StillRivers-Mevion, IBA

c) Cyclotron (IBA, Varian-Accel, Sumitomo)

Diam 4m
235 MeV

d) Synchrotron

(Mitsubishi, Hitachi, Optivus, Siemens,..



Diam 12m
250 MeV

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How many of you think cyclotrons are better than synchrotrons for hadrontherapy ?

And the opposite ?

Why?

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	Cyclotrons	*Synchrotrons*
size	**small**	**big**
weight	**heavy**	**light**
operation	**small number of parameters**	**double stage of acceleration**
energy	**fixed, need degrader**	**variable at accelerator**
intensity	**high, easy**	**limited**
activation	**high upstream**	**low upstream**
shielding	**larger (degrader)**	**lower**
frequency	**continuous**	**pulsed**
intens mod	**Easy … to complex**	**Easy… to complex**
extraction	**steering, septum**	**resonance**
extracted beam	**symetrical**	**asymetrical**
power	**stable load**	**peak power**
….	**….**	**….**

(arguments given by a cyclotronist…)

Ions !

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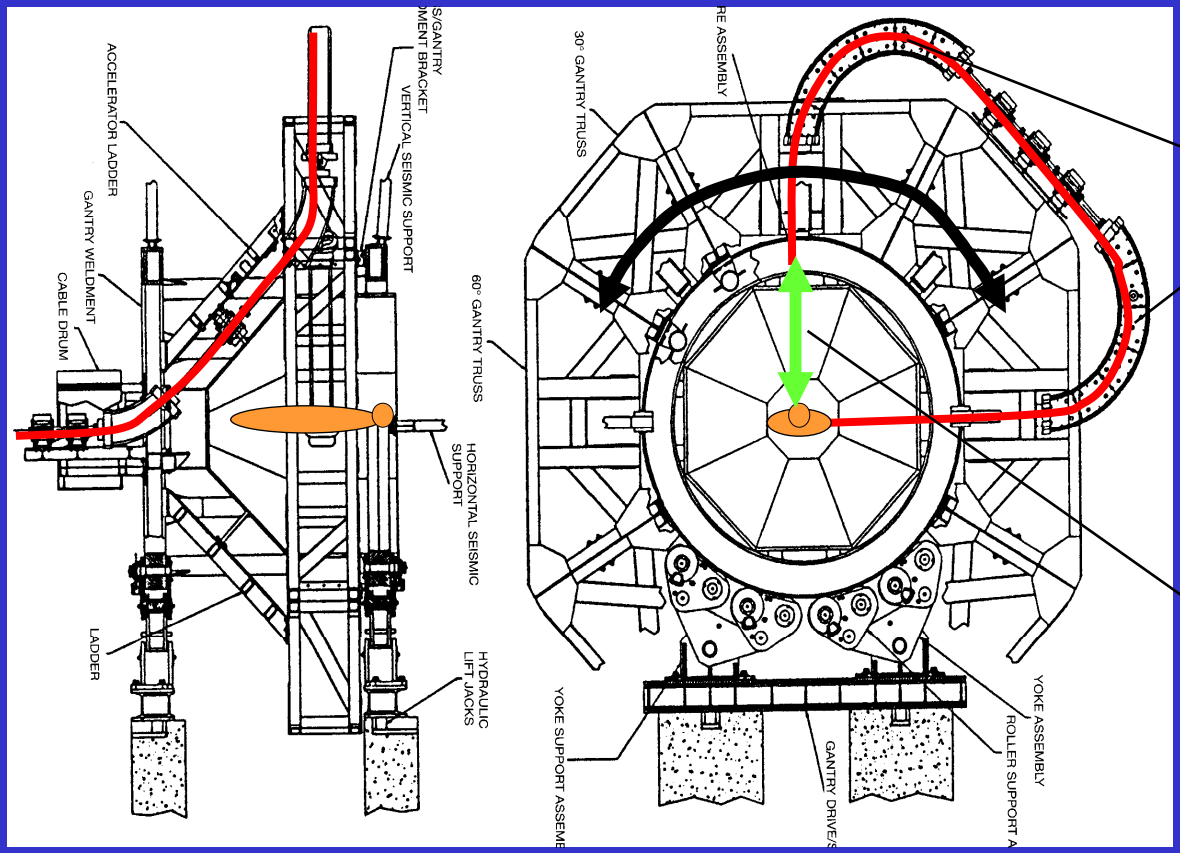
Proton treatment gantries

The Loma Linda passive scattering proton gantry

12 meter diameter



Bending magnets

Drift space to patient

Side view

Front view

From T.Lomax & E.Pedroni, PSI & G.Coutrakon, LomaLinda

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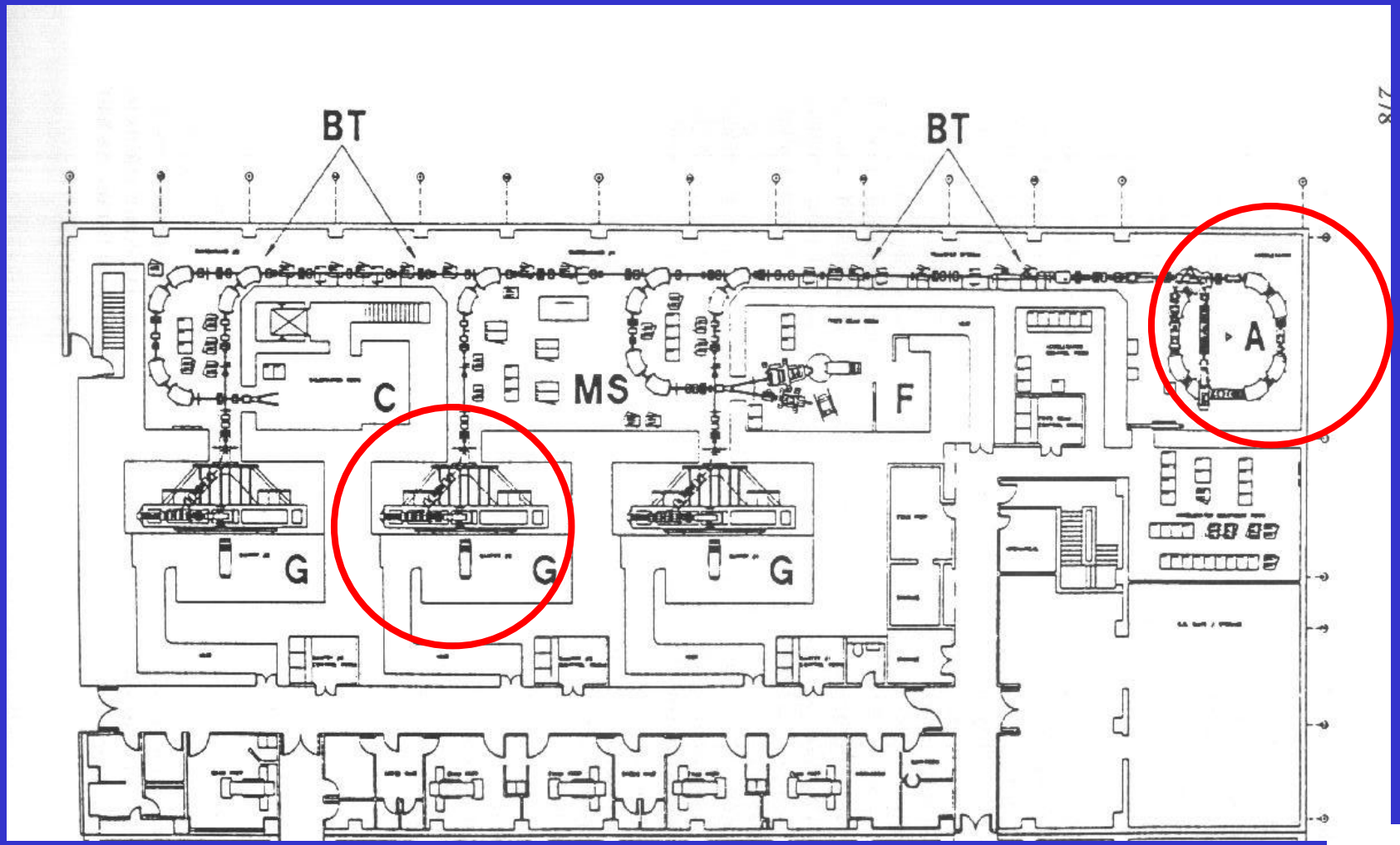
A typical hospital-based protontherapy center



Loma Linda, Ca, USA

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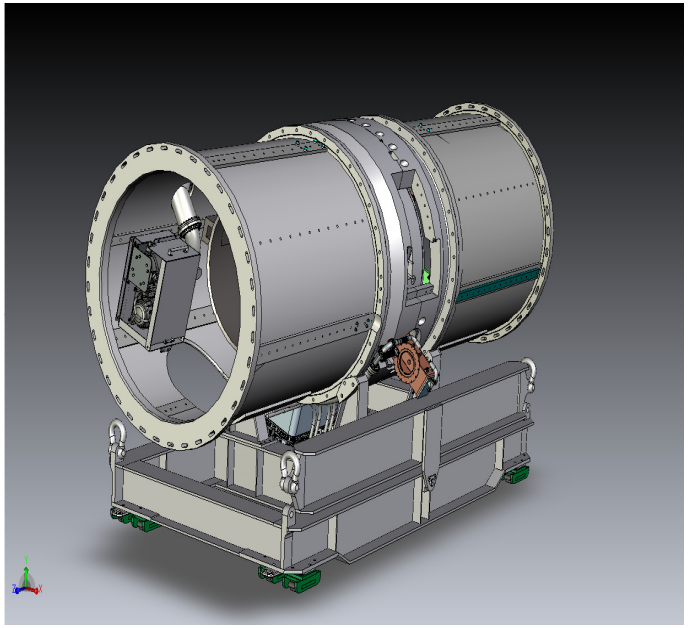
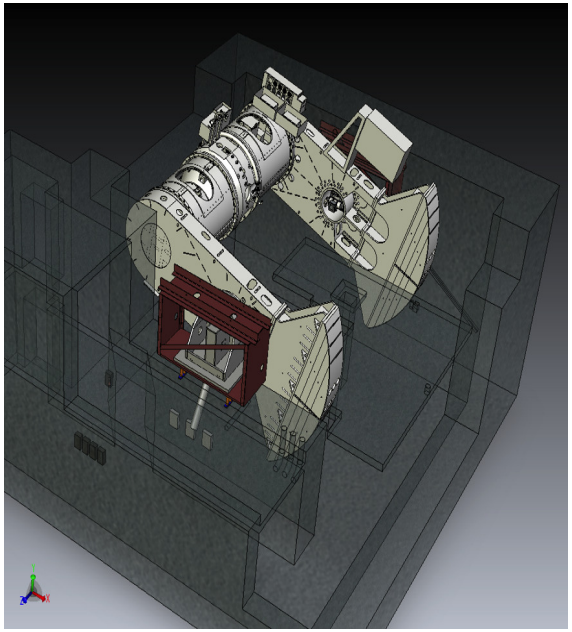
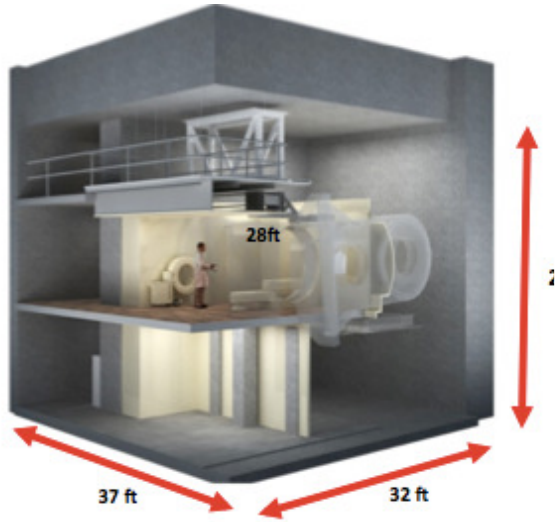
Accelerator Installation (U.Washington, 2011)

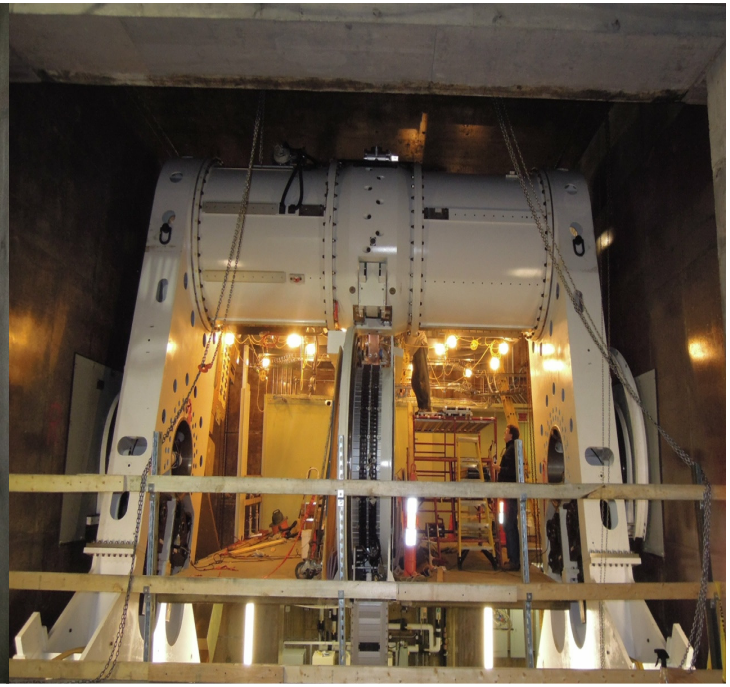




MEVION medical systems

(Ex Still-Rivers)





“20-25M$”
(+ building)?

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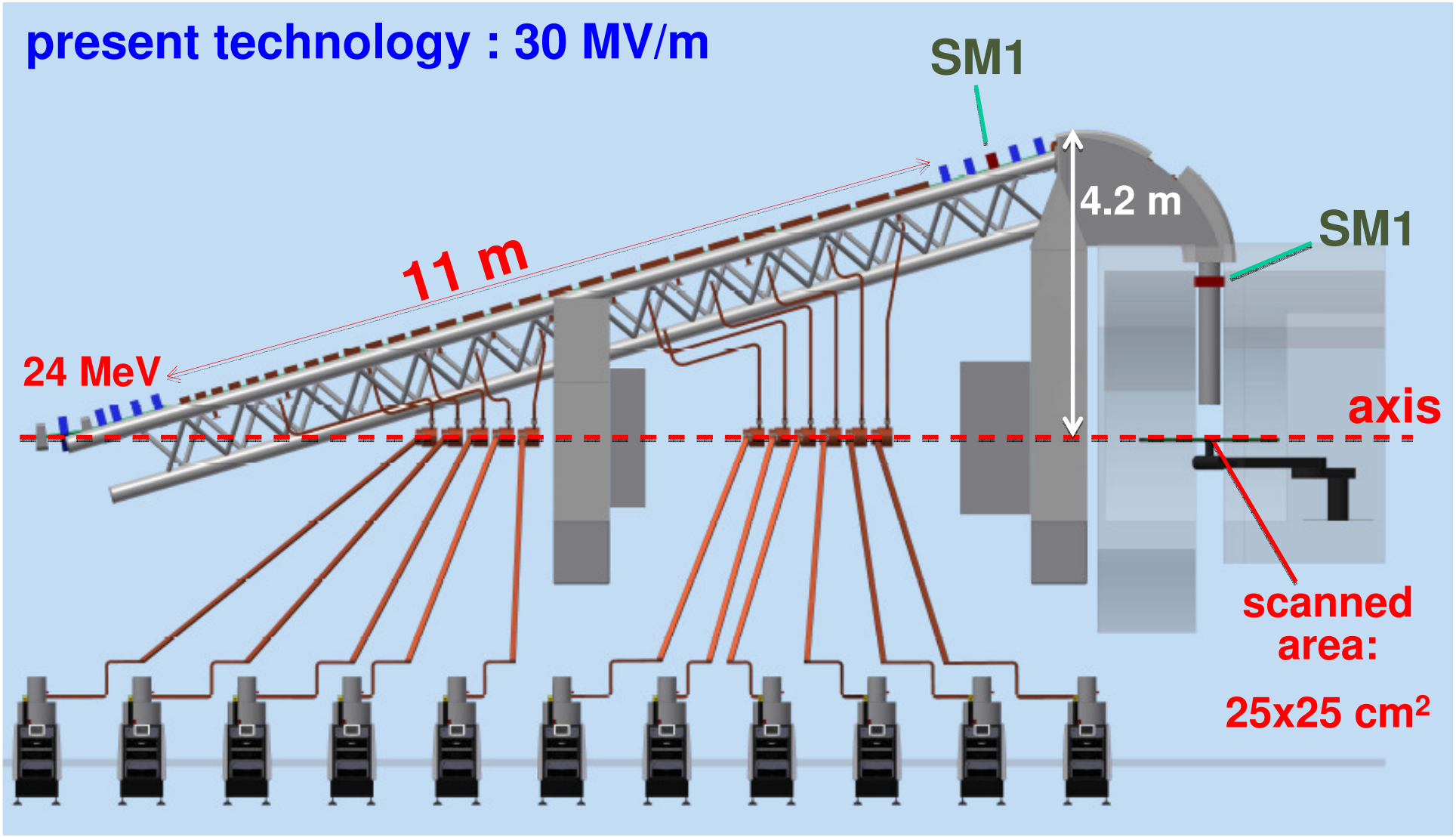
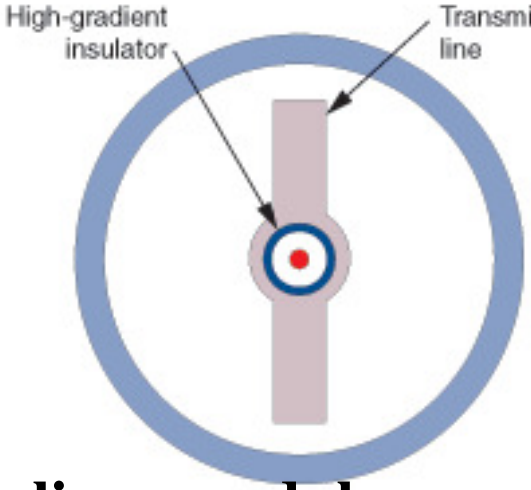
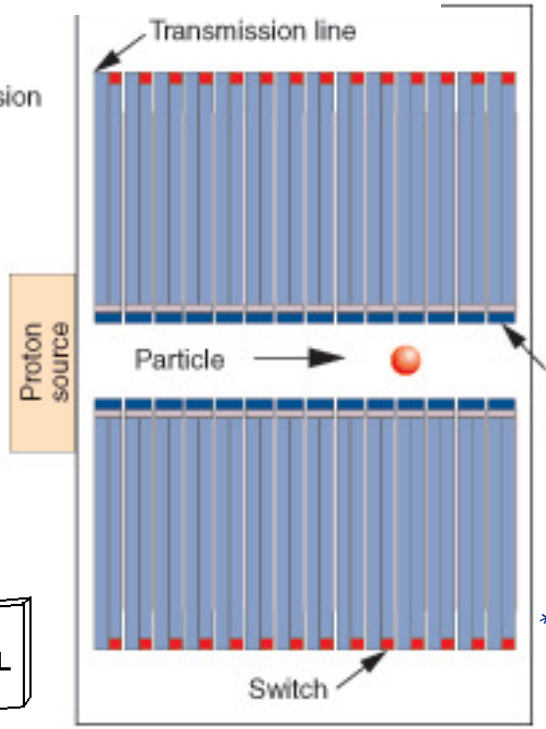
TULIP at 3 GHz with E_0 = 30 MV/m



Courtoisie : Amaldi et al

DIELECTRIC WALL ACCELERATOR → Proton linac





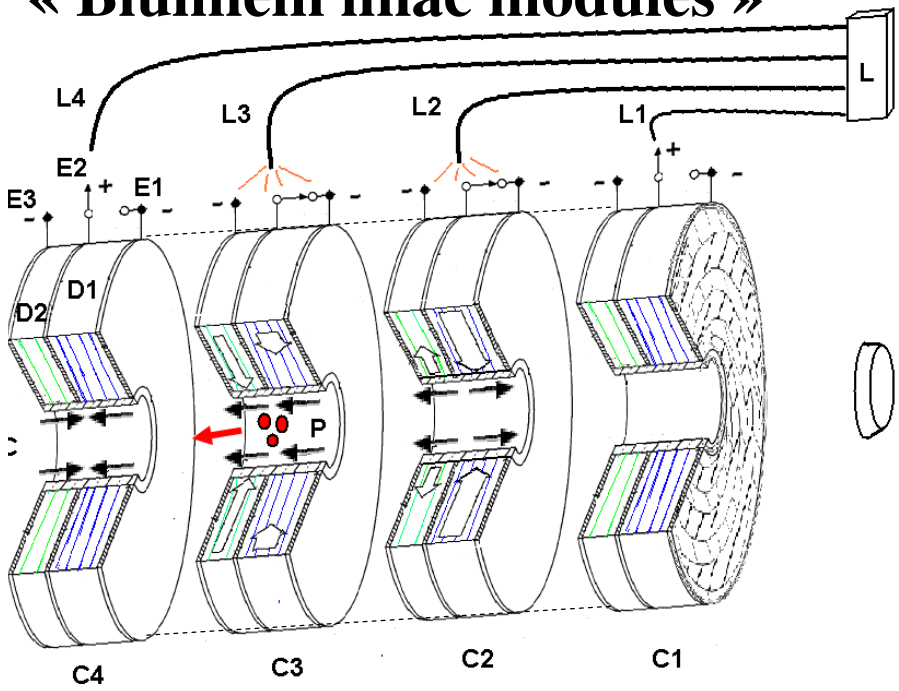
(c)

Freepatentsonline.com

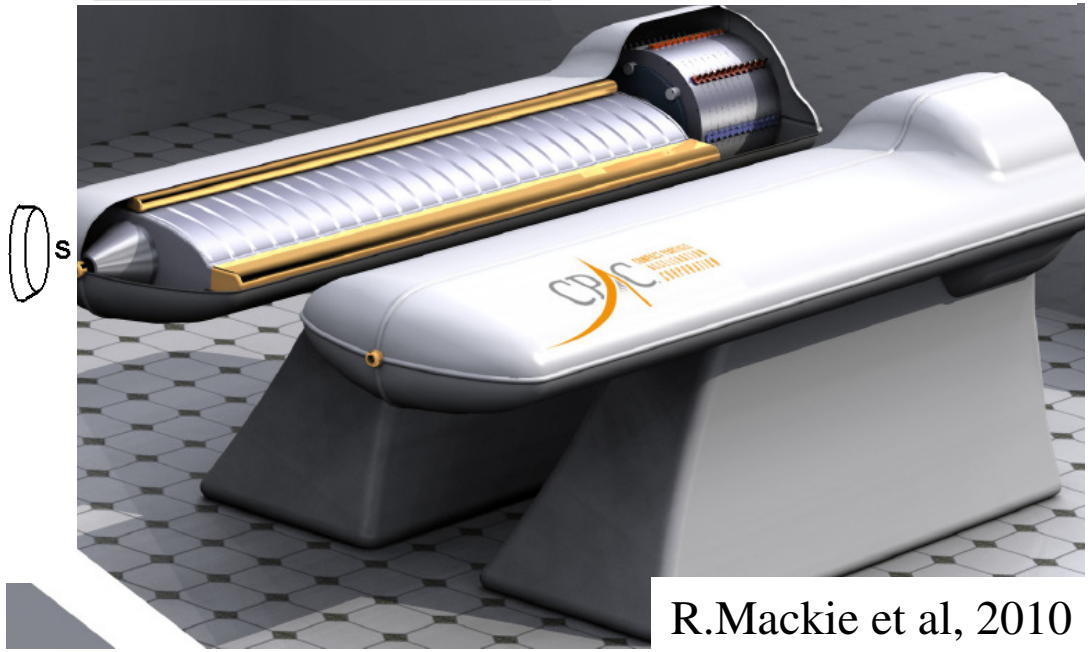
George Caporazo et al

**Lawrence Livermore National Laboratory, Livermore CA*

« Blumlein linac modules »



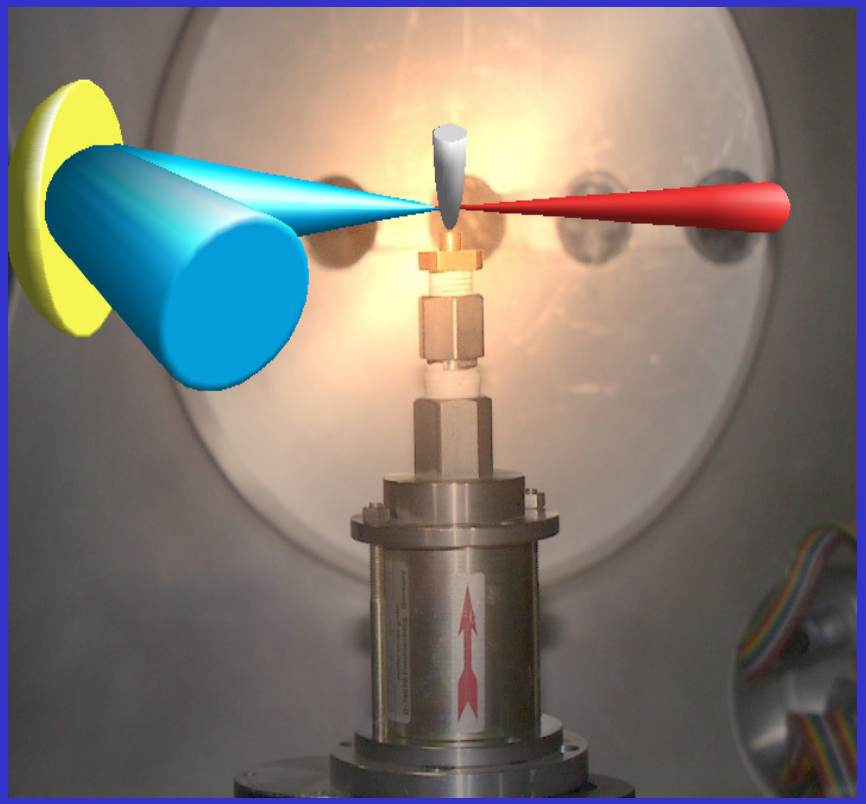
Mazal et al, 2010

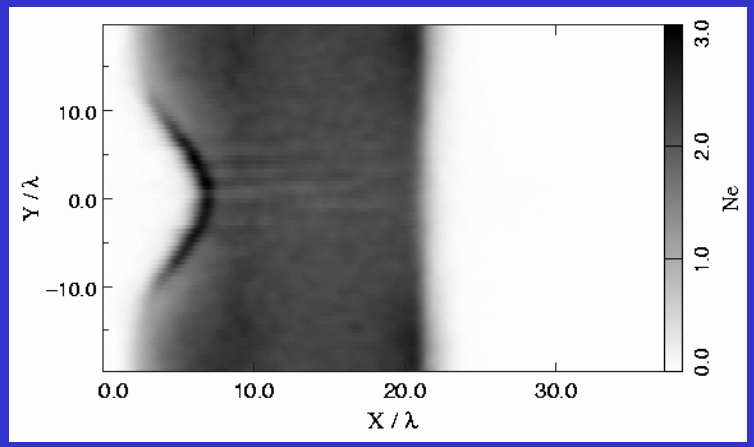


R.Mackie et al, 2010

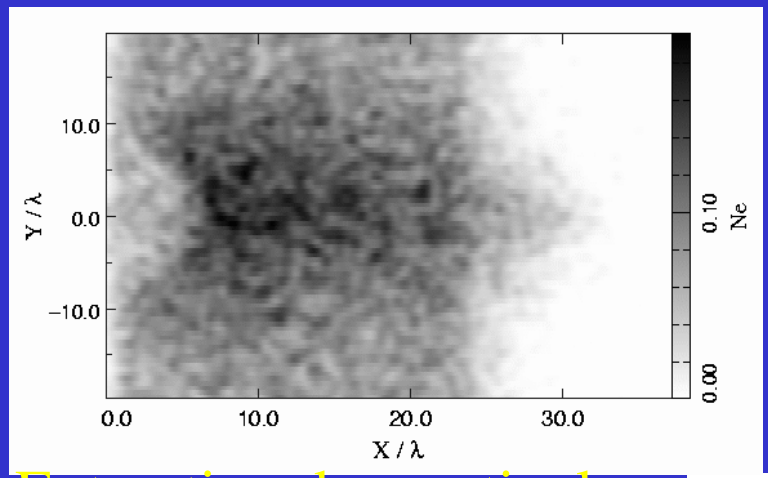
Laser-based proton beams

Laboratoire d'Optique Appliquée Polythechnique/ Palaiseau // IGR // CPO





Impact de l'impulsion (P~3GBar)



Extraction des particules (E~TV.m^{-1})

Fréquence des pulses : 10 Hz
Durée d'impulsion : 30 fs
Puissance sur la cible : 10^{20} W.cm^{-2}
Diamètre d'impact : quelques µm^2

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Optimistics or pesimistics ?
How many of you think we can have
Medical laser accelerators
in less than 10 years ?

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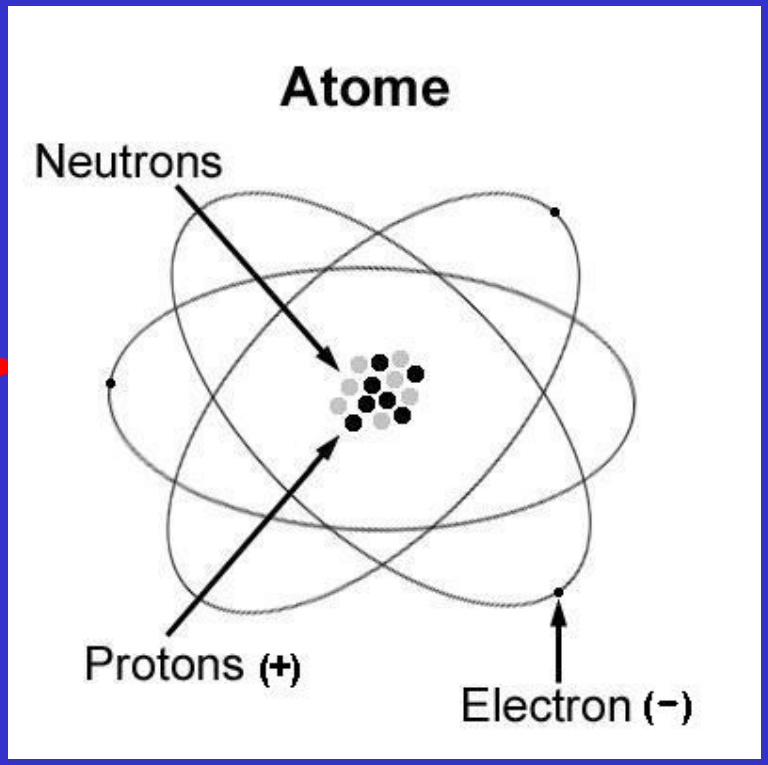
III. BEAM-TARGET INTERACTIONS :

- Elastic & inelastic collisions
- Coulomb Forces : (+) & (-) charges

Incident Proton or Ion (+)



Which are the Main Interactions of Interest in our field?

