Treatment Planning in protontherapy

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In behalf of
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Enlight, Utrech
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MENU

1. The Planning Process,
   the beam models
   and the uncertainties.

2. Some clinical examples
   with passive beams.

3. Planning with PBS,
   advantages and still some limits

4. The future,
   examples of research and development

5. Conclusions

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The planning process in general

(M.Goitein)

step	
1	Evaluate the patient using all relevant diagnostic tools, and decide whether to employ radiation therapy.
2	Obtain and inter-register imaging studies with the patient lying in the position to be used for therapy.
3	Delineate on the planning CT the target volumes (GTV, CTV and PTV) and normal tissues.
4	Establish the planning aims for the treatment.
5	Design one or more sets of beams, together with their weights, each of which fulfills, to the extent possible, the requirements of the prescription.
6	Evaluate these plan(s) and either select one of them for use OR revise the planning aims and return to step 5.
7	Finalize the prescription.
8	Simulate the selected plan to ensure it is deliverable.
9	Deliver the treatment, and verify that the delivery is correct.
10	Re-evaluate the patient during the course of treatment and, if necessary, return to step 5, or even 2, to re-plan the remainder of the treatment.
11	Document and archive the final treatment plan.
12	Review the treatment plan at the time of patient follow-up or possible recurrence.

Steps are common
for any approach in RT…

The planning process in general – and the differences between protons and x-rays

(M.Goitein)

step		•protons vs. photons
1	Evaluate the patient using all relevant diagnostic tools, and decide whether to employ radiation therapy.	~same
2	Obtain and inter-register imaging studies with the patient lying in the position to be used for therapy.	Same
3	Delineate on the planning CT the target volumes (GTV, CTV and PTV) and normal tissues.	~same
4	Establish the planning aims for the treatment.	same
5	Design one or more sets of beams, together with their weights, each of which fulfills, to the extent possible, the requirements of the prescription.	different
6	Evaluate these plan(s) and either select one of them for use OR revise the planning aims and return to step 5.	same
7	Finalize the prescription.	same
8	Simulate the selected plan to ensure it is deliverable.	same
9	Deliver the treatment, and verify that the delivery is correct.	~same, but QA harder.
10	Re-evaluate the patient during the course of treatment and, if necessary, return to step 5, or even 2, to re-plan the remainder of the treatment.	same
11	Document and archive the final treatment plan.	same
12	Review the treatment plan at the time of patient follow-up or possible recurrence.	same

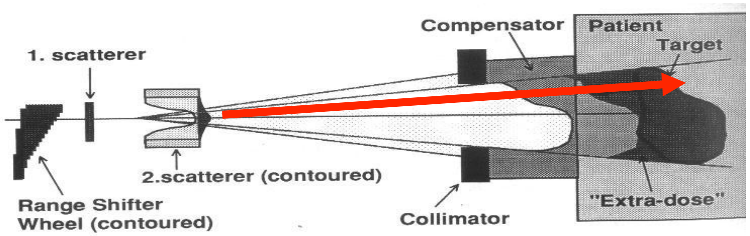
- Dose algorithm (depth-dose, lateral profile, field-size dependence, inhomogeneities, MU)

  Set up the configuration data for the dose calculation algorithm
- The effects of inhomogeneities
- Compensation for inhomogeneities
- Beam delivery techniques
- The planning target volume (PTV)
- Design of single beams:
- Design of plans
- Immobilization, localization and verification
- Uncertainty analysis

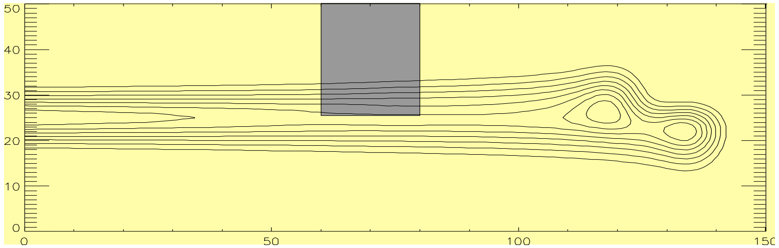
TPS : beam models

- 3 families :

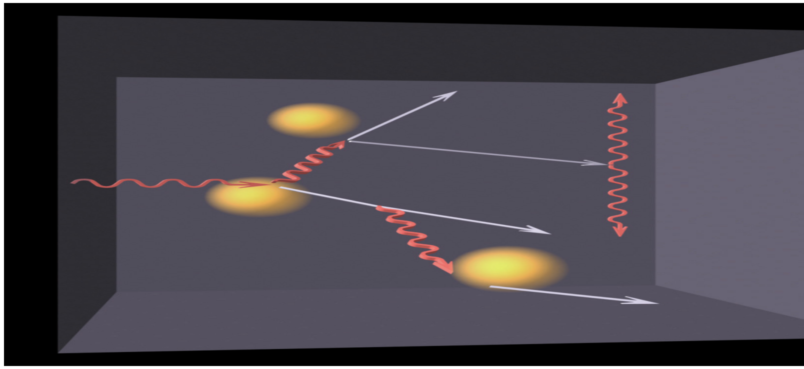
1) Ray tracing



2) Pencil beam



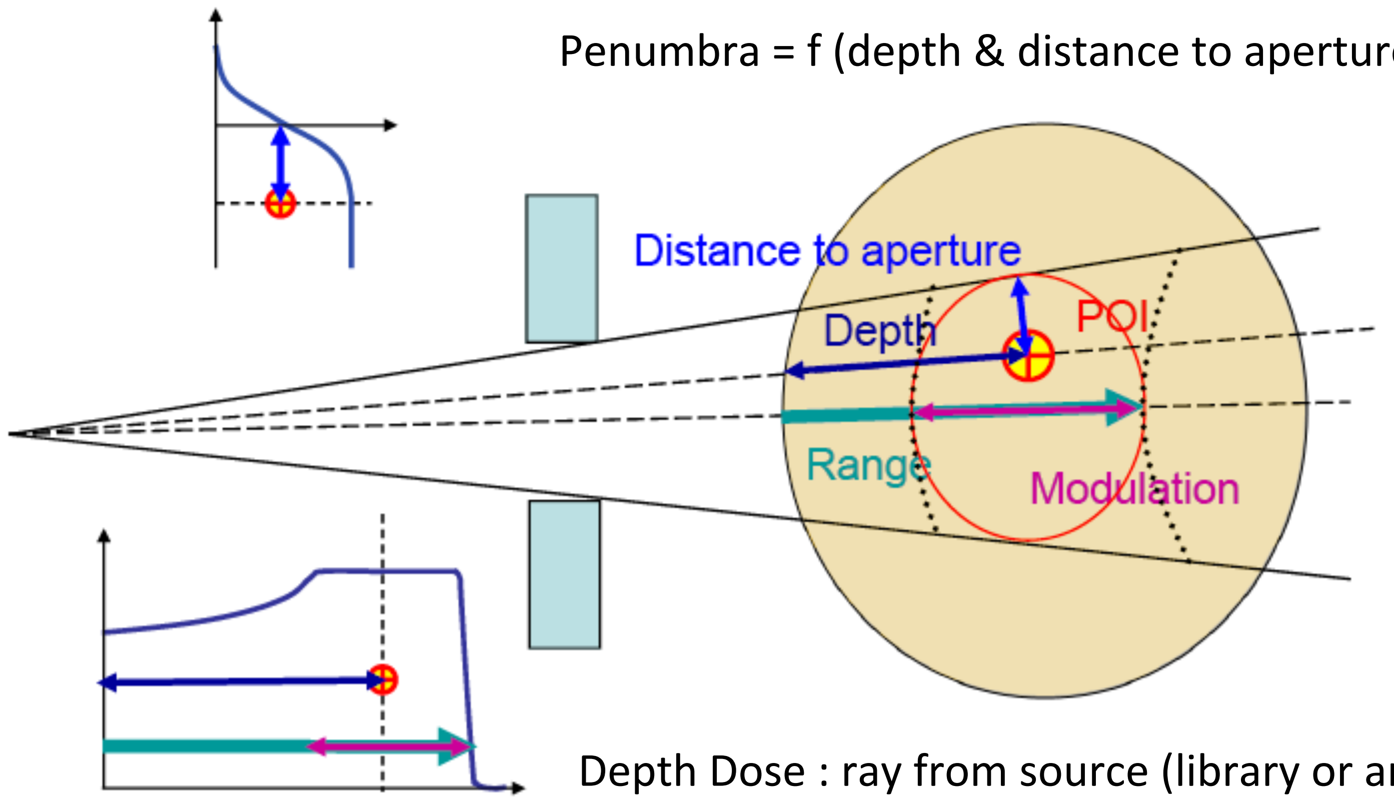
3) Monte Carlo



1) Ray tracing :

Broad beam algorithm - Concept

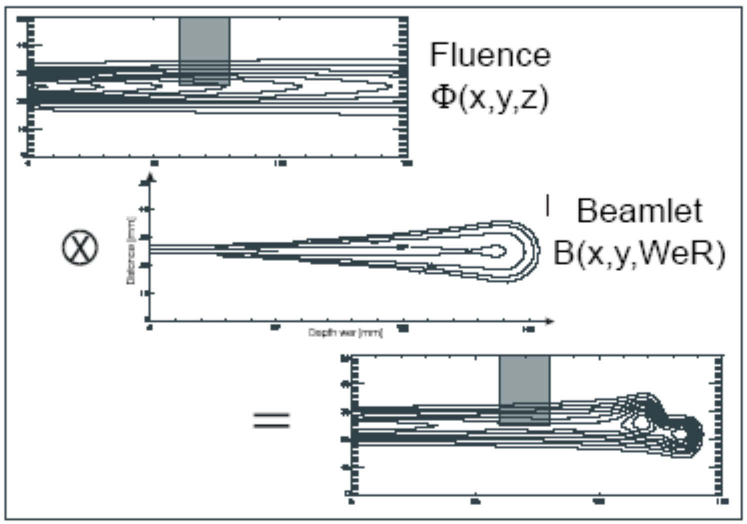
Penumbra = f (depth & distance to aperture)



Depth Dose : ray from source (library or analytical)

2) Pencil Beam

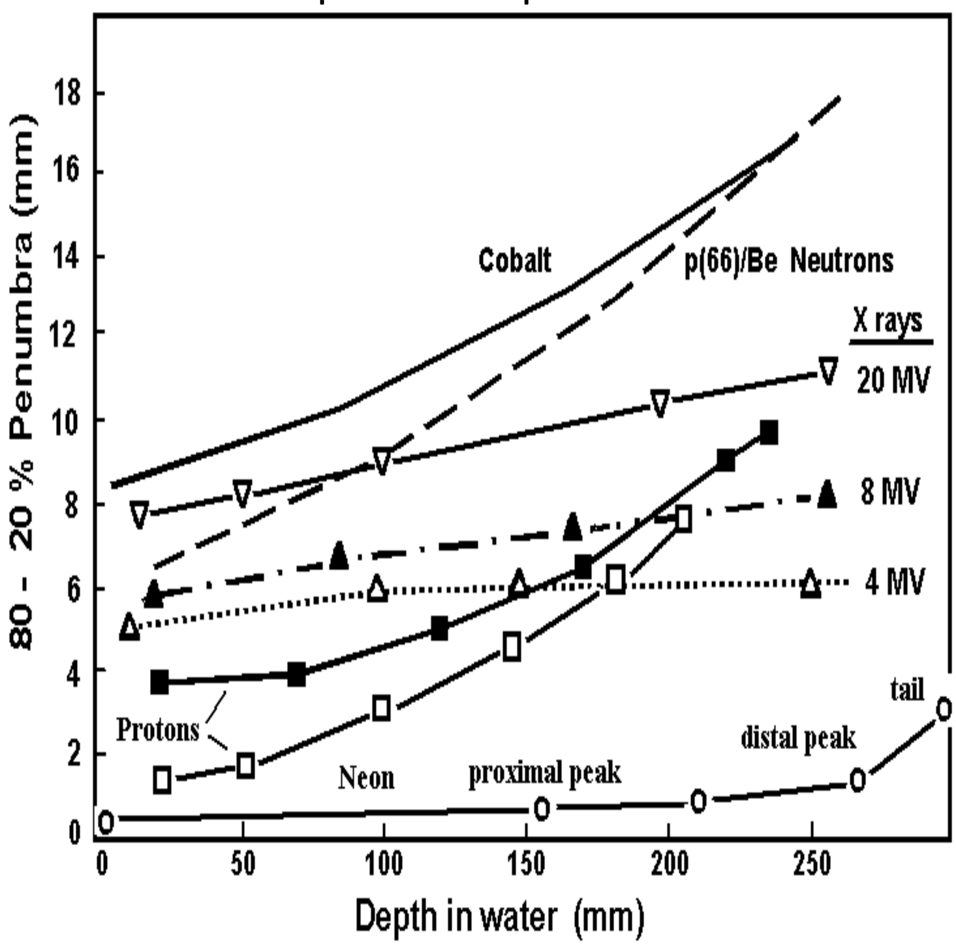
Eclipse pencil beam algorithm - Concept



- Principle
  - Convolution of 3D undisturbed proton fluence in air with a ‘beamlet’ in water.
- In practice
  - Superposition of inhomogeneity - corrected beamlets and multiplication with fluence at calculation position.

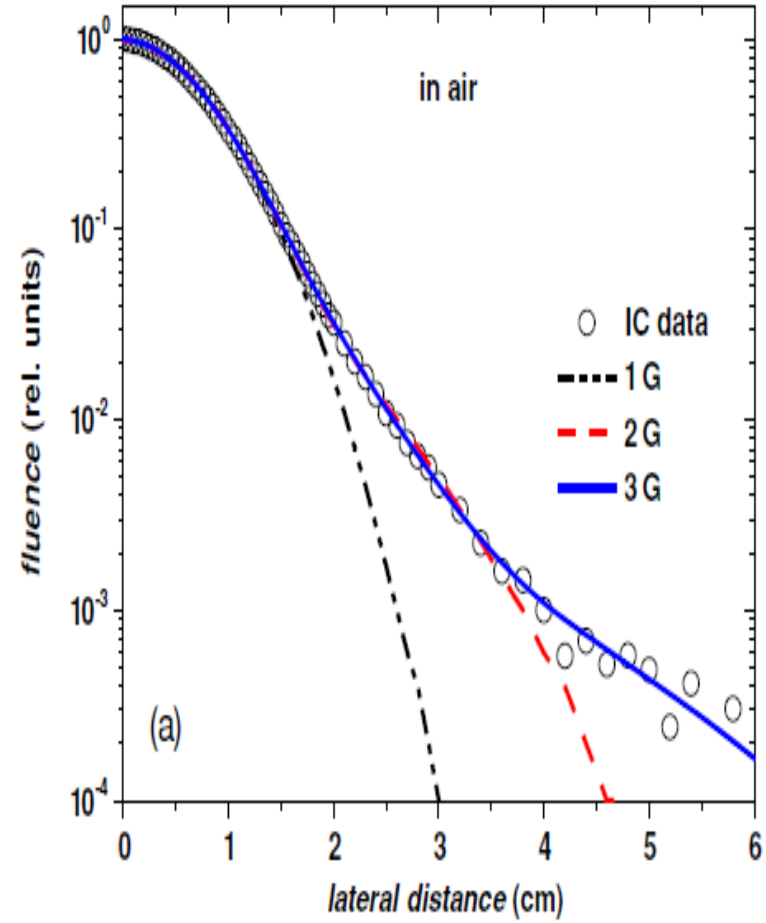
-Lateral penumbra

Protons passive vs photons



Mazal et al

Pencil Beam modeling



DeMarzi et al

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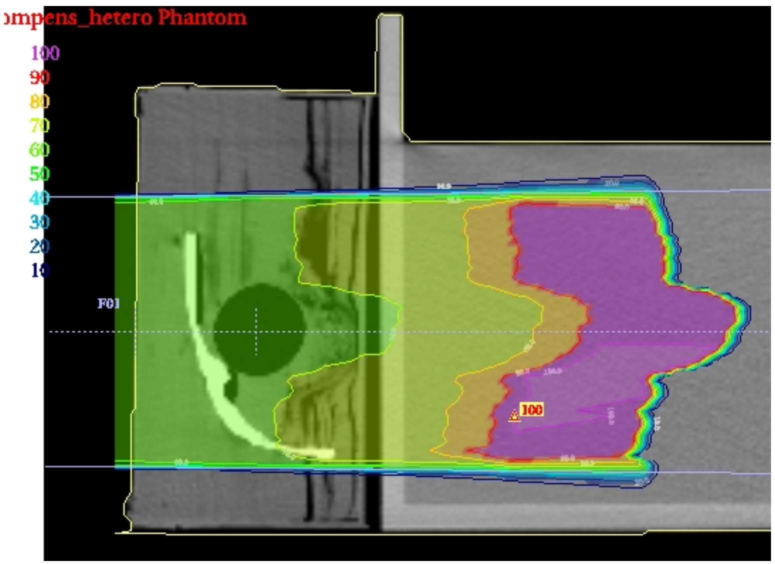
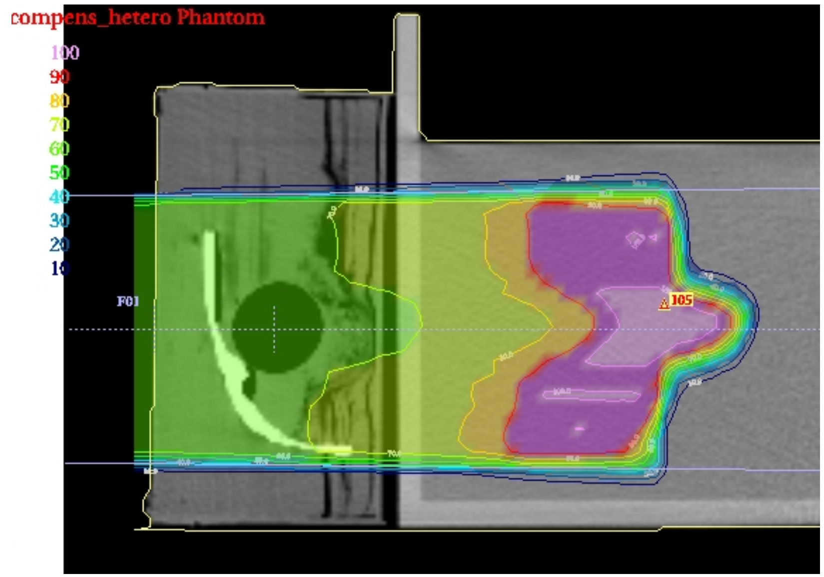
Quality assurance and validation for different TPS models (example)





Ray tracing

Pencil beam

- antropomorphic phantom (skull + fat + air)
- shoot through beam
- Absolute comparison : isodoses in water fantom + TPS isodoses

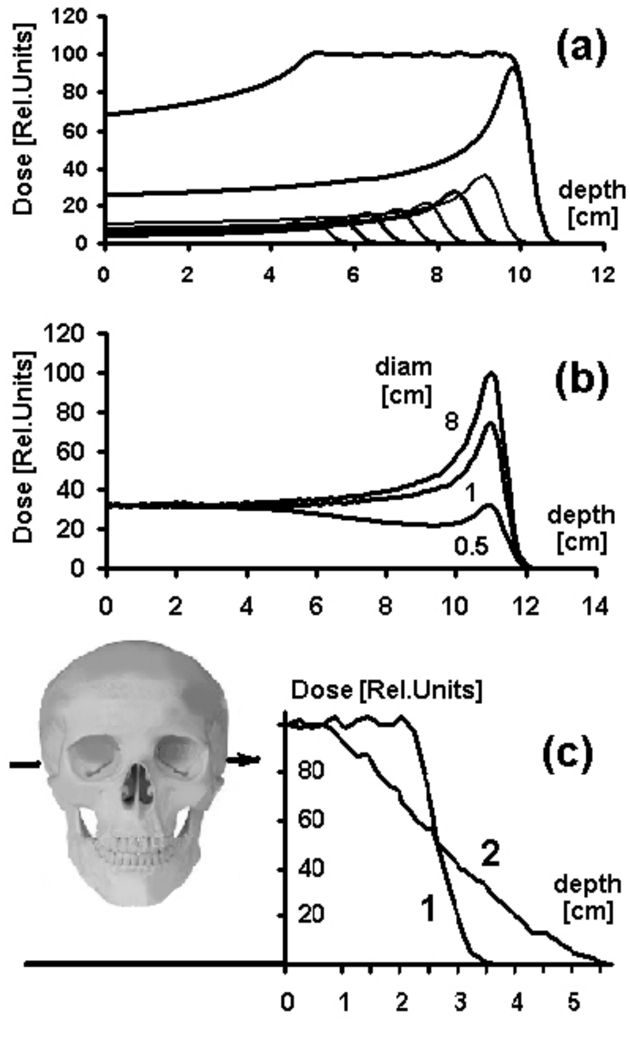
(R.Ferrand, L.DeMarzi et al)

Limits: Degradation of balistic properties

Entrance dose
(& small buildup)

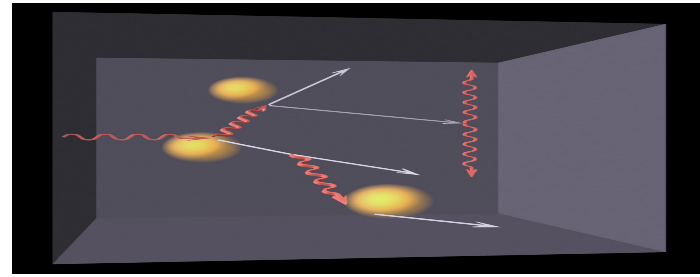
Small field size
< peak/entrance

Degradation
After complex
Inhomogeneities
(and problem of
CT artifacts)

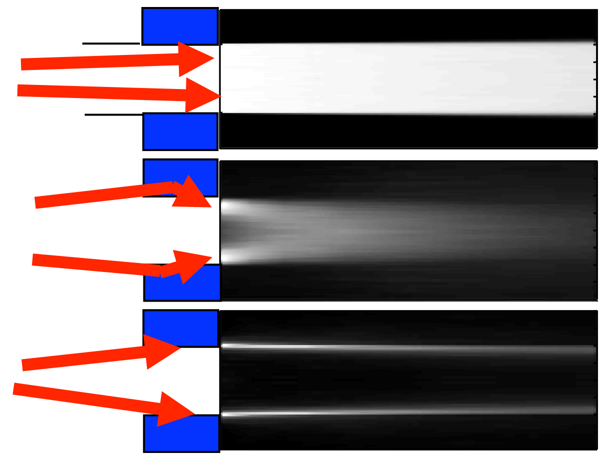


⇒ Check that TPS
takes
all this into account

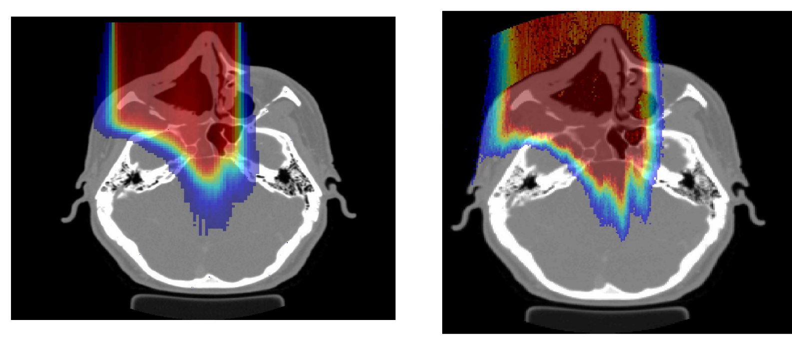
3) Monte Carlo



- Tracking of each particle : protons, électrons, neutrons…
- Tracking of all types of interactions: electronic, nuclear (important to take RBE into account)
- Upstream effects and in the patient body
- results « sharper » than with pencil beams
- Powerful, in expansion

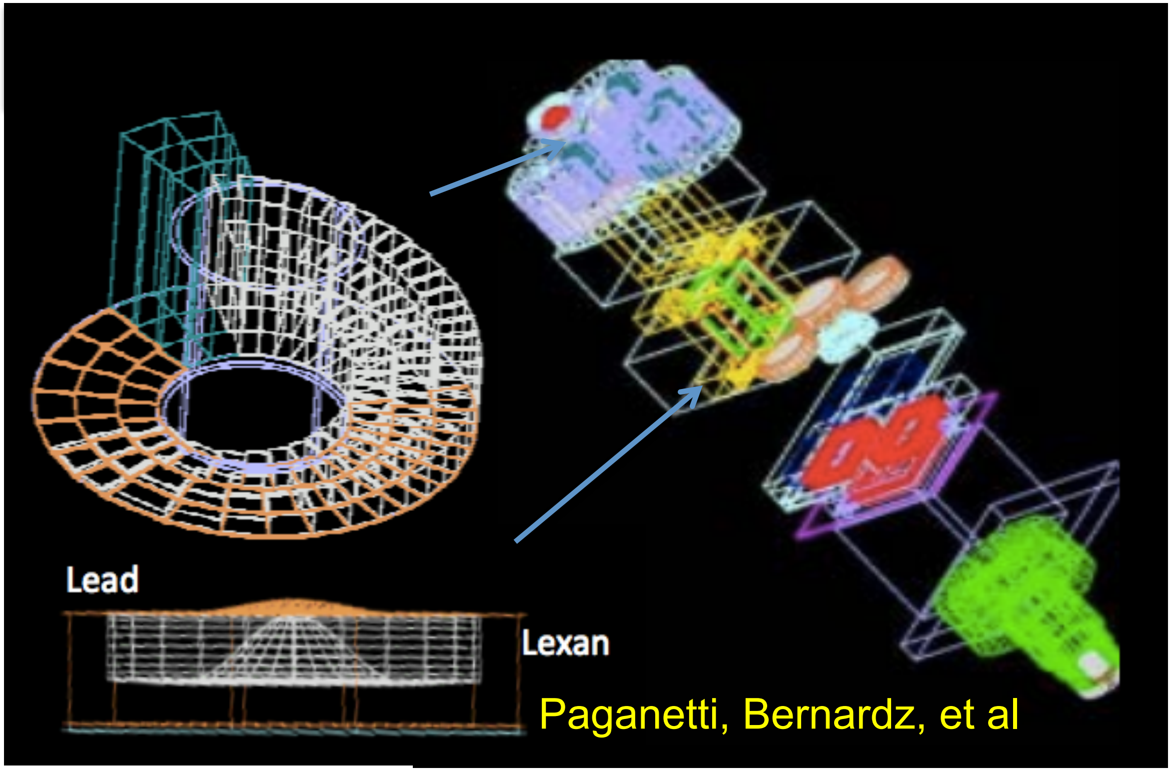


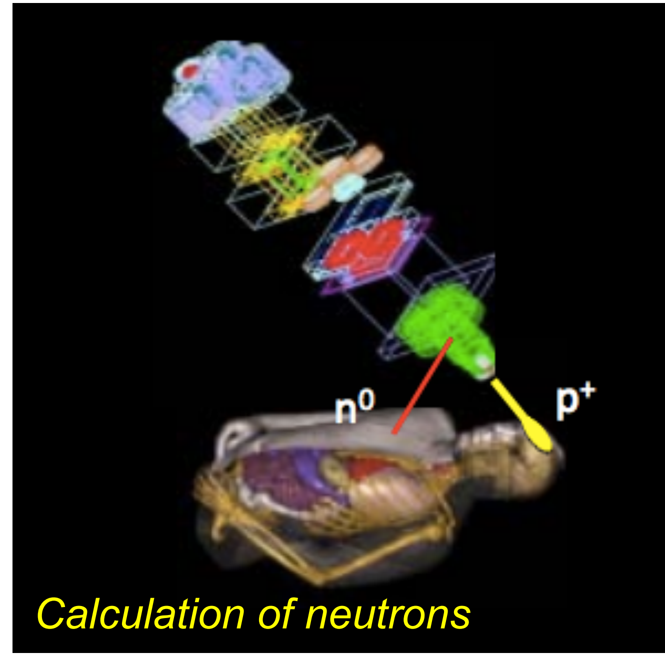
(van Lujik et al)

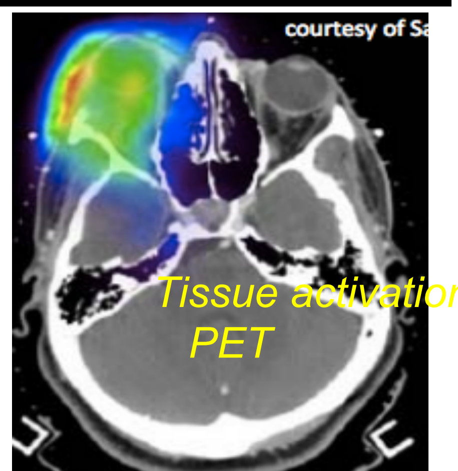


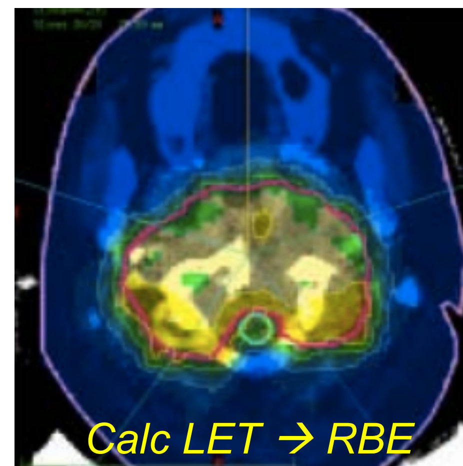
Comparison PB-MC (Paganetti)

Limits in Beam models : towards Monte Carlo









	Uncertainties	**Eliminate / Links/ Mitigate / Take in charge**
	PATIENT PREPARATION AND IMAGING	
1	Patient immobilisation & contention devices	Minimise & Homogeneous material in beam path
2	CT calibration, QA, use and constancy	Methods, frequency, evaluation,…
3	CT conversion Hounsfield to Stopping power	Stoichiometric, analytical, data base, double E,…
4	CT grid size	Tests, compromises
5	CT artifacts (eg metals)	Acquisition parameters, MVCT, double energy, others…
6	Protocols for image acquisition	Conceive, Compromises, Verify use, human error, evolut
7	Movement management, breath holding, gating,…	4D CT, breath holding, gating, (tracking), repainting,…
8	Patient imaging and tumor volume delineation	Image & correlation QA
9	Target & critical organs delineation	MD experience & goals, protocols, procedures, tools
	TECHNOLOGY: DEVICES & MEASUREMENTS	
10	Facility Commissioning (eg beam data)	Detectors, redundancies, small tolerances, interlock
11	Beam on line range monitoring and feedback	Detectors, fast feedback and/or interlocks
12	Measuring errors : devices, procedures, human errors	Detectors, check lists, automatic tools and filters
	CALCULATIONS IN THE PREPARATION PHASE	
13	Range calculation algorithms	Improve & validate algorithm; comparisons and tests;
14	Compensator calculation, optimisation, fabrication, validation	Improve algorithm; Quality Control, smearing, drill size,
15	Dose calculation models (including multiple scattering and biological effects)	Improve algorithm; Quality Control, compensate, reoptimise,…
16	Management of Inhomogeneities (lung, metals, …)	Improve algorithms; tests, avoid incidences, reject cases,...
17	Accessories in beam path (eg table, masks, …)	Avoid or Verify, measure, model, test,…
	TRANSFER AND TREATMENT	
18	Patient specific QA on range	Detectors, redundancies,tolerances, stats, models
19	Accessories in beam path (eg table, masks, …)	Avoid or verify
20	Patient setup	Immobilise, margins, IGRT (CBCT, orthogonal X, vision, …)
21	Management of movements	Immobilise, margins, gate, track, repaint, monitor range
22	Changes in anatomy	in room - off room imaging, monitor range
23	Beam modifiers choice (compensator and others)	Check lists, test, interlocks, imaging, monitor range
24	Beam modifiers setup (compensator and others)	Fixations, verification, monitor range
25	Beam delivery (pattern, position, interruptions,…)	Monitoring, testing
26	Delivered Range (abs value, reproducibility,…)	QA, monitor range

CT

Detectors

Algorithms

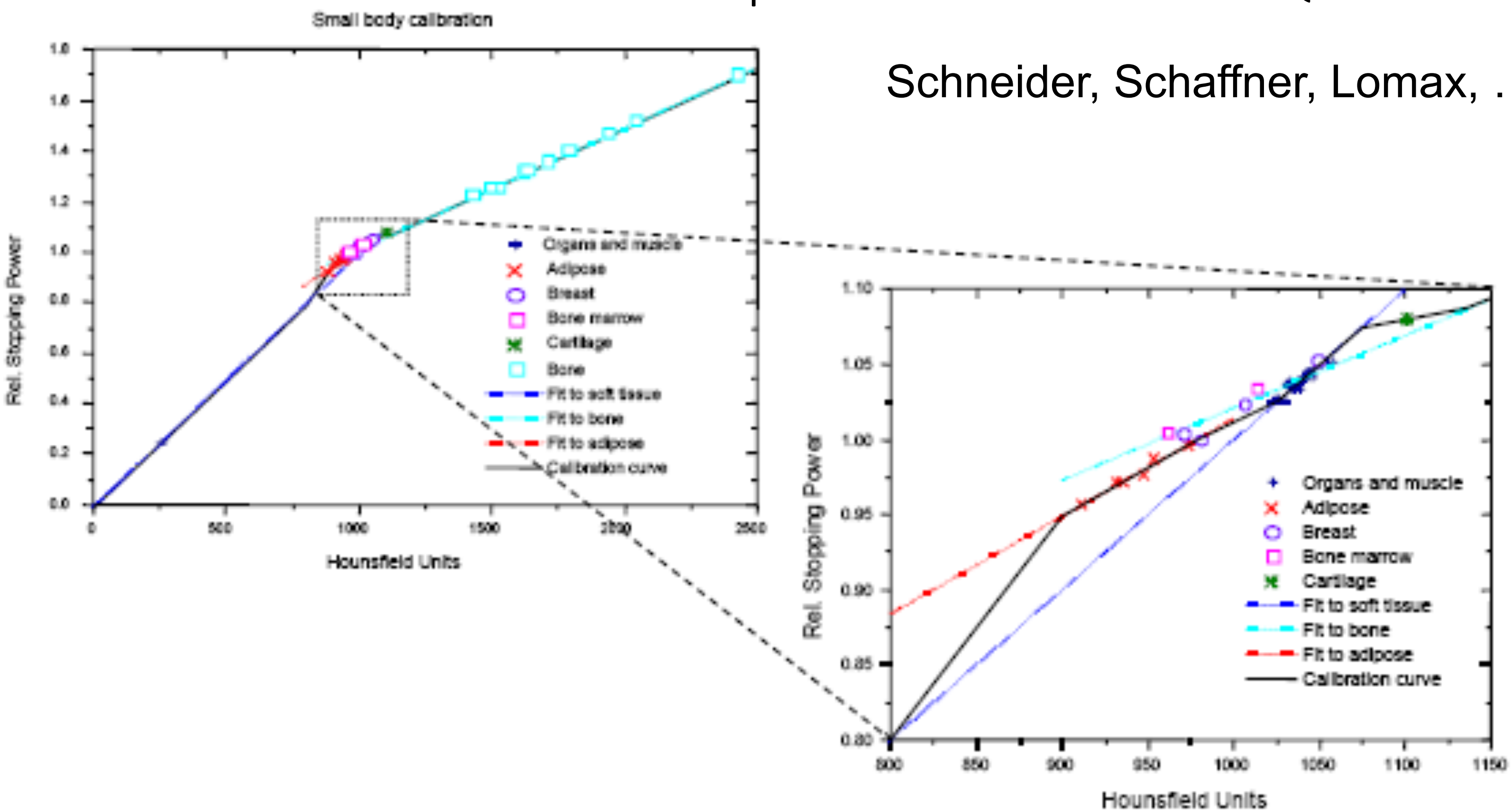
IGRT

Monitoring

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

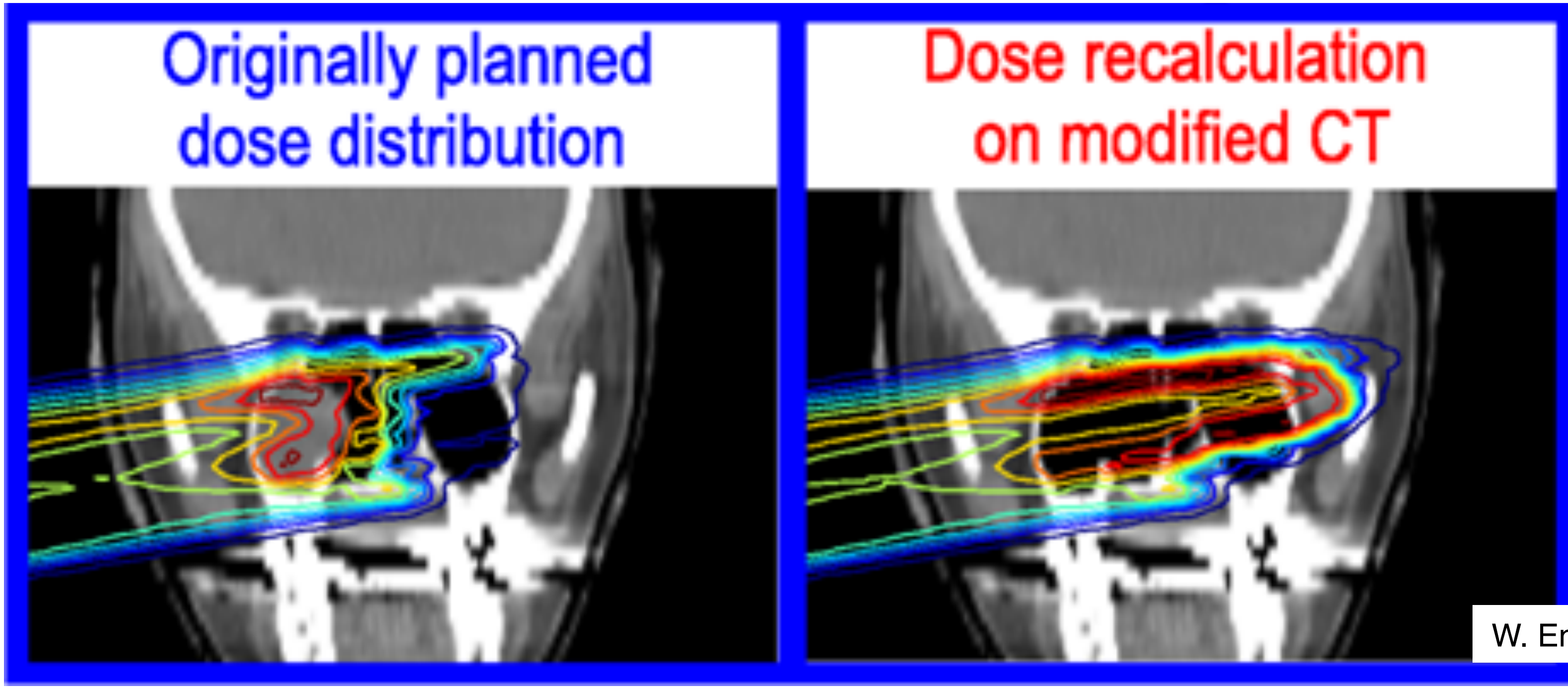
Importance of CT calibration & QA = RANGE

Schneider, Schaffner, Lomax, …

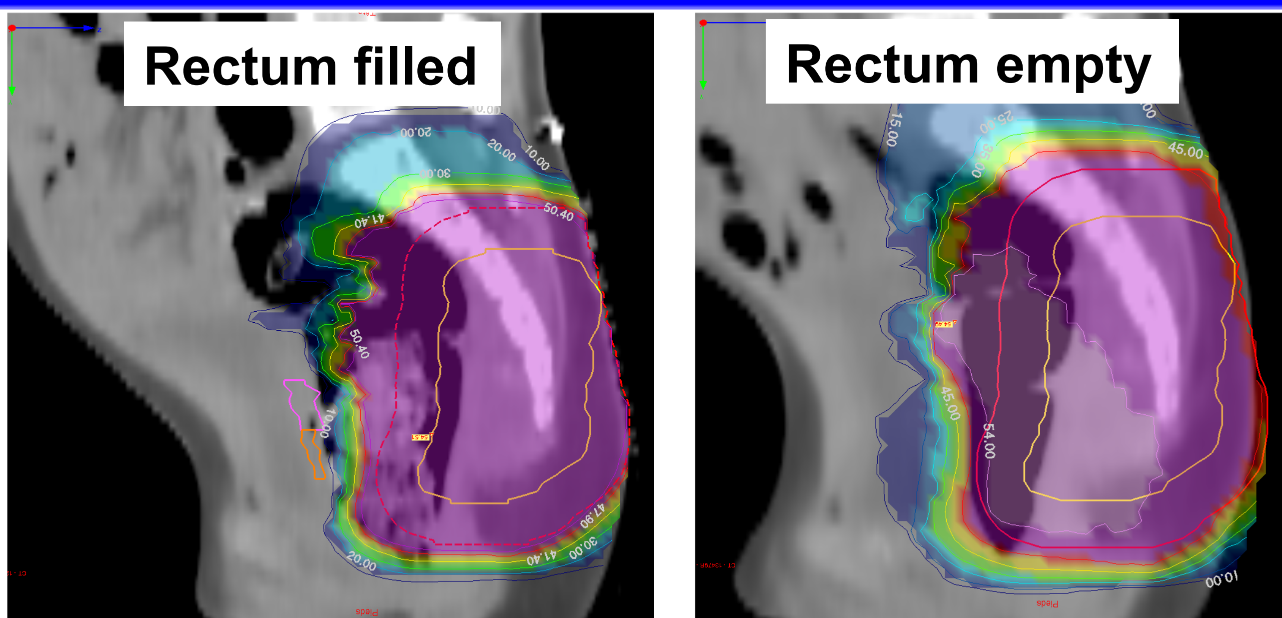


UNCERTAINTIES IN THE RANGE

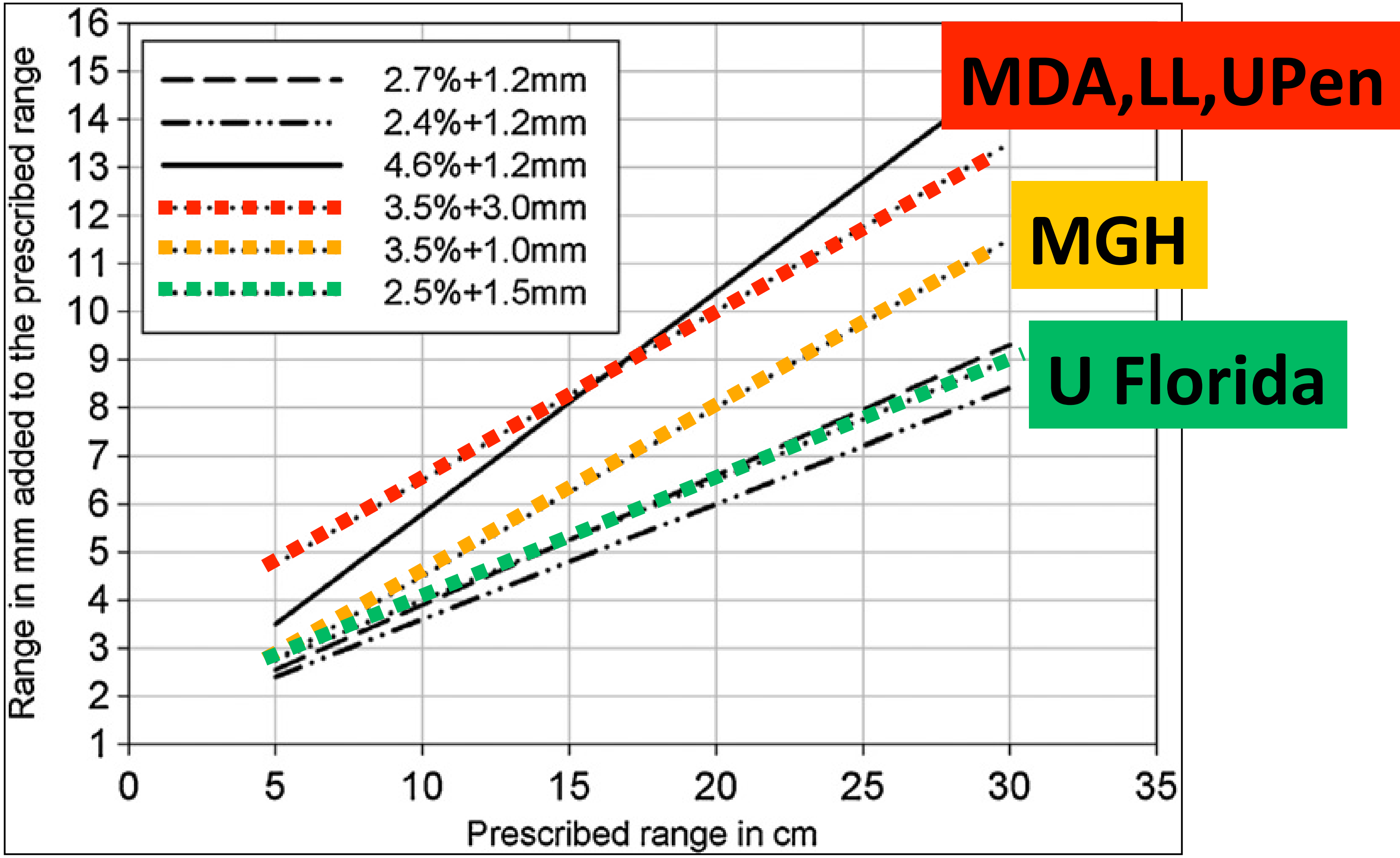
ex : Effect of density changes (eg : in the target volume or in the beam path)



W. Enghardt et al.



De Marzi et al. , CPO



Dotted lines: typically applied range uncertainty margins in proton therapy treatment planning as currently typically applied at the MGH (3.5% + 1 mm), the MD Anderson Proton Therapy Center in Houston, the Loma Linda University Medical Center and the Roberts Proton Therapy Center at the University of Pennsylvania (3.5% + 3 mm) and the University of Florida Proton Therapy Institute (2.5% + 1.5 mm). Note that these centers may apply bigger margins in specific treatment scenarios.

Dashed line: estimated uncertainty without the use of Monte Carlo dose calculation. Solid line: estimated uncertainty for complex geometries without the use of Monte Carlo dose calculation. Dashed-dotted line: estimated uncertainty with the use of Monte Carlo dose calculation.