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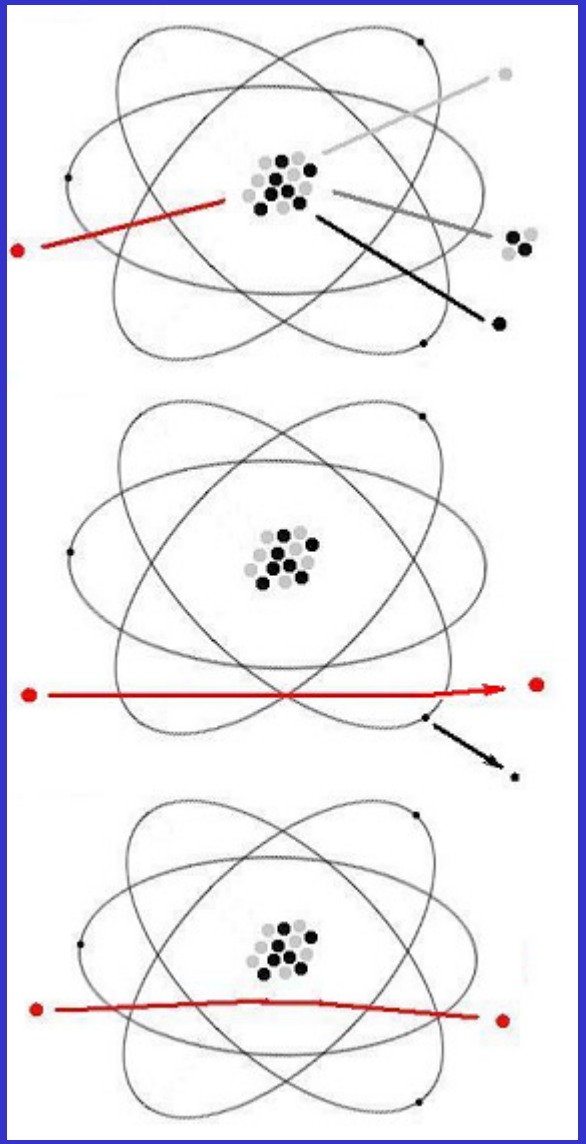
Many interactions of particles with matter …
but keep 3 :



Inelastic collision w/nuclei : neutrons…

Inelastic collision with electrons: Dose

Elastic collision w/nuclei:
« multiple Coulomb scattering » :
all the effects you do not know why

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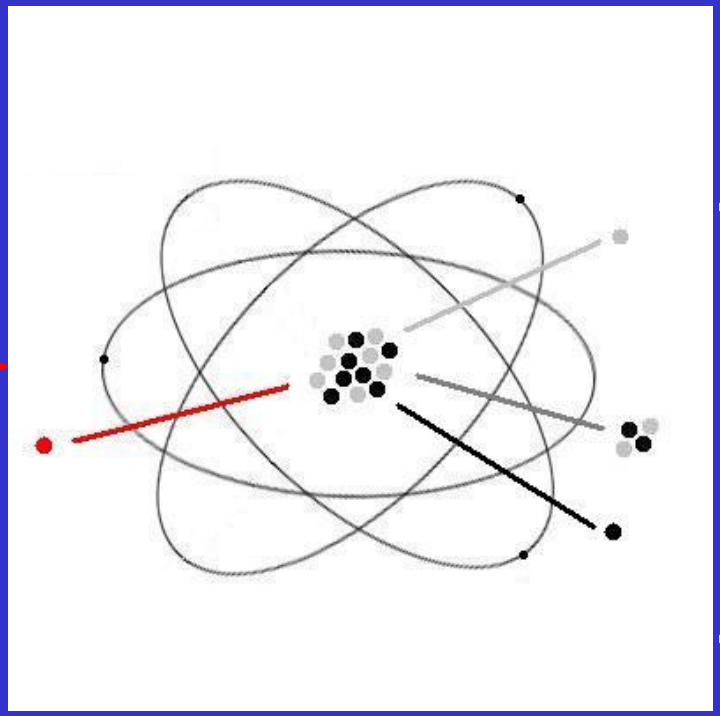
BEAM-TARGET INTERACTIONS :

Mid & High Energy :
(10-250 MeV protons)

Inelastic collision w/nucleus & nuclear reactions

Incident Proton or Ion (+)



- Neutrons:
  - shielding
  - patient dose
- Fragments
- Protons (large angles)
- Activation → gamma,…
  - Accelerator, Beam line
  - Patient →PET, …

→ *Disappearance of incidental protons*

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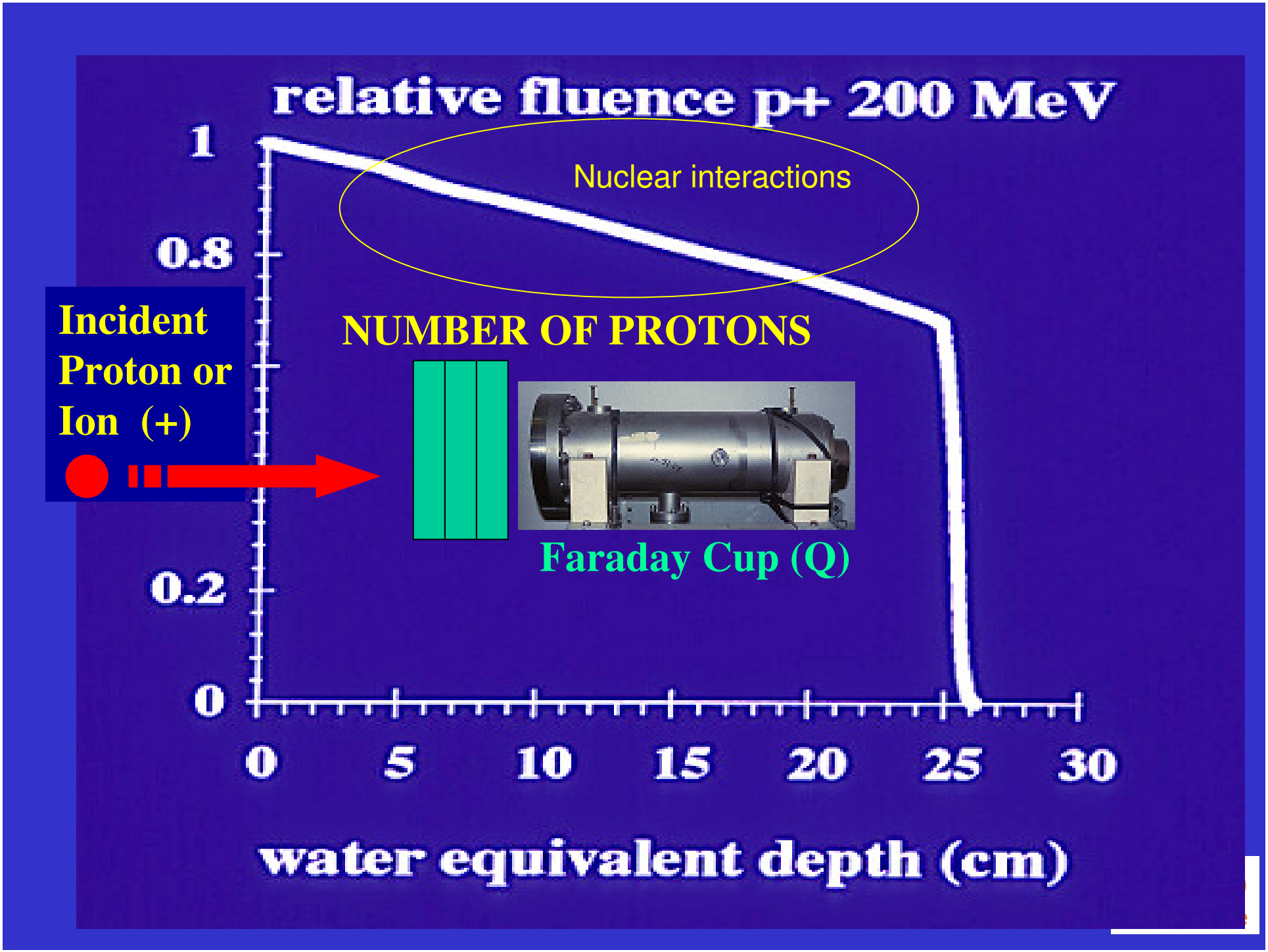
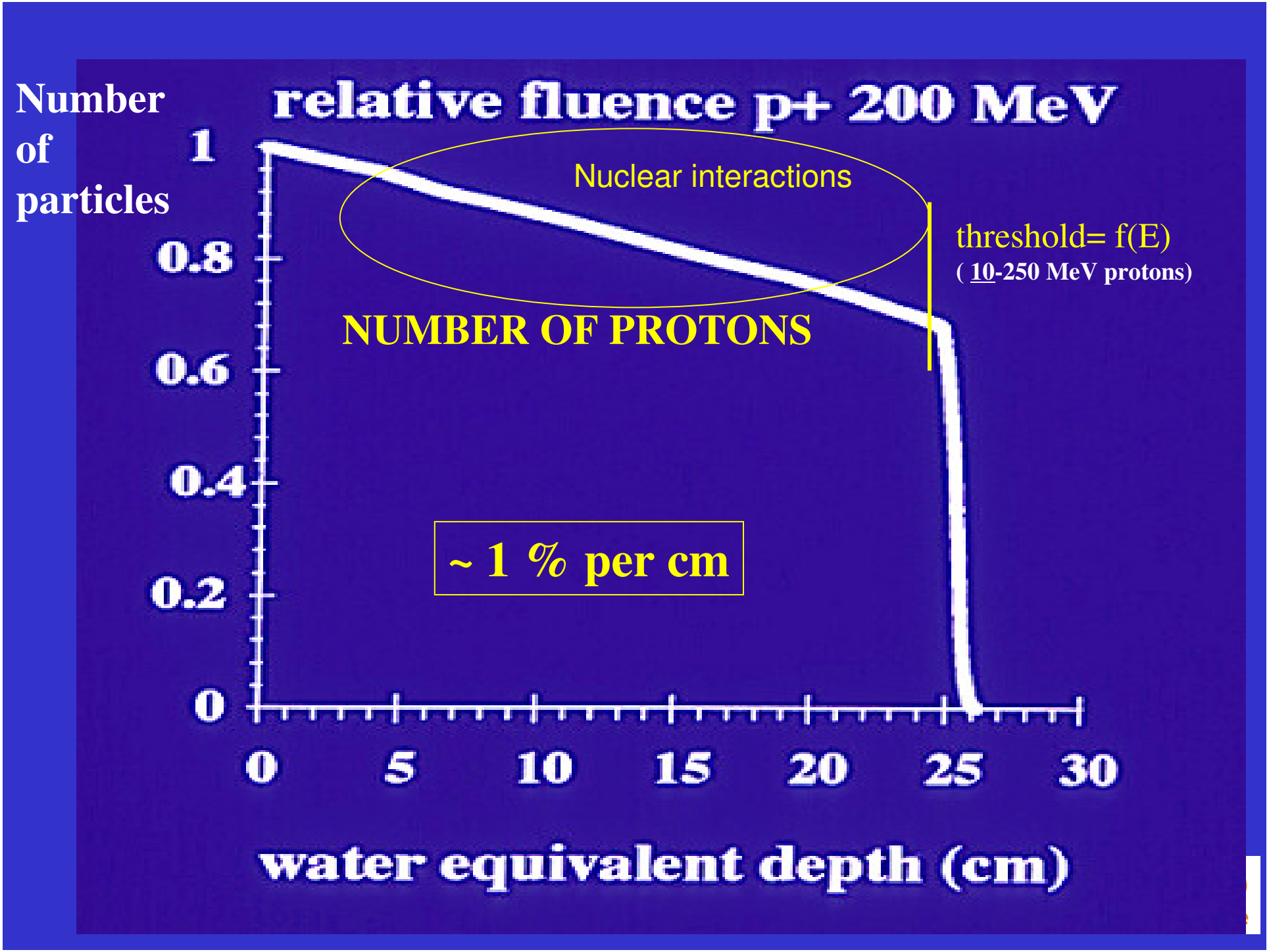

relative fluence p+ 200 MeV
1
0.8
0.2
0
Nuclear interactions
Incident Proton or Ion (+)
NUMBER OF PROTONS
Faraday Cup (Q)
0
5
10
15
20
25
30
water equivalent depth (cm)

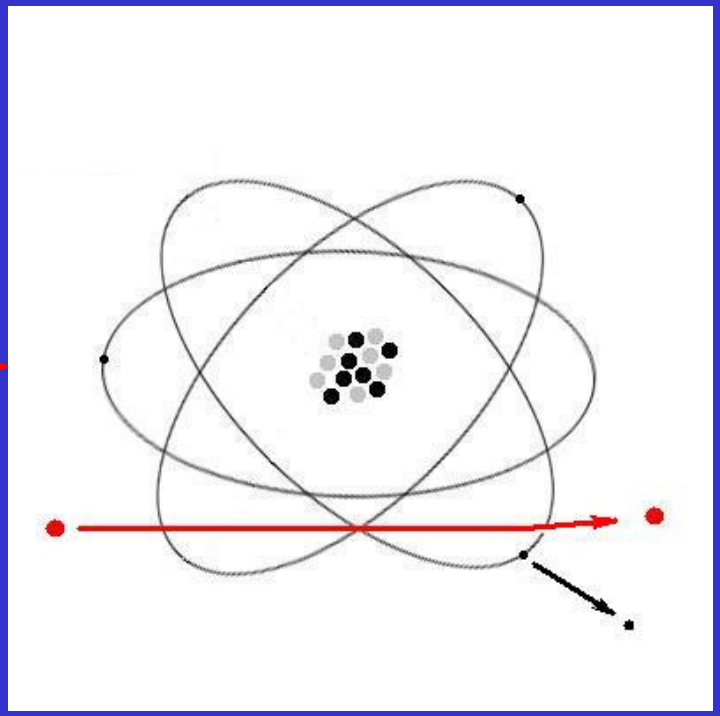

relative fluence p+ 200 MeV
Number of particles
1
0.8
0.6
0.4
0.2
0
Nuclear interactions
threshold= f(E)
(10-250 MeV protons)
NUMBER OF PROTONS
~ 1 % per cm
0
5
10
15
20
25
30
water equivalent depth (cm)

BEAM-TARGET INTERACTIONS :
Why the bragg peak…?

\# Intermediate Energy (0.1- 250 MeV)

Inelastic Collision with electrons

Incident Proton or Ion (+)



-Protons : E loss & very small angle

-Electrons: Ionization, excitation

= Dose

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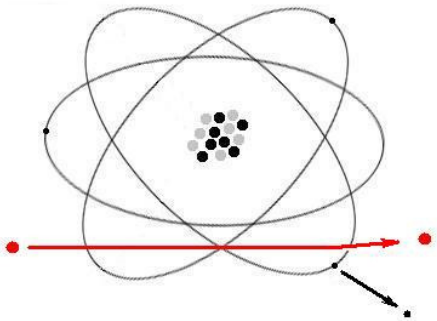
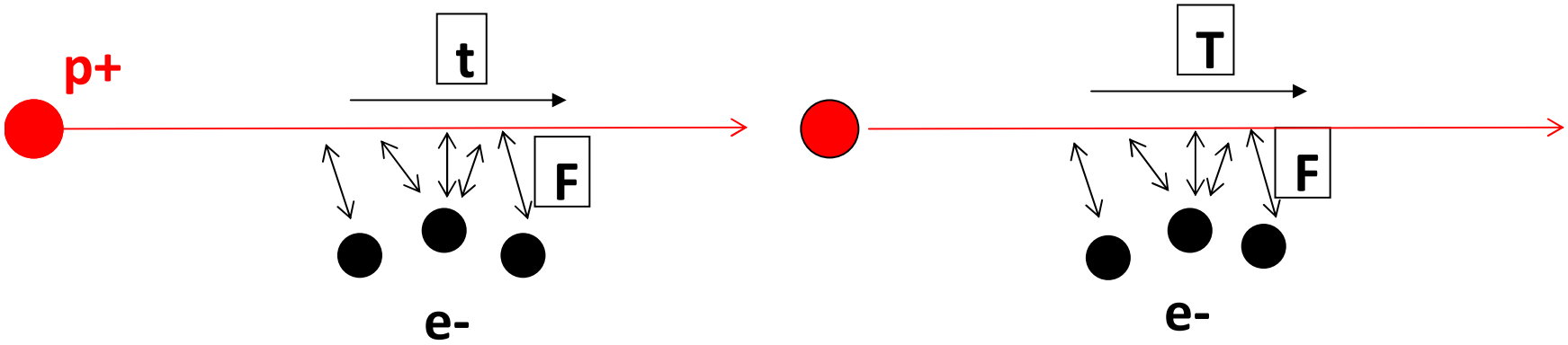
ionisations =f(Energy)





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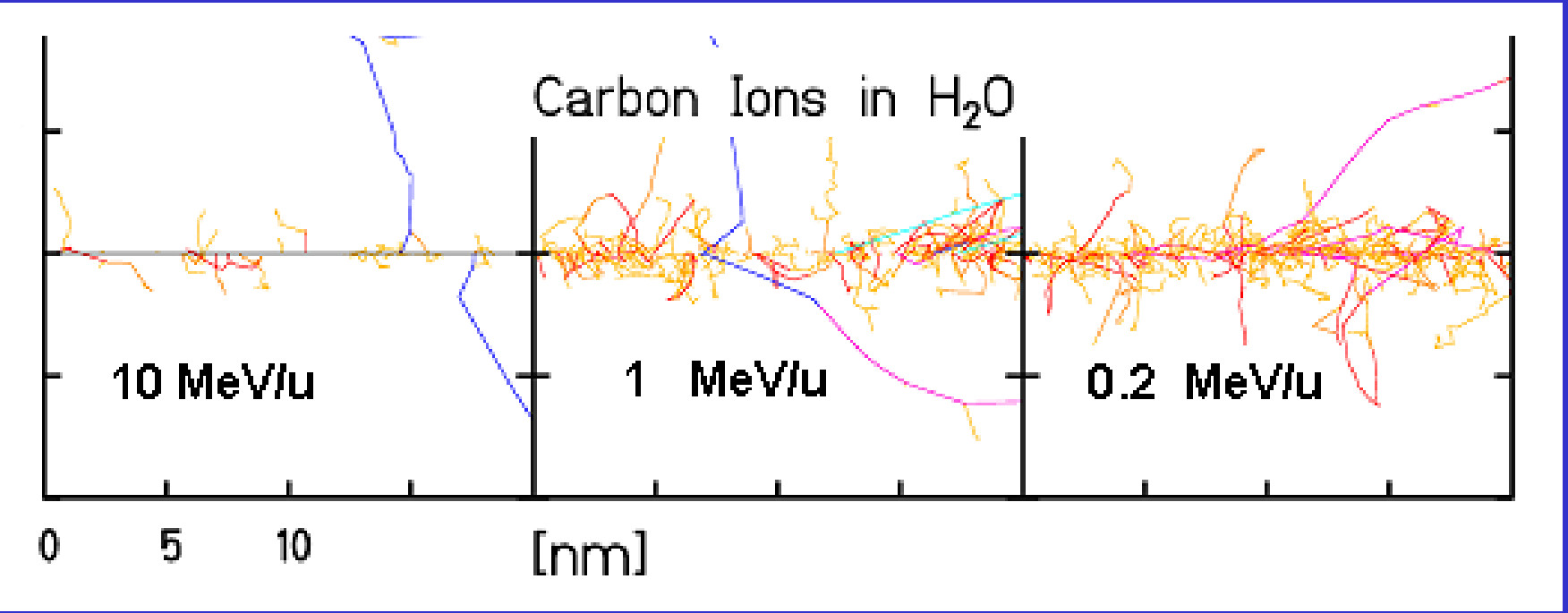
Dose distribution in nanometer scale



M. Kraemer, M. Scholz

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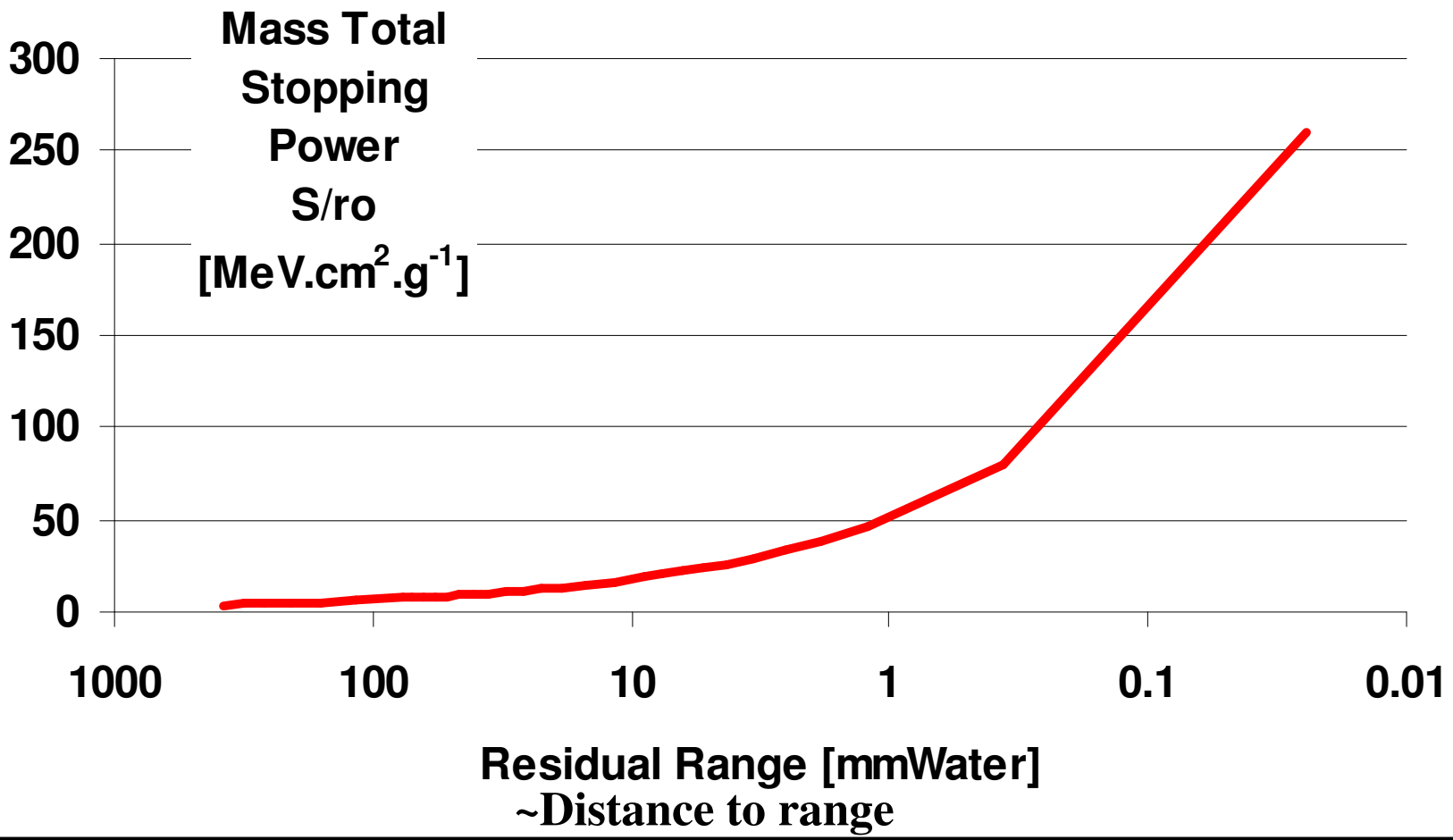
Stopping Power