H.Paganetti , PMB 57 (2012) R99-R117 & personal comm

MENU

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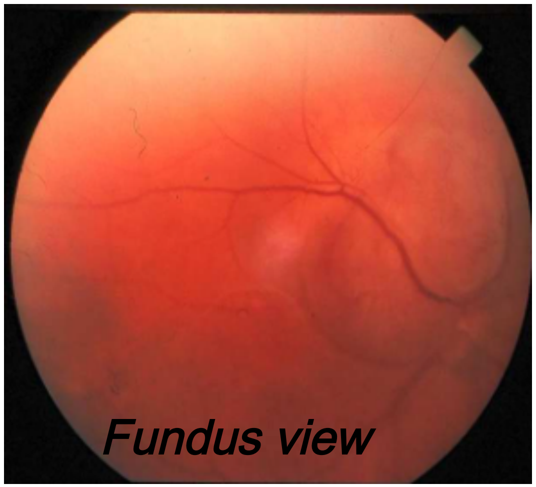
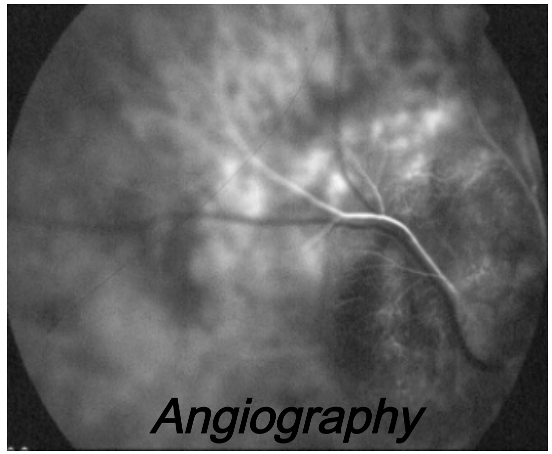
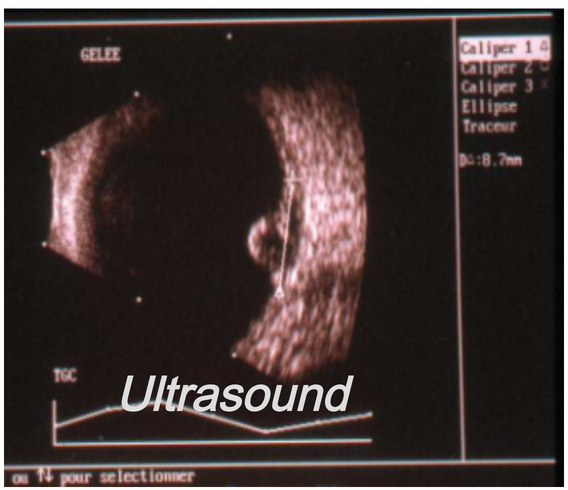
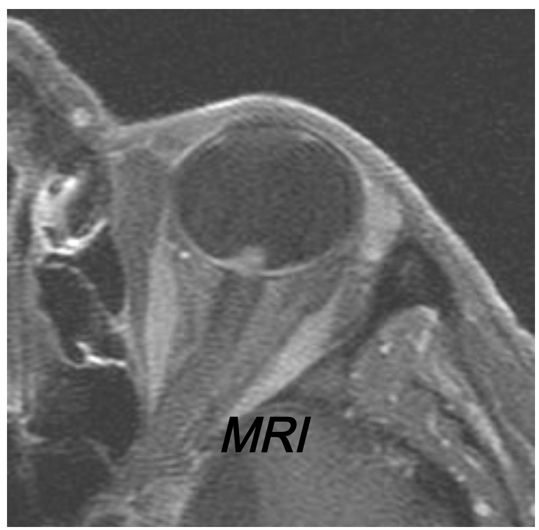
2. Imaging

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







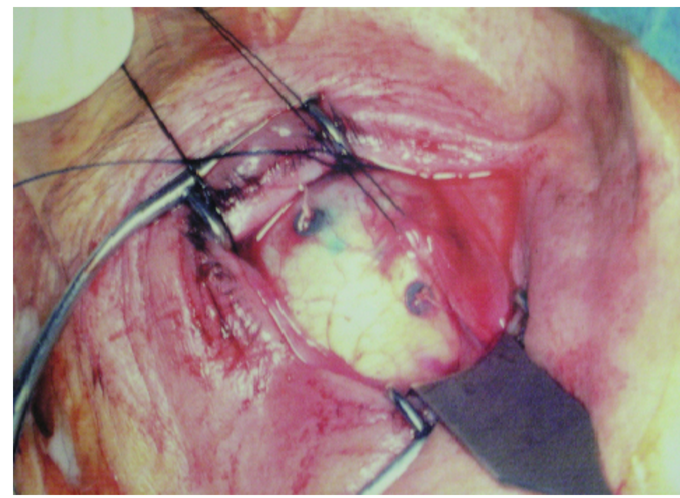


Immobilisation
& reference coordinates :

masks, frames,…

and/or…

Use of implanted fiducials



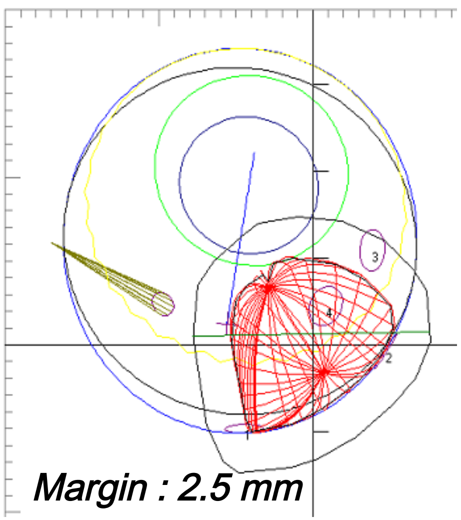
5. Beam design

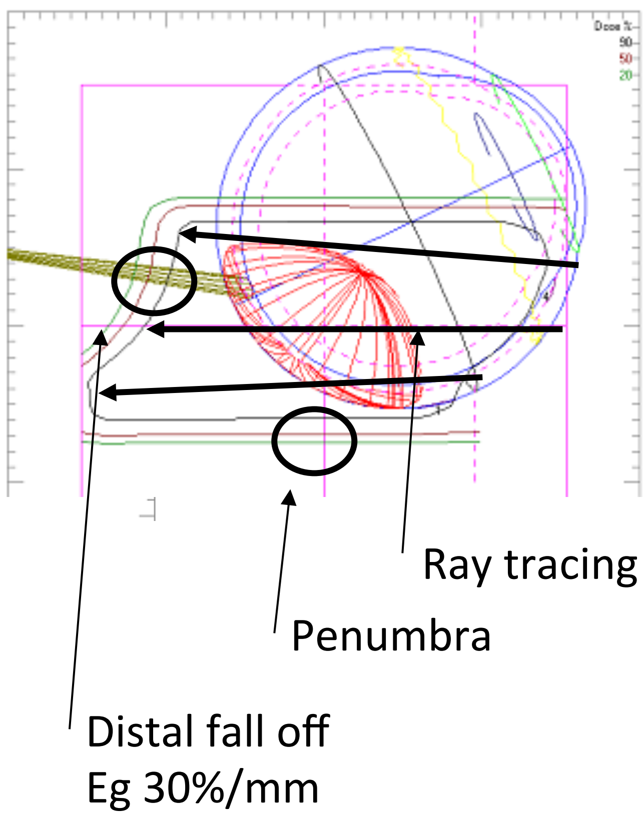
Design sets of beams

- *Choice of the gaze angle to avoid critical organs*

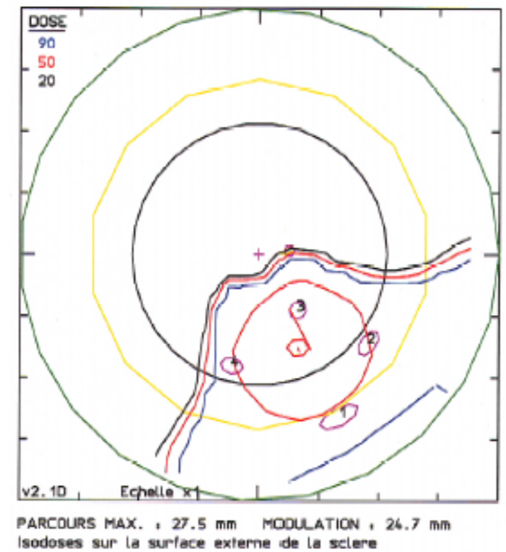
  -In the beam's eye view: Design a collimator

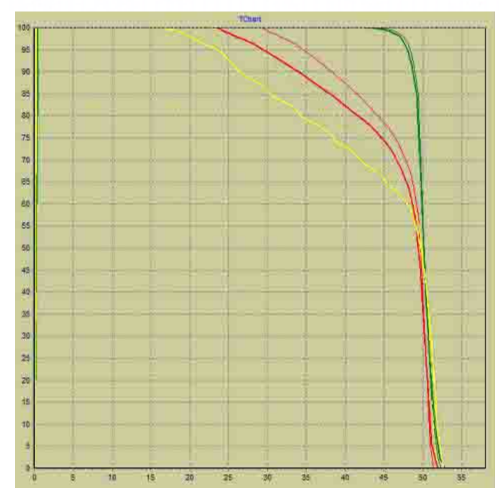
- *Calculate dose distribution*





6 & 7 : Evaluation & final prescription



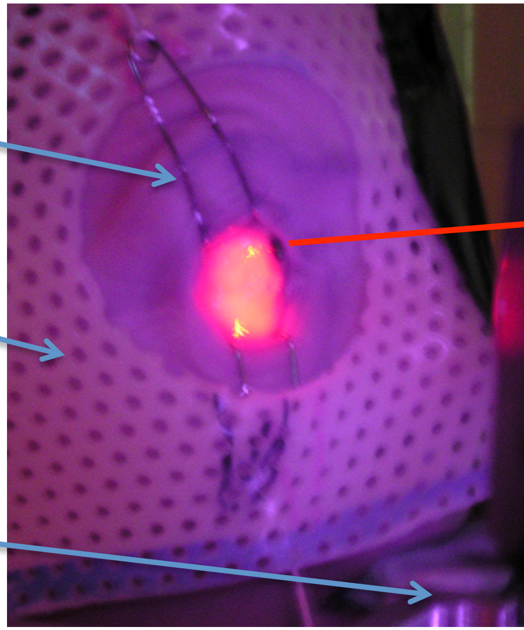


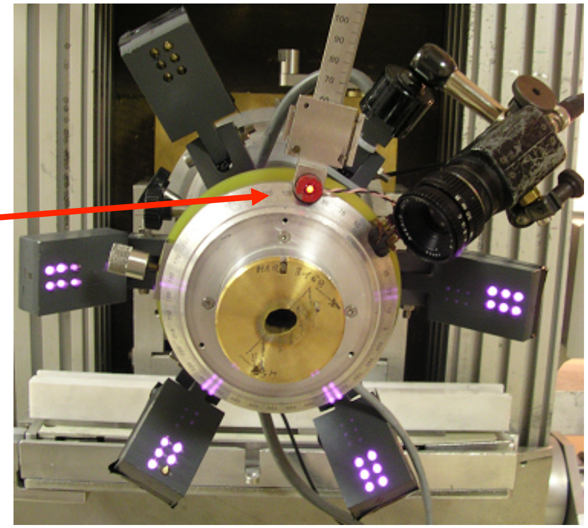
8, 9 & 10 : Simulate, Daily set-up & Treat, re-evaluate

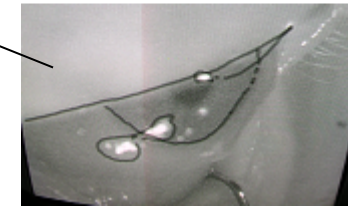
Eyelids retractors

Thermo plastic mask

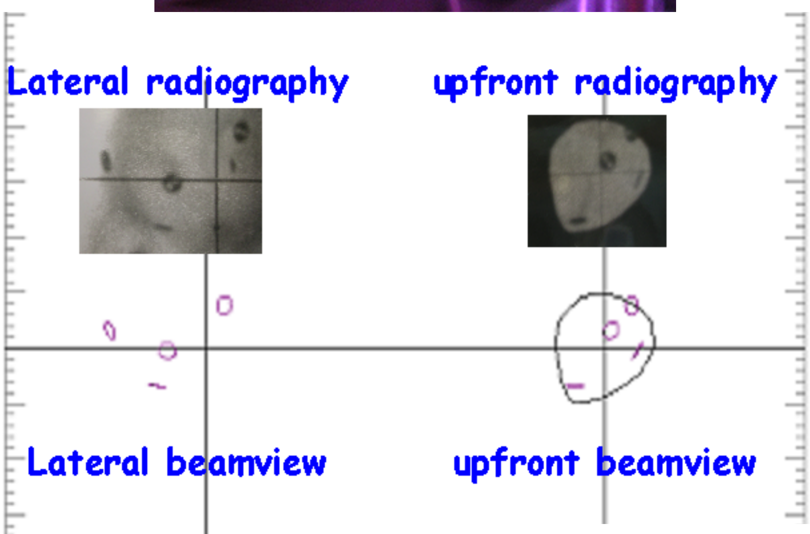
Bite block

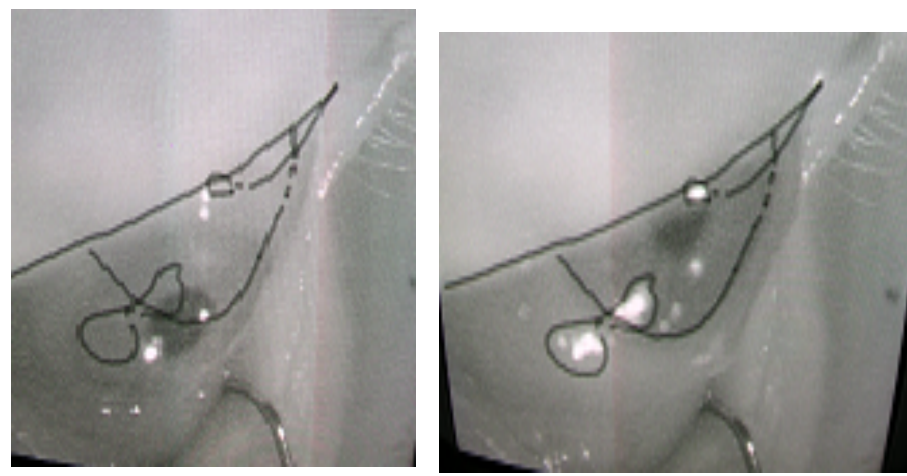






Infrared diodes and camera



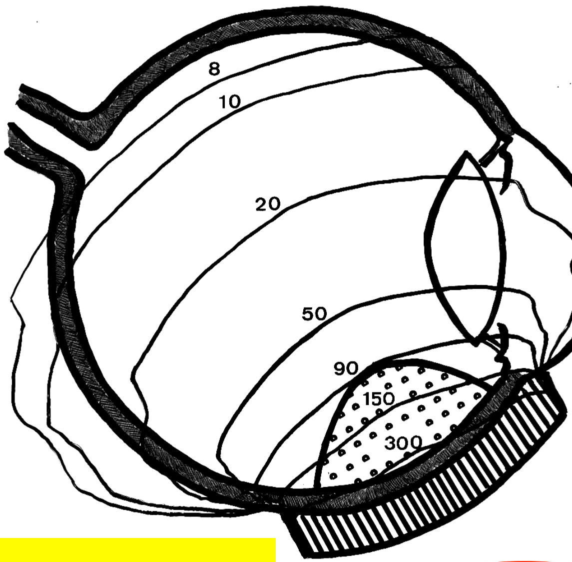


« Image Guided Radiation Therapy IGRT»

Classical and rare locations :
>5000 EYE treatments with radiation therapy, Institut Curie

In 2015

I-125 Plaques

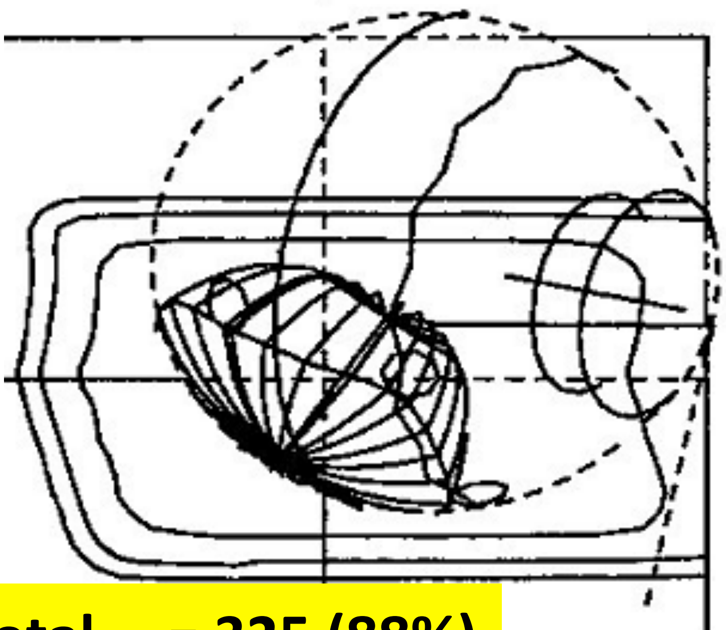


Total = 46 (12%)

Total Melanomas = 29 (10%)

Small Ant
Large Ant-Temporal
(lacrimal)

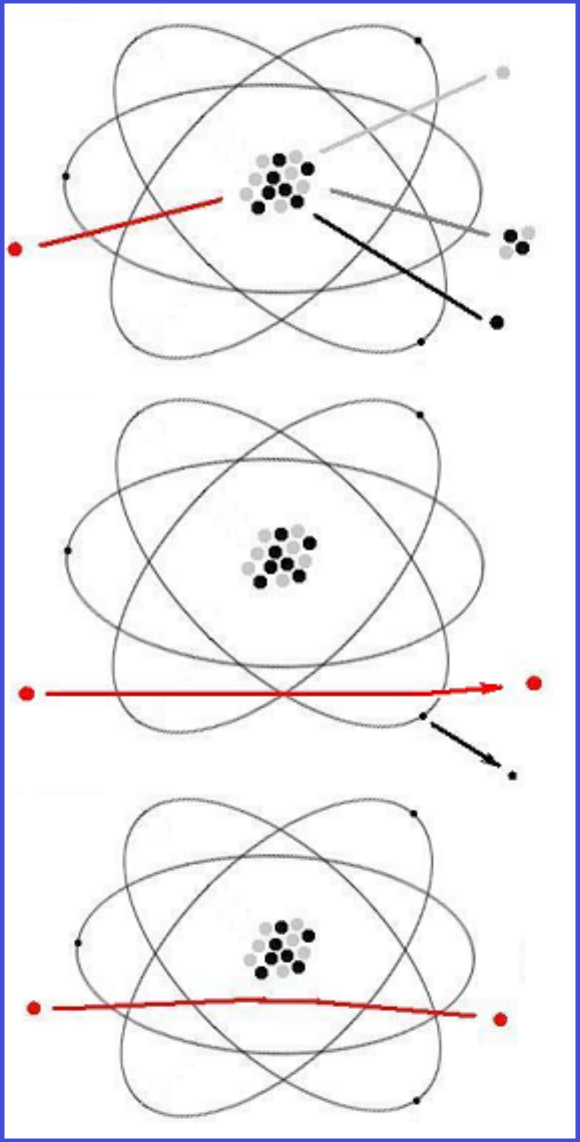
Protons



Total = 325 (88%)

Total Melanomas = 264 (90%)

Main interactions of particles with matter :



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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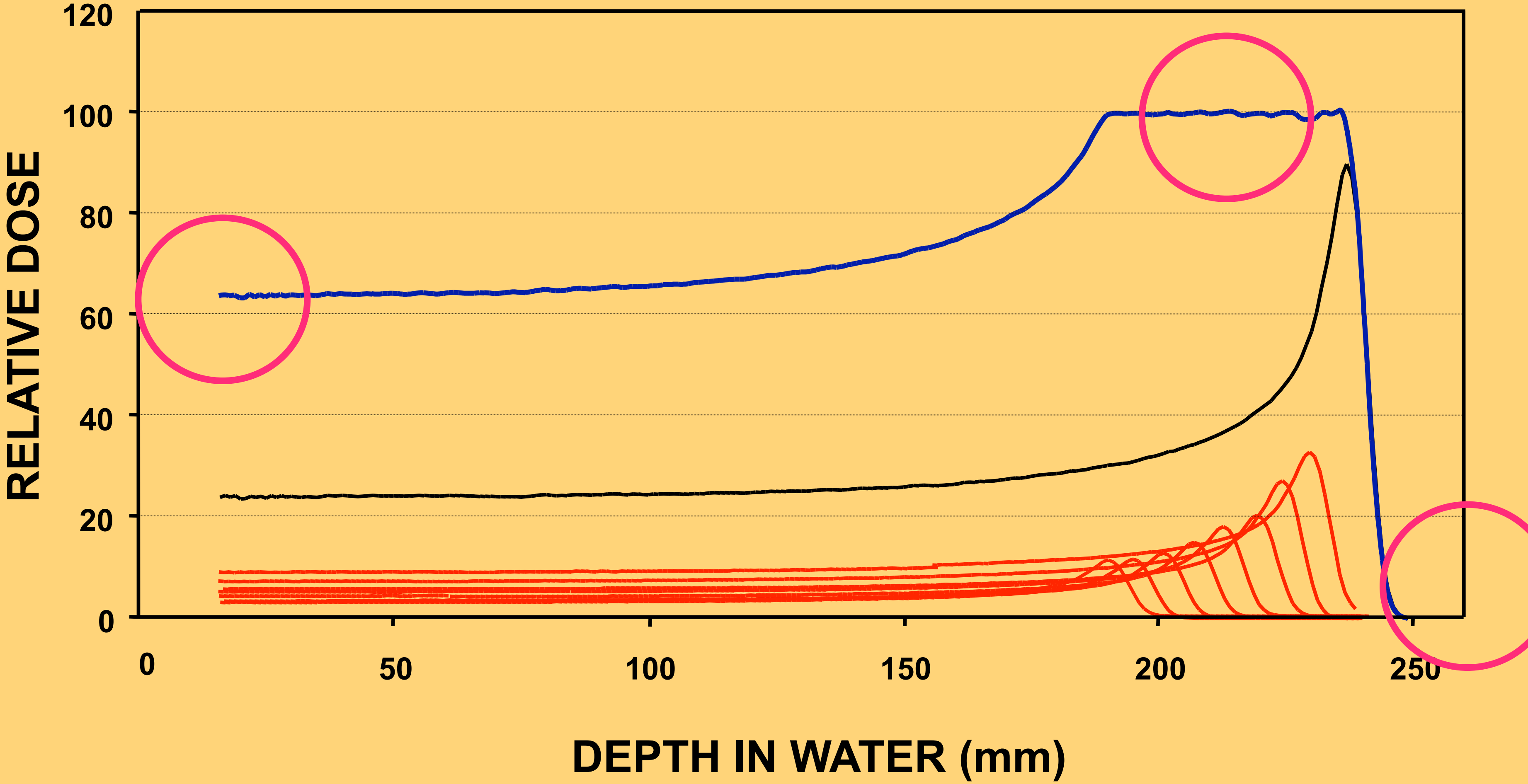
Spread-out Bragg Peak (SOBP)



(Concept : Andy Kohler // graph : Niek Schreuder)

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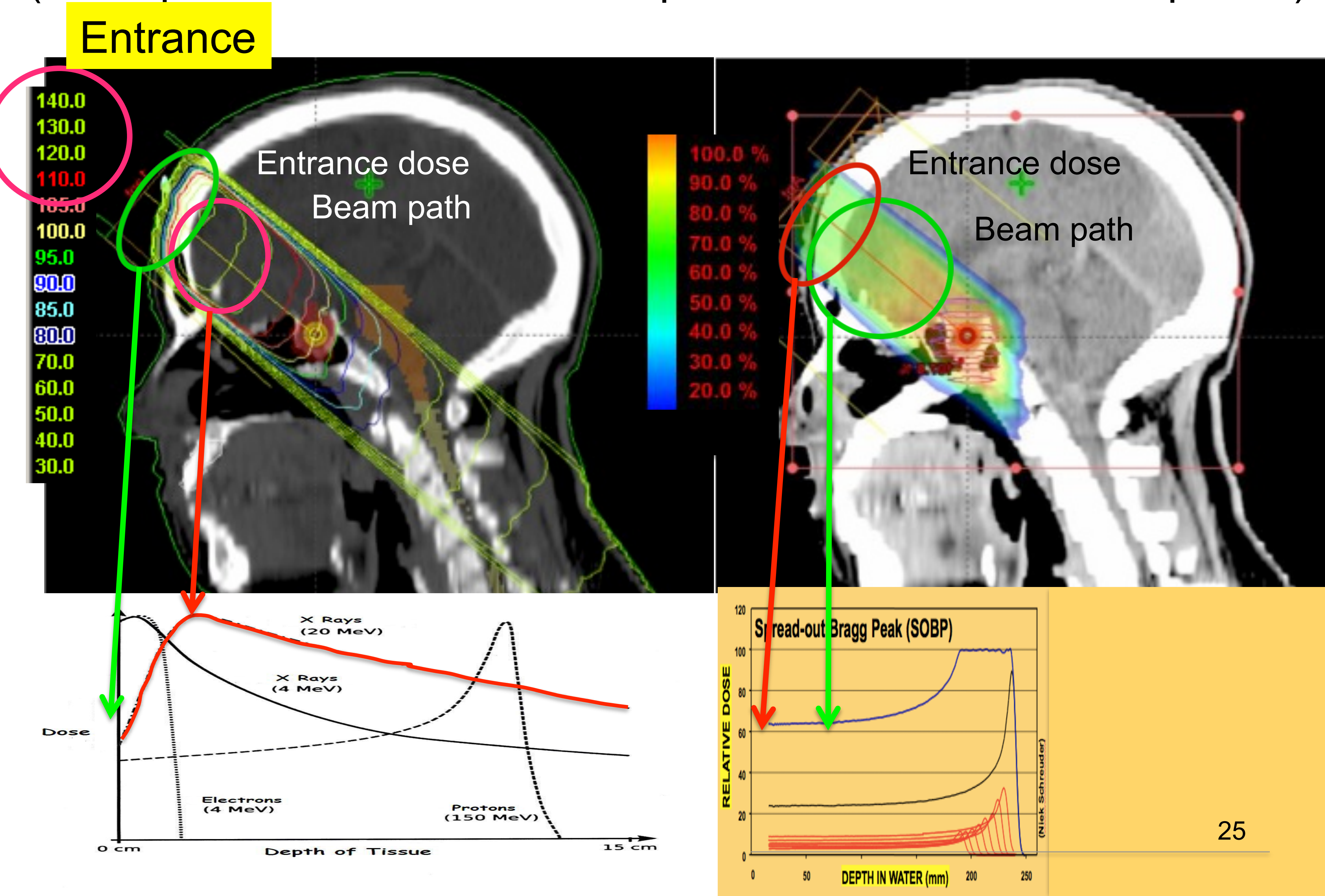
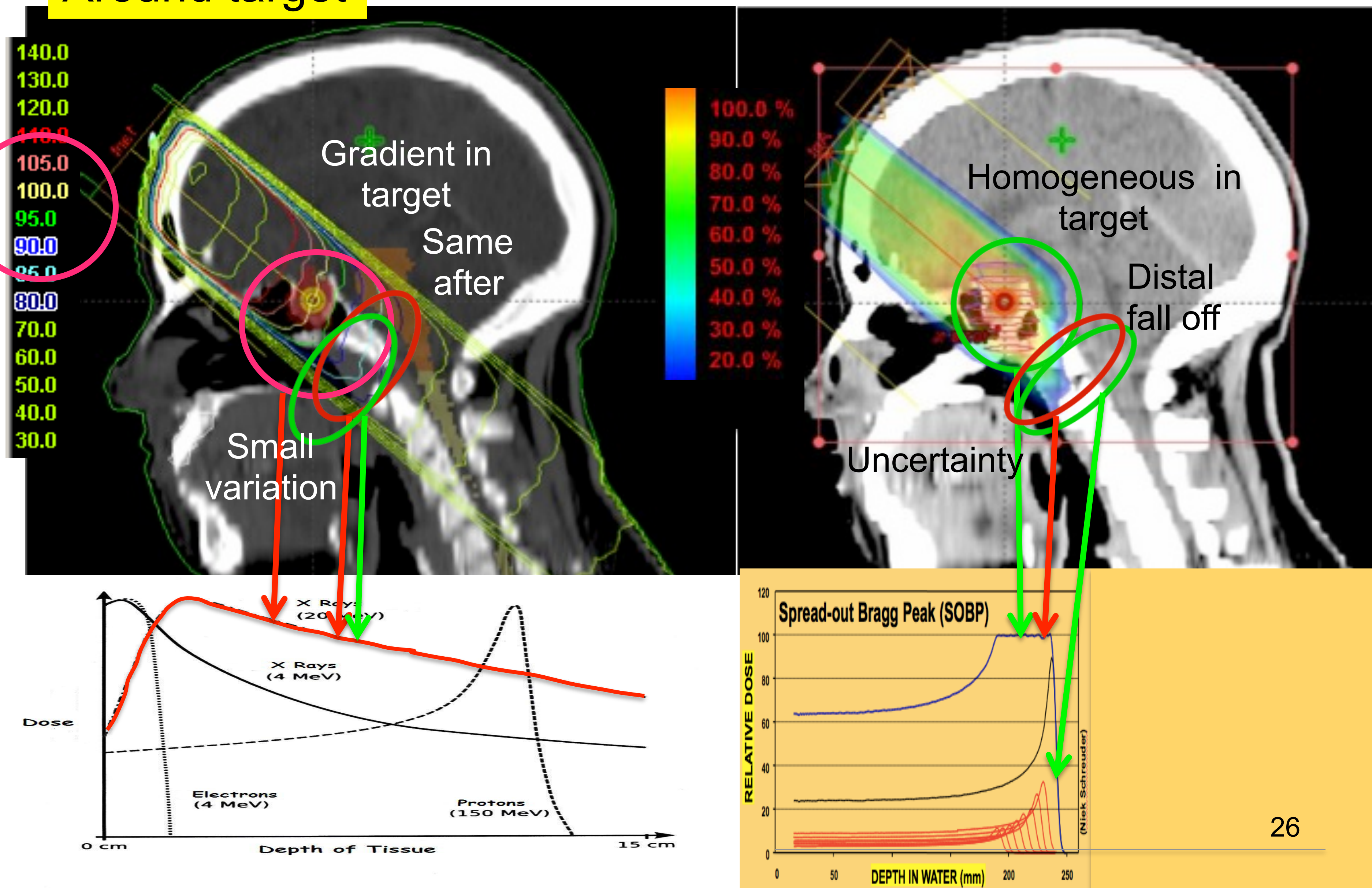
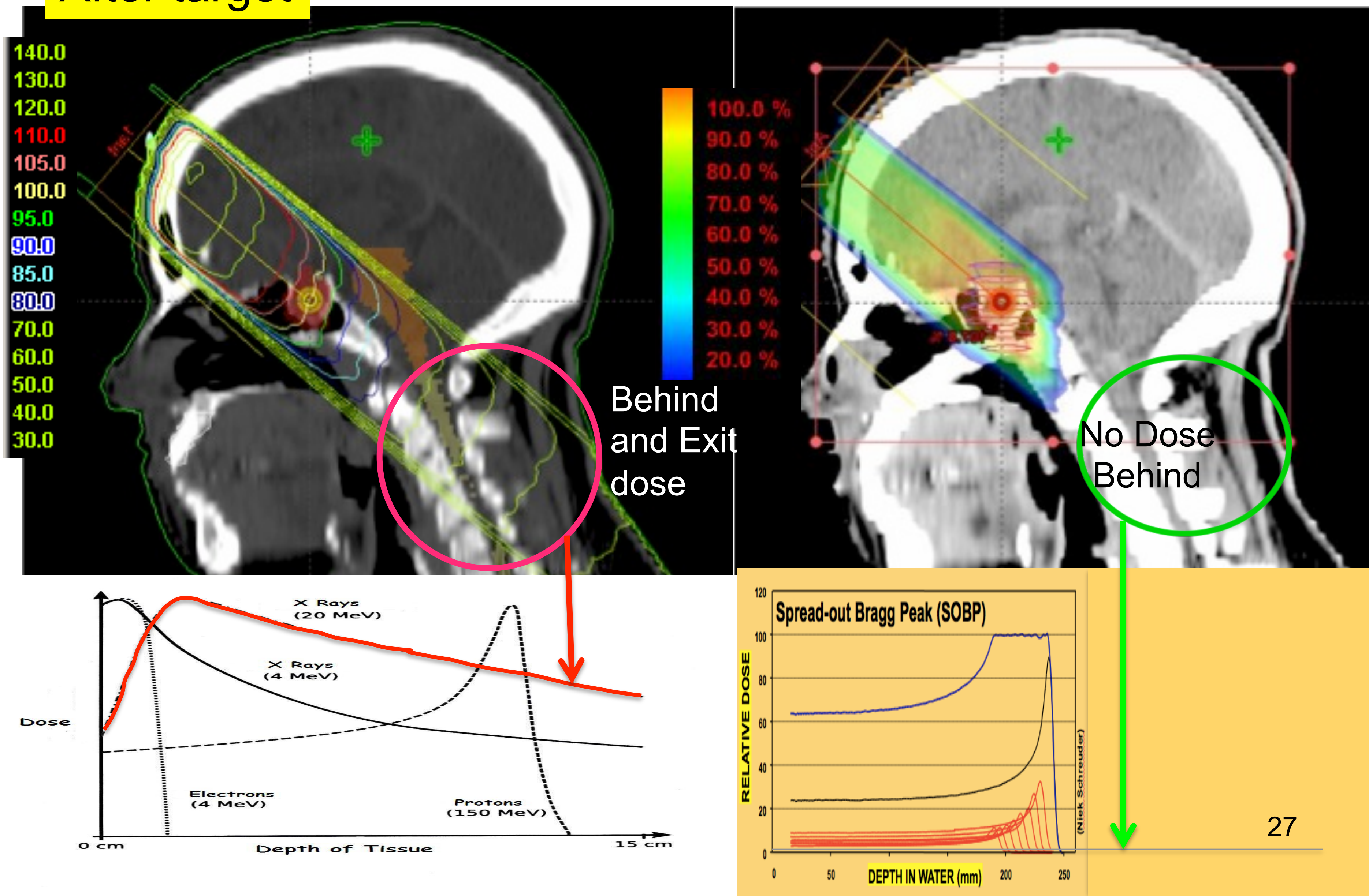
Moving from planning with photons to protons? (Isodoses)
(concepts for 1 beam ~ valid for passive and active techniques…)