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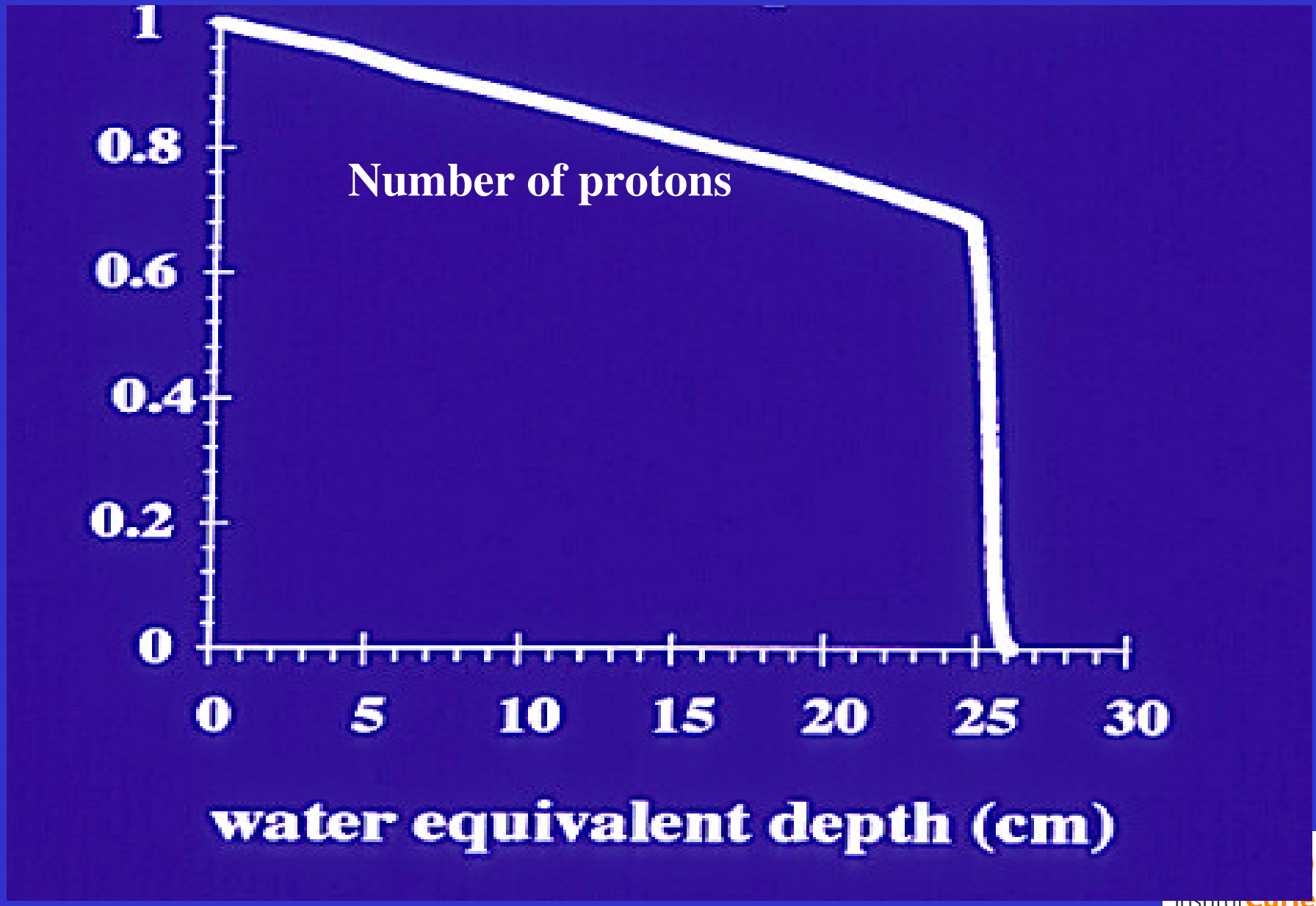
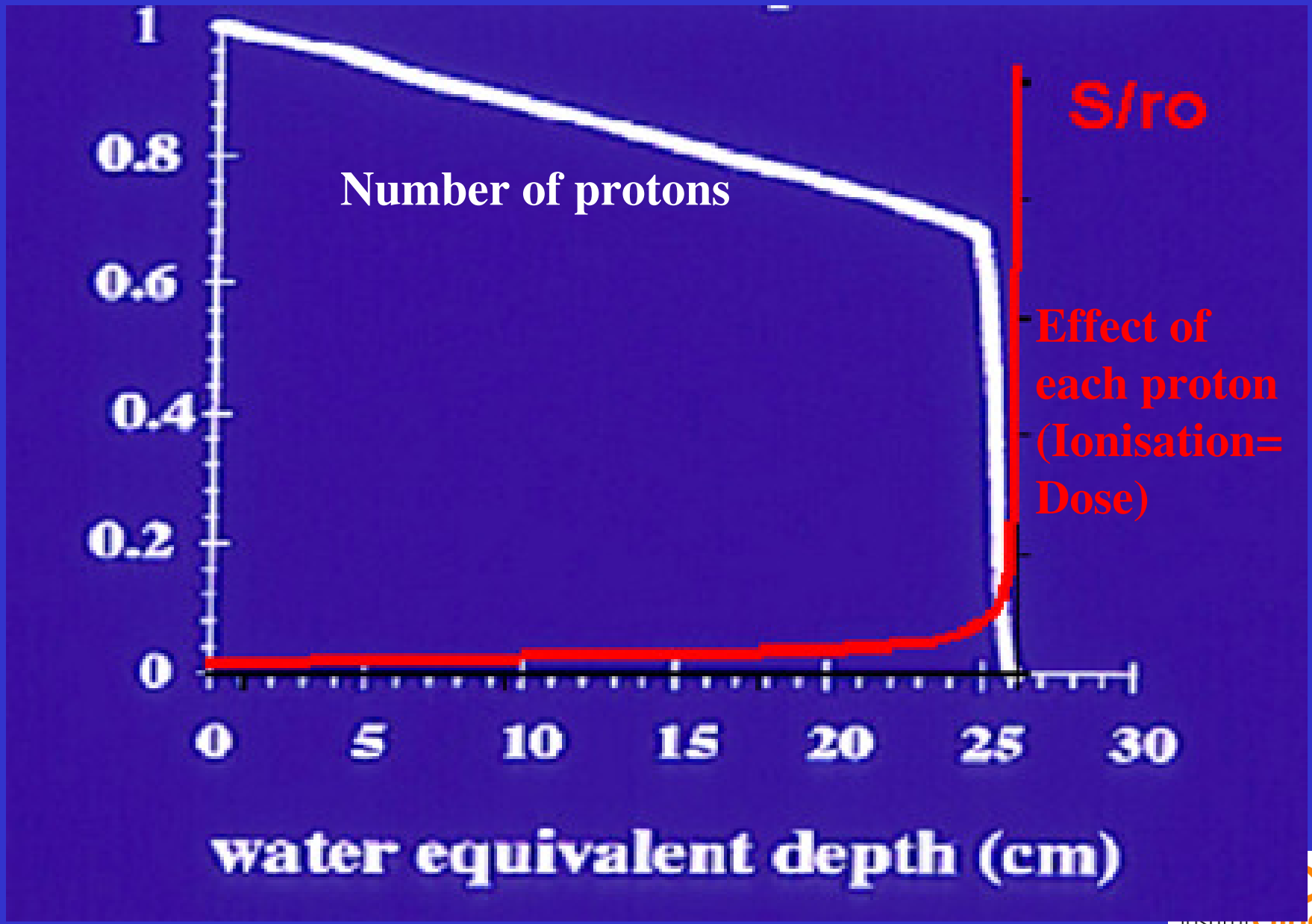
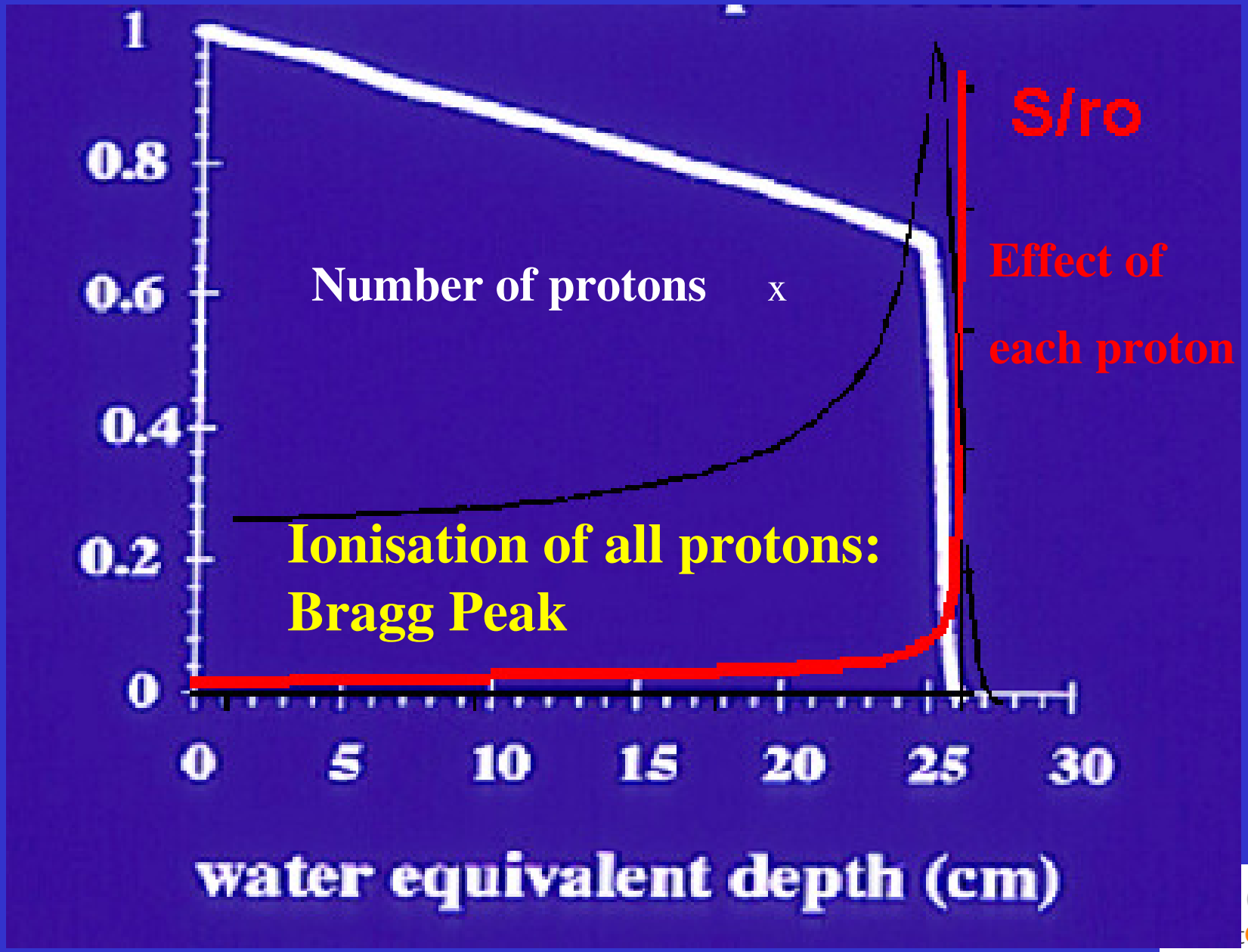
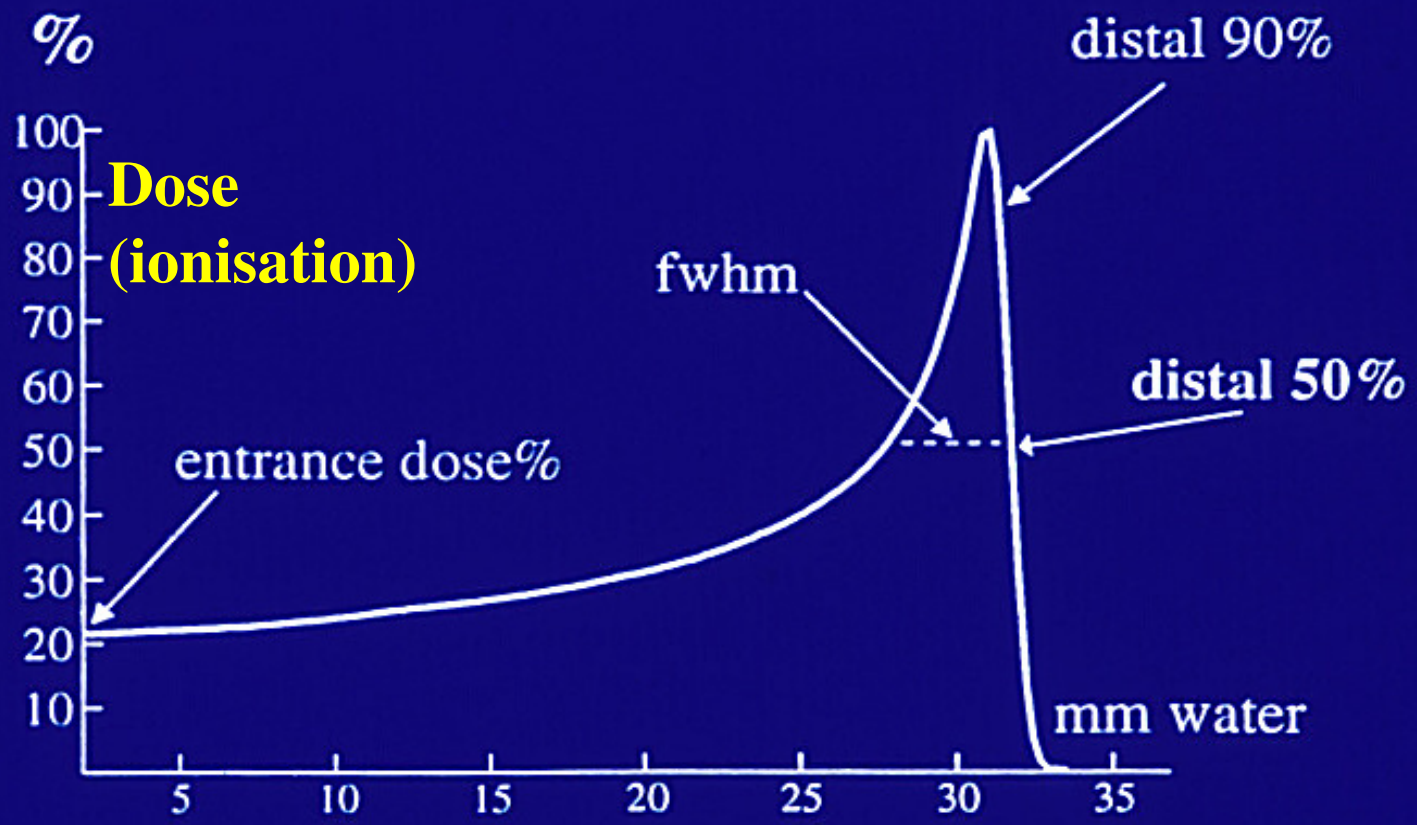

1
0.8
0.6
0.4
0.2
0
Number of protons
0
5
10
15
20
25
30
water equivalent depth (cm)


1
0.8
0.6
0.4
0.2
0
Number of protons
S/ro
Effect of each proton (Ionisation= Dose)
0
5
10
15
20
25
30
water equivalent depth (cm)


1
0.8
0.6
0.4
0.2
0
Number of protons x
S/ro
Effect of
each proton
Ionisation of all protons:
Bragg Peak
0
5
10
15
20
25
30
water equivalent depth (cm)

Characteristics of Bragg Peak



Pure Bragg peak depth of 60.4 MeV protons

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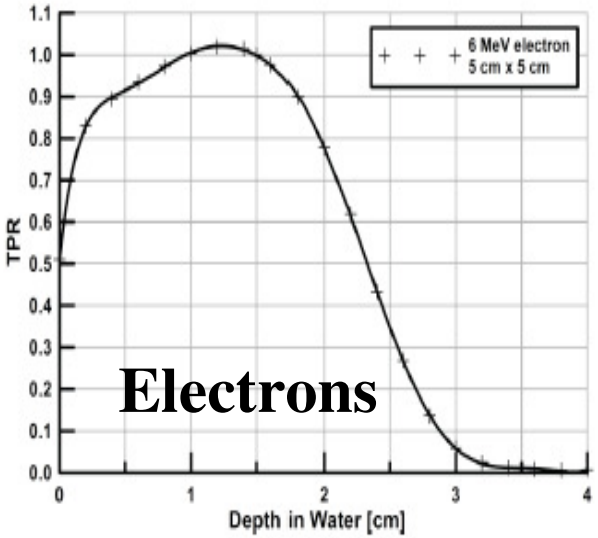
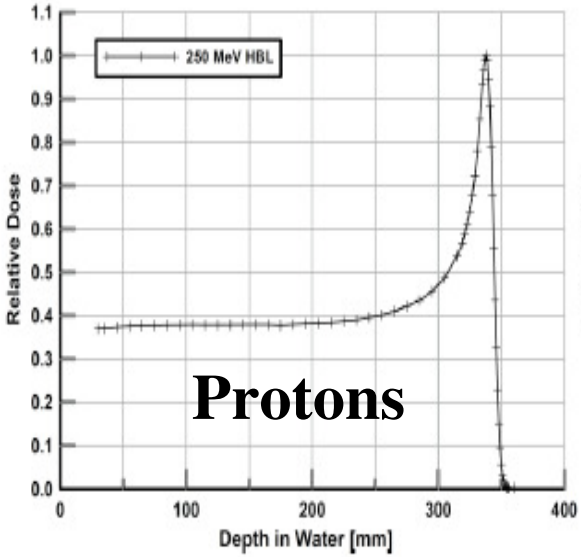
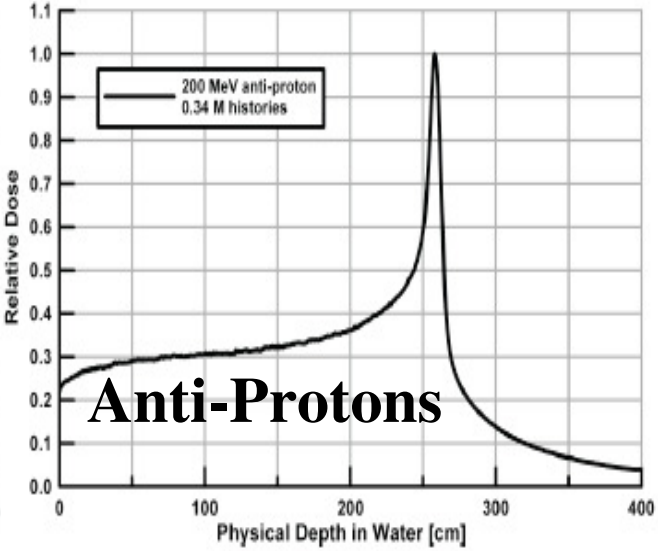
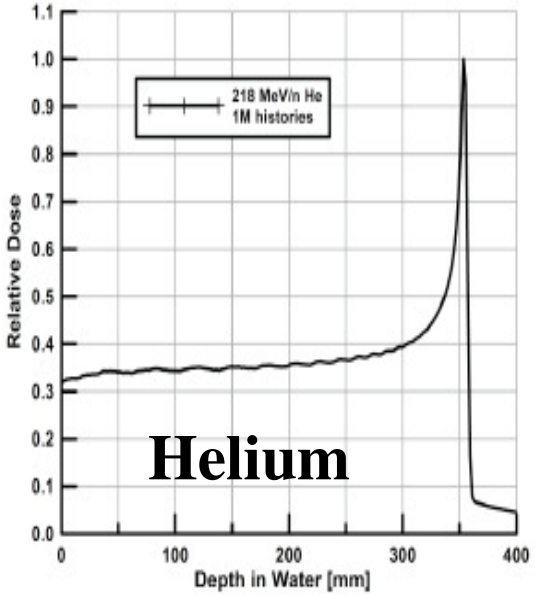
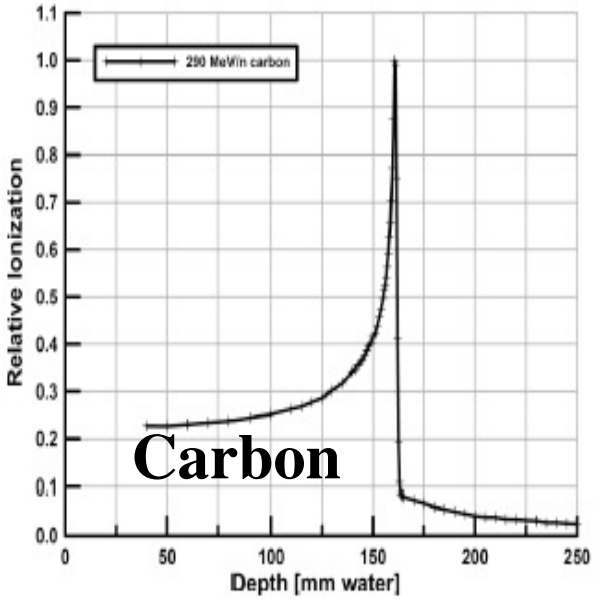
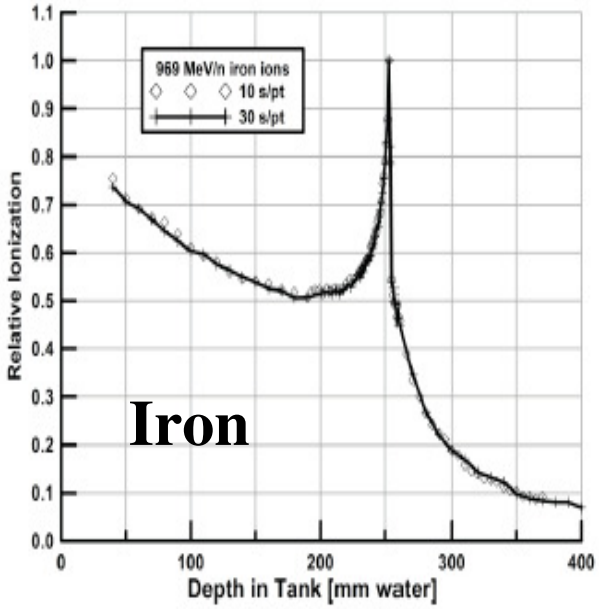








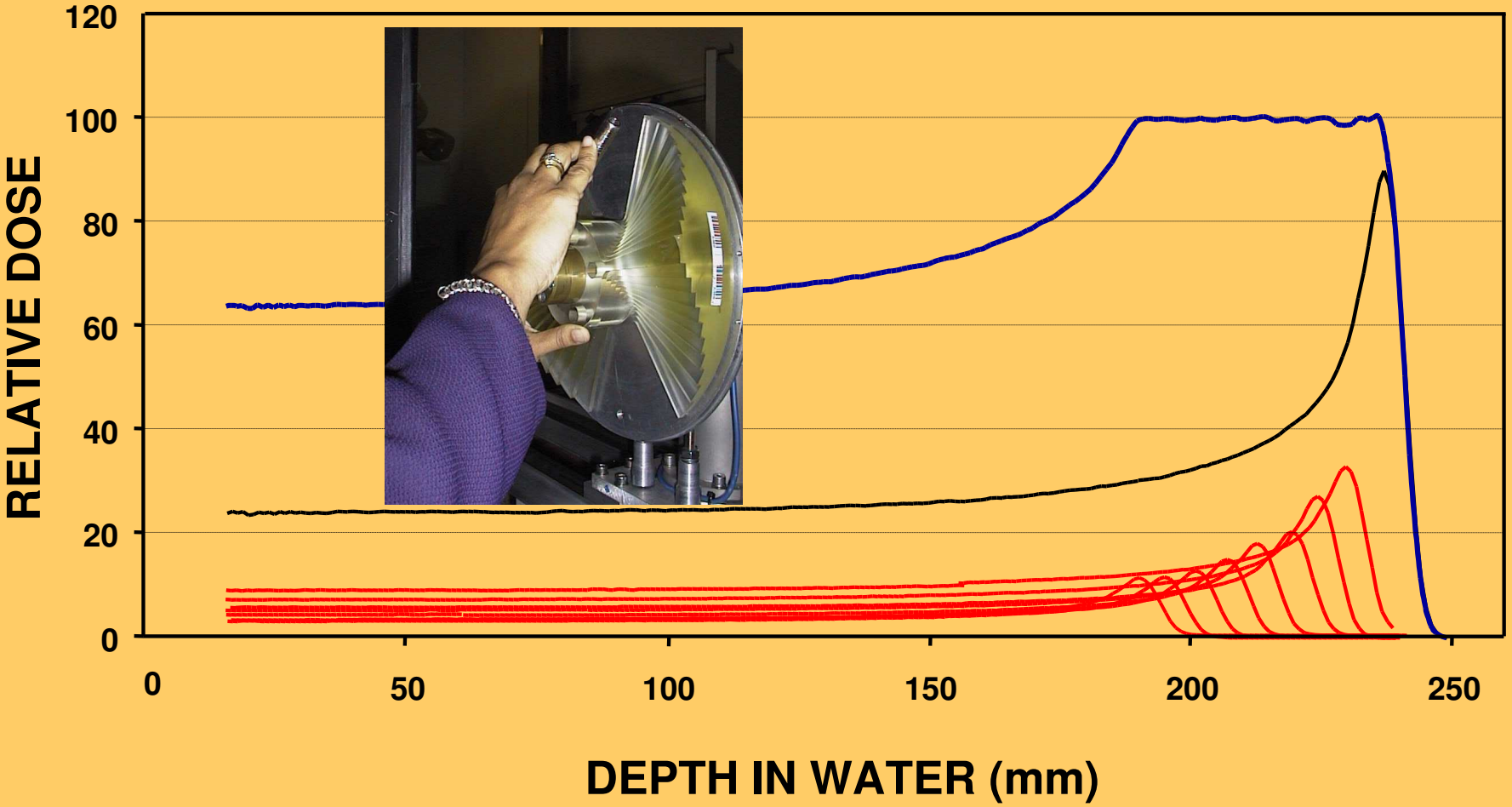




Moyers

PTCOG 2008

Spread-out Bragg Peak (SOBP)



(Niek Schreuder & Orsay)

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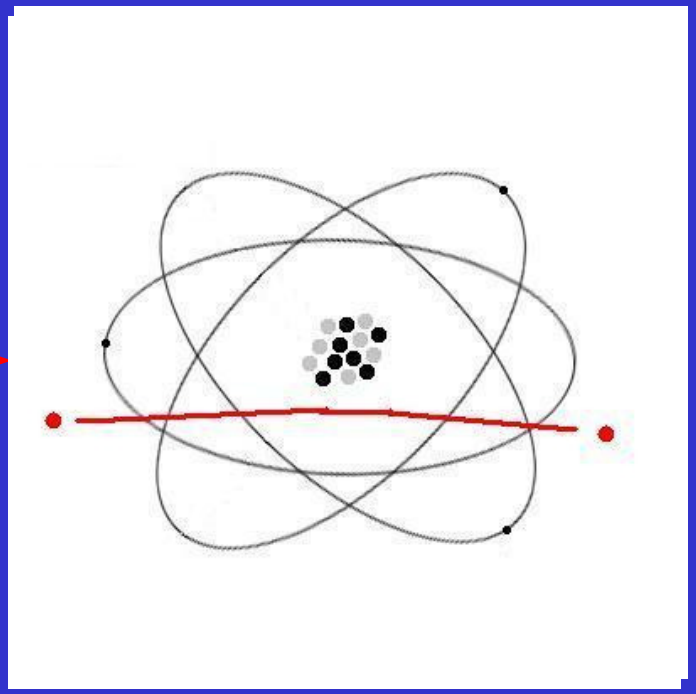
BEAM-TARGET INTERACTIONS :

Elastic collision w/nucleus

Incident
Proton or
Ion (+)



Coulomb
multiple small angle
scattering

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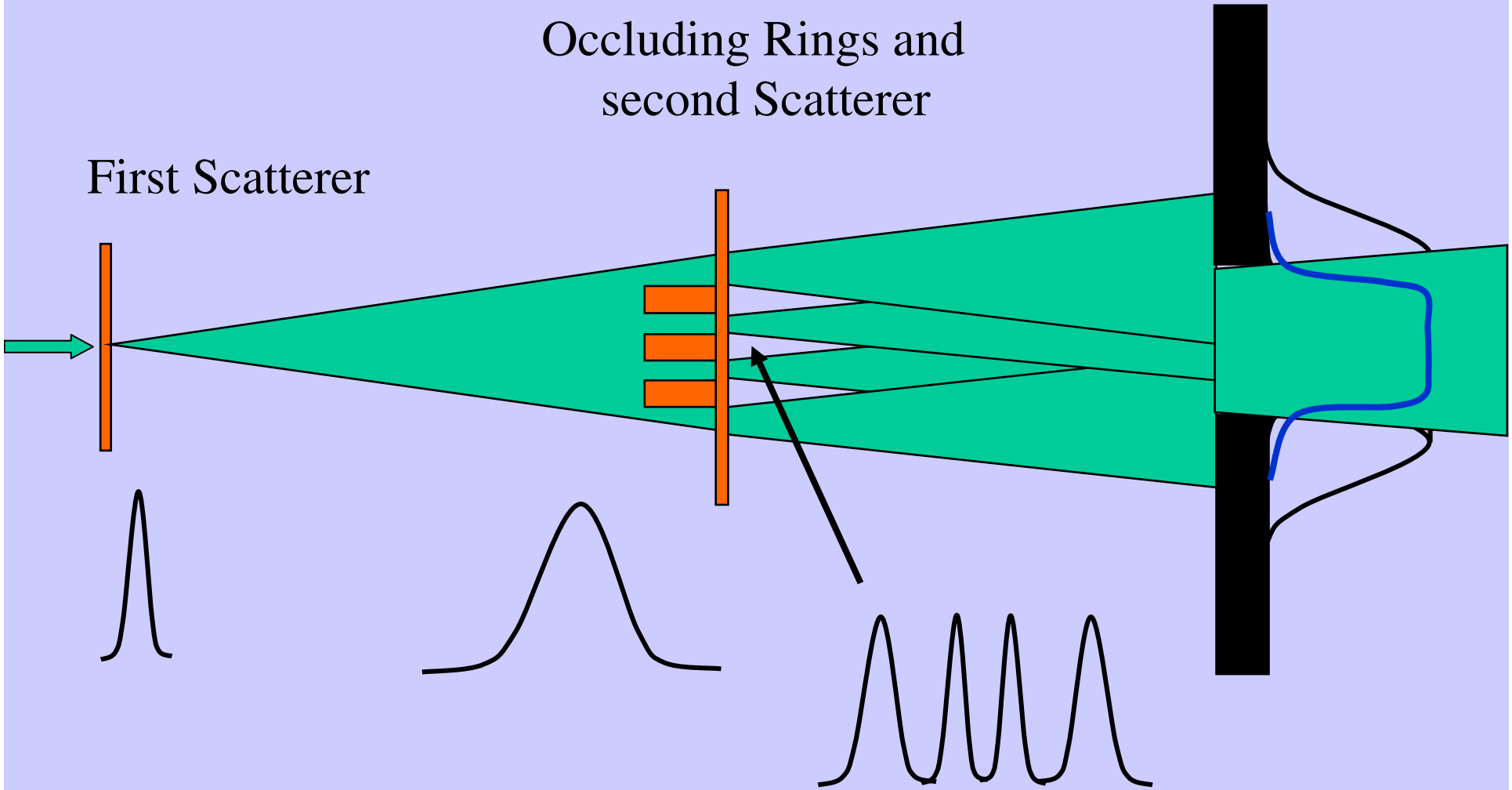
« Get profit » of this ! : Clinical passive lines



(from Niek Schreuder,Indiana)

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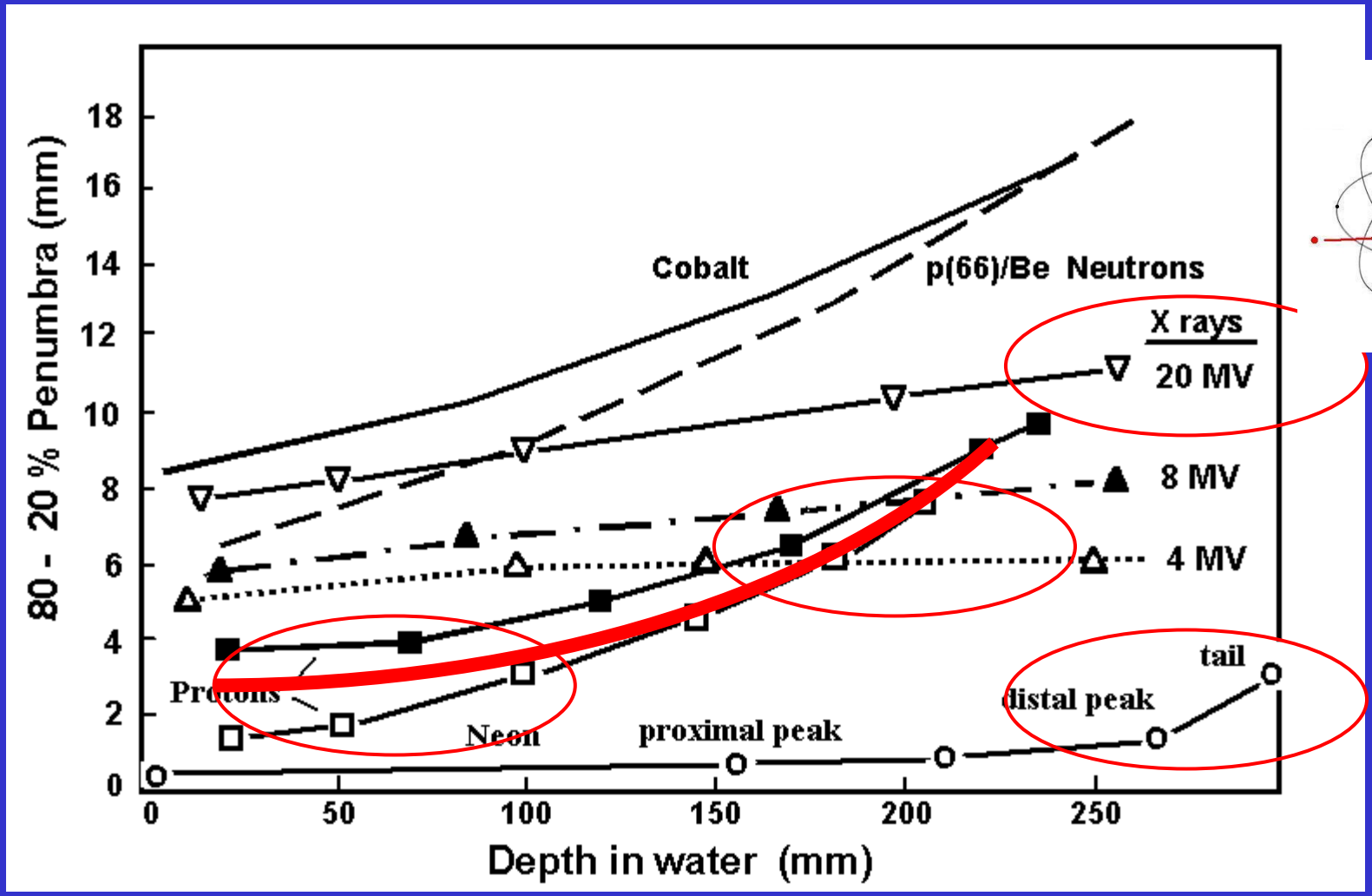
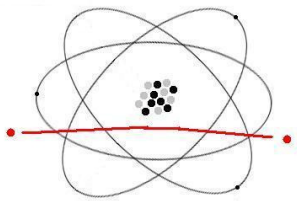
Lateral penumbra in depth : (multiple) Scattering Power





Data: Curie, NAC, Darmstadt

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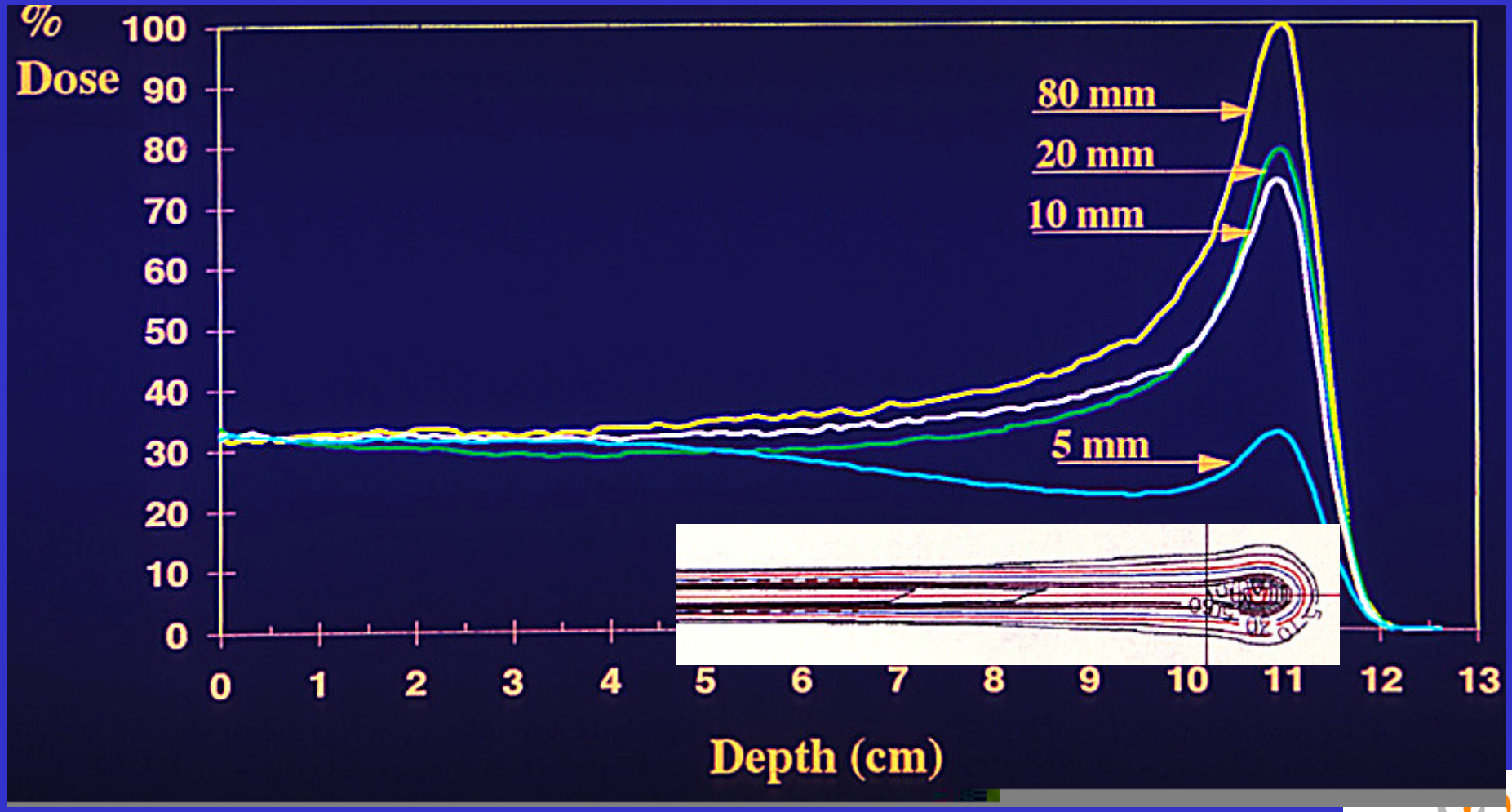
Scattering effect in small beams



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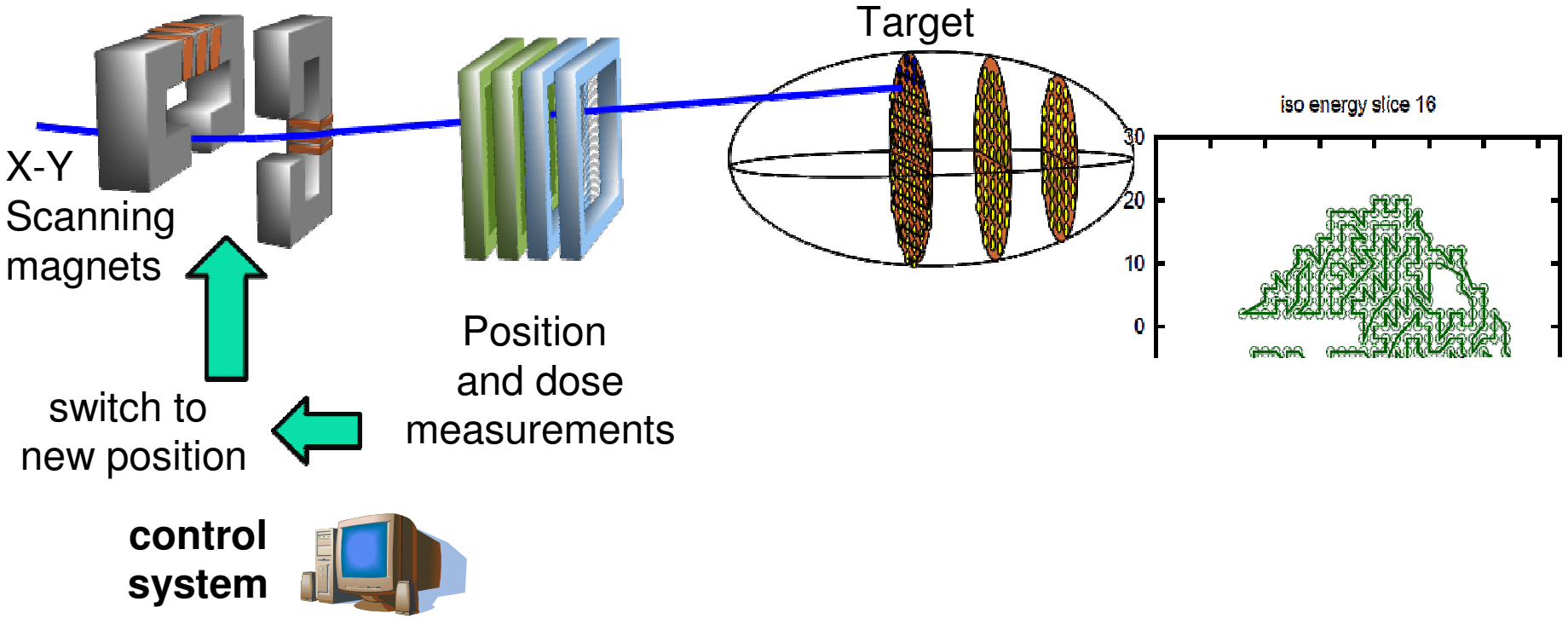

Adapted from Naumann et al, PTCOG 2010 // Heidelberg Ion Therapy Center

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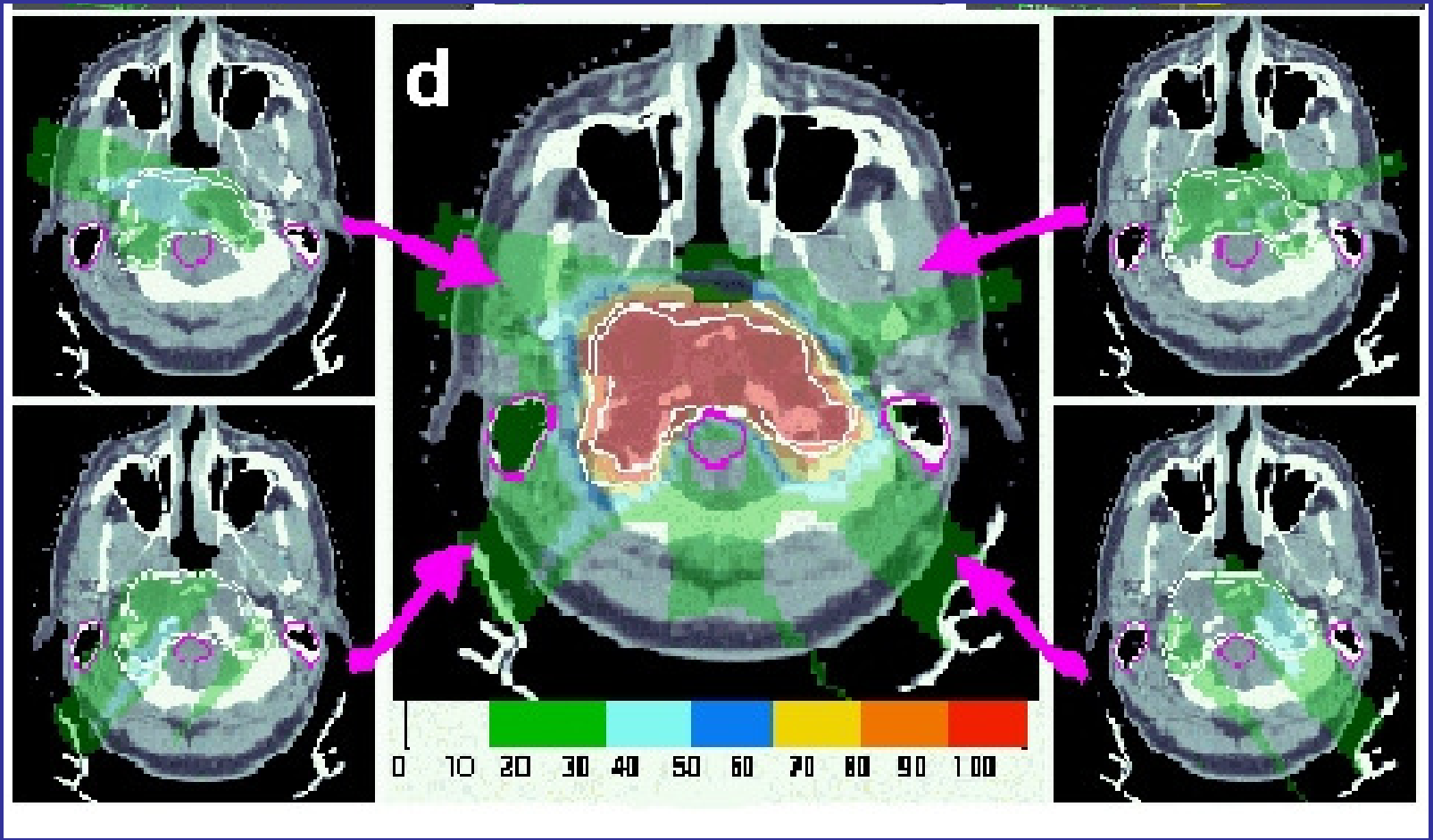
Intensity Modulated IMPT-IMZT



T. Lomax, A. Trofimov, …

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How many of you prefer scanning than passive?

Why ?
Any specif concern or limitation ?

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Conclusions at Estro Course

Passive and scanning delivery compared.

Passive		Scanning	
Mature technology	+	New technology	-
Insensitive to organ motions	+	Very sensitive to organ motions	-
Relatively inflexible	-	Very flexible	+
Field specific hardware required	-	No field specific hardware required	+
Large gantries required	-	Smaller gantries	+
Integral dose	-	Integral dose	+

From Tony Lomax, Estro Particles 2011

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Menu :

I. Medical Physics in RT: past, present

I. Hadrontherapy :

1. Types of particles
2. Interactions with electric (E) and magnetic fields (B)
3. Interaction with matter (eg: beam line, patient)
4. Planning and treating with particles
5. Moving towards heavier ions

III. The future : revisiting radiation biology

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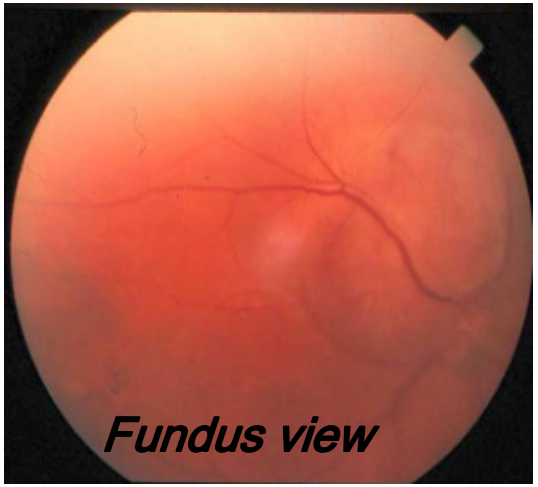
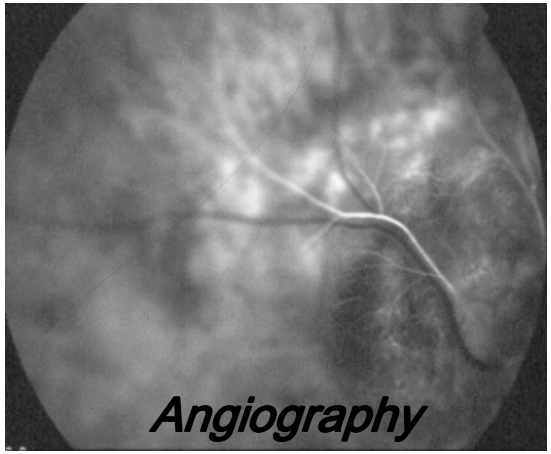
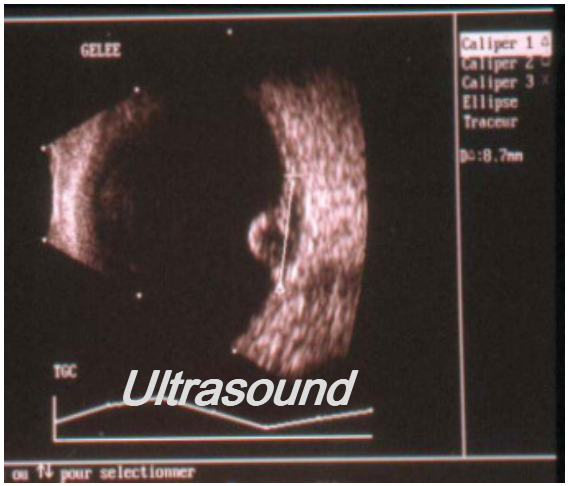
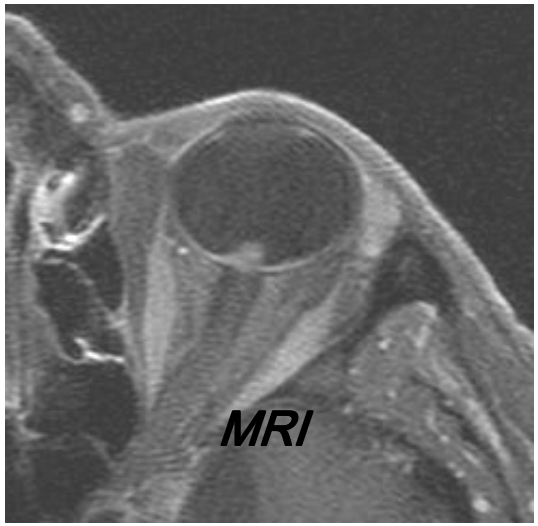
2. Imaging

Obtain and inter-register imaging studies :
CT, MRI, fundus, angiography, ultrasound





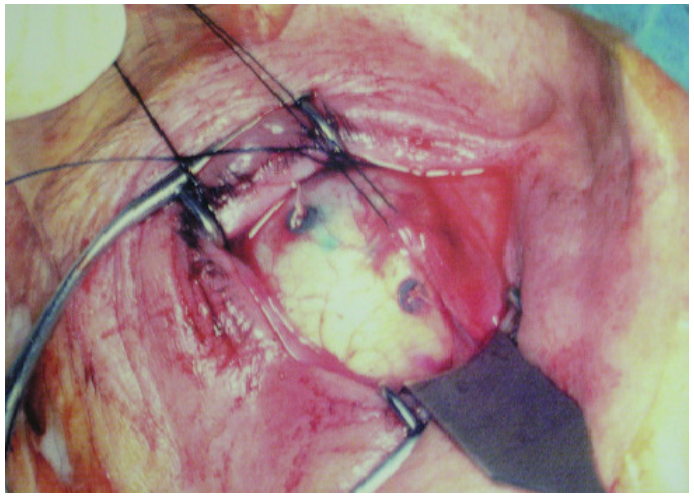




Immobilisation
& reference coordinates :

masks, frames,…
and/or…

Use of implanted fiducials



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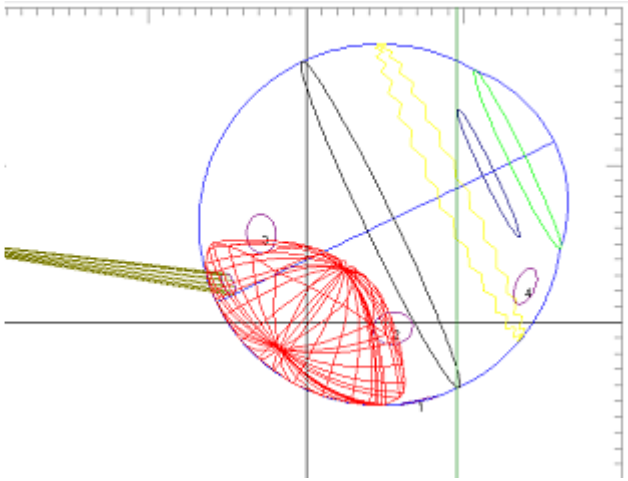
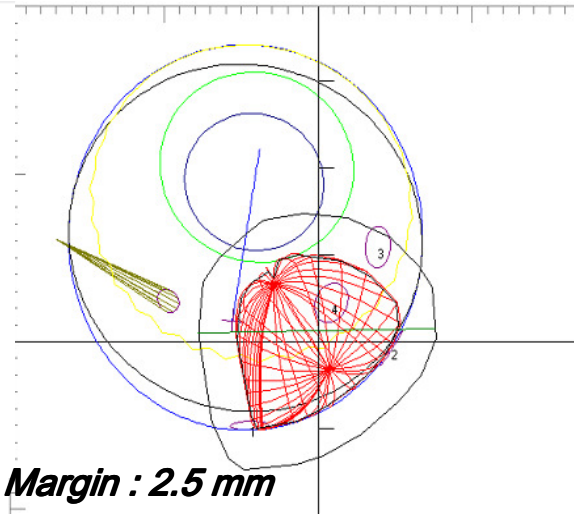
5. Beam design

Design one or more sets of beams

Indeed for eyes:
Choice of the gaze angle
to avoid critical organs

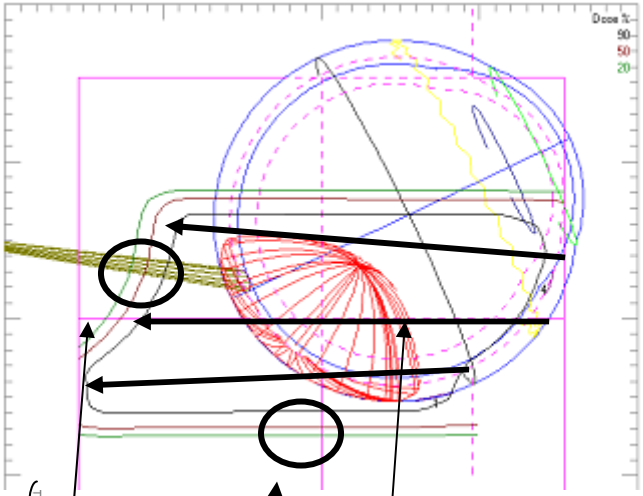


In the beam's eye view:
Design a collimator



Margin : 2.5 mm

Calculate dose distribution



Beam model
(see later)

Ray tracing

Penumbra

Distal fall off
Eg 30%/mm

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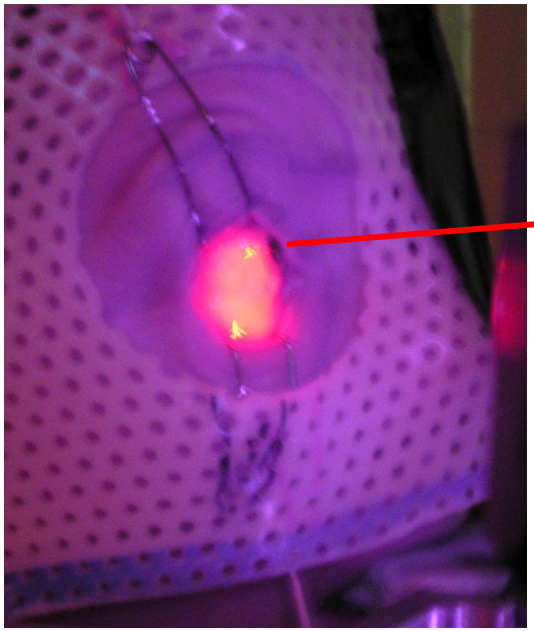
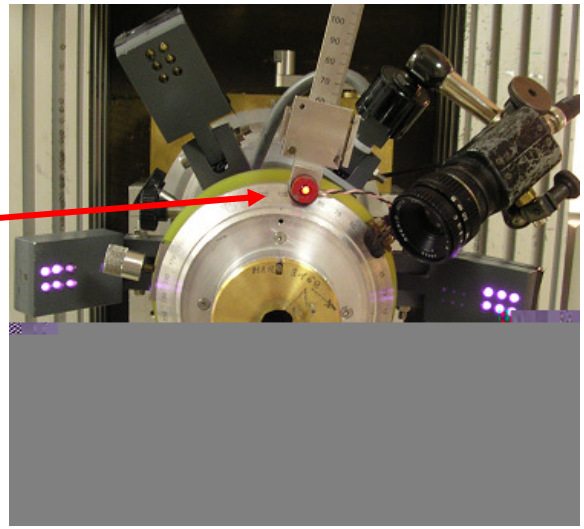
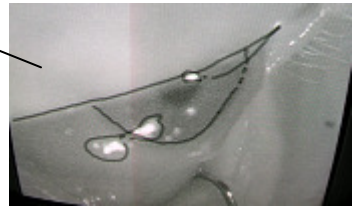
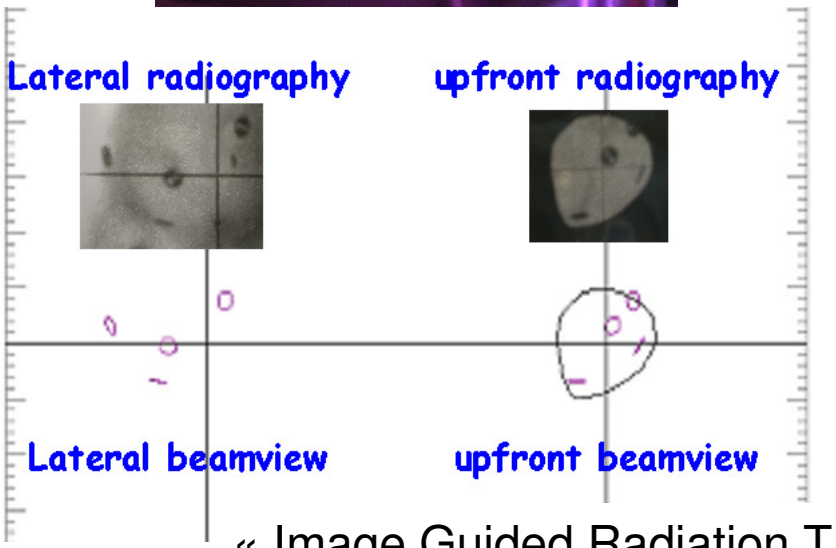
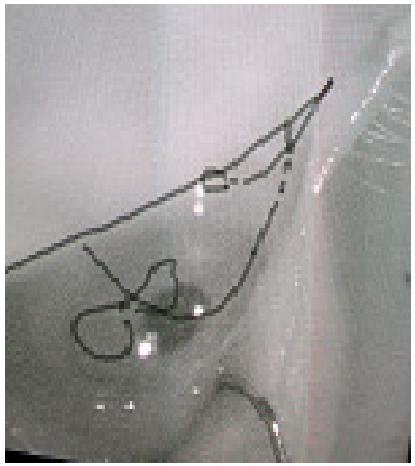
9 & 10 : Daily set-up control

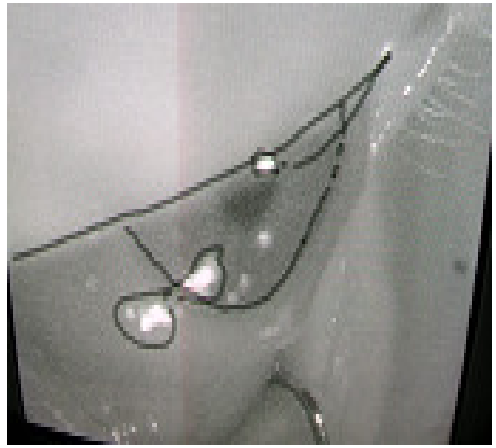












« Image Guided Radiation Therapy IGRT» with gating

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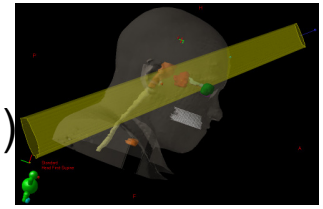
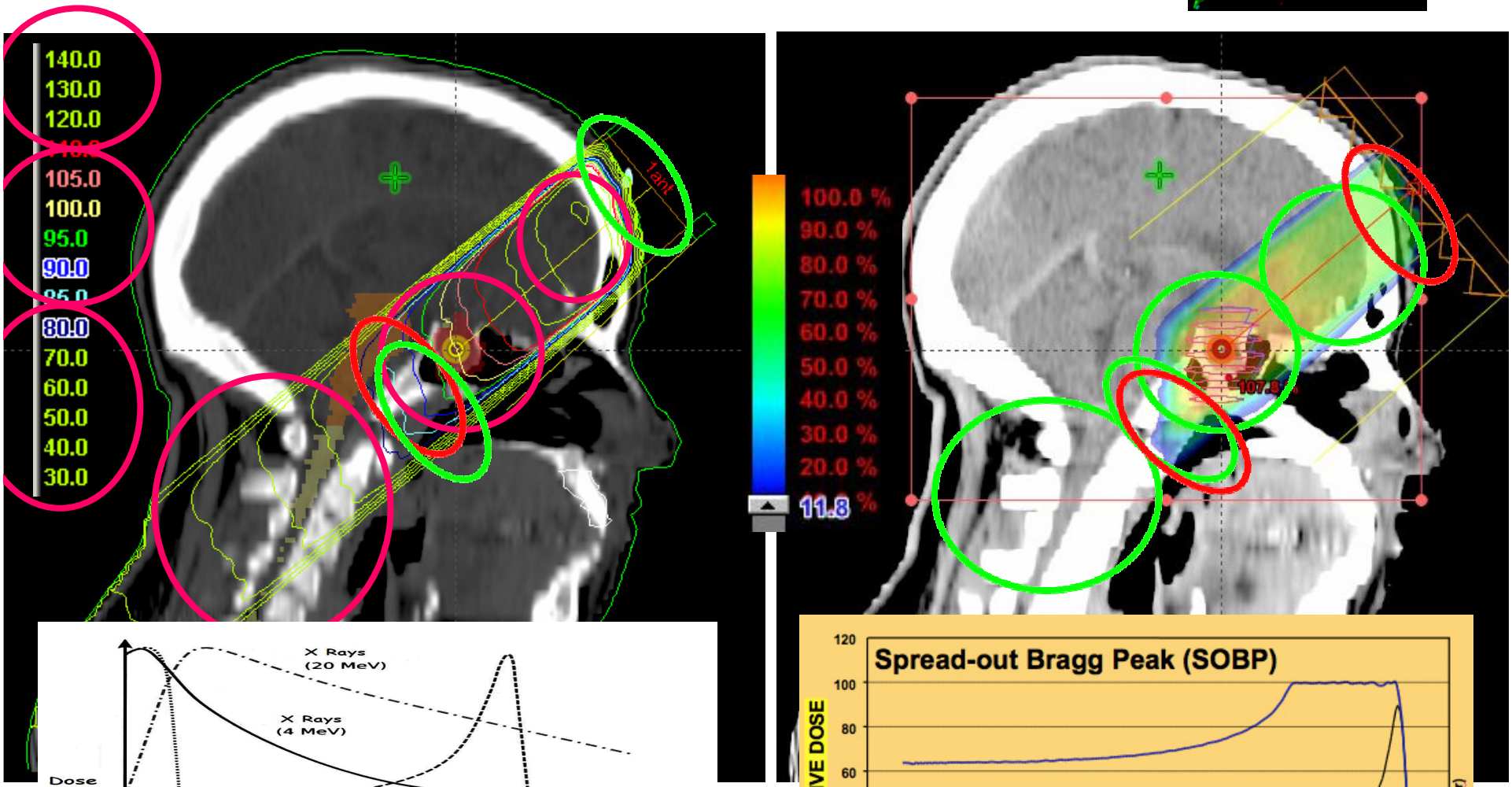
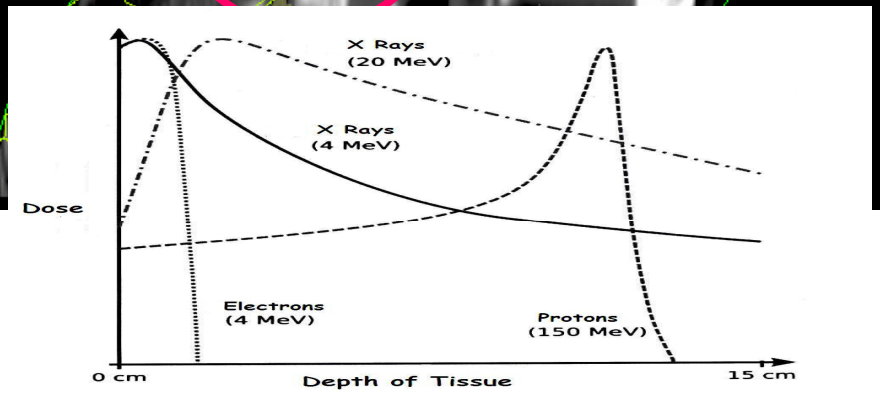
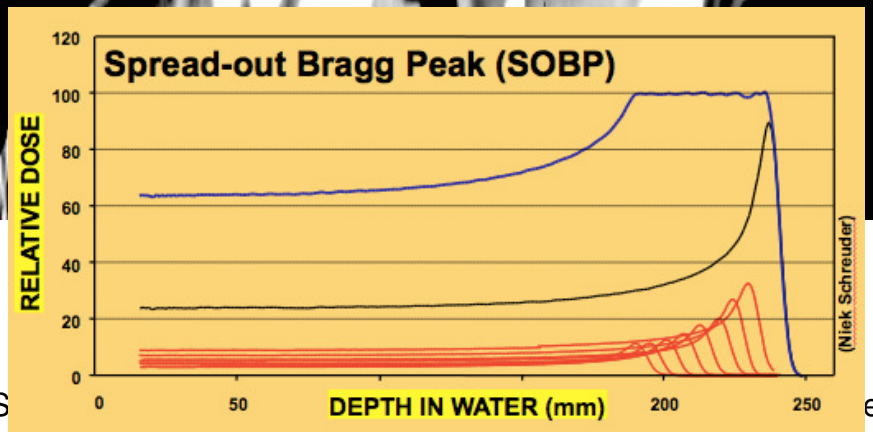
What can we see when we are used to plan with photons
… and move to protons? (~ concepts valid for passive and active…)