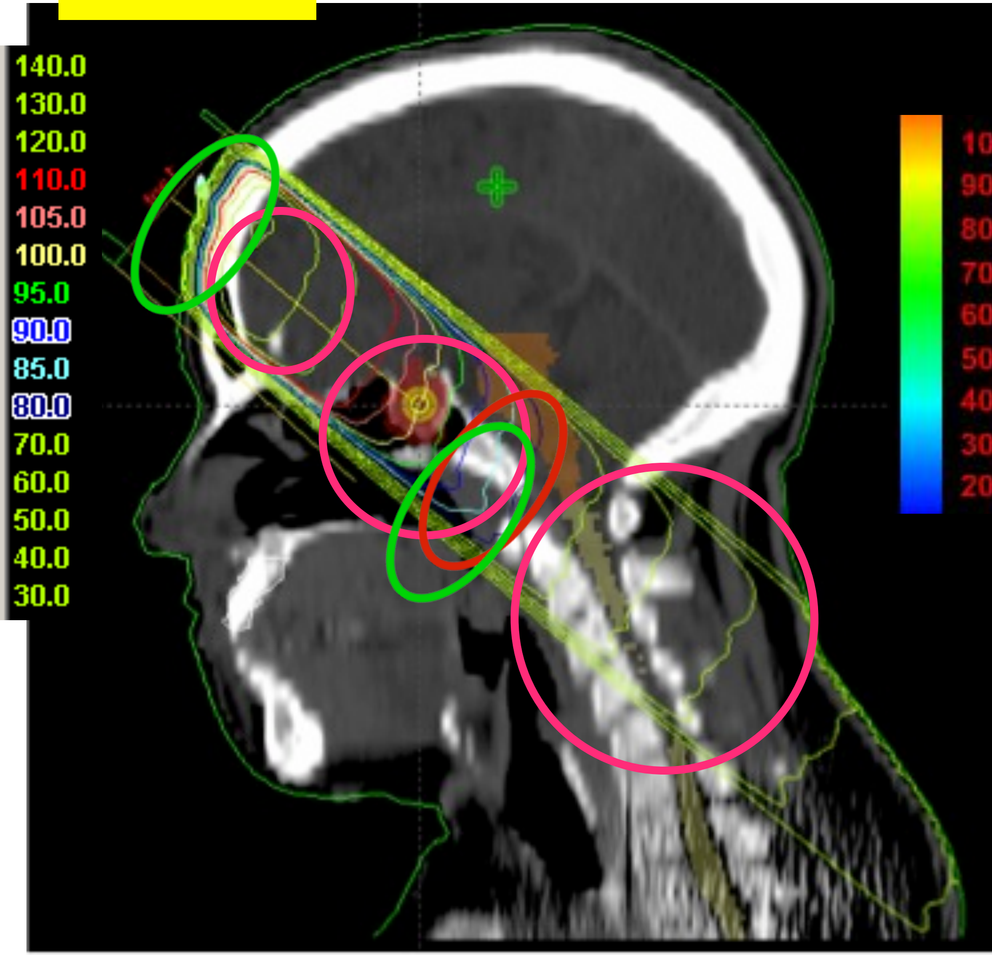
Around target

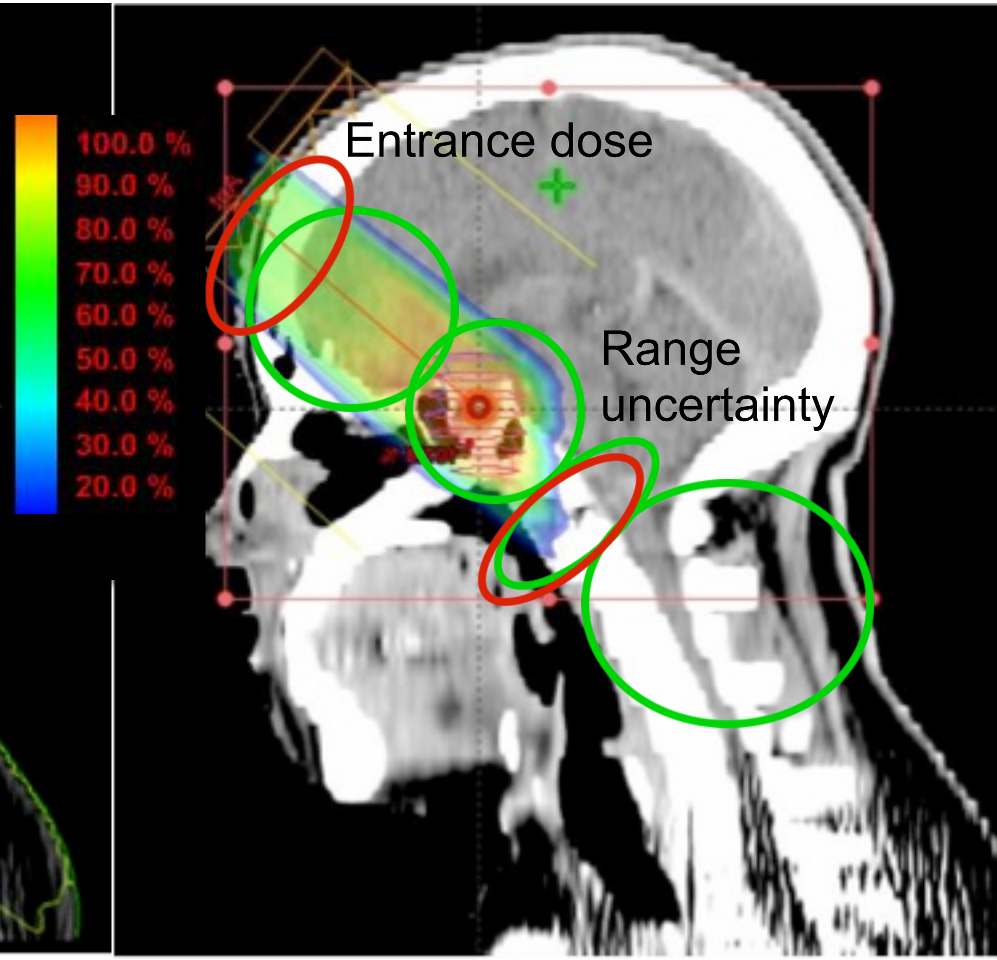


After target

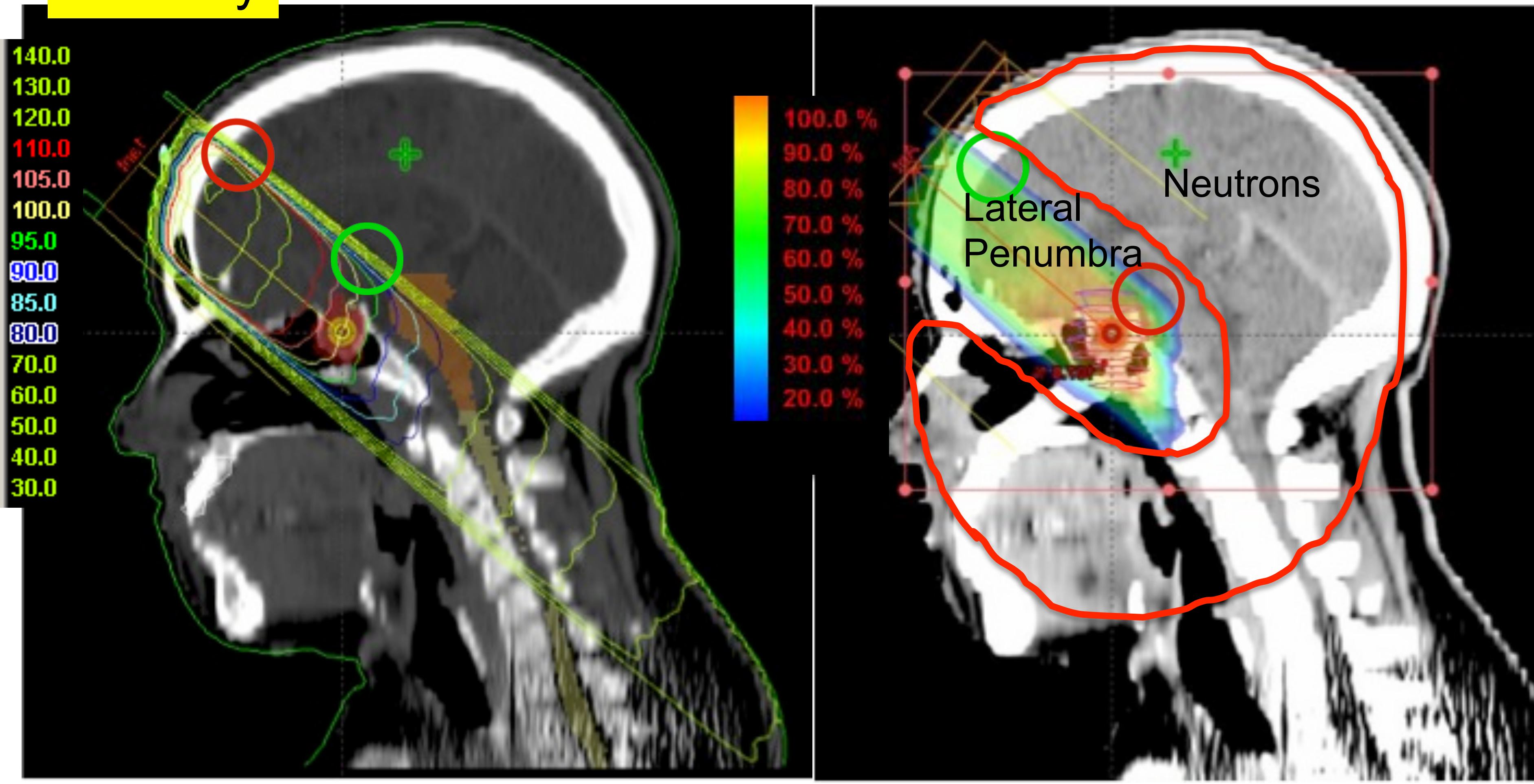


On axis

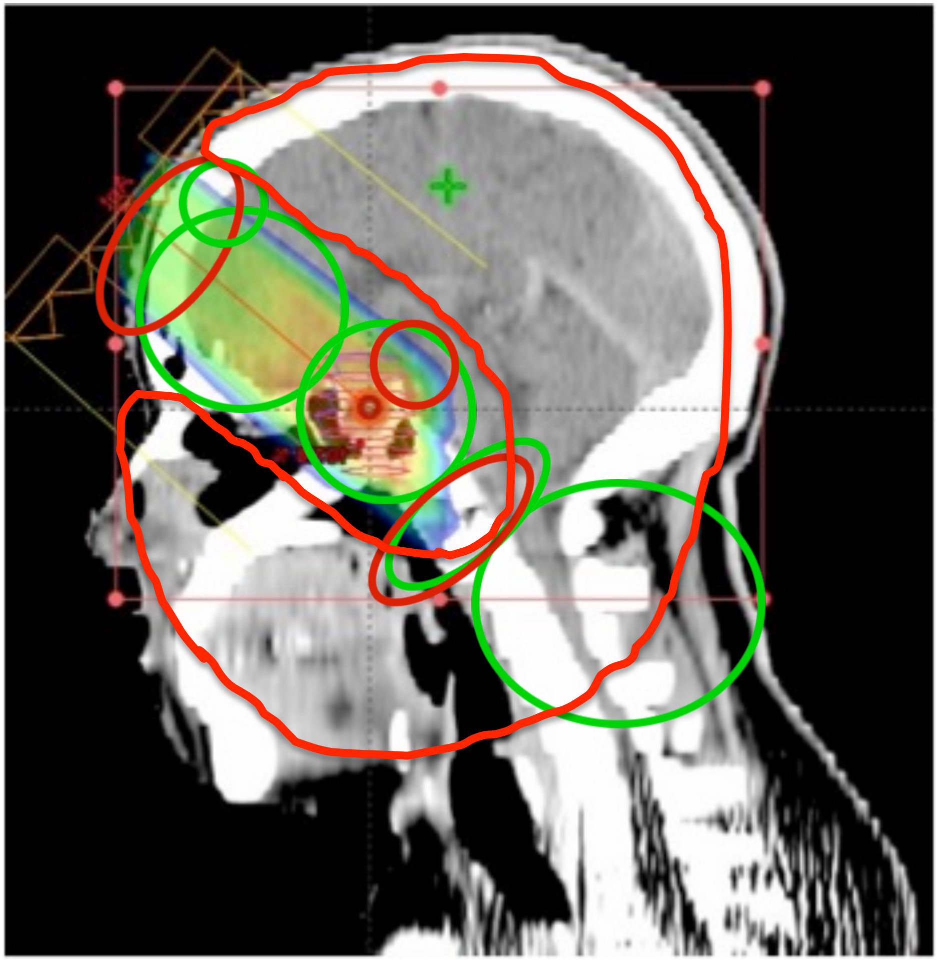

140.0
130.0
120.0
110.0
105.0
100.0
95.0
90.0
85.0
80.0
70.0
60.0
50.0
40.0
30.0

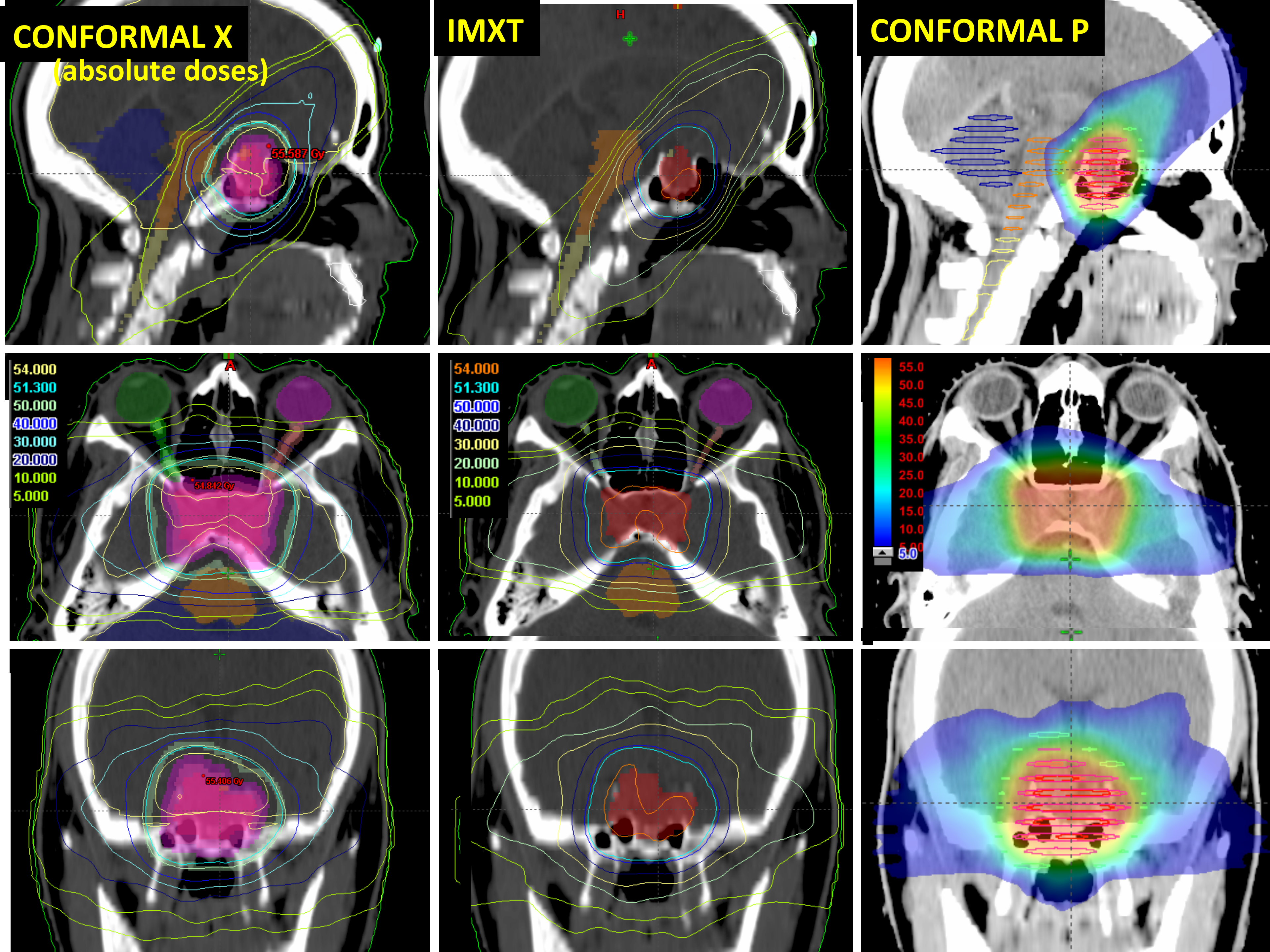

100.0 %
90.0 %
80.0 %
70.0 %
60.0 %
50.0 %
40.0 %
30.0 %
20.0 %
Entrance dose
Range uncertainty

Laterally


140.0
130.0
120.0
110.0
105.0
100.0
95.0
90.0
85.0
80.0
70.0
60.0
50.0
40.0
30.0
100.0 %
90.0 %
80.0 %
70.0 %
60.0 %
50.0 %
40.0 %
30.0 %
20.0 %
Lateral
Penumbra
Neutrons

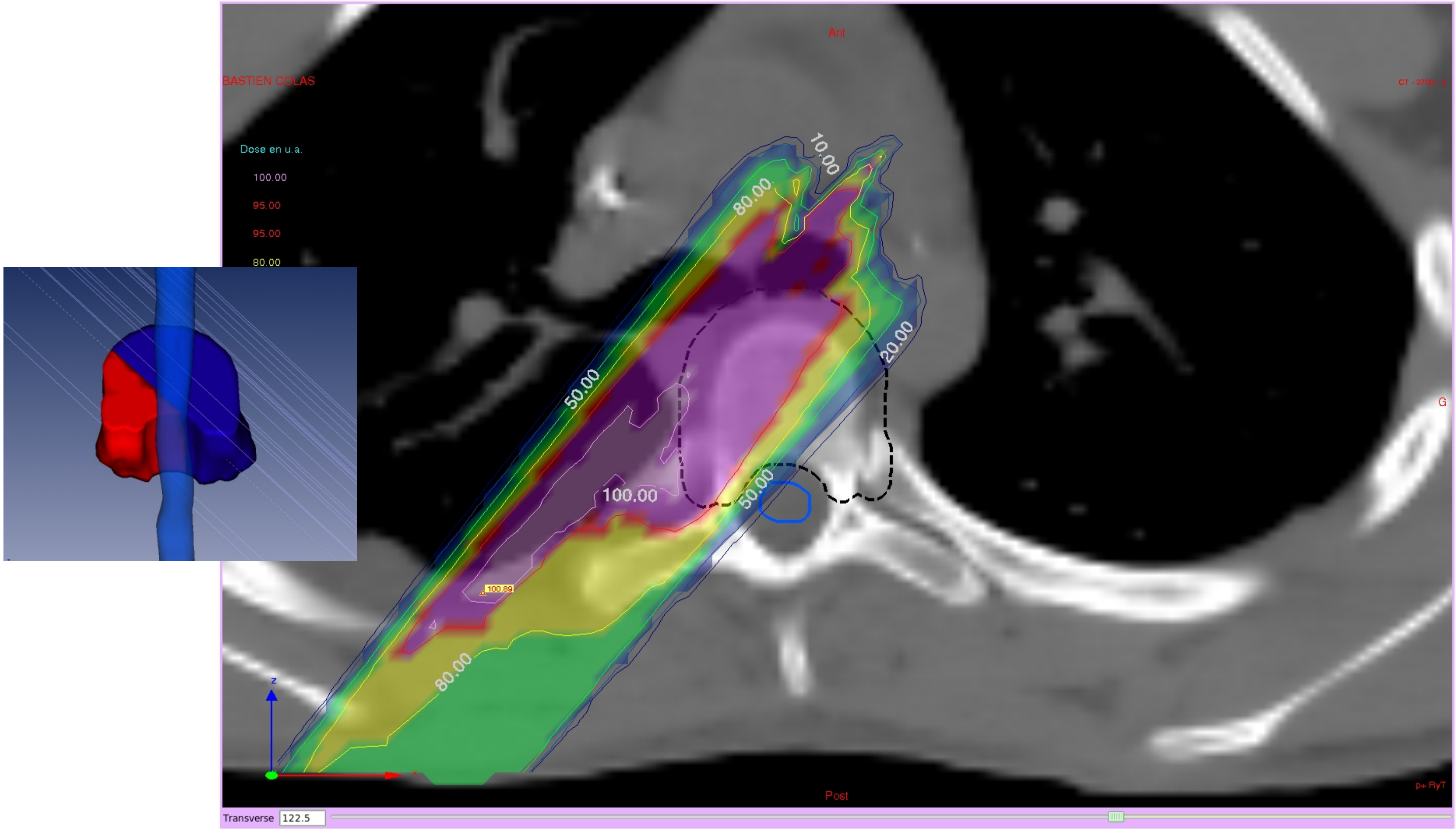
Advantages and limits with particle beams in therapy





CONFORMAL X
(absolute doses)
IMXT
CONFORMAL P
55.587 Gy
54.000
51.300
50.000
40.000
30.000
20.000
10.000
5.000
54.842 Gy
55.0
50.0
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
55.406 Gy

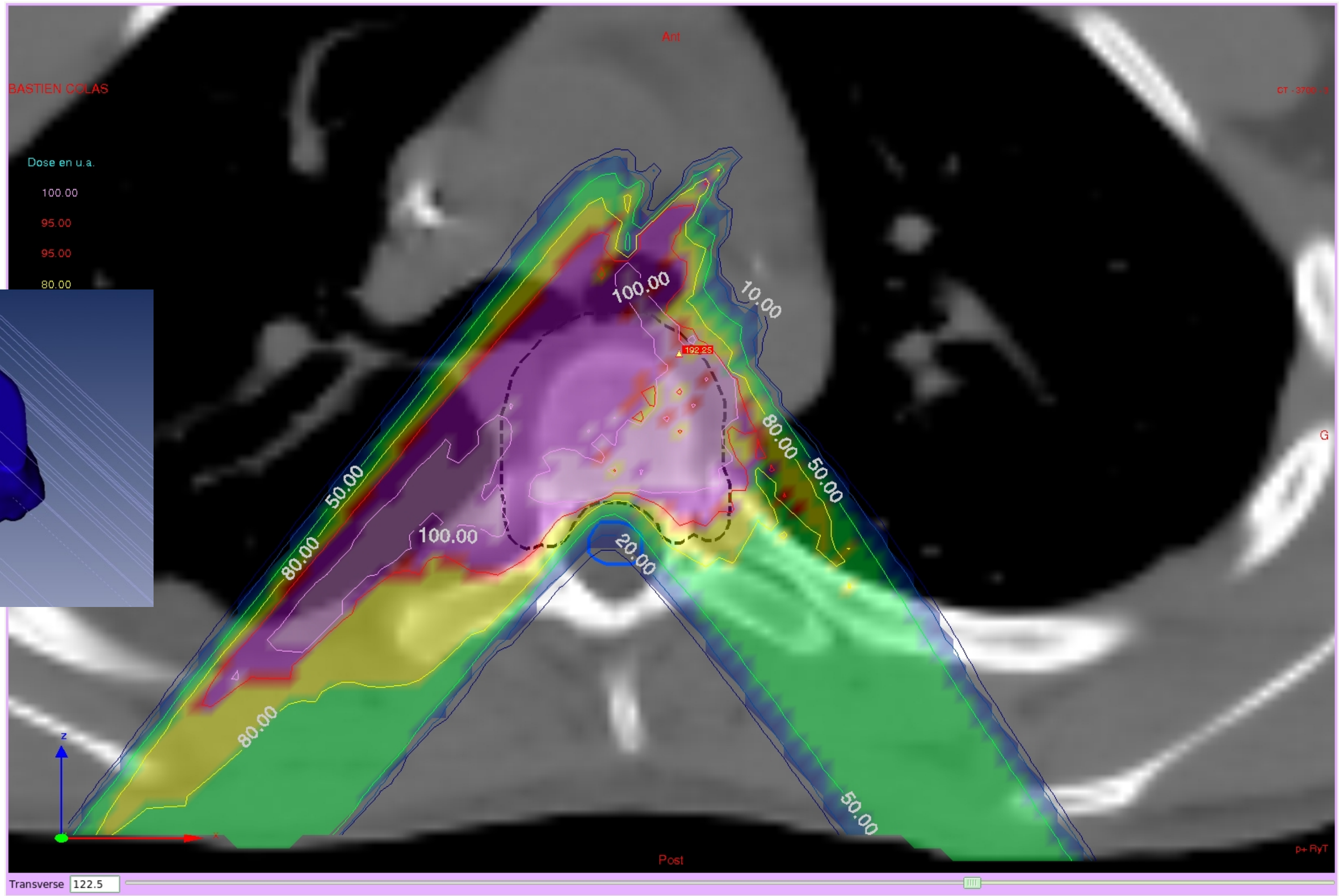
Applications cliniques: les patchs

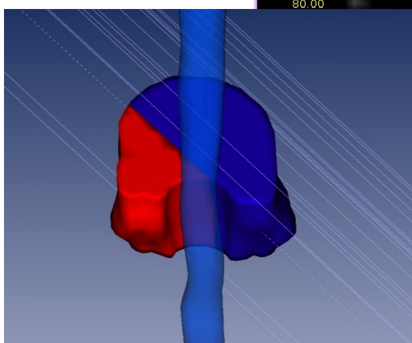


DeMarzi et al

institutCurie

Applications cliniques: les patchs



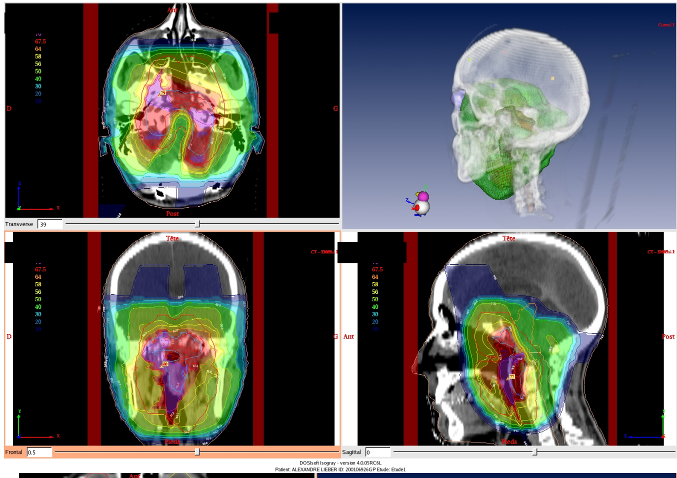


DeMarzi et al

General planning tricks and some useful rules

- Entrance dose (++) =>

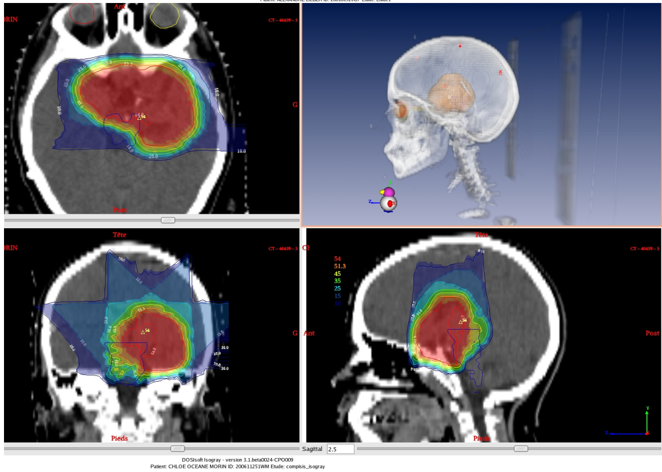
- multiply the ports, combine with photons



- Patch fields risky (hot & cold spots) =>

- limit the dose/patch (eg < 8 CGE)

- design several patch fields



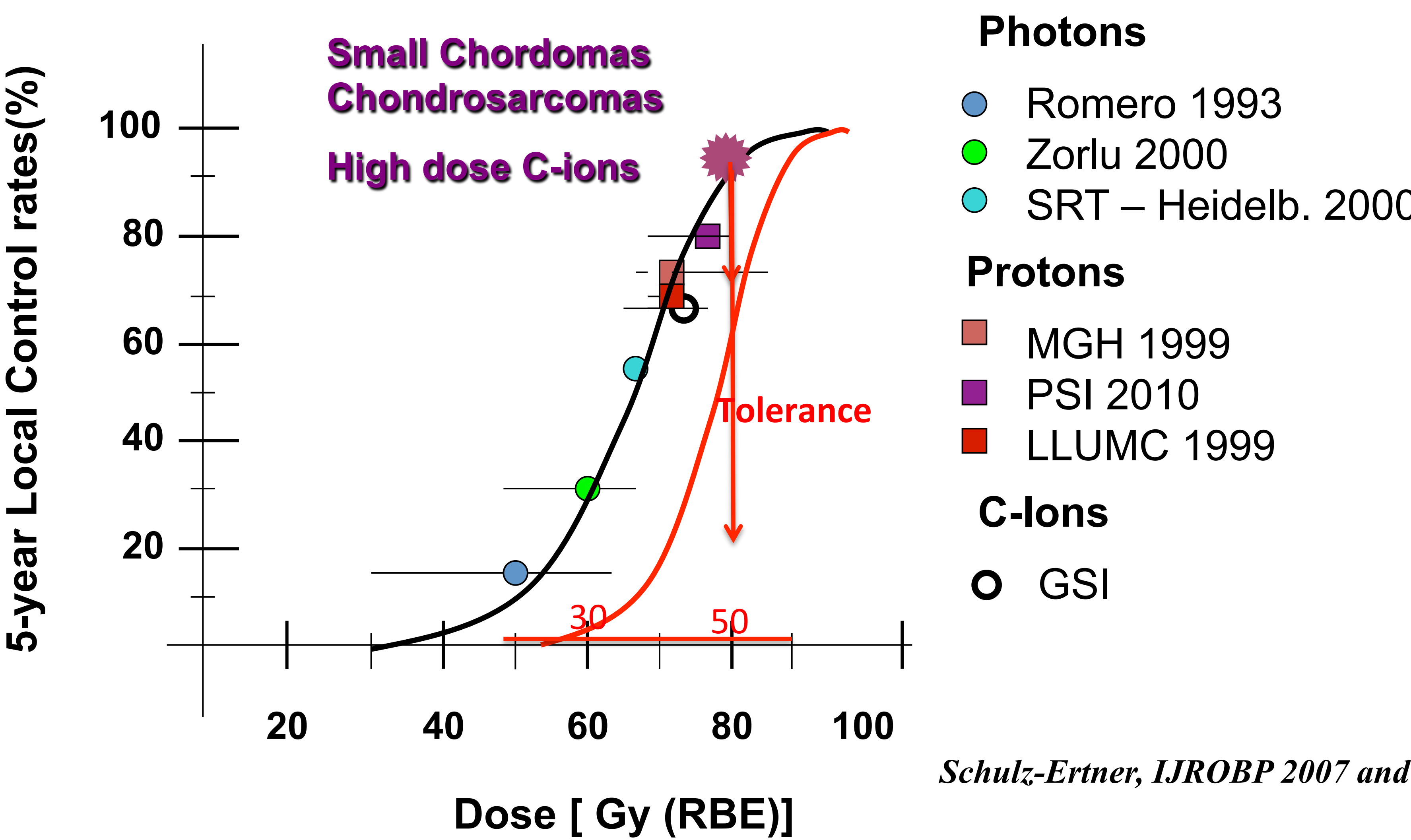
- Uncertainties on distal edge position (mask, inhomogeneities) + RBE =>

don't stop beams with high dose in front of OAR (if possible…)

- avoid « risky » ports (through nose, tongue, …)

Local control
(photons, protons, carbon…)

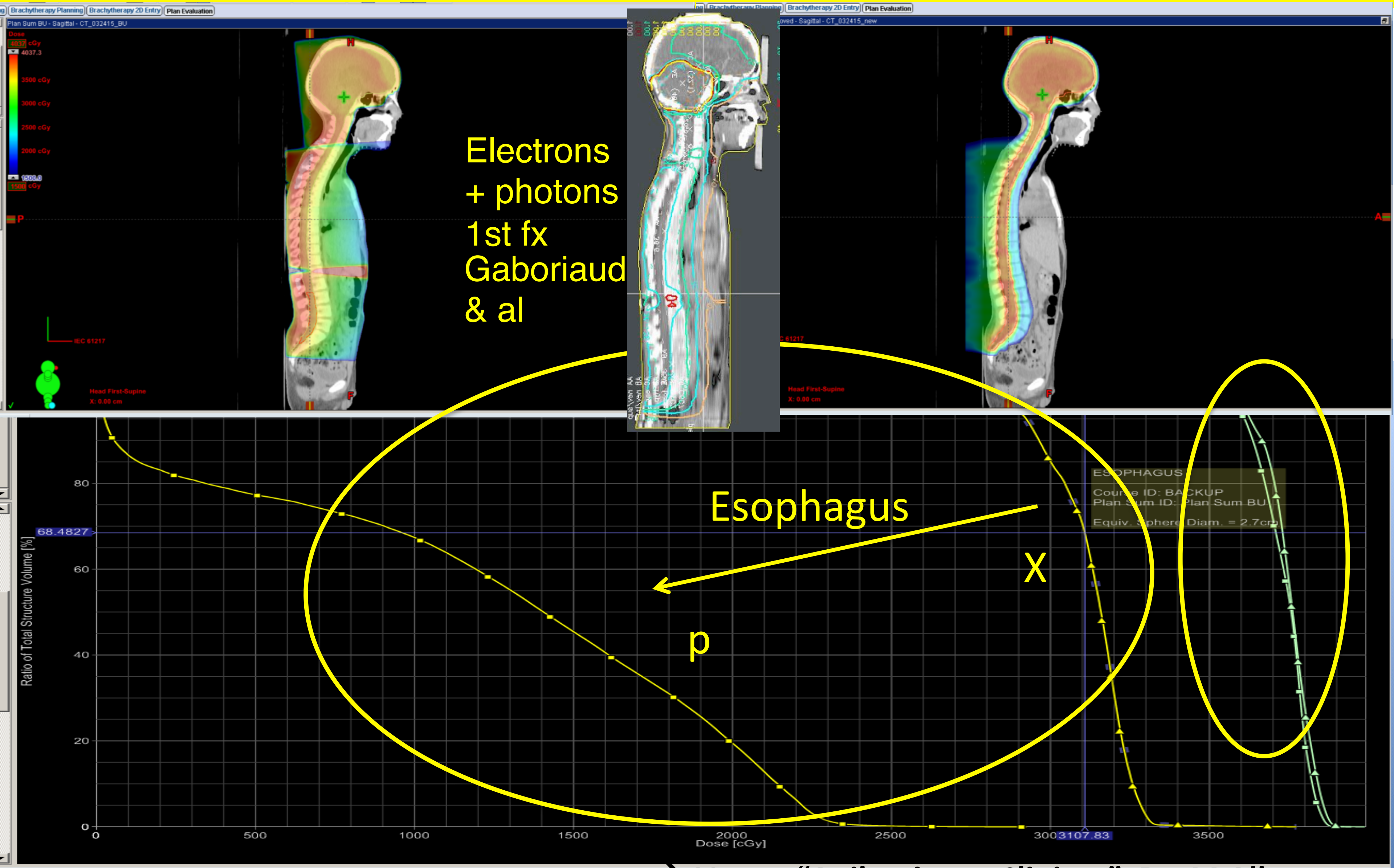
Chordomas of the Base of Skull



Schulz-Ertner, IJROBP 2007 and

CSI: Photons (left & triangles), PBS (right & squares)