F1



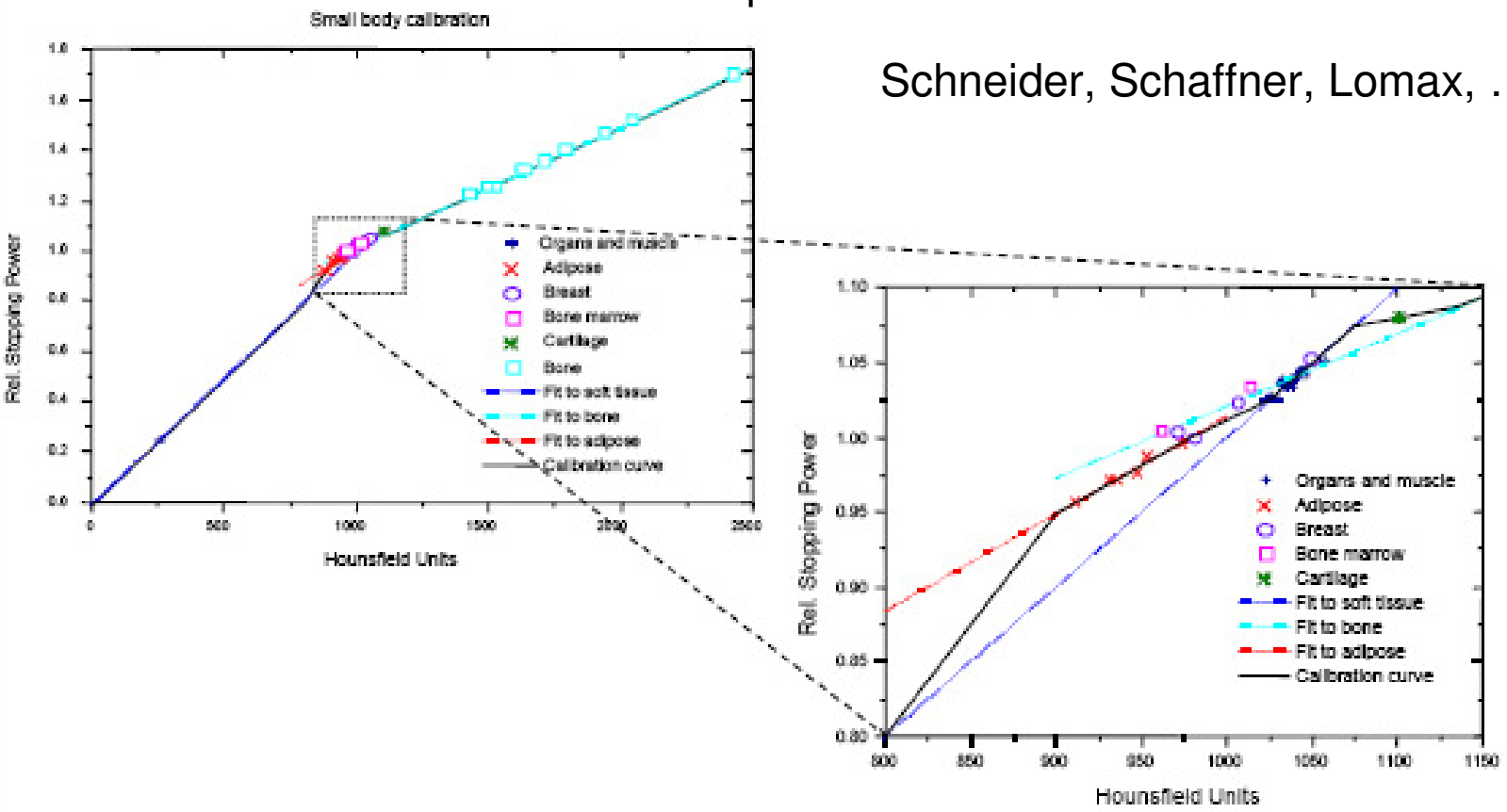




Plot of calculated (HU_{sc},SP_{rel}) pairs and linear fits

Importance of CT calibration & QA = RANGE

Schneider, Schaffner, Lomax, …



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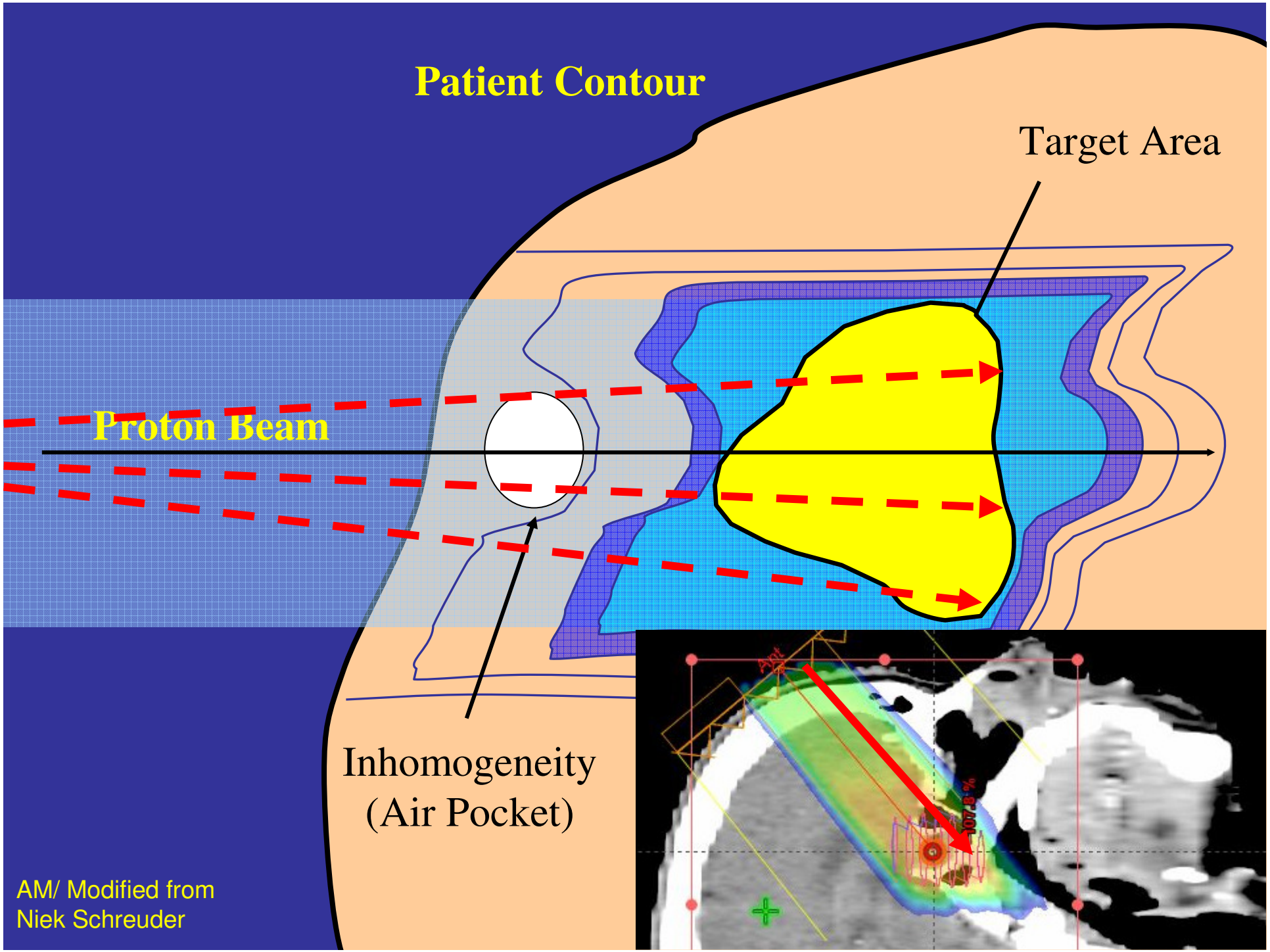
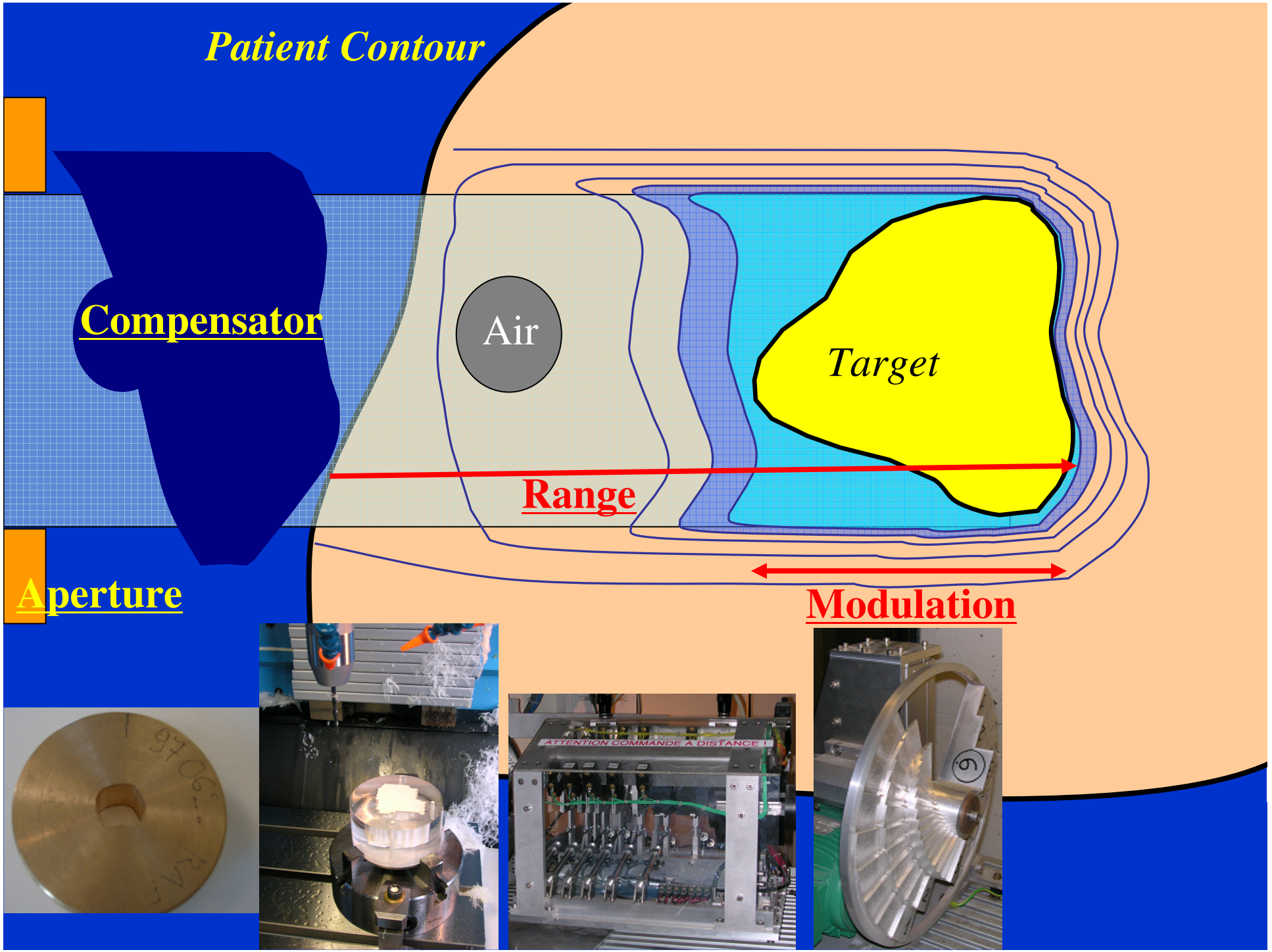
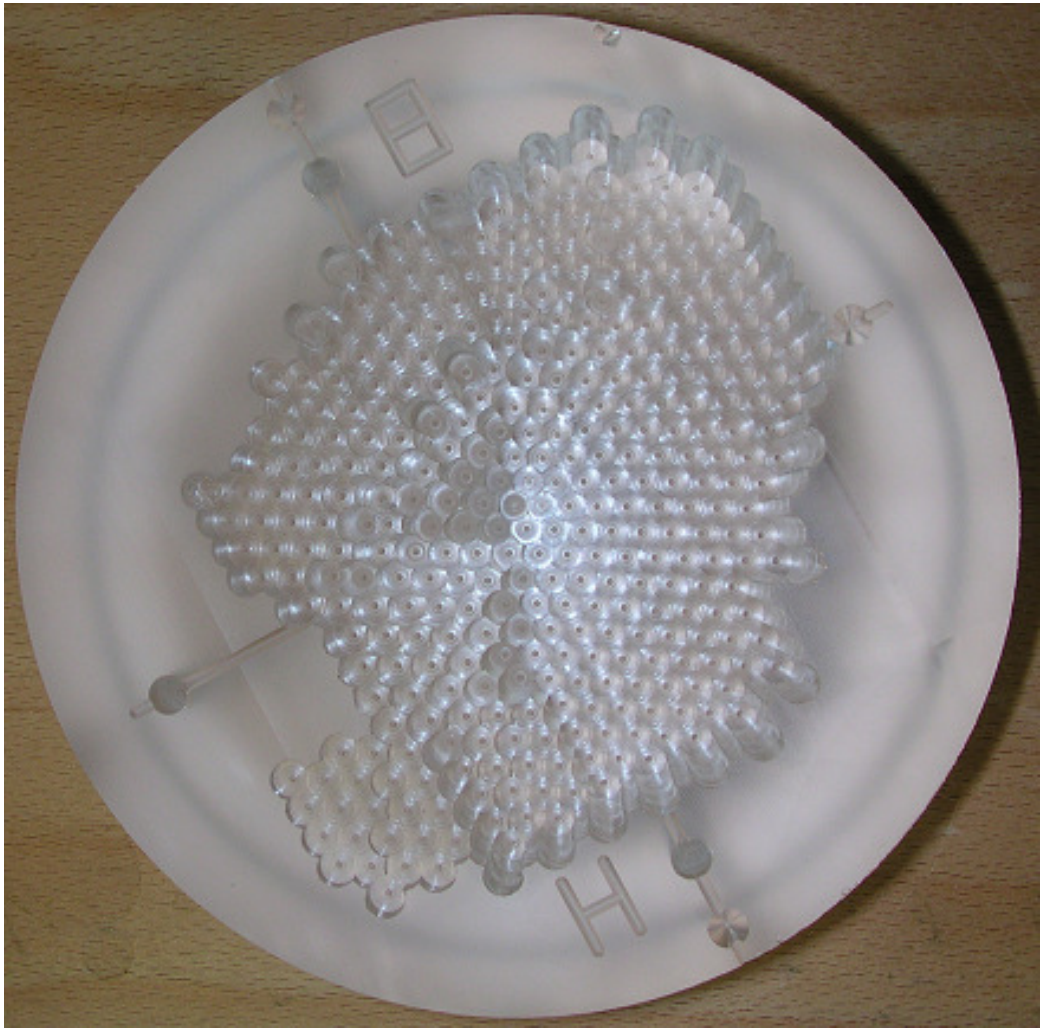

Patient Contour
Target Area
Proton Beam
Inhomogeneity
(Air Pocket)
AM/ Modified from
Niek Schreuder


Patient Contour
Compensator
Air
Target
Range
Modulation
Aperture



2nd reason to smear : Mis alignements and/or organ movement

→ See other presentation in this course

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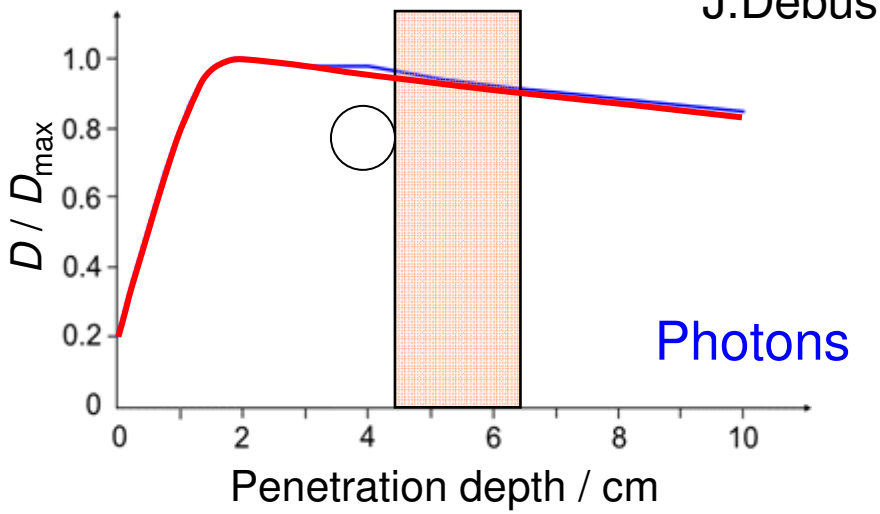
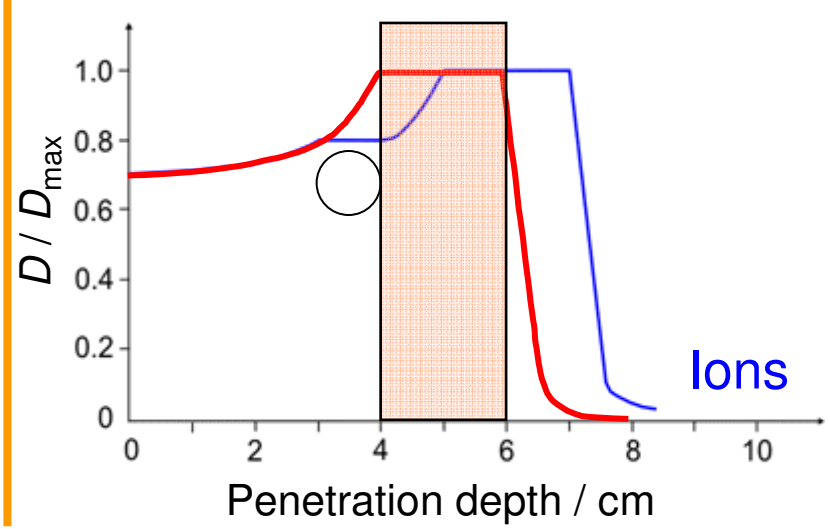
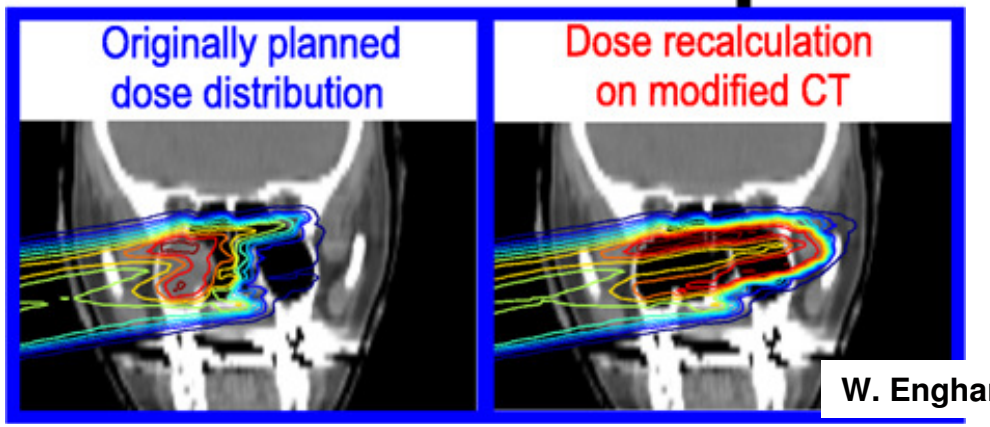
Effect of density changes (eg : in the target volume or in the beam path)

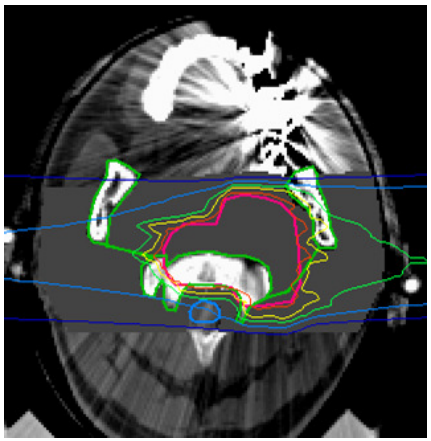
J.Debus







W. Enghardt et al.



Similar effects for CT artifacts, contrast, mispositioning or organ movement

Need to survey the anatomical changes in the path
after the planning CT and till the end of the treatment

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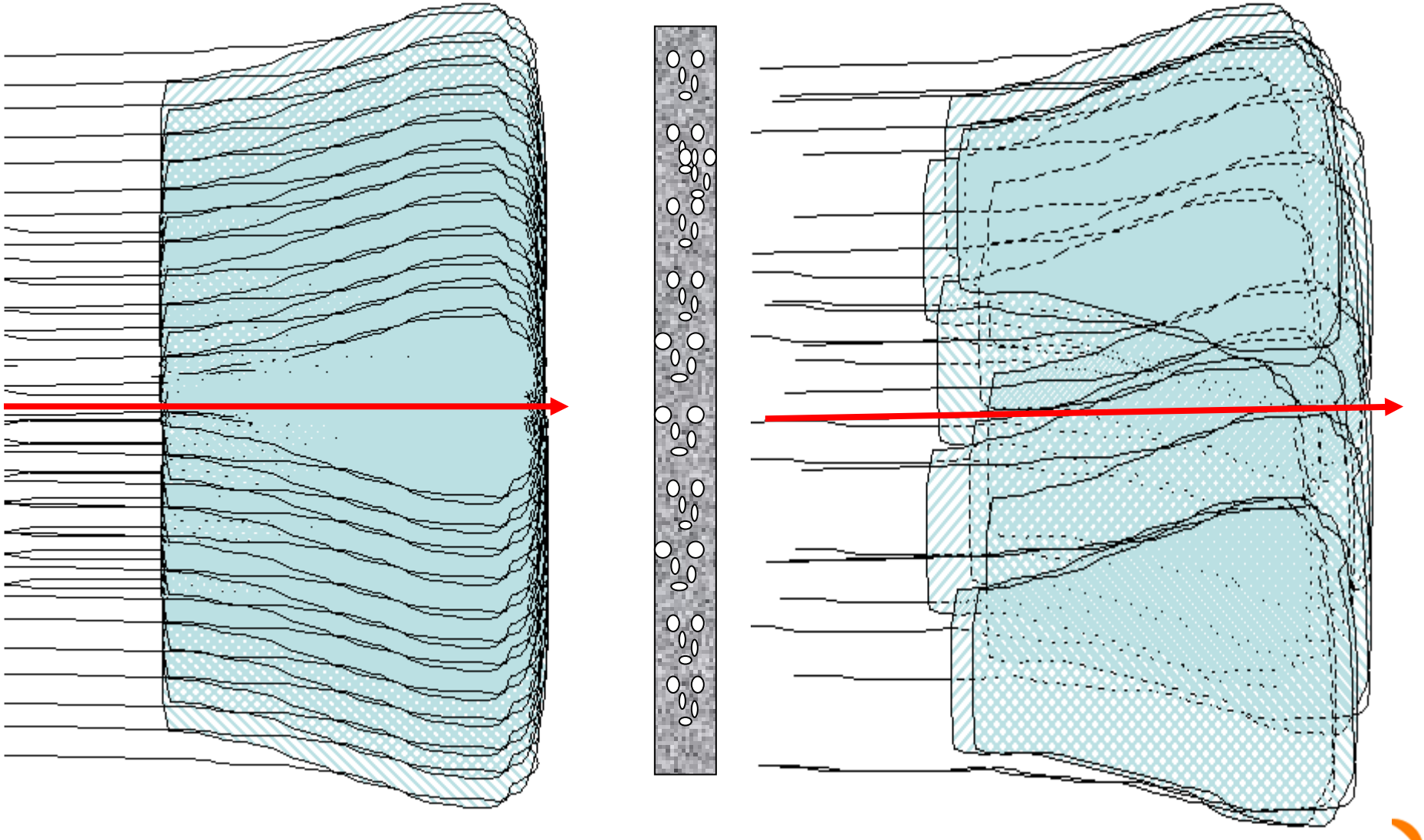
But… if « complex » heterogeneities : not only a « ray tracing approach », also multiple scattering effects :



This effect is even more evident with borders along the beam direction…

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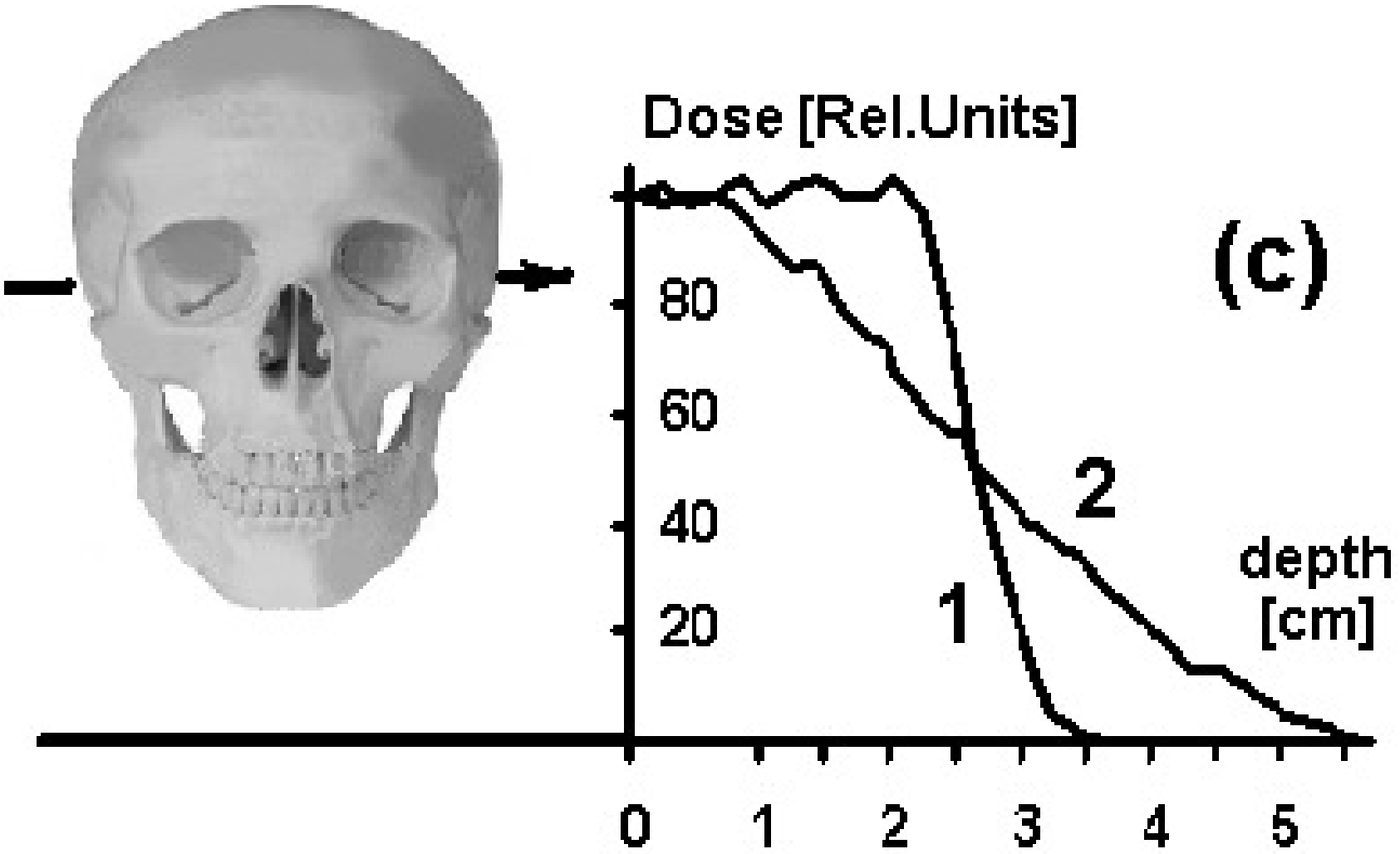
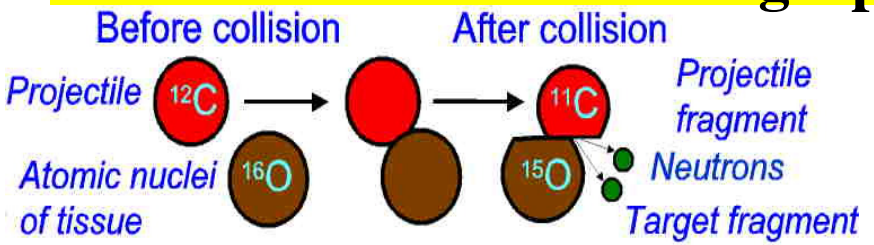


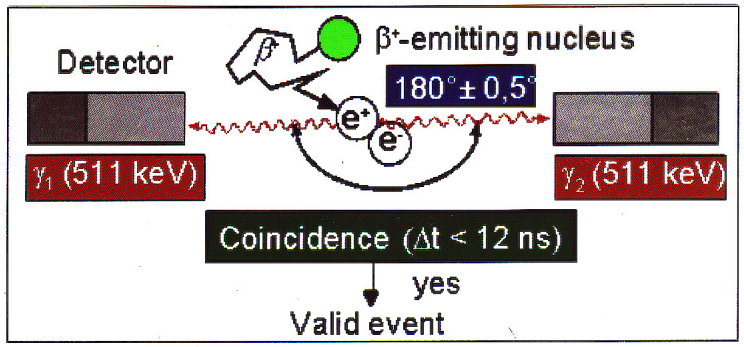
Need to change the range

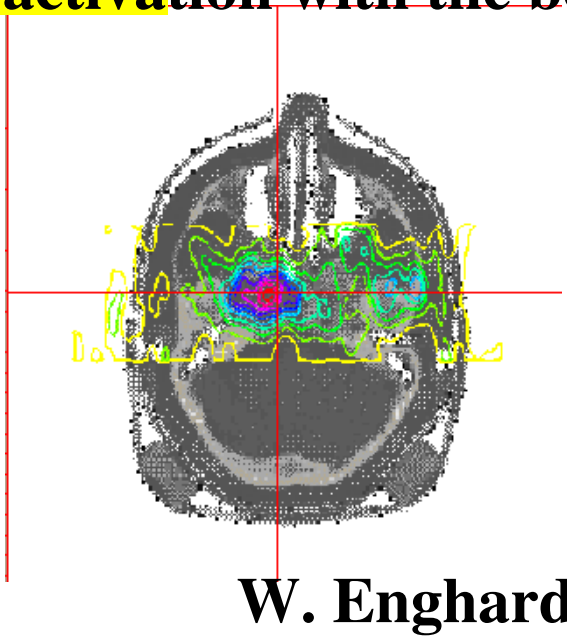
→ change the incidence !!

Urie et al

Positron Emission Tomography from patient activation with the be





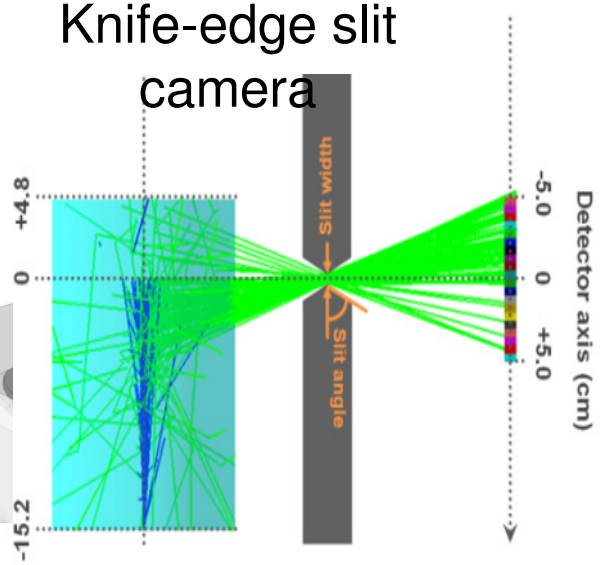


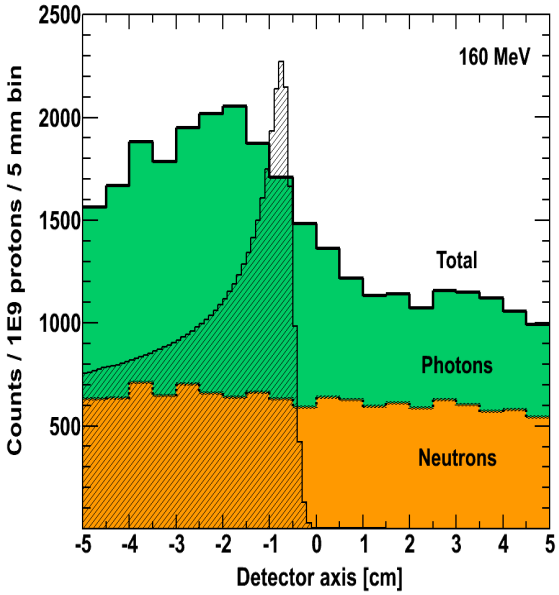
W. Enghardt

Prompt Gamma

F.Roellinghoff.
PhD, IBA.

Knife-edge slit camera

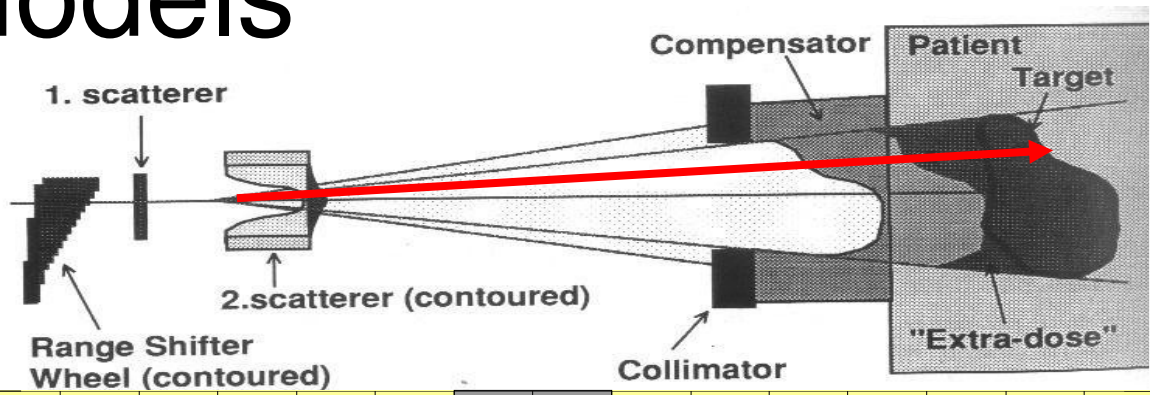




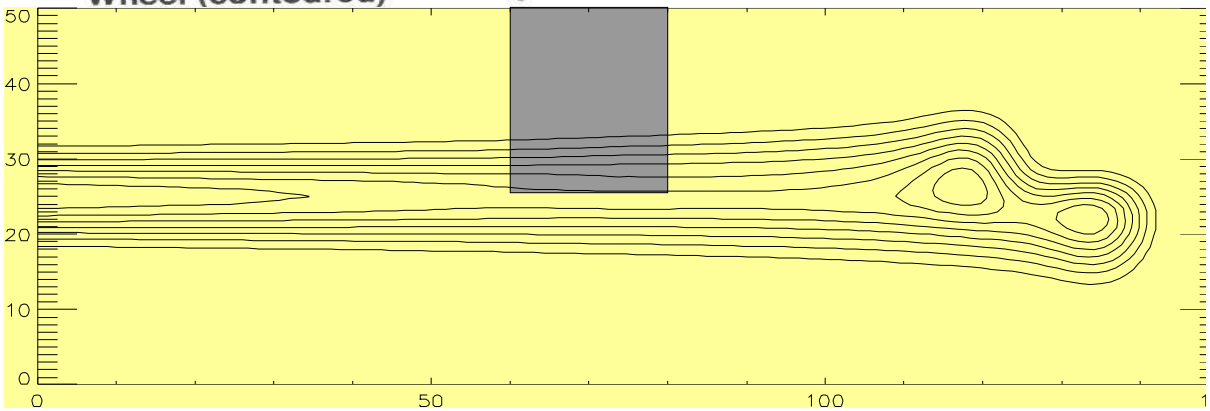
TPS : beam models

3 Families

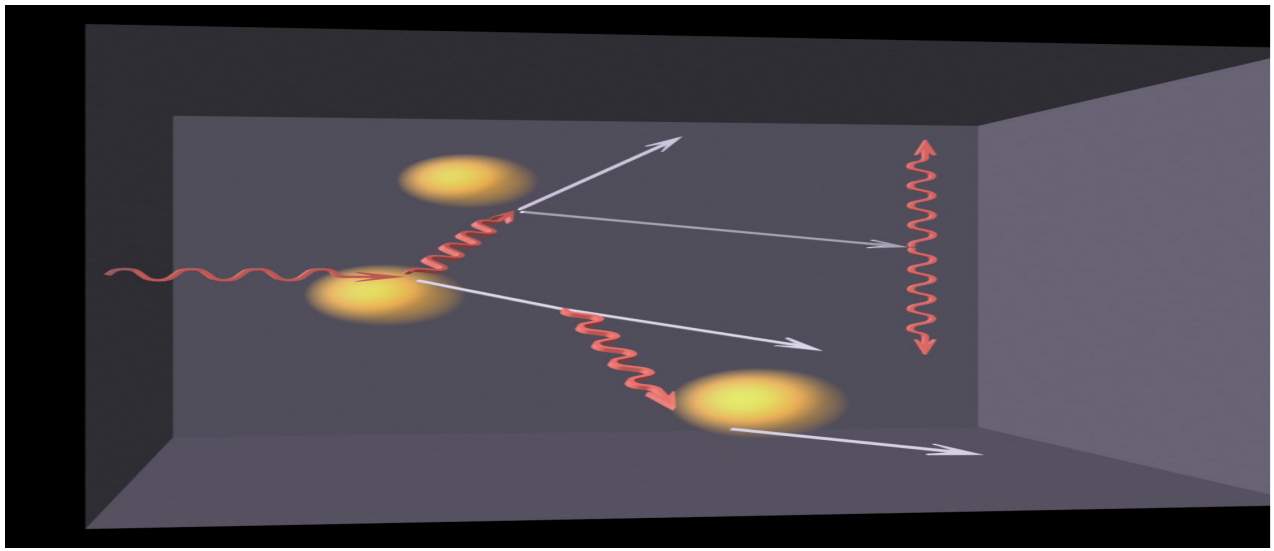
1) Ray Tracing



2) Pencil Beam



3) MonteCarlo



Why MonteCarlo?

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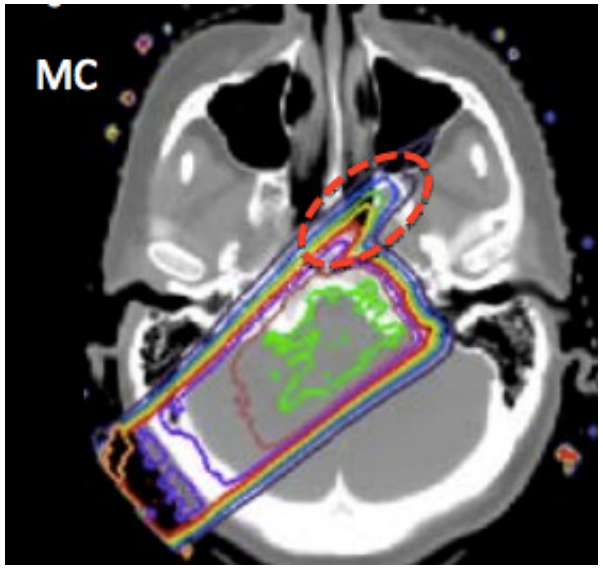
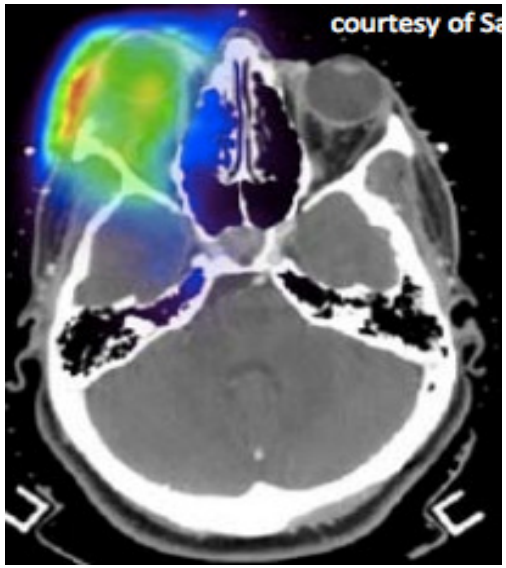
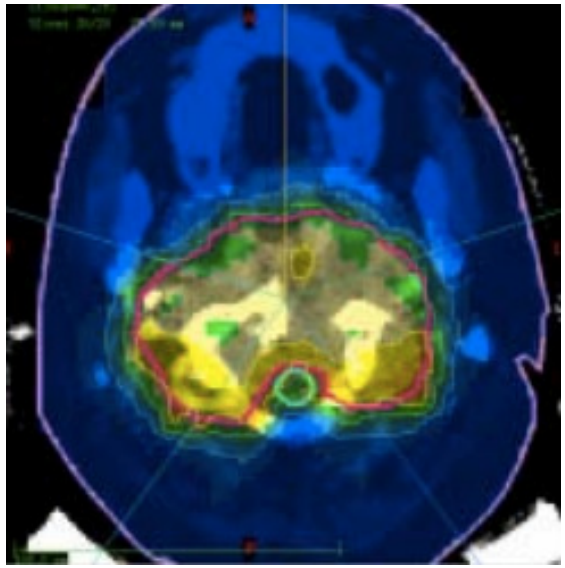
Applications of Monte Carlo :



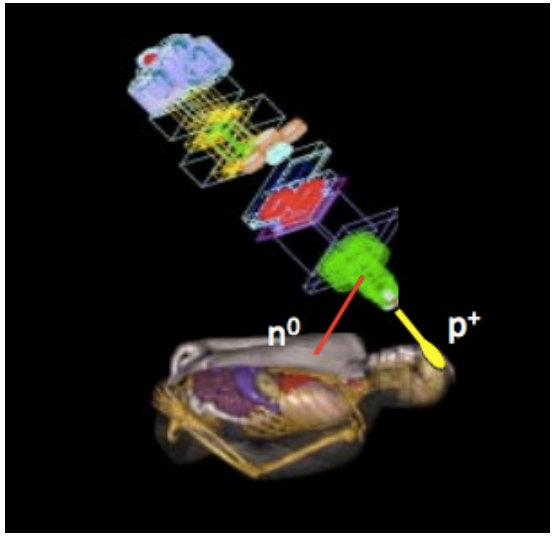
Precise dose calcs with inhomog



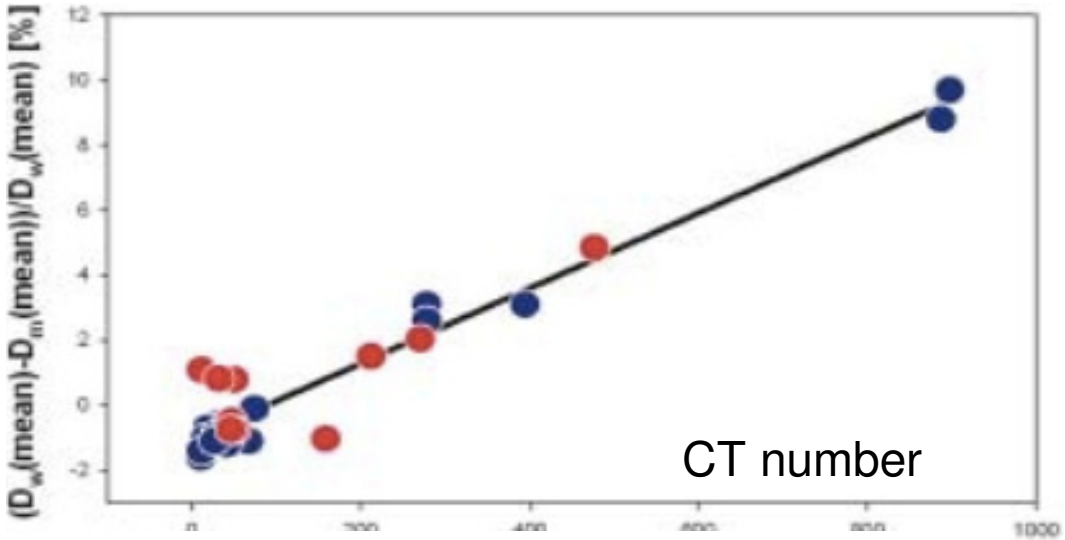
Tissue activation for PET QA



Calculation of LET → RBE



Calculation of neutrons



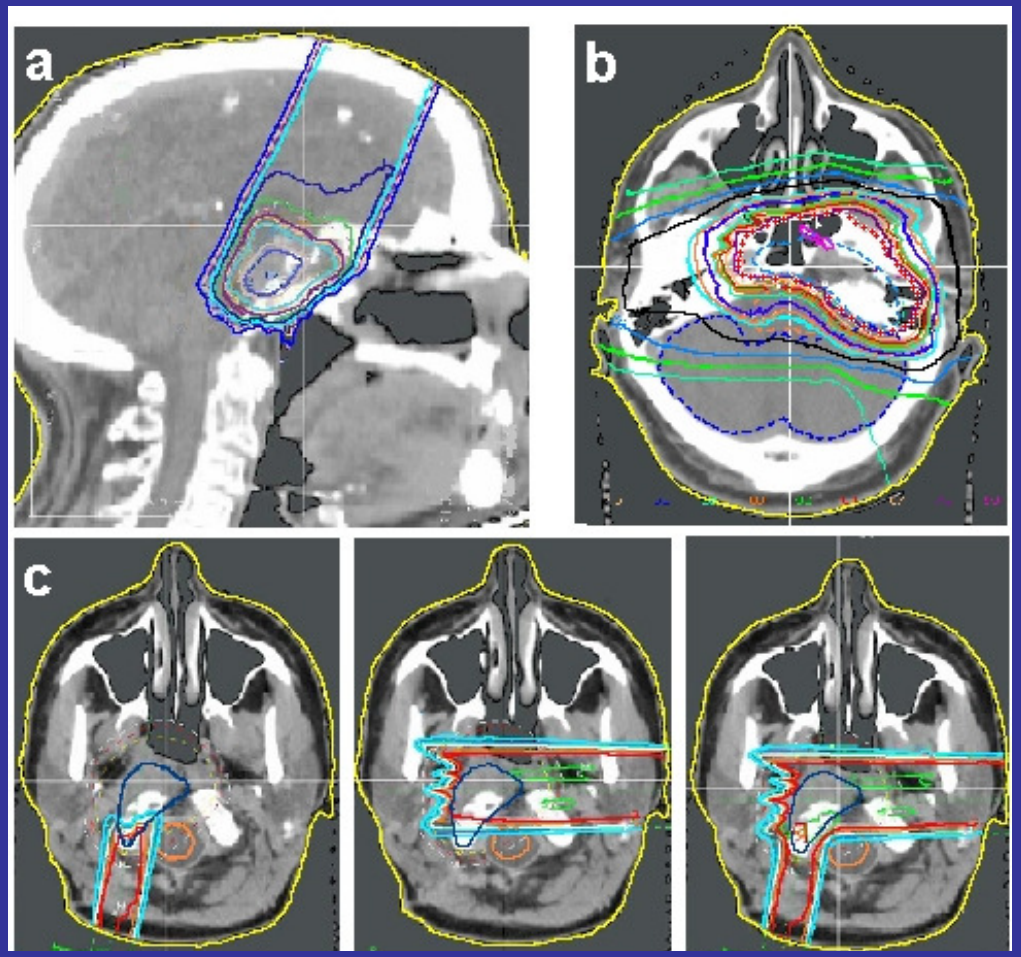
Conversion from water to tissue dose

Bednardz, PTCOG49 / Data from Paganetti, Shin, Espana, Oelfke, Athar, Xu and Bolch)

Clinical applications:
Eg: Base of the skull tumors

Photons-protons
Non coplanar beams

Junctions, patching



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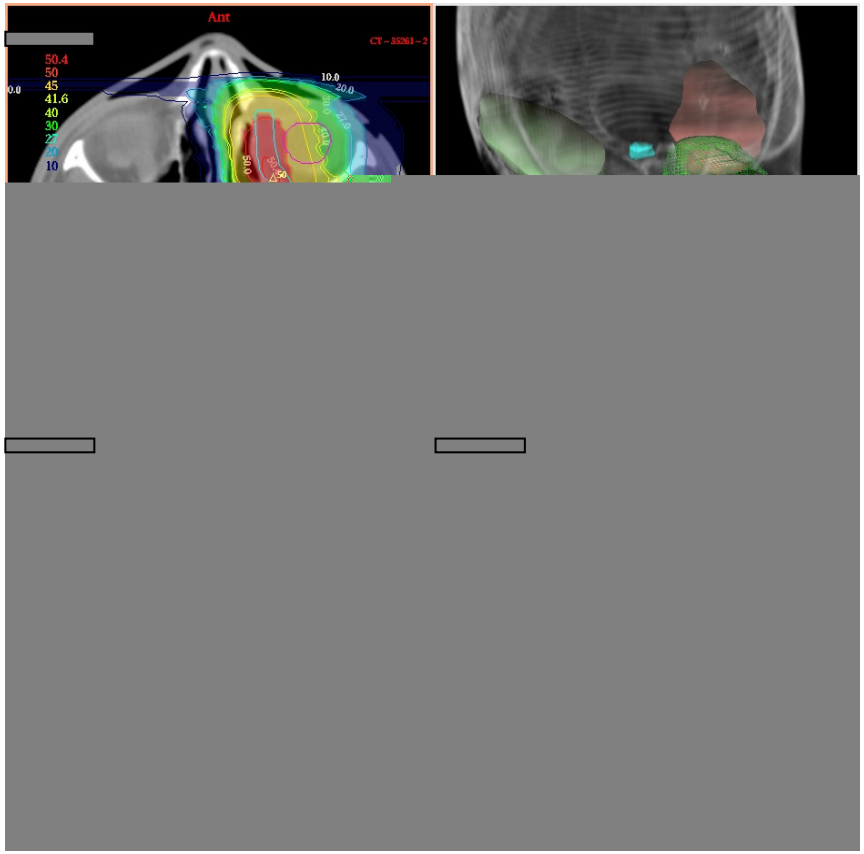
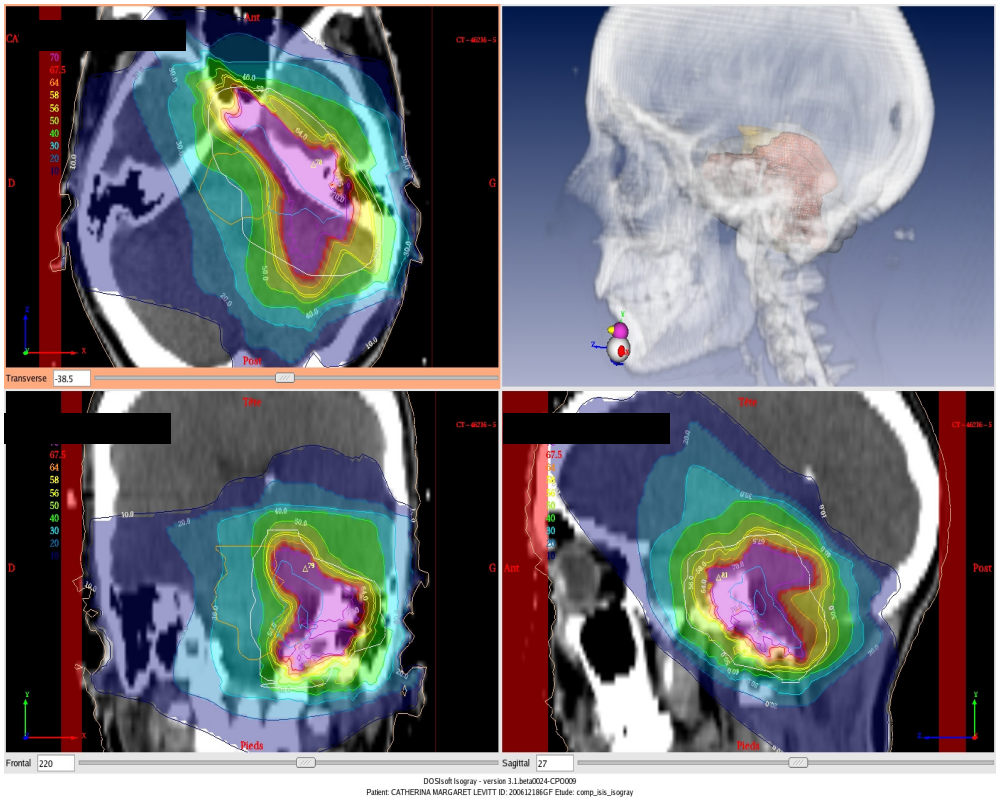
Practical examples (CPO)



Rhabdomyosarcoma



Chondrosarcoma (X + p)

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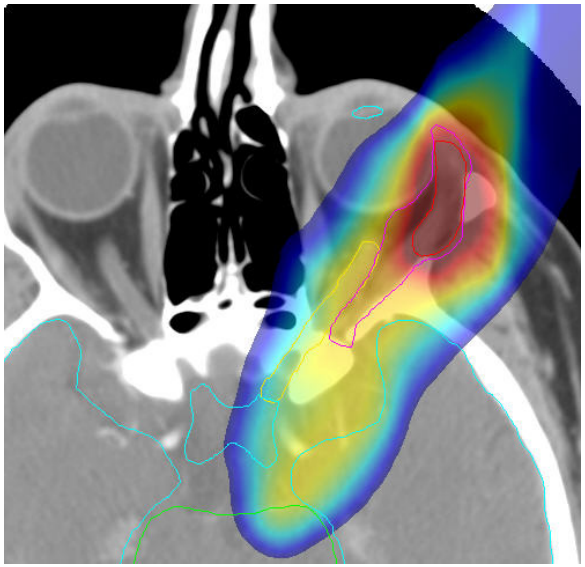
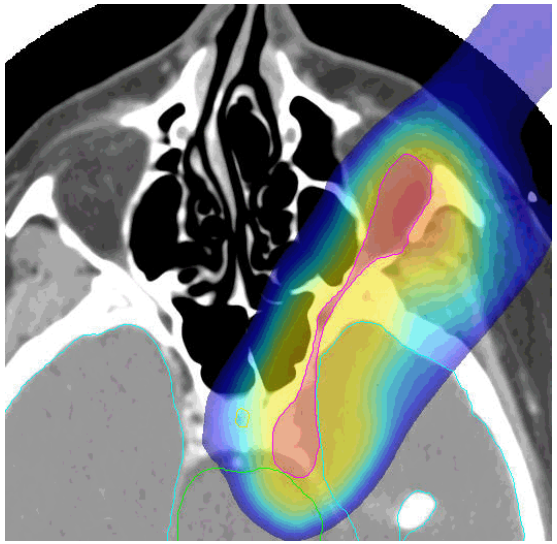
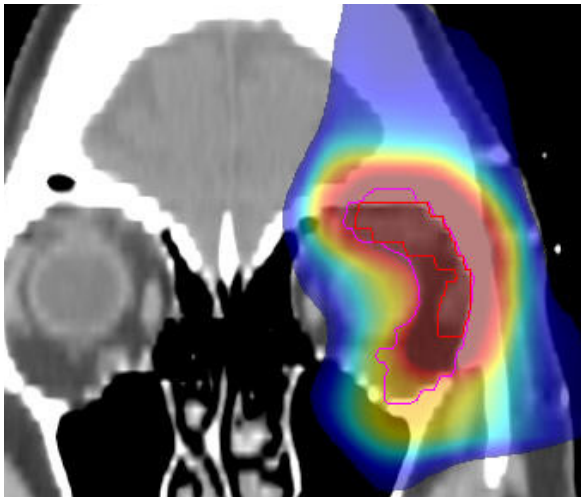
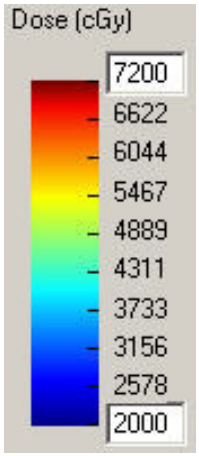
Practical example (MGH)









Judy Adams et al,
Skin sparing
Lacrimal gland

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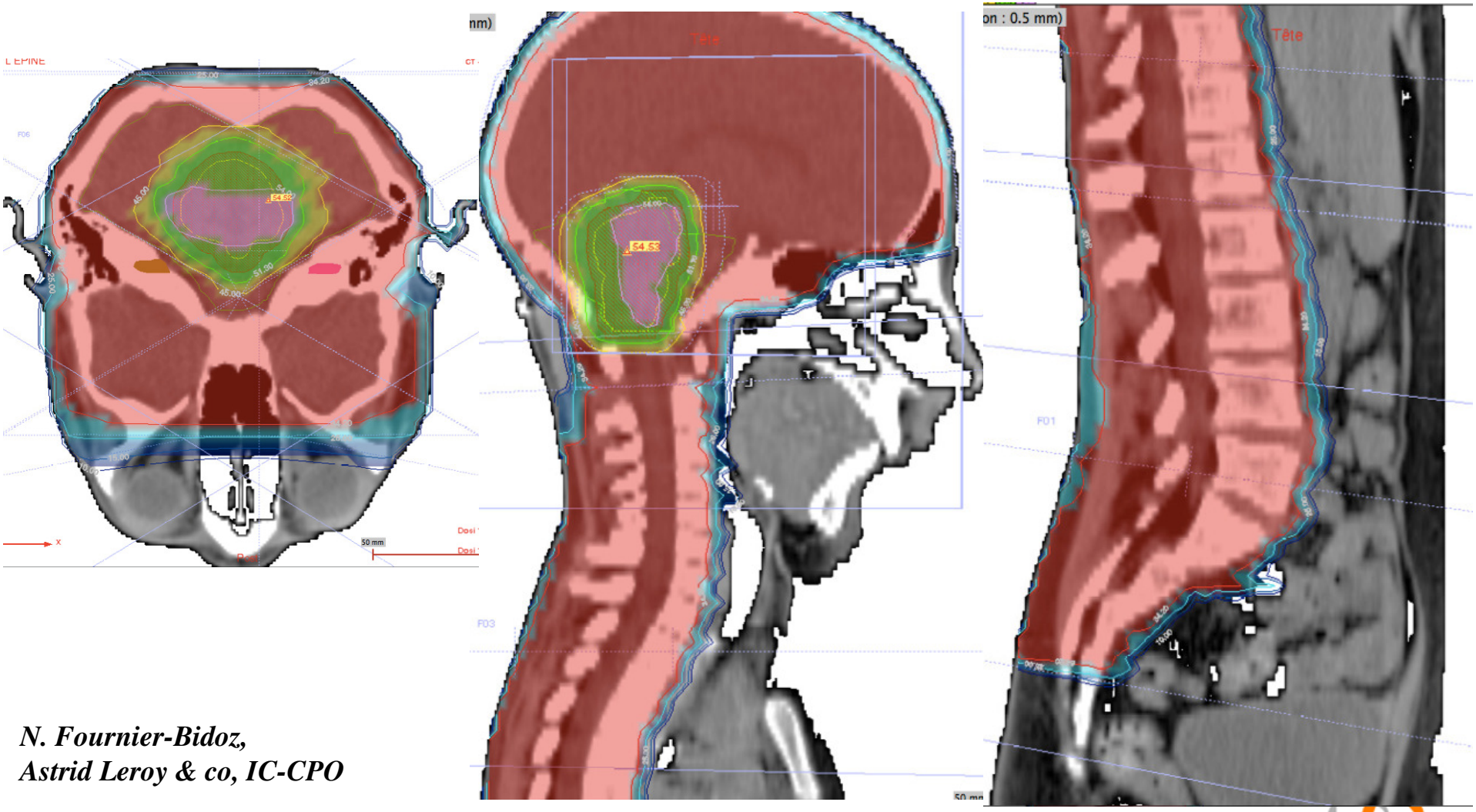
Pediatric tumors (ex: medulloblastome)



N. Fournier-Bidoz,
Astrid Leroy & co, IC-CPO

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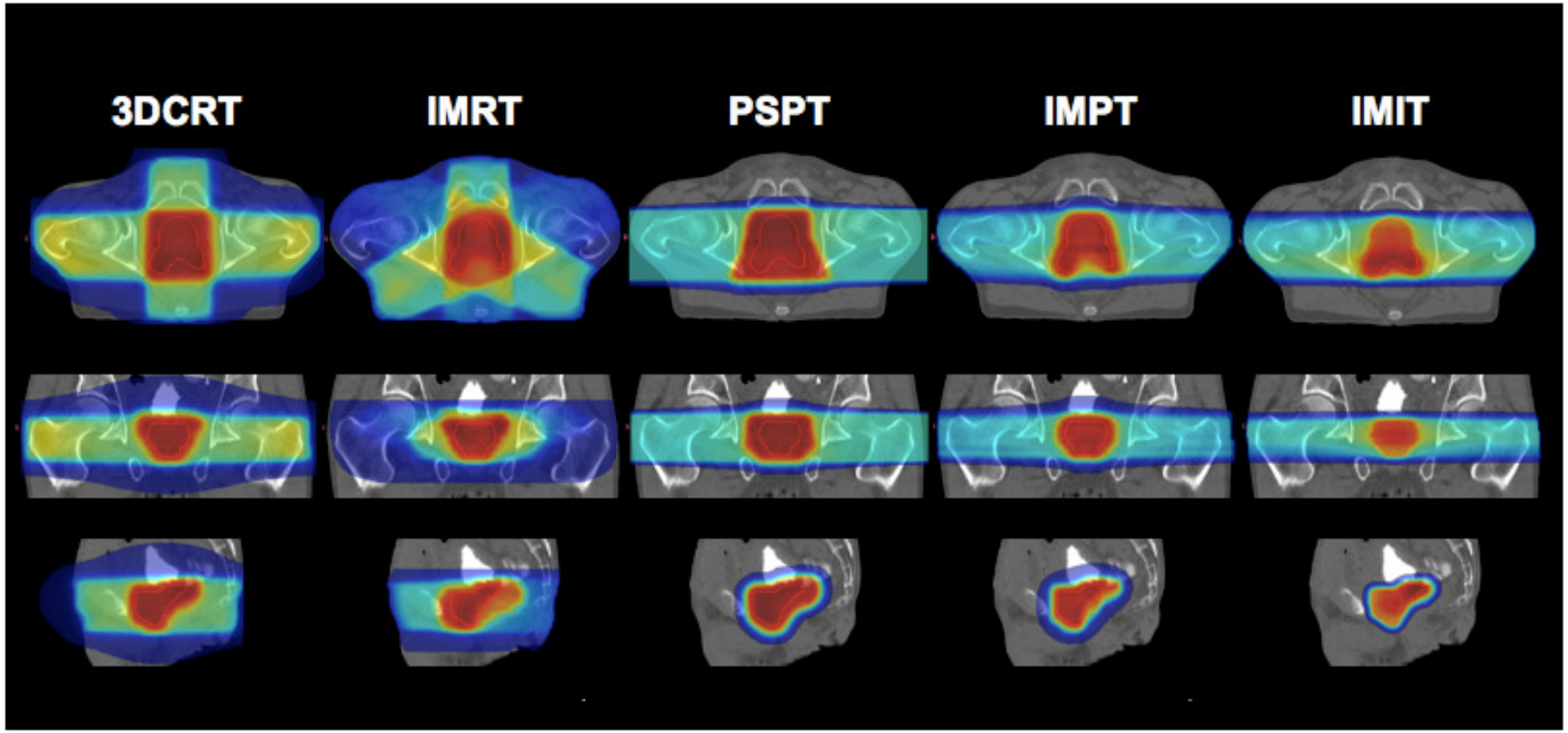
ROCOCO (Maastro & > 15 institutions involved)