Jim McDonough, U. Penn



→ Vean : "Apilcaciones Clinicas" Dr. M Albert

M.D.Anderson, Houston// Komiki et al//PTCOG

LUNG

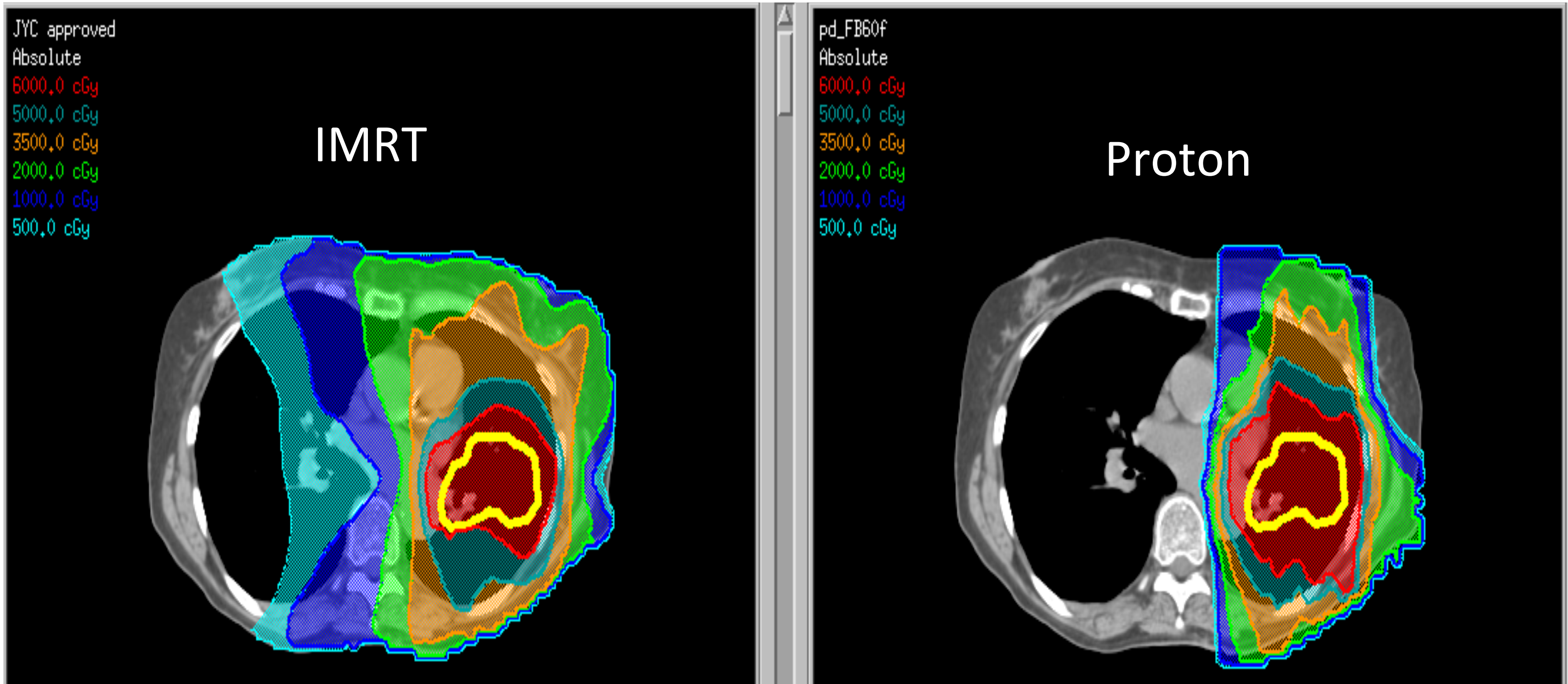
Proton dose escalation still spares more normal tissues

Proton 87.5 GY vs photon 60 GY in stage I

Proton 74 GY vs photon 60 Gy in stage III

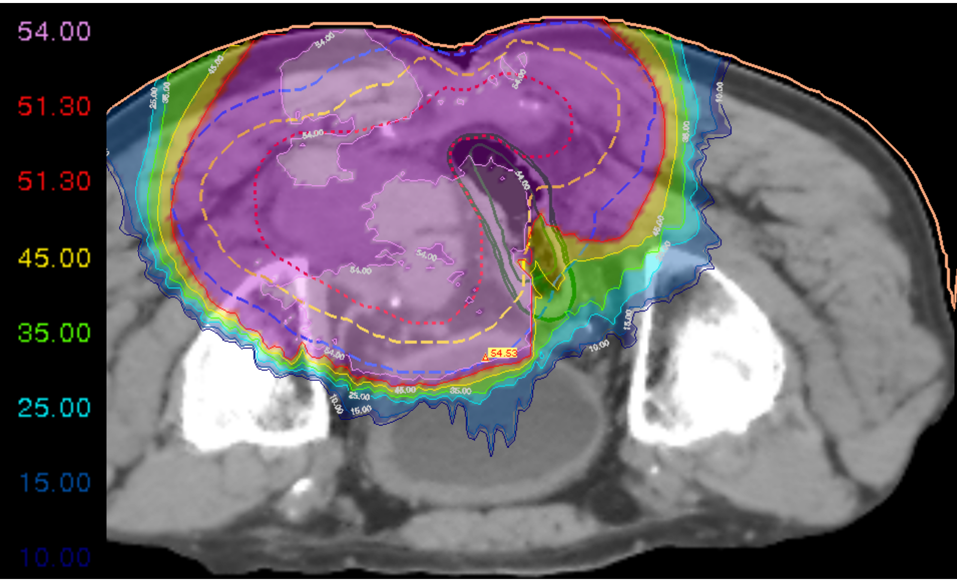
(Chang et al: Int J Rad Onc Bio Phys 65:1087-96, 2006)

Stage III

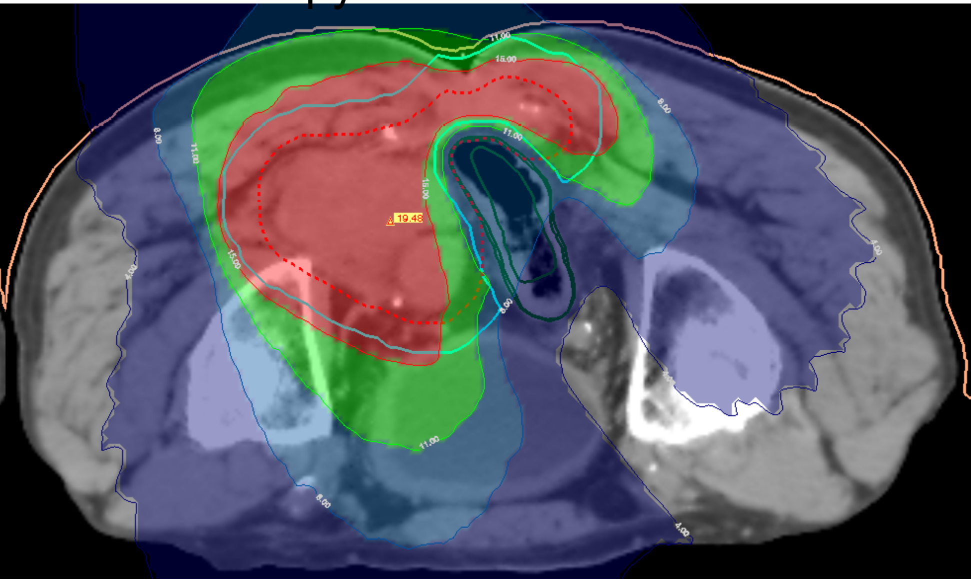


Ex Large sarcoma

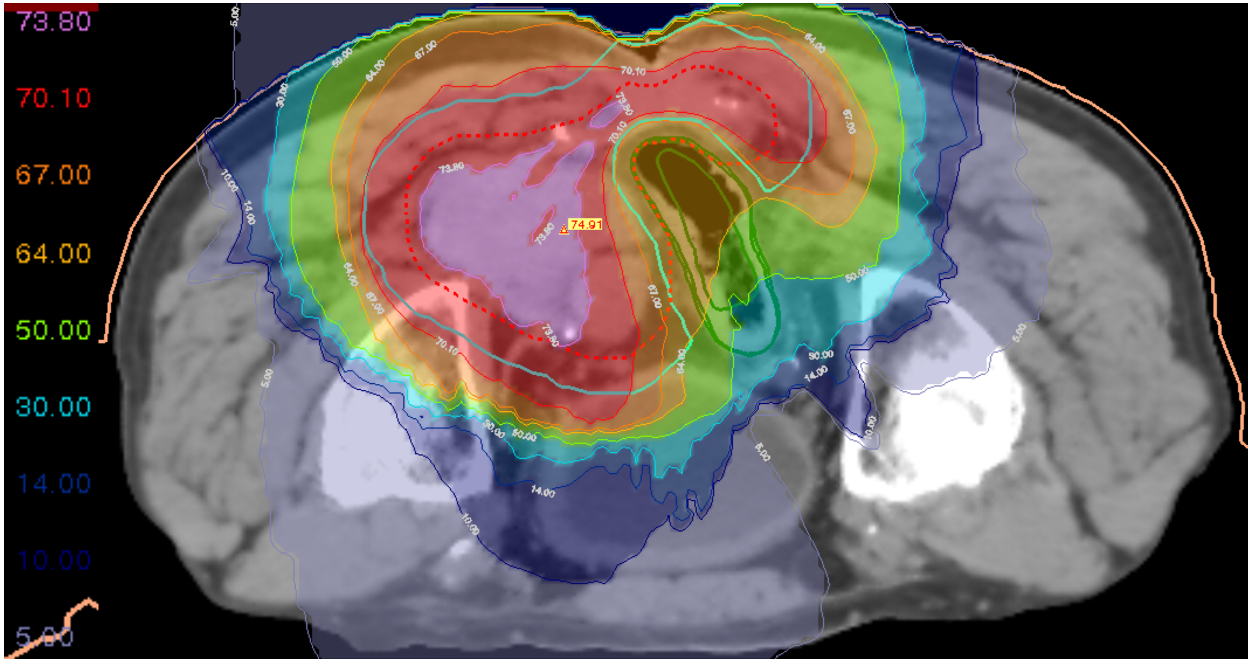
Protons



Tomotherapy



Cumulated



N.Fournier-Bidoz et al, I. Curie

Less Hardware !

TO REDUCE ALL ASPECTS RELATED TO APERTURES AND COMPENSATORS

- CALCULATION, OPTIMISATION (air gap,…)
- WORKSHOP or OUTSOURCING
- QUALITY ASSURANCE
- DAILY SETUP
- NEUTRONS
- STORAGE
- DISPOSAL
- COST

→ **PBS** ☺

MENU

1. The Planning Process,
   the beam models
   and the uncertainties.

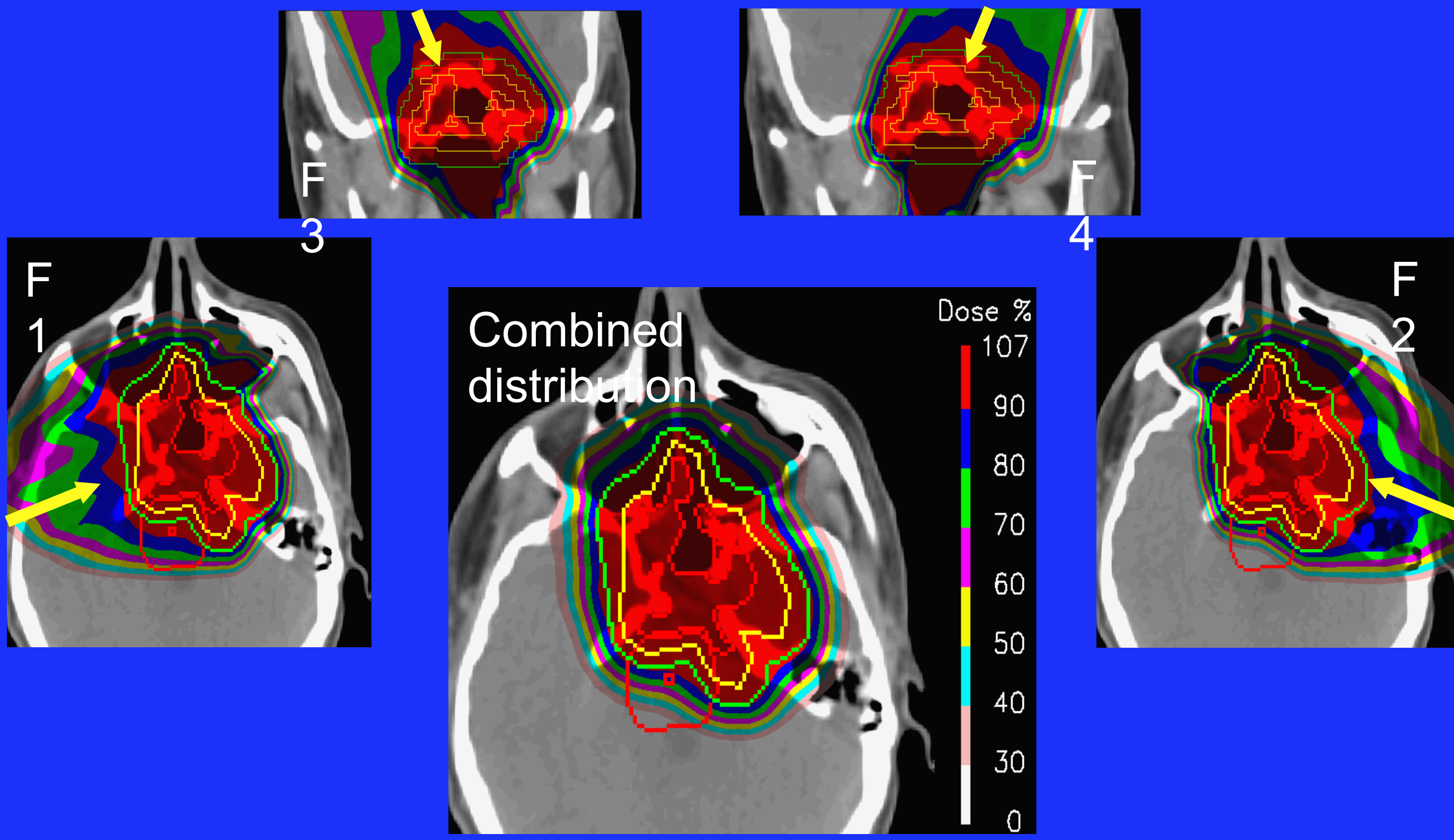
2. Some clinical examples
   with passive beams.

3. **Planning with PBS,**
   advantages and still some limits

4. The future,
   examples of research and development

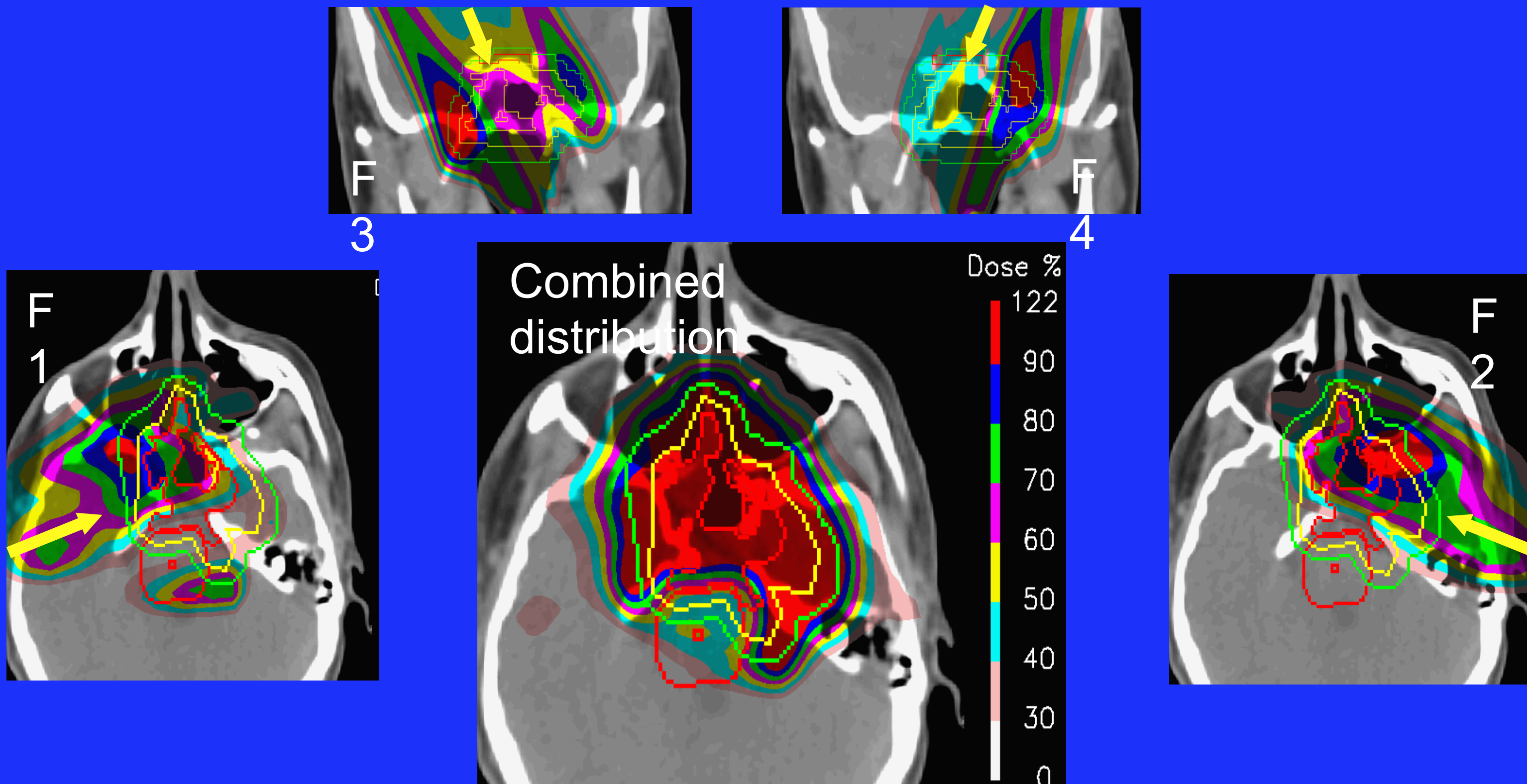
5. Conclusions

An example SFUD plan.



Note, each individual field is homogenous across the target volume

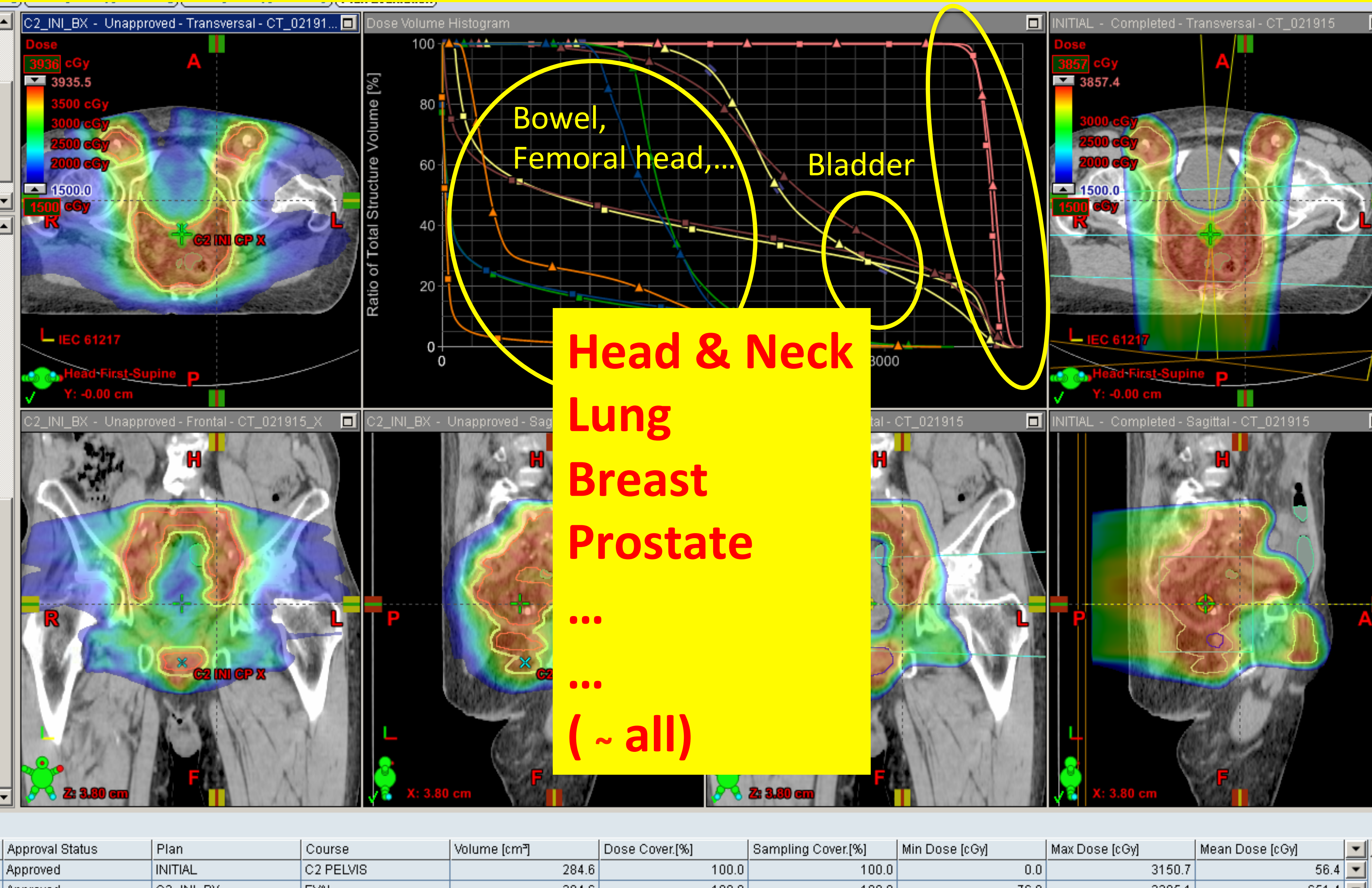
An example IMPT plan



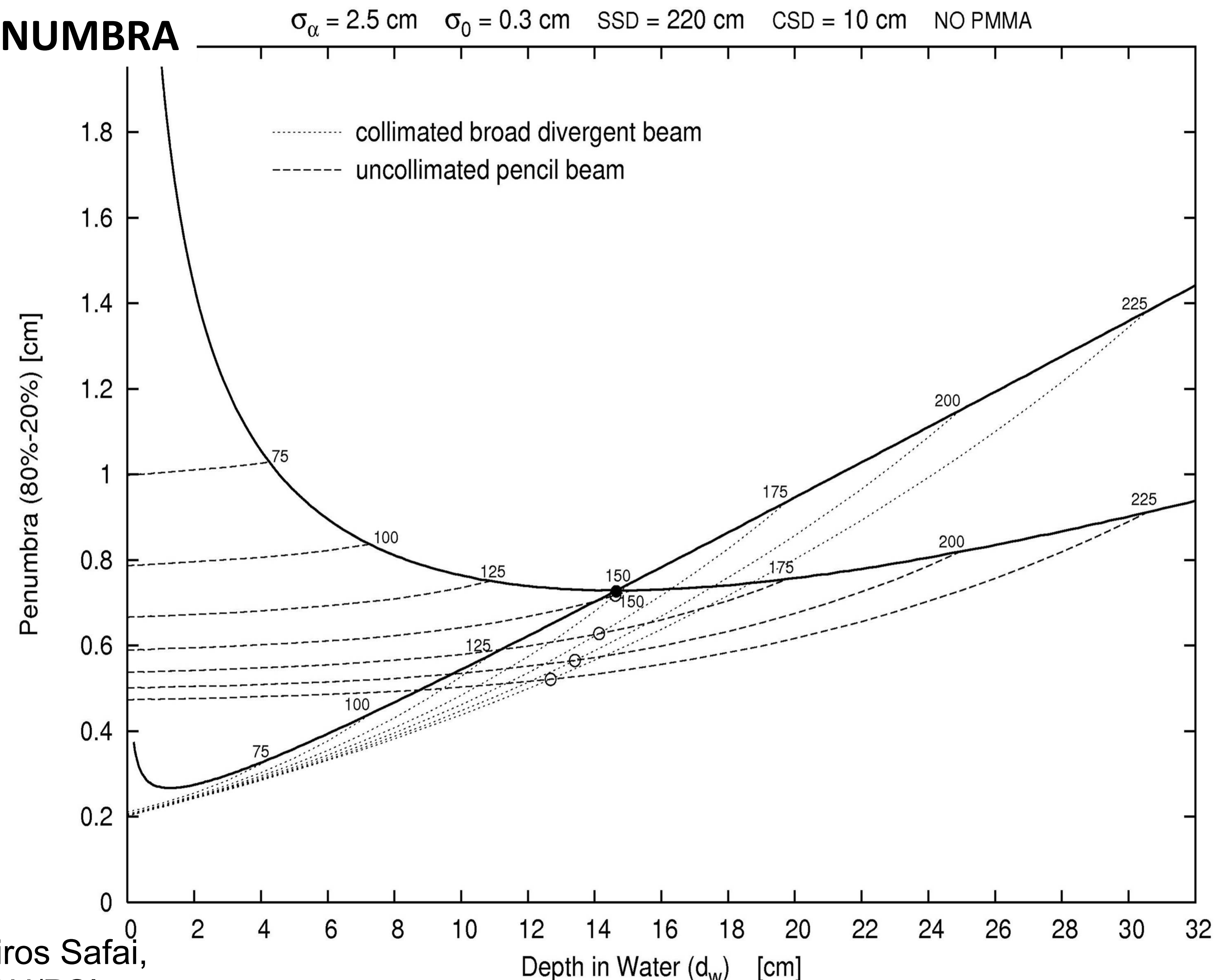
Note, each individual field is highly in-homogenous (in dose) across the target volume (c.f. SFUD plans)

Jim McDonough, U. Penn

Pelvis: Rapid Arc (left & triangles), PBS (right & squares)



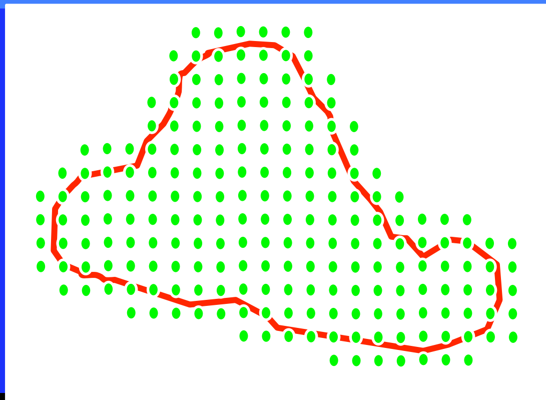
PENUMBRA

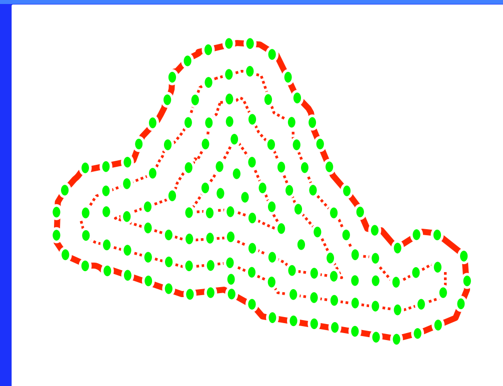


Sairos Safai, MGH/PSI

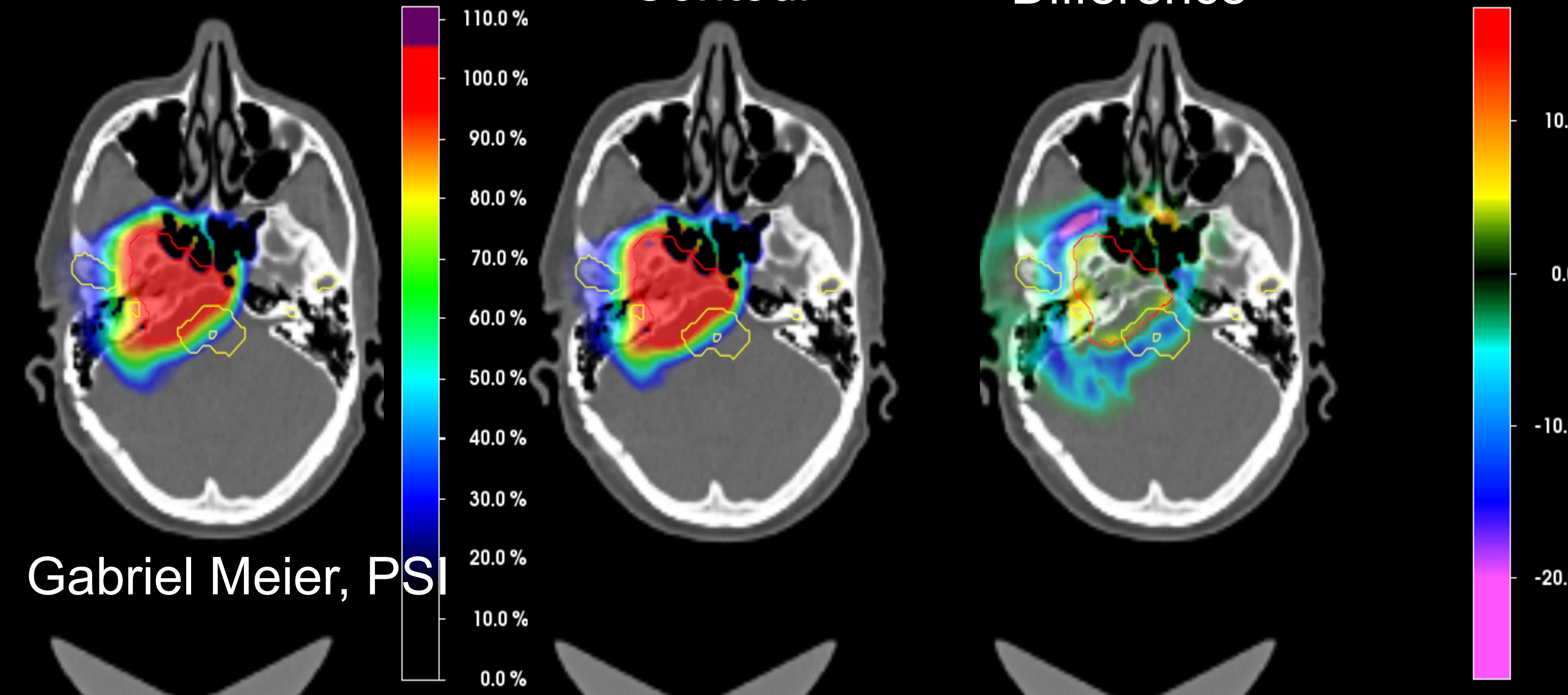
Contour scanning

PAUL SCHERRER INSTITUT





Grid | Contour | Difference



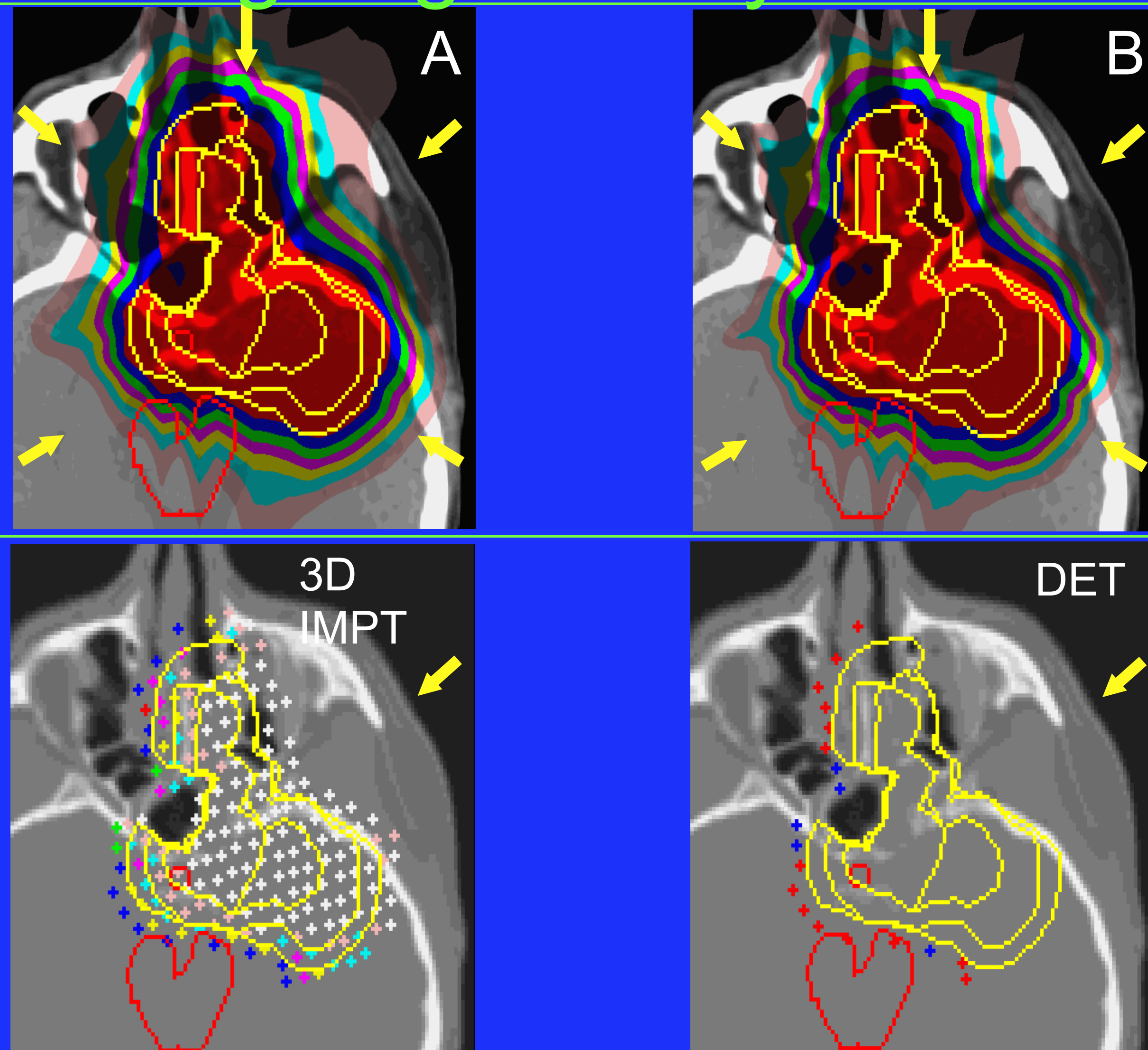
Gabriel Meier, PSI

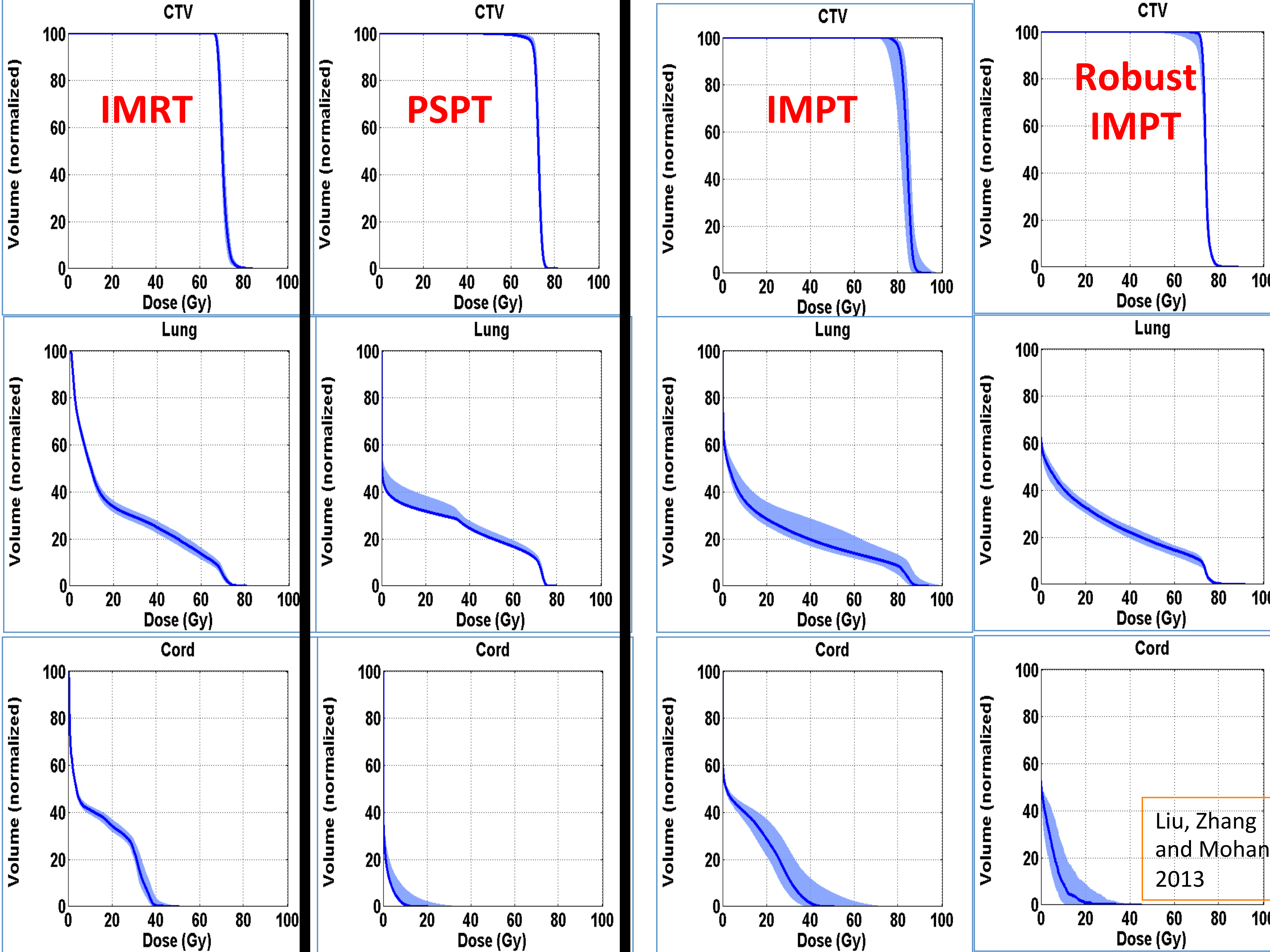
Planning degeneracy

Two exs,

5 field IMPT dose distributions

Corresponding spot weight distributions from field 2

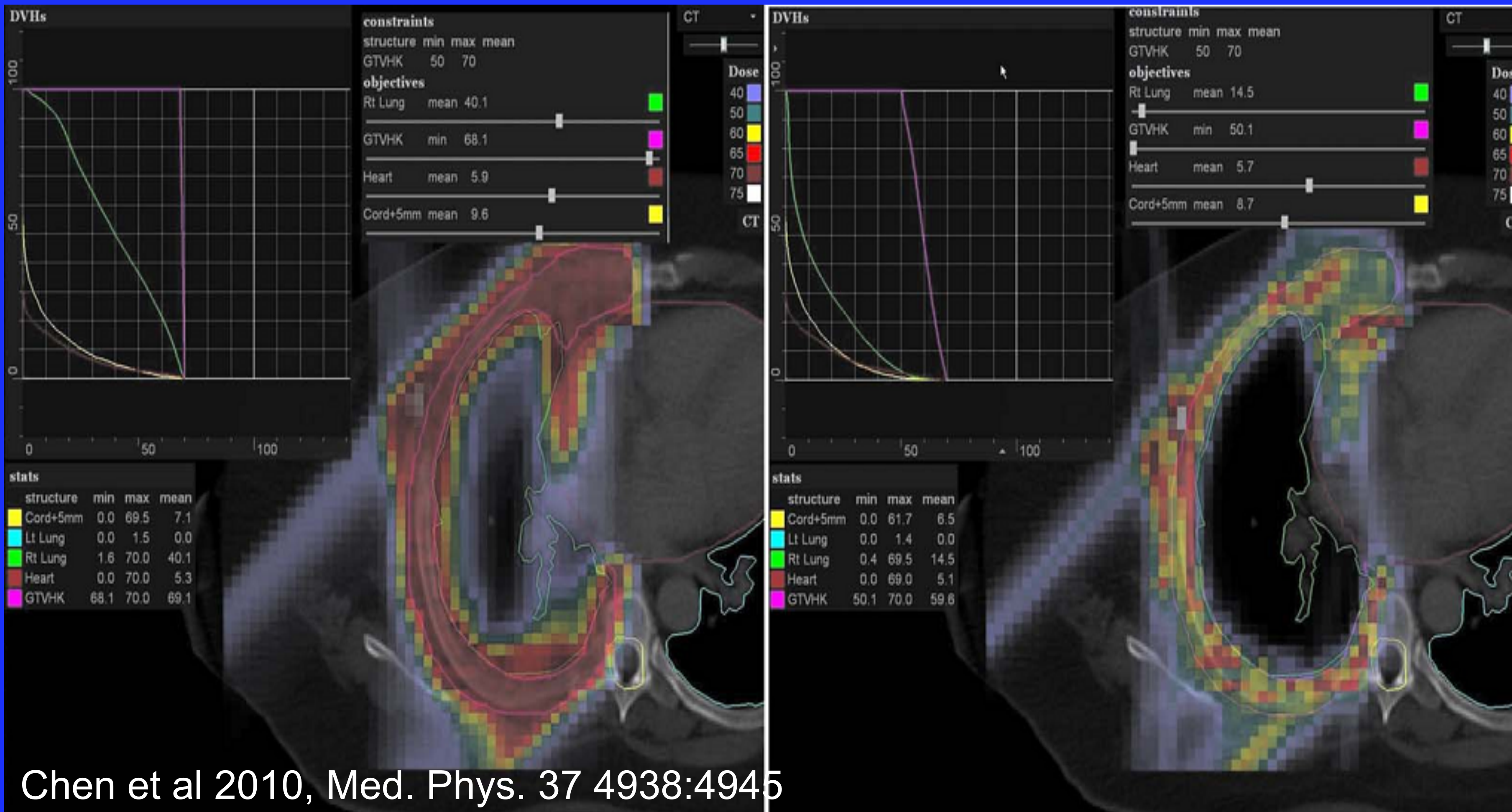




IMRT
PSPT
IMPT
Robust IMPT
CTV
Lung
Cord
Volume (normalized)
Dose (Gy)
Liu, Zhang and Mohan 2013

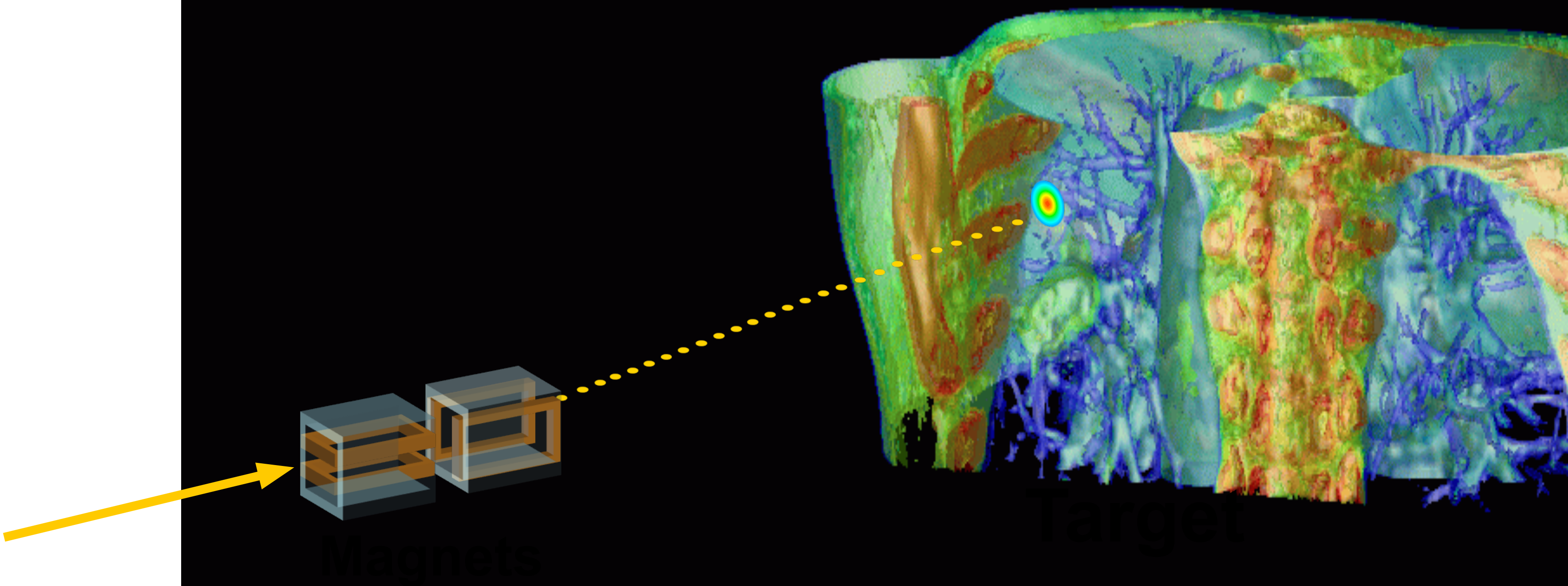
PAUL SCHERRER INSTITUT

Multiple Criteria Optimisation (MCO)