Erik Roelofs et al, ROCOCO Trial, PTCOG 51, 2011

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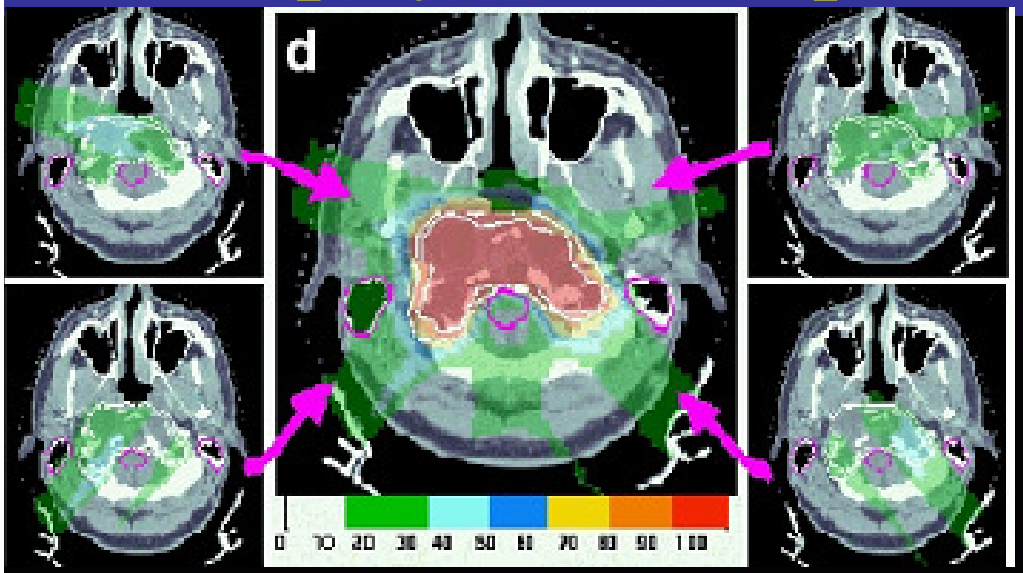
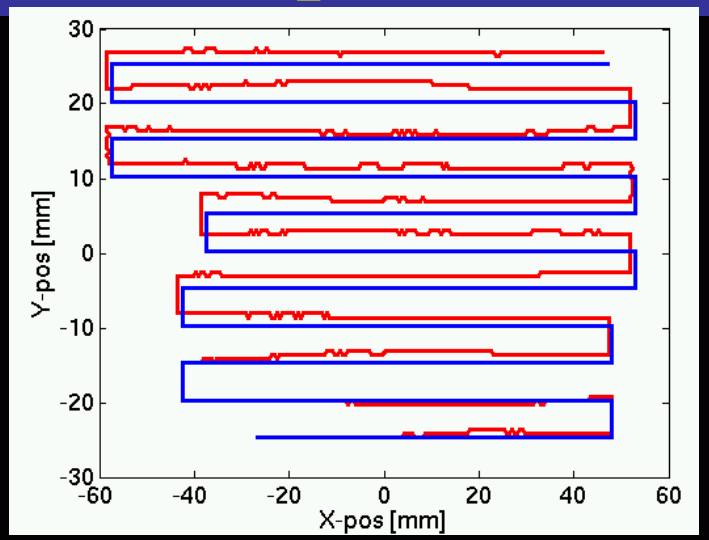
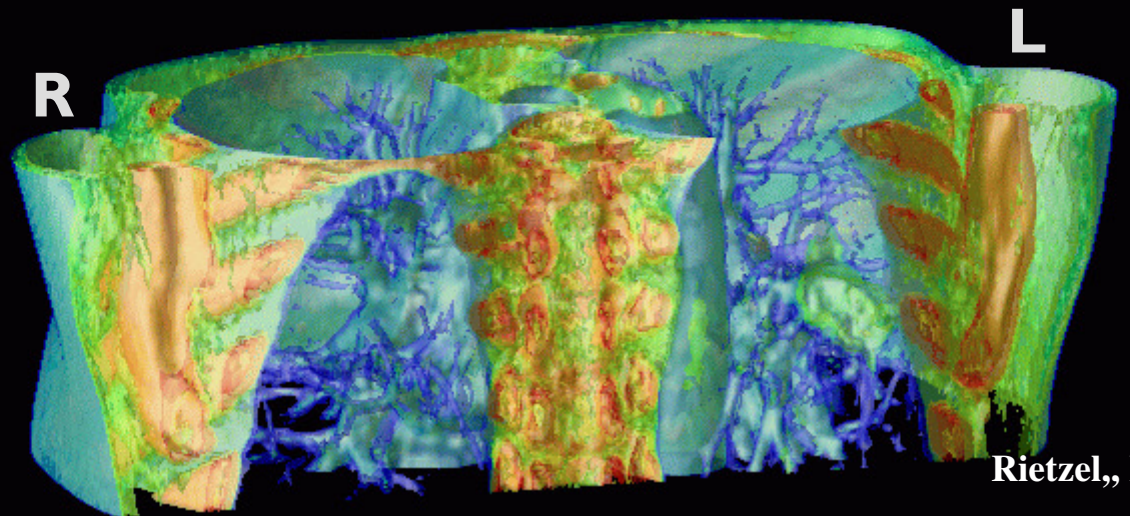
Towards dynamic delivery systems while being able to treat moving organs: « interplay » & « repainting » concepts

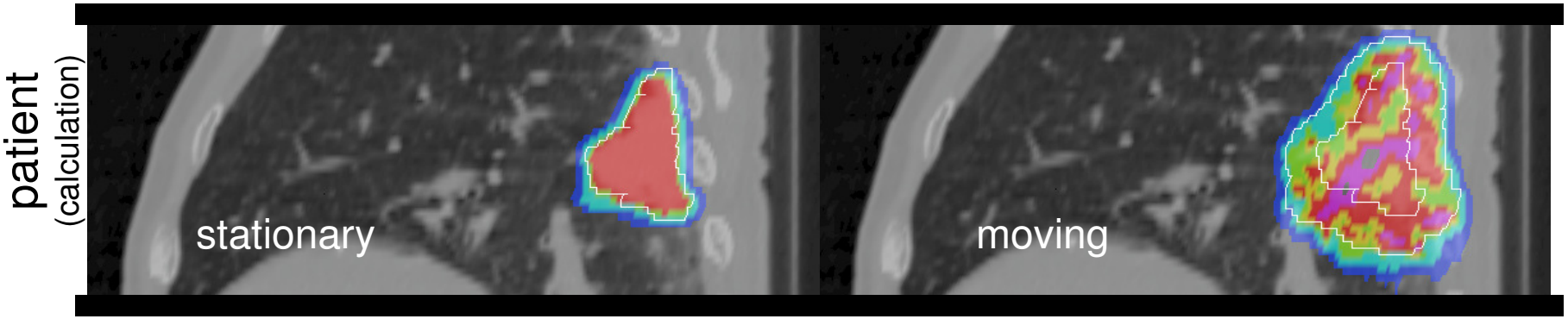


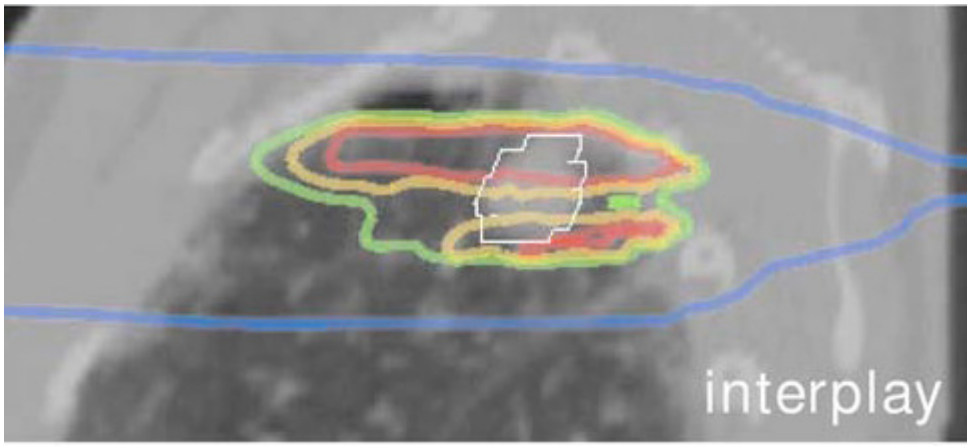




Rietzel,, Bortfeld, Lomax,Trofimov,…

Effect of target movement with scanned beams





(Local under and over dosage)

Mitigation techniques :
- Breath holding
- Compression
- Beam Gating
- Beam Tracking
- Repainting

Status and perspectives : specifications to vendors are evolving.

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C. Bert et al., Phys. Med. Biol.(2008), Rietzel et al Med.Phys (2010)

« Hadrons » in therapy

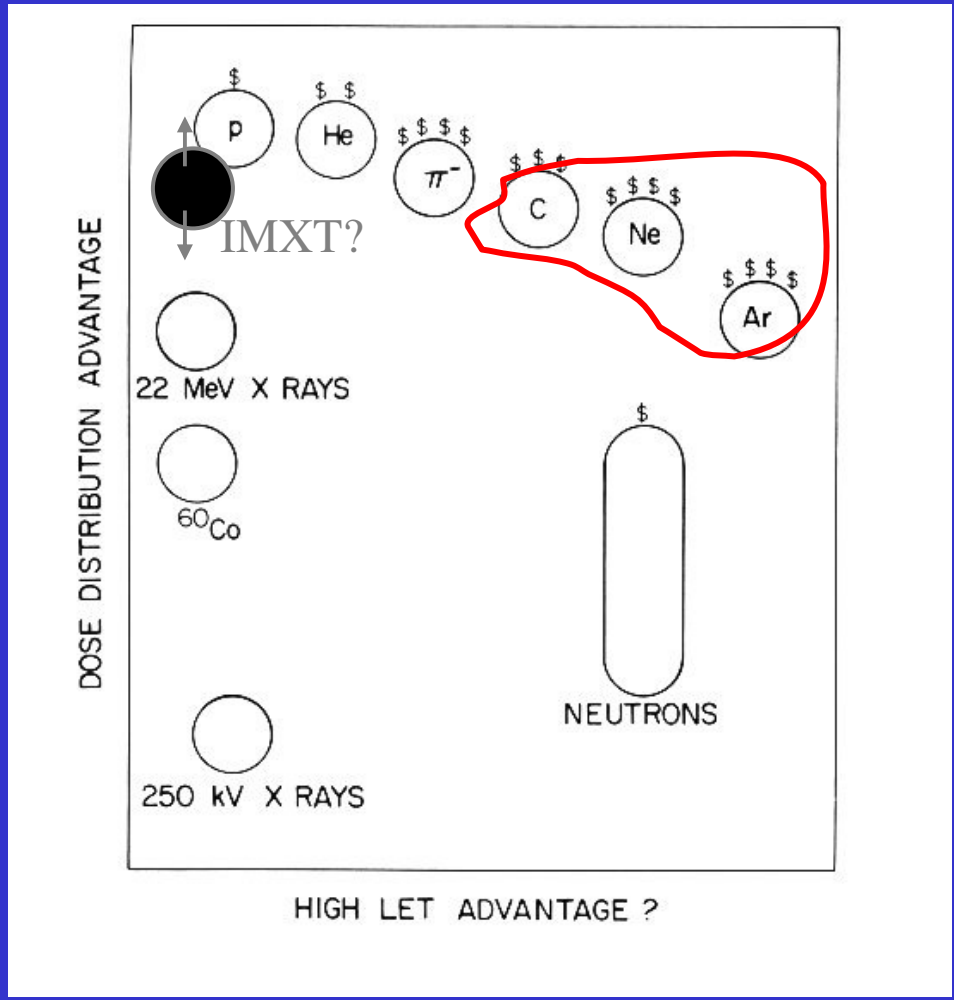
Physical selectivity and/or Radiobiological effects

* pions

* fast
& slow neutrons

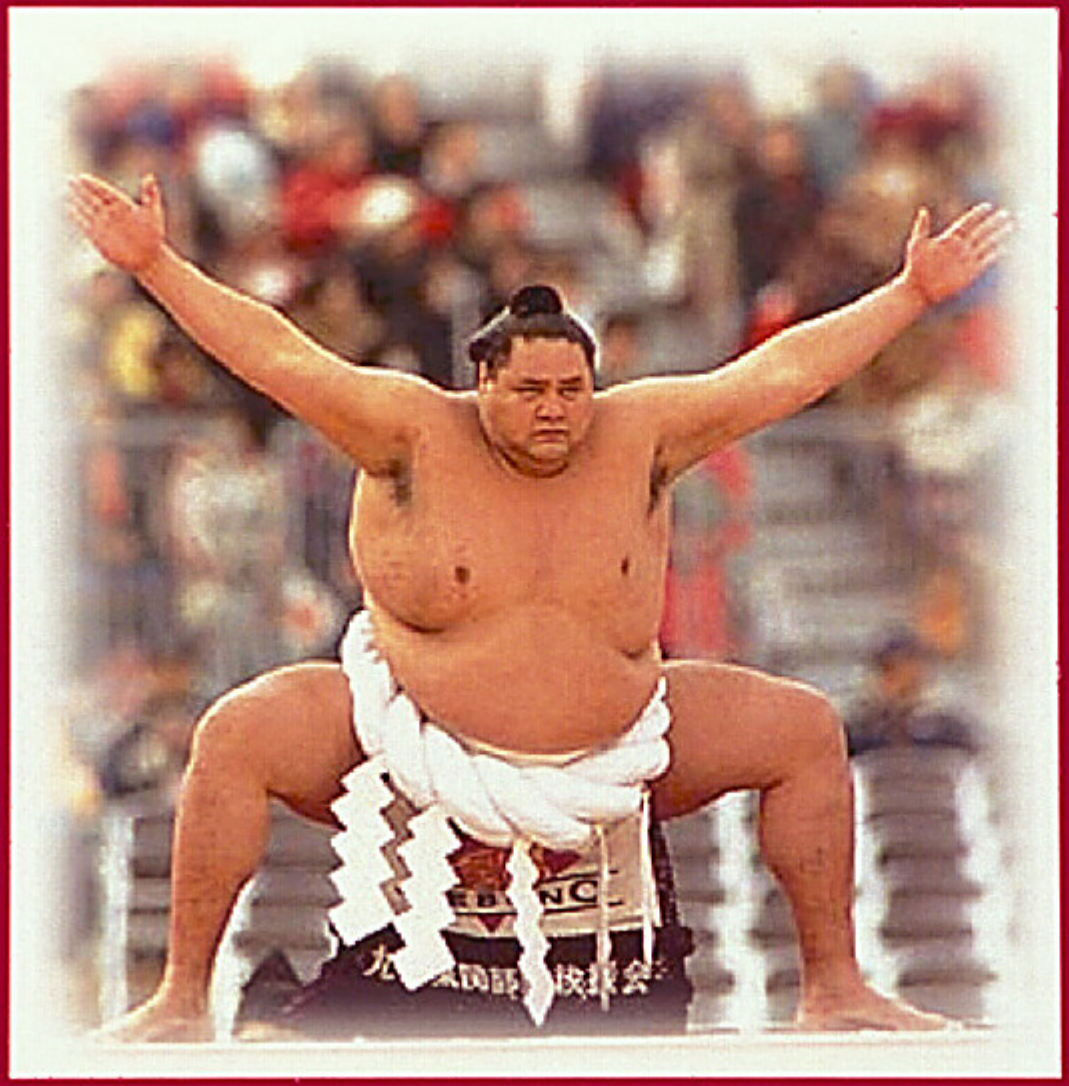
* protons

* light and heavy ions



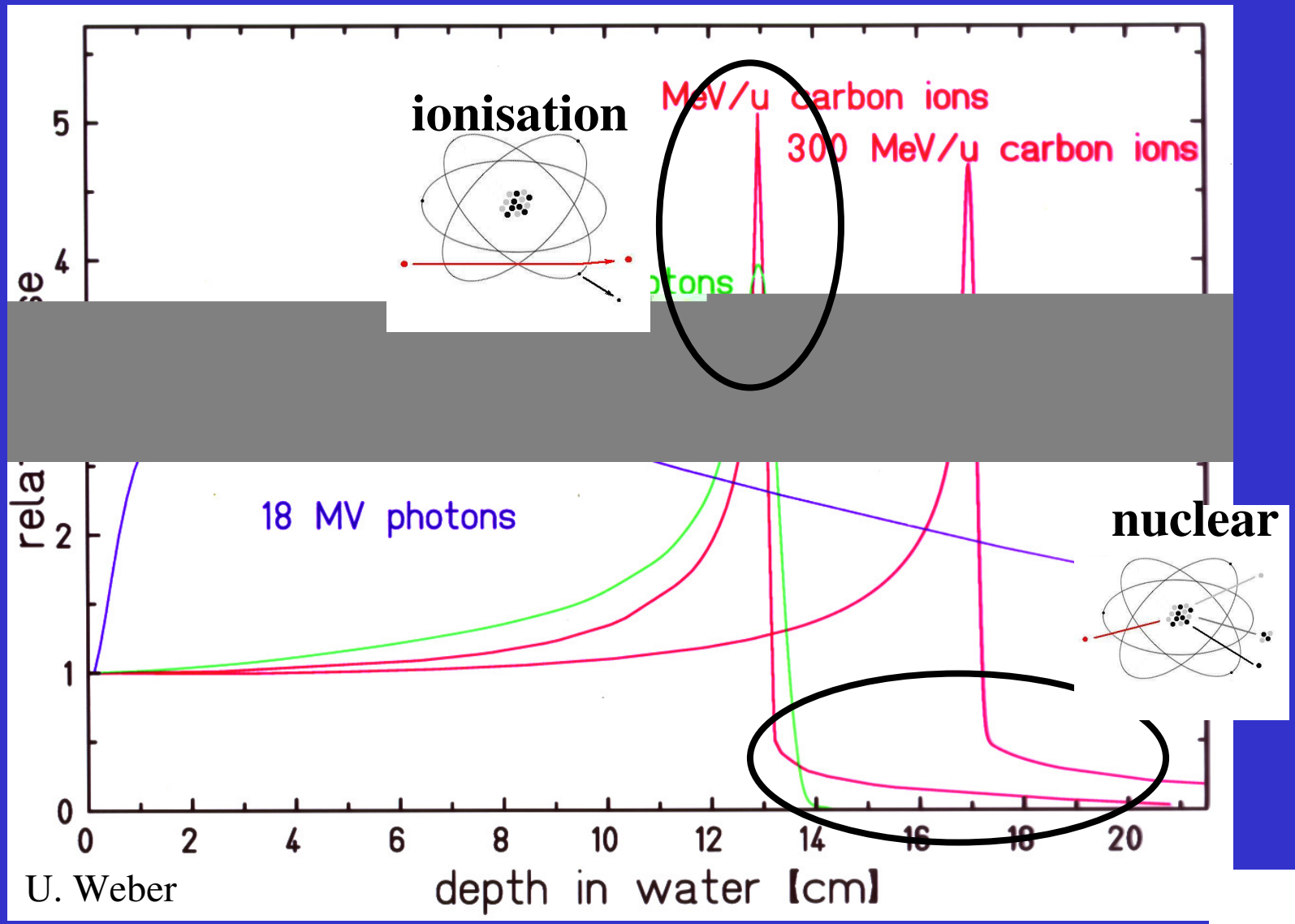
Raju & Koehler, 1980

HEAVY IONS



… having.the Stopping power as a larger « **weighting** » factor

Depth dose distribution of various radiation modalities



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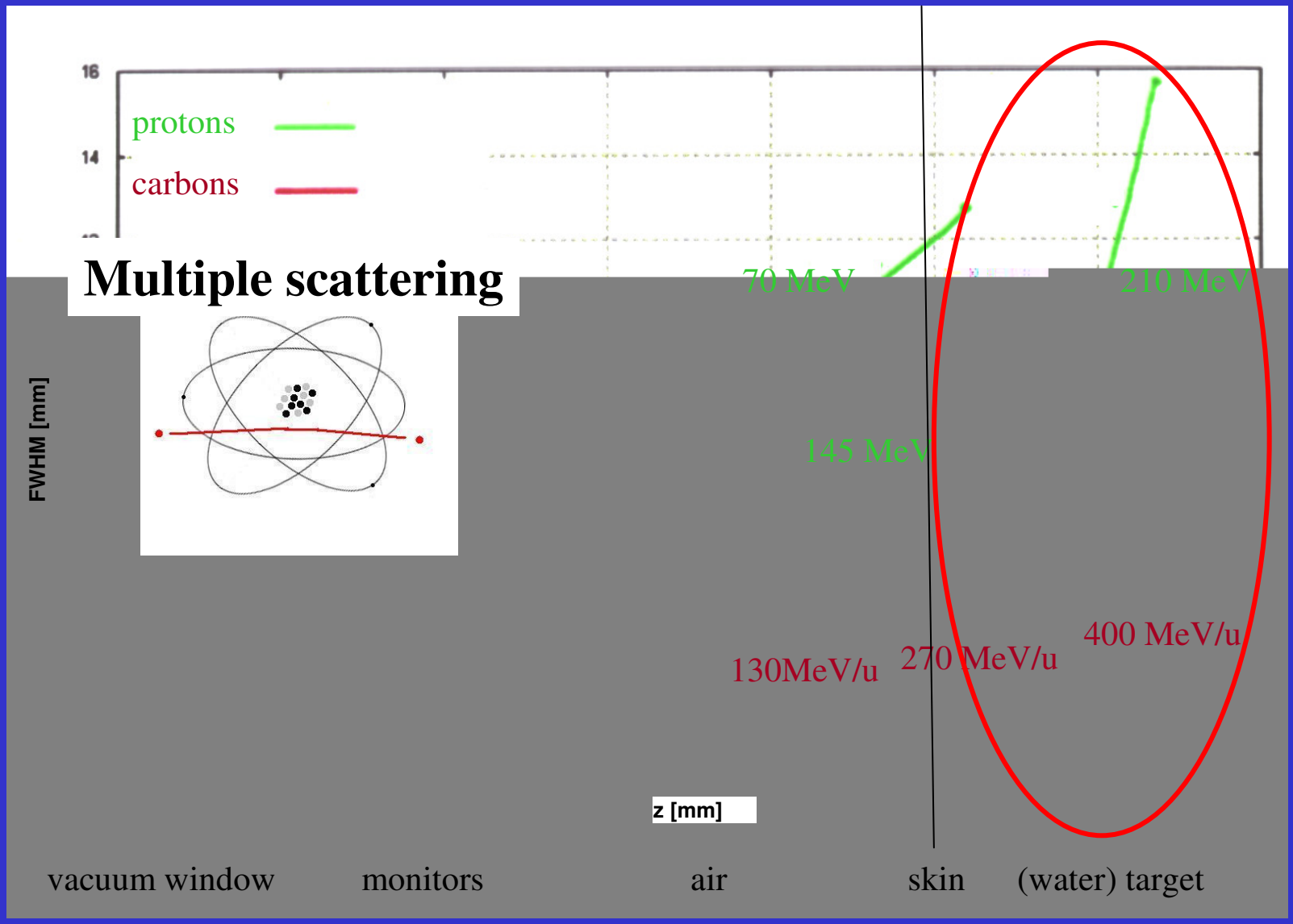
Beam scattering for a real scanning setup (exit window, monitors, air, patient)



Calc. U.Weber, RKA AG

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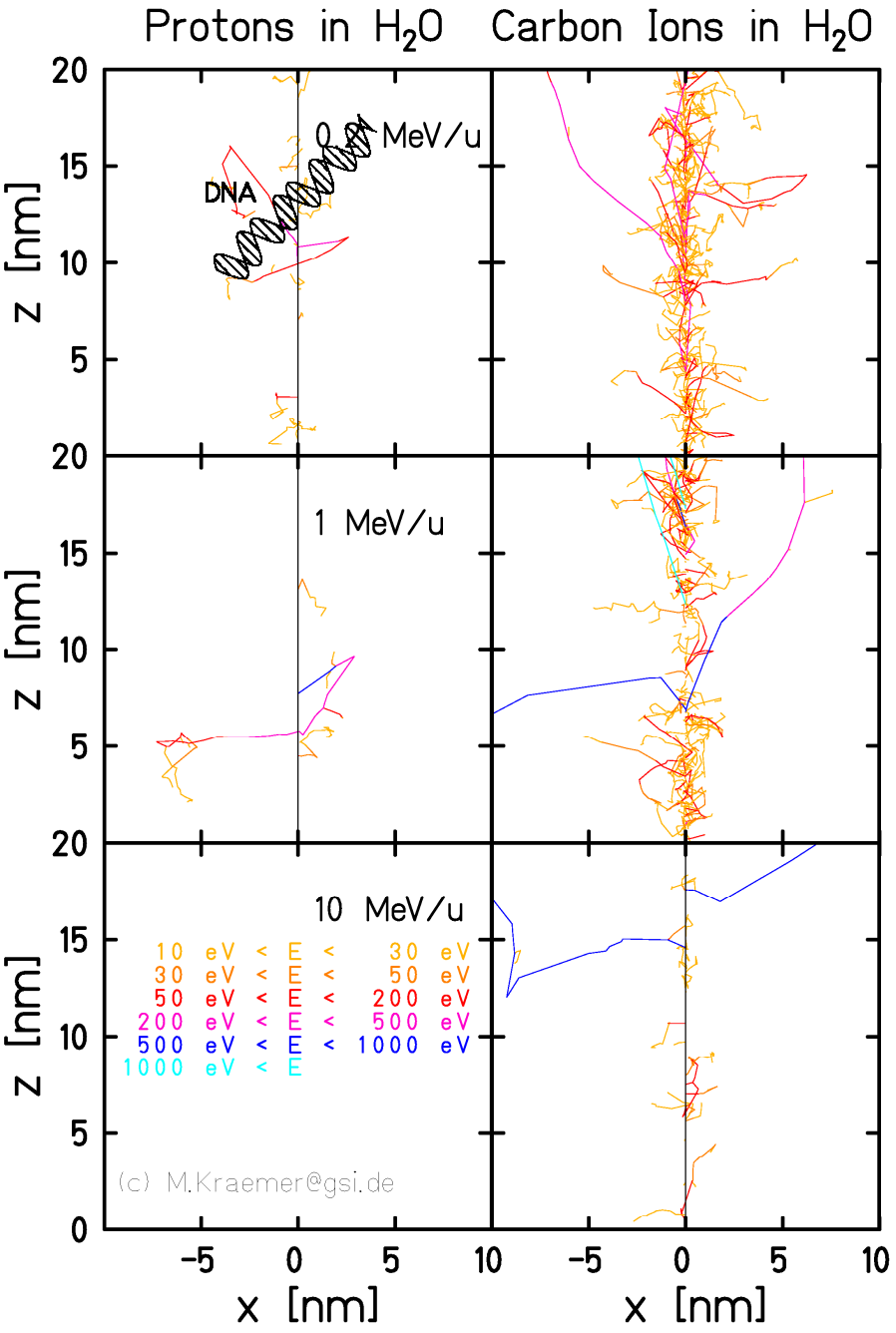
Radiation Biology:

Dose distribution in nanometer scale

M. Kraemer



Menu :

I. Medical Physics in RT : past, present

I. Hadrontherapy :
   1. Types of particles
   2. Interactions with electric (E) and magnetic fields (B)
   3. Interaction with matter (eg: beam line, patient)
   4. Planning and treating with particles
   5. Moving towards heavier ions

III. The future : revisiting radiation biology

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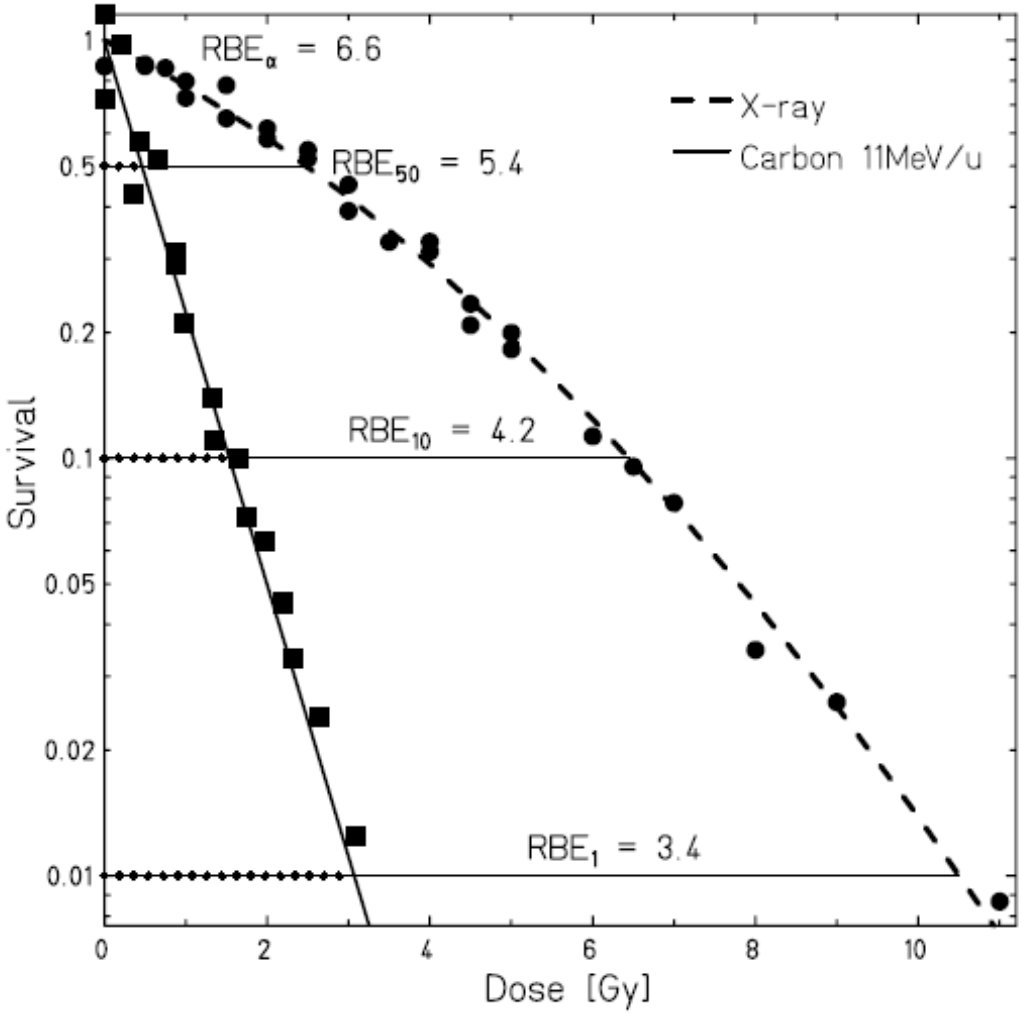
Relative Biological Effectiveness (RBE)

Definition: **RBE is defined as the ratio of X-ray dose to particle dose to produce the same biological effect.**



RBE is not a fixed parameter . . . .

Krämer et al.
Technology in Cancer Research & Treatment 2: 2003

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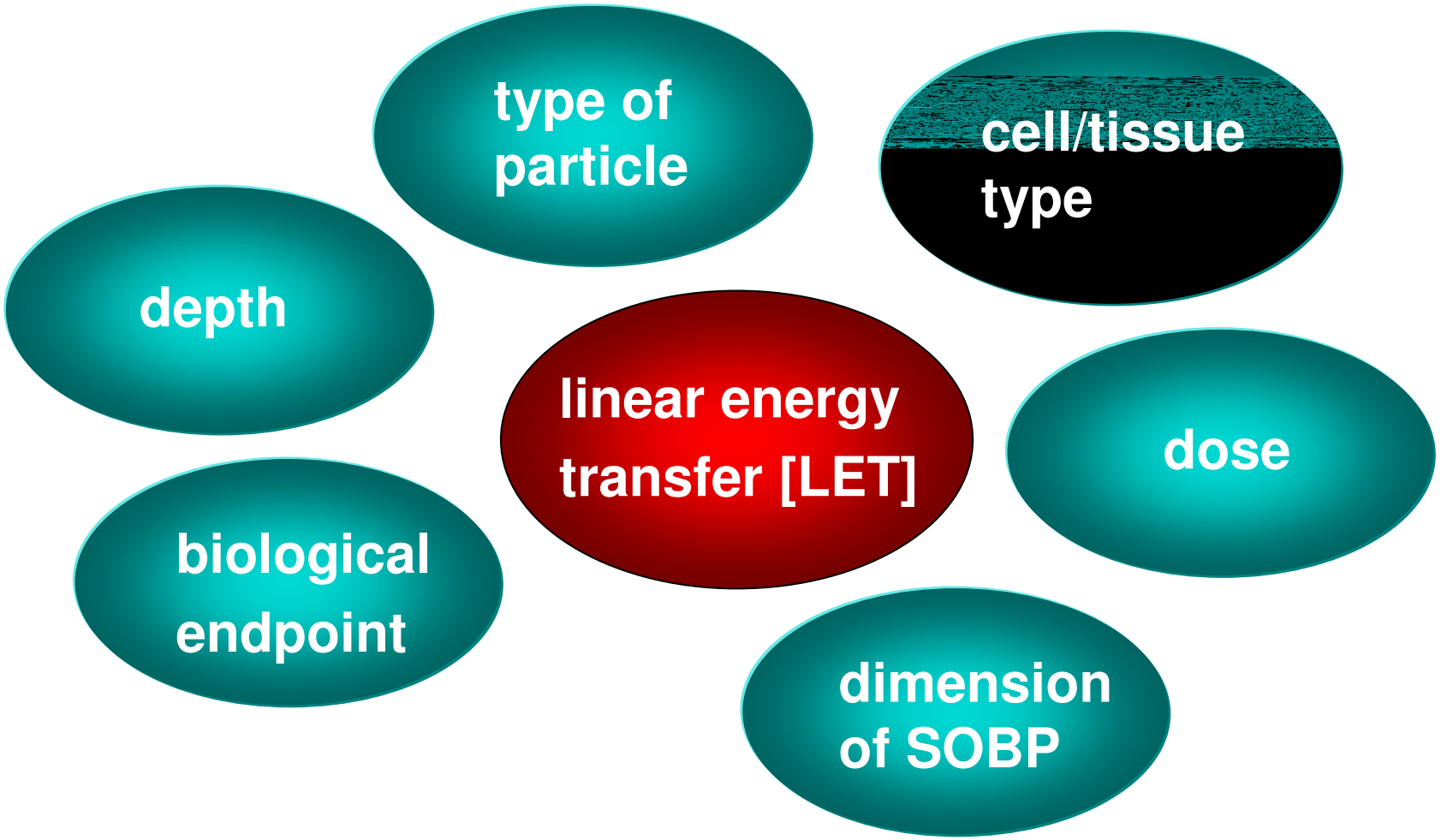
Relative Biological Effectiveness (RBE)

RBE depends on:

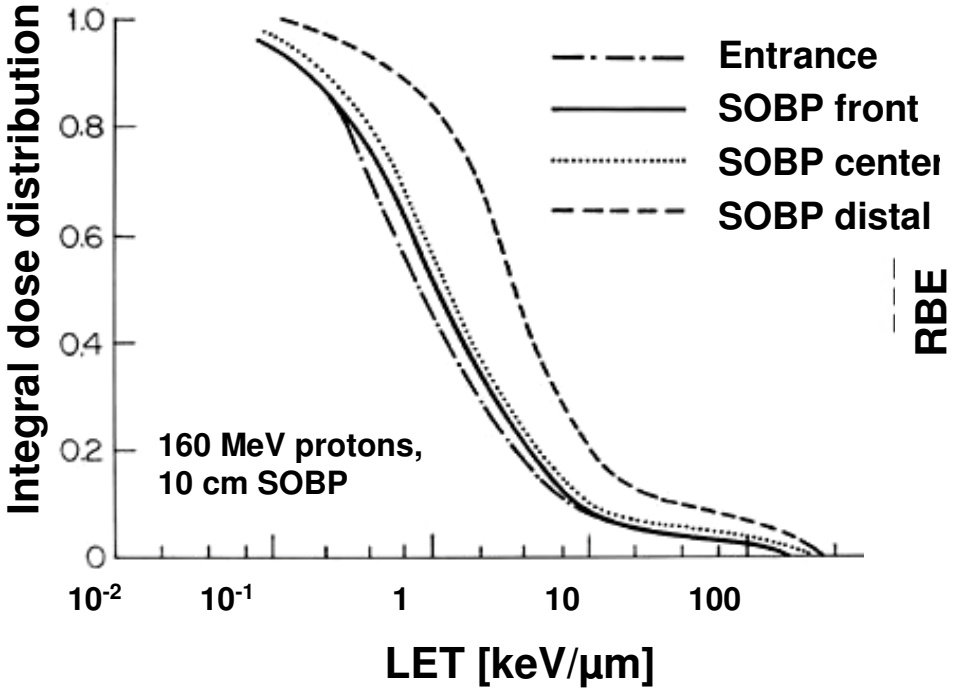


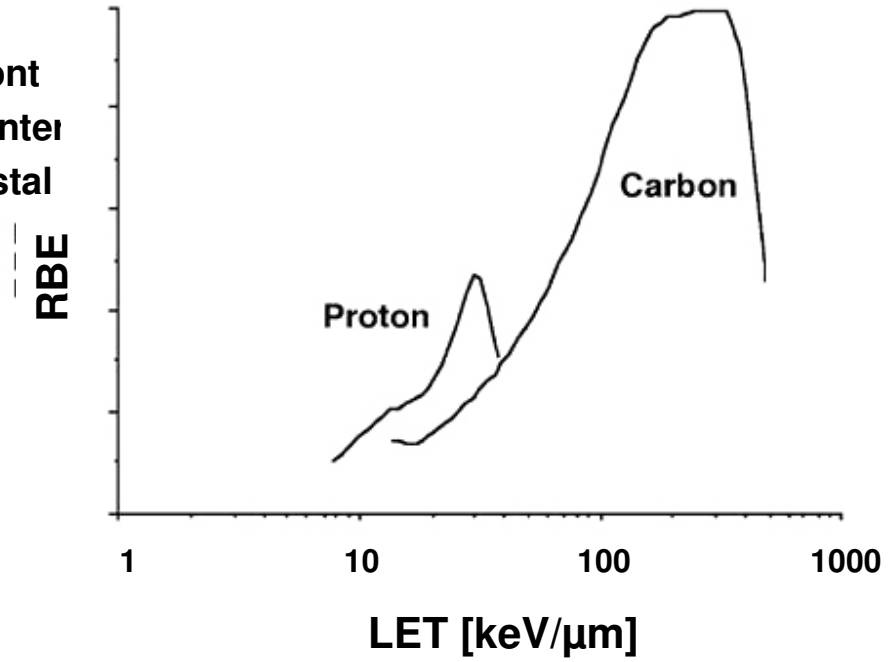
Peschke, Estro 2011

Particles: LET dependencies

(Gerwick 1999)

Protons: For a small volume within the distal part of a radiation field RBE increases throughout the SOBP. Estimated range 10 -15 %.





Kilagua et al. 1978

Belli et al. 1997; Weyrather et al.1999

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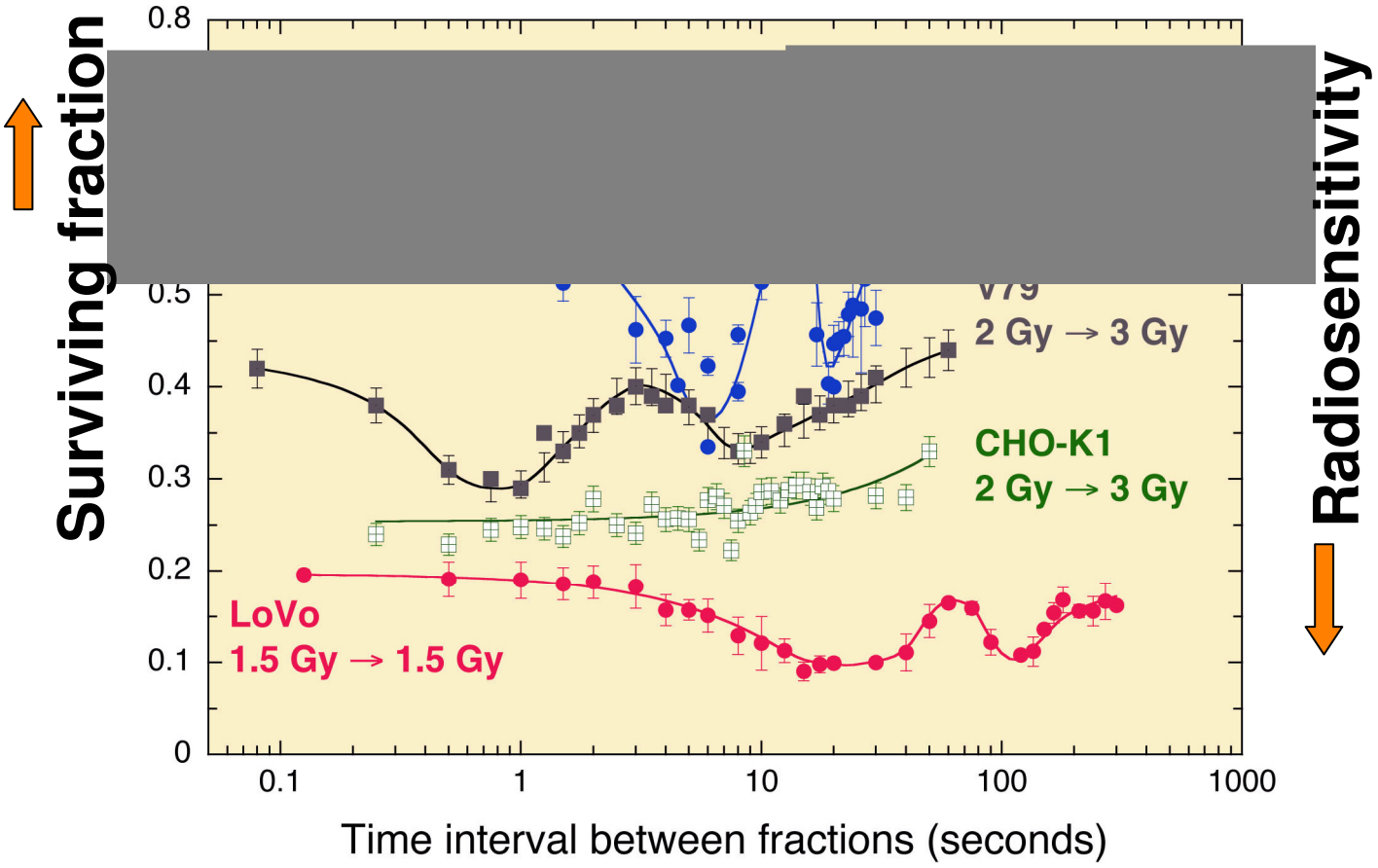
Early cell response to split-dose irradiation

"W-Effect"

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



V.Favaudon et al, I. Curie

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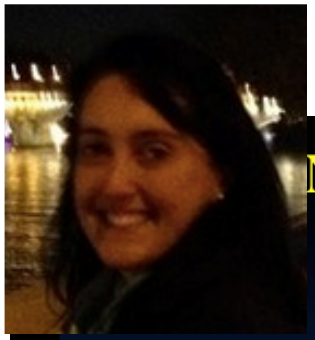


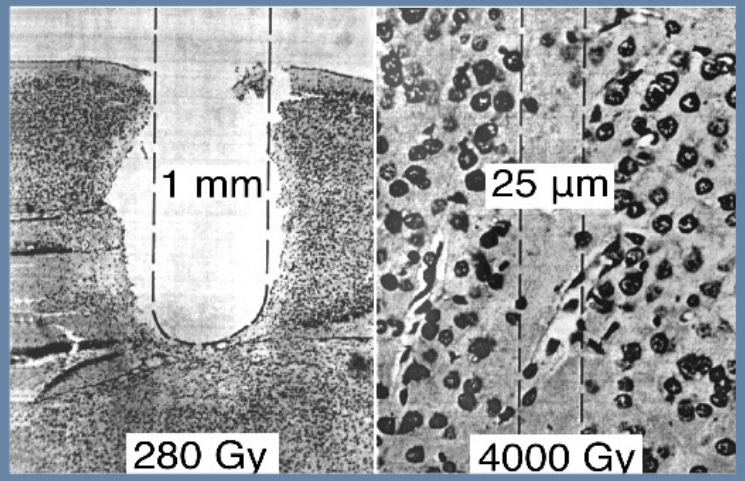
Yolanda Prezado, France

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

Combination

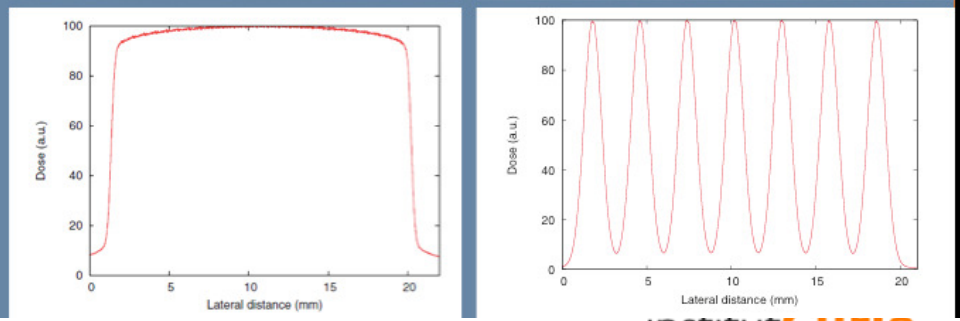
Very small field sizes (< 1mm²) + **spatial fractionation of the dose**

Dose-volume effects



Zeman et al., Science (1959)

Conventional RT



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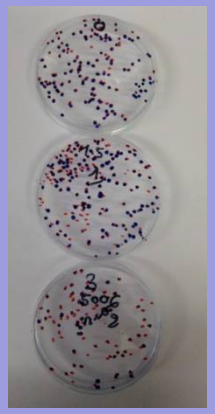
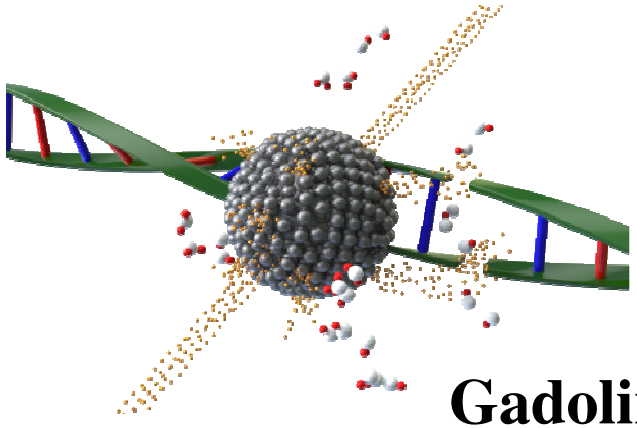
Erika PORCEL
Institut des Sciences Moléculaires d'Orsay

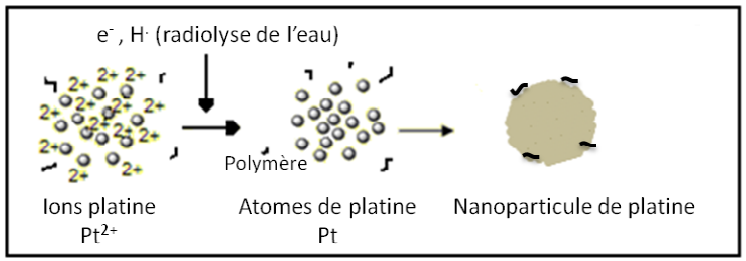
Soutenance de thèse
Direction : S. LACOMBE



Use of nanoparticles to improve the performance of hadrontherapy

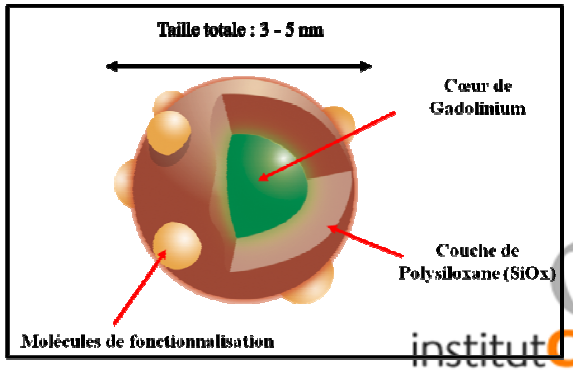


Platine



Remita et al

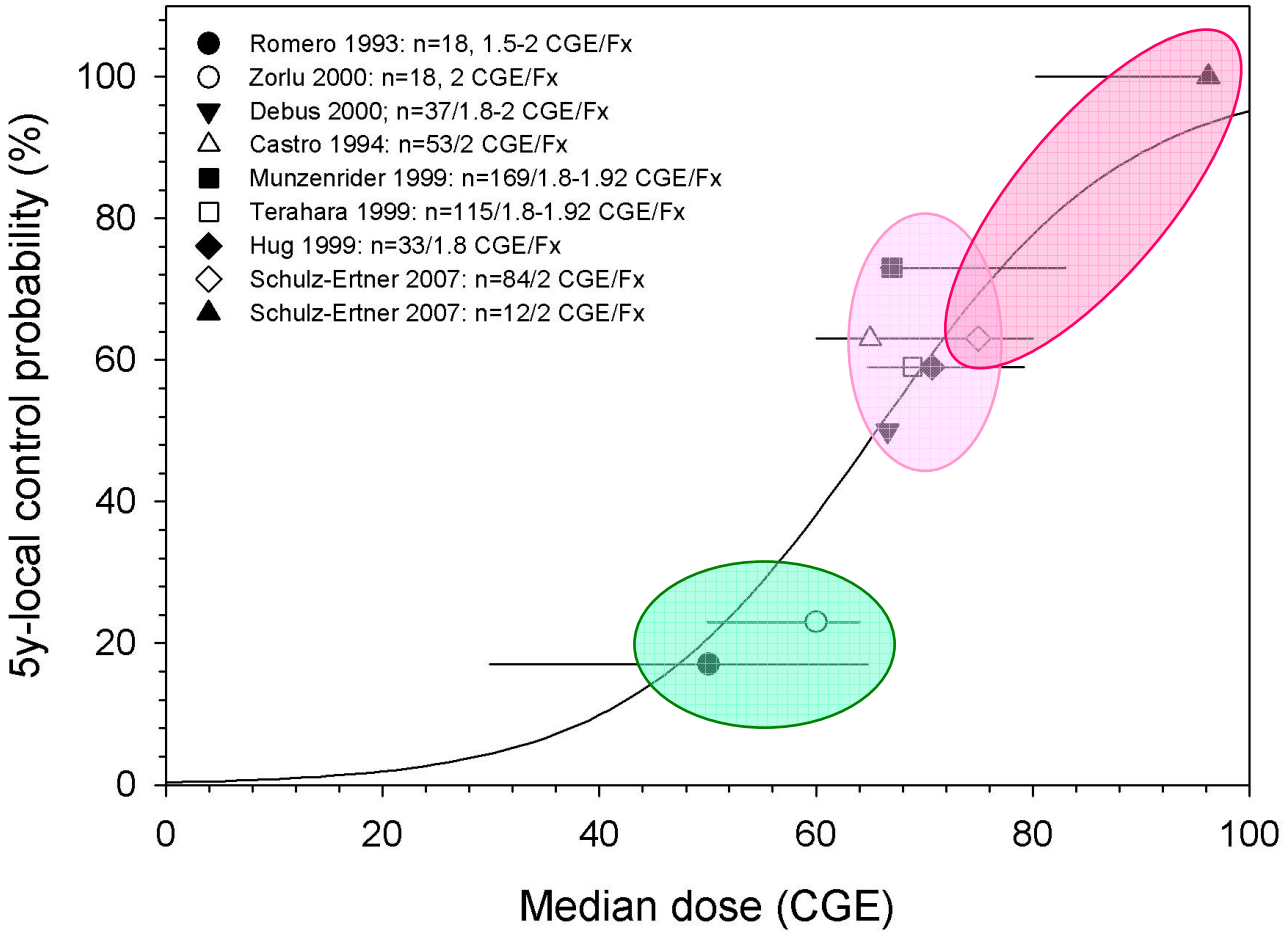
Gadolineum



Mowat et al

Dose-effect-relationship

Au top de la sygmoide de contrôle local ??



C-Ions

Protons

Conventional RT

BoS chondrosarcomas

Schulz-Ertner, IJROBP 2007

Darmstadt & Heidelberg

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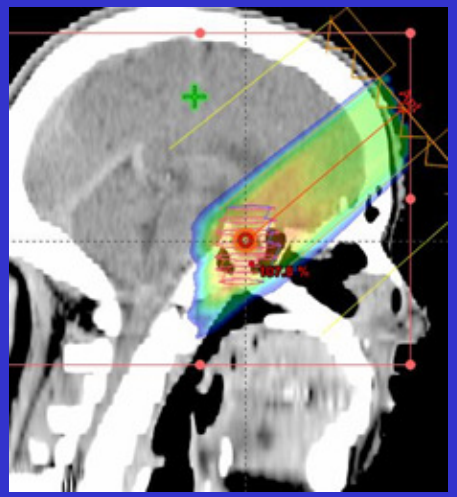
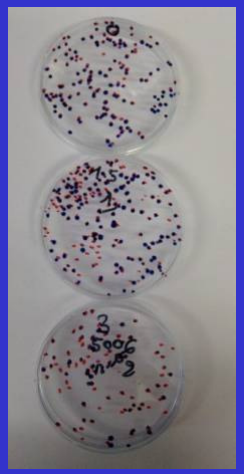
« This is not an apple »

Magritte

« This is not a patient »





→ Go to clinics !

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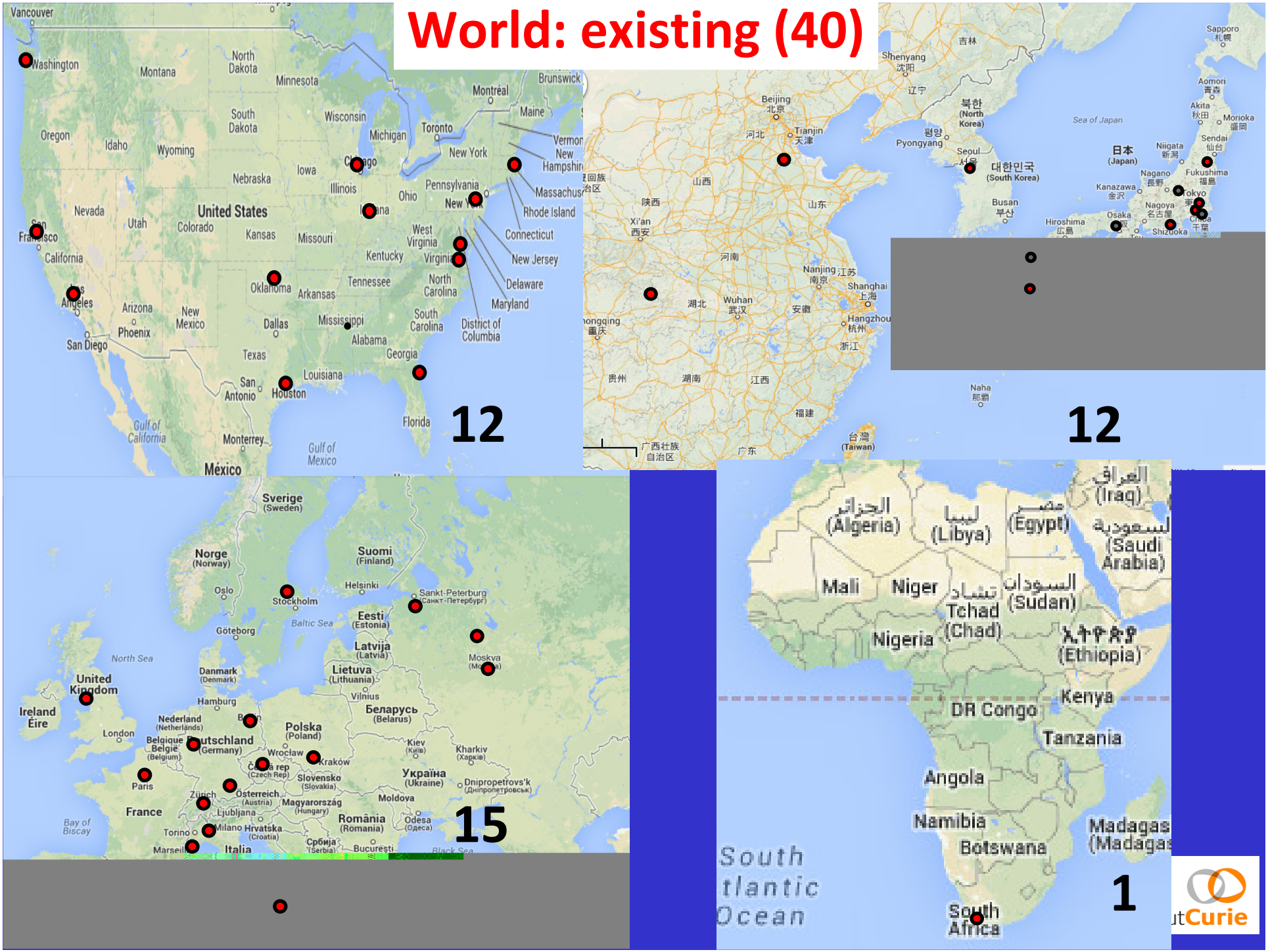
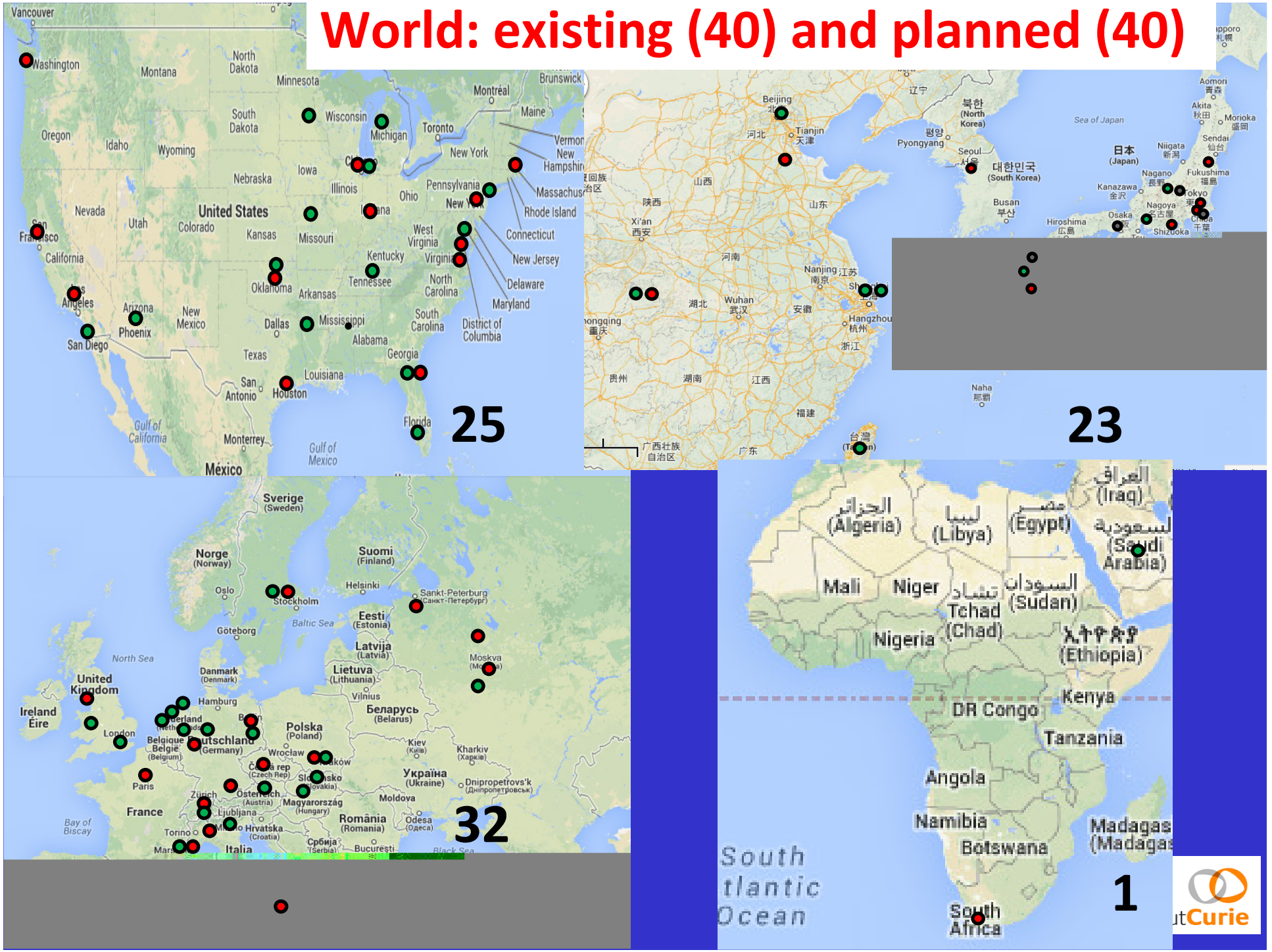
World: existing (40)



World: existing (40) and planned (40)



Conclusions : a lot of job !

→ **Synergy**
between basic research and medical physics
with engineering, biologists and physicians
and institutional and political administrators

Thank you ! Questions ?

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