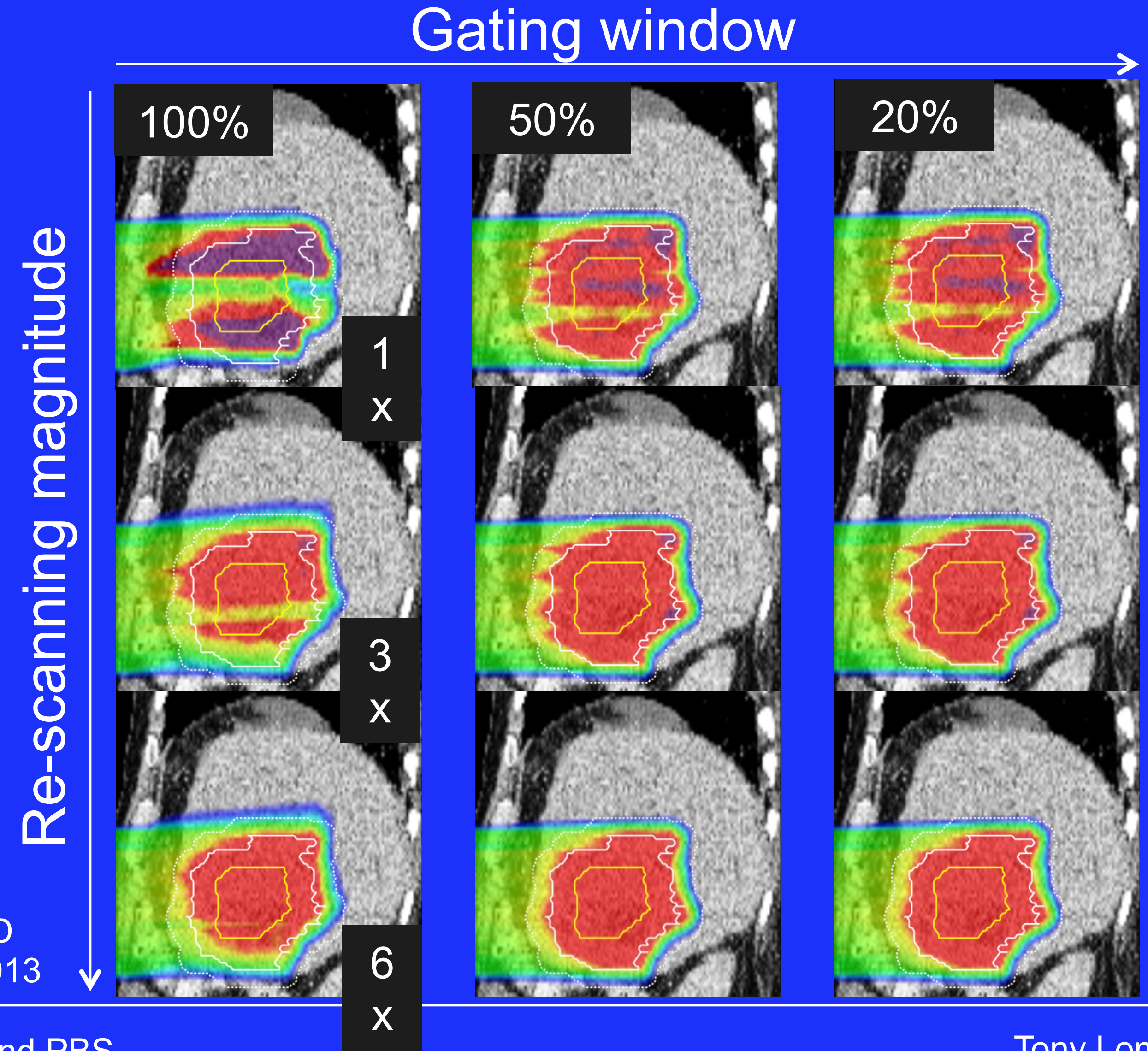
Chen et al 2010, Med. Phys. 37 4938:4945

Beam Delivery : 3D Pencil Beam Scanning



4D by Rietzel, Beam by Kamada

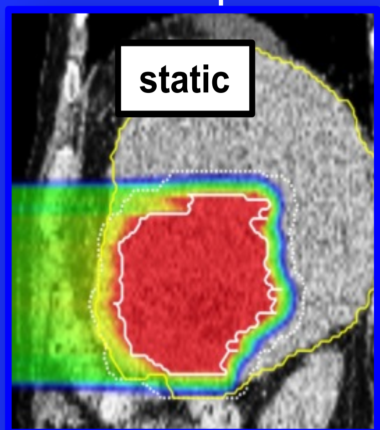
Gating and re-scanning combined



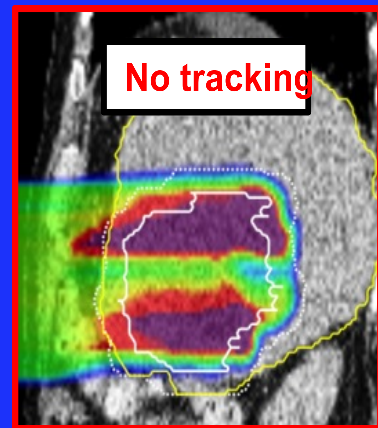
Ye Zhang, PhD thesis, PSI, 2013

Re-scanning and re-tracking compared

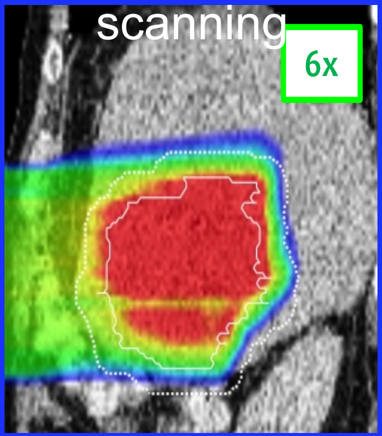
Static plan



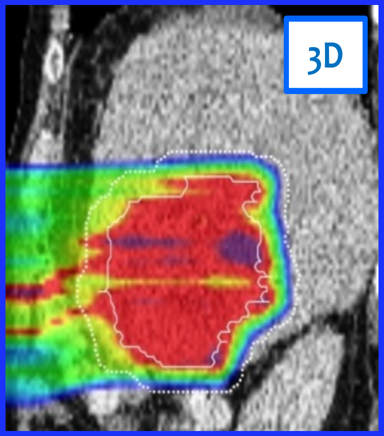
4D – no mitigation



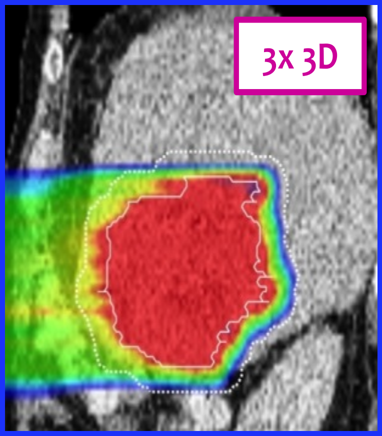
4D – 6x re-scanning



4D – tracking



4D – 3x re-tracking



Zhang et al 2014, PMB, 59:7793-7817

MENU

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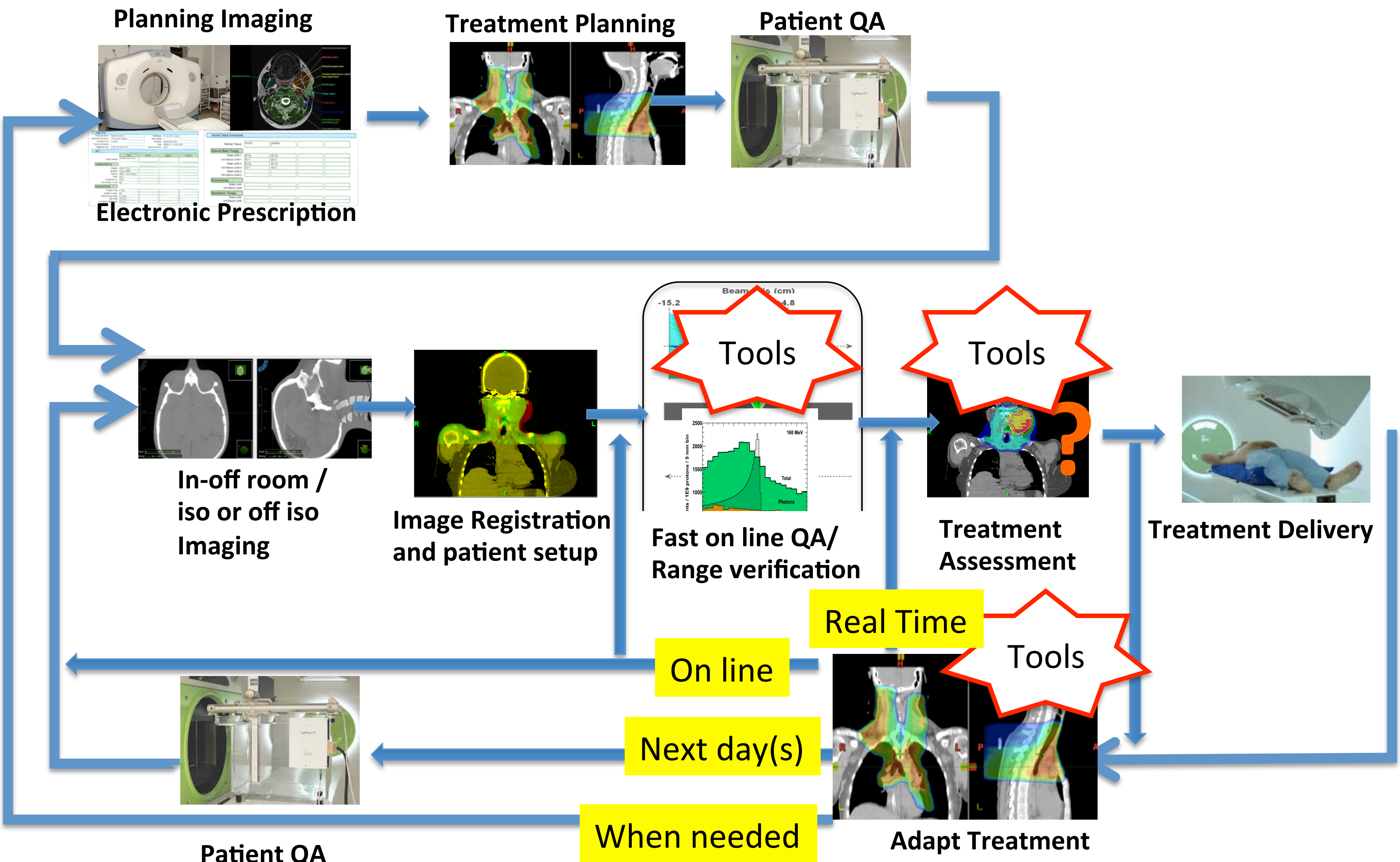
   examples of research and development

5. Conclusions

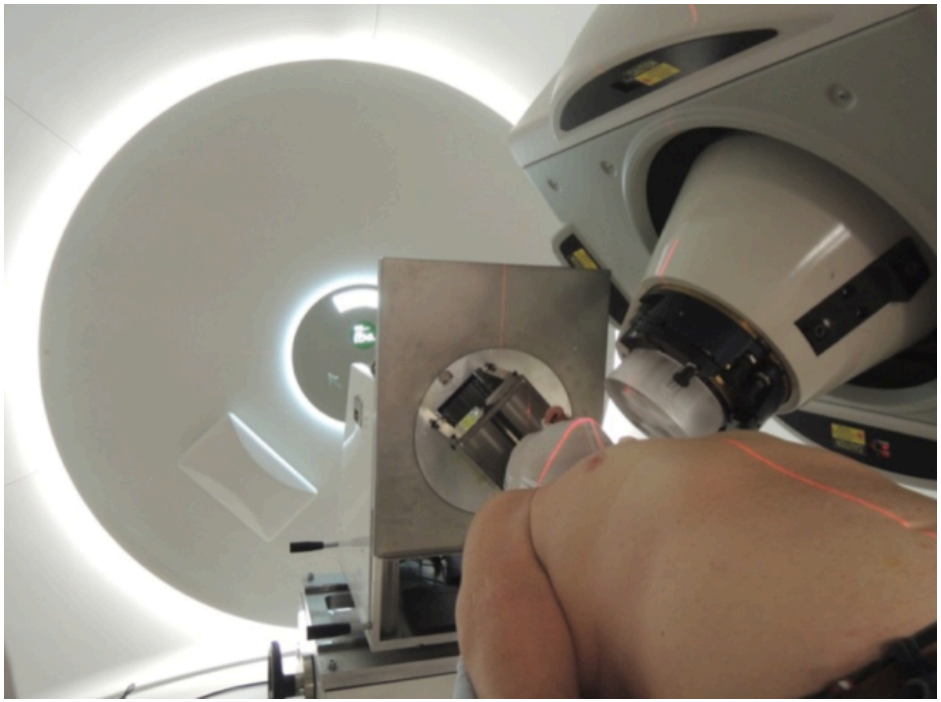
adaptive workflow with pencil beam scanning



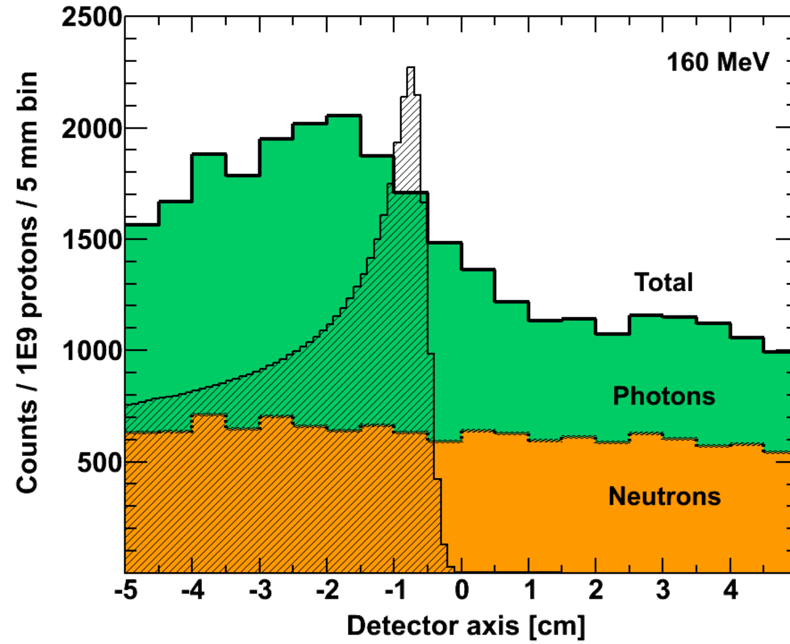
(G. Olivera, A.Mazal)

Range calculation : double E CT, MonteCarlo models, …
Range verification : PET, proton radiography, ionoacustic, …

Gamma prompt detection



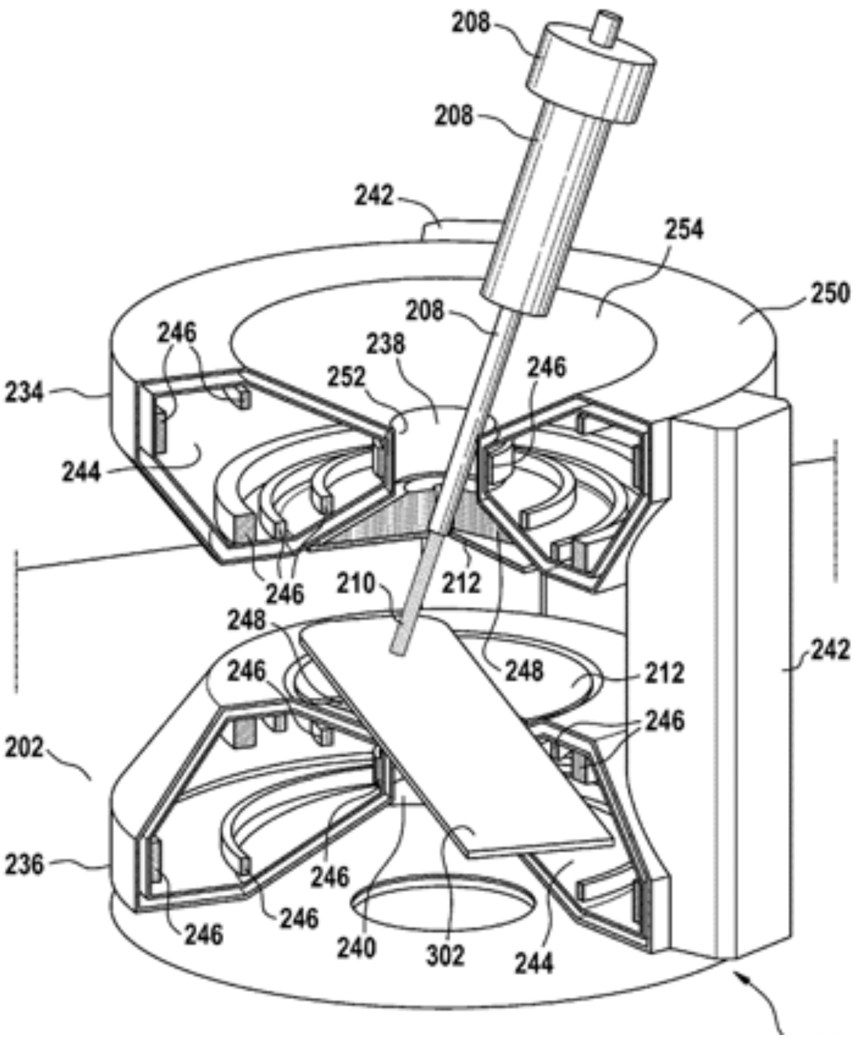
Courtesy G. Pausch, Dresden



1st clinical application, Dresden Aug 2015,

Coming:
Compton cameras , spectrometry, time analysis of gamma prompts…

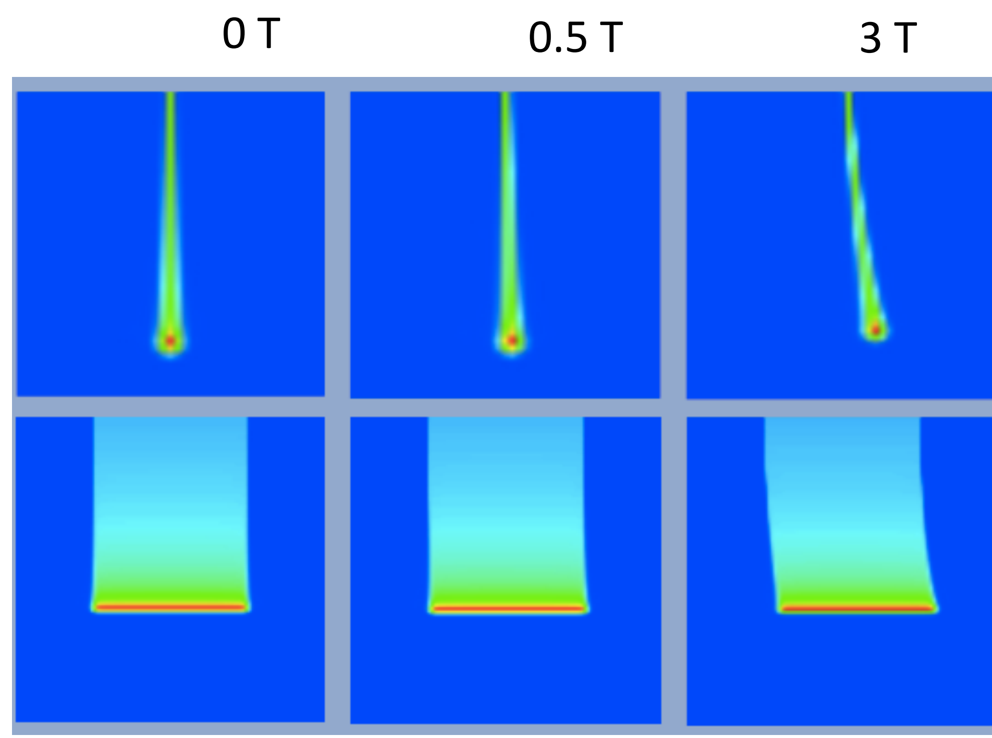
Integrating 1.5T MRI functionality with a radiotherapy accelerator   Lagendijk et al, Utrech



Patent Overweg Philips

Feasibility of MRI guided Proton Therapy:
Magnetic Field Dose Effects

90 MeV proton beam in water



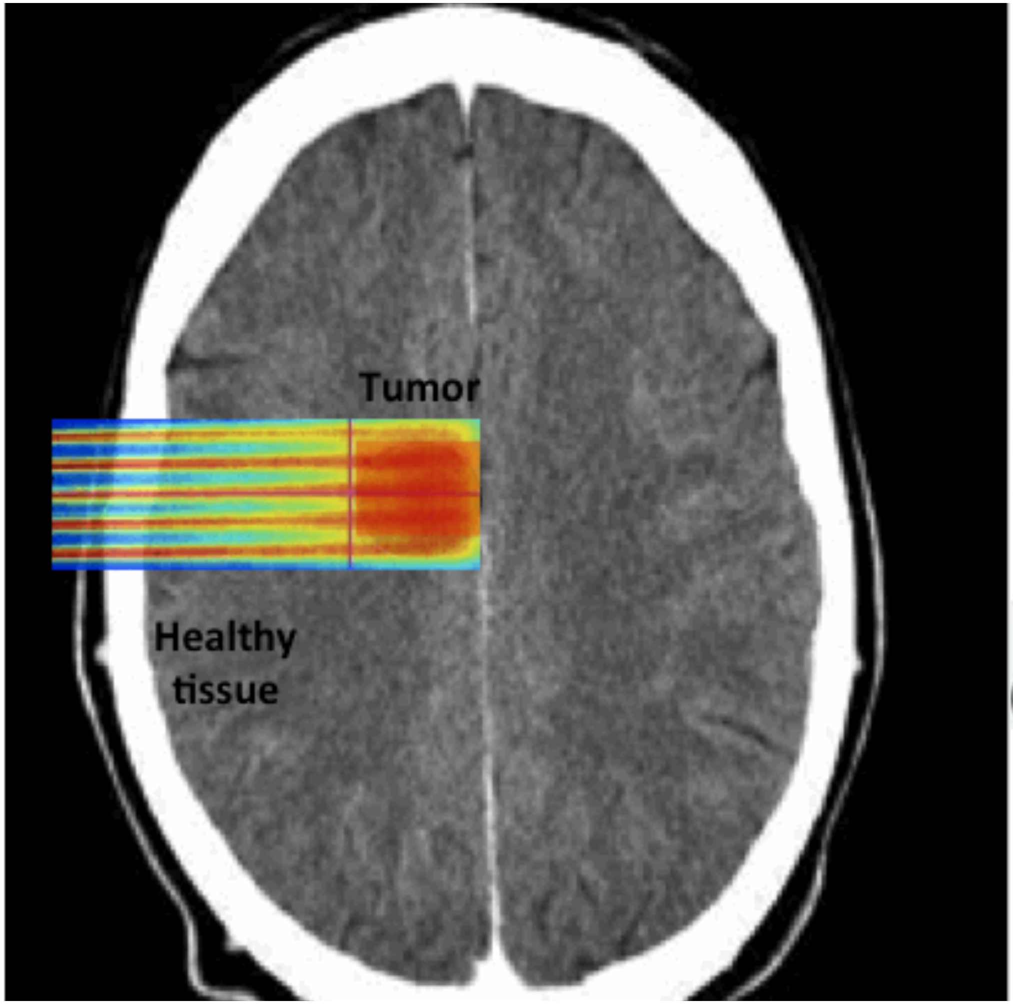
Raaymakers et al, AAPM

www.umcutrecht.nl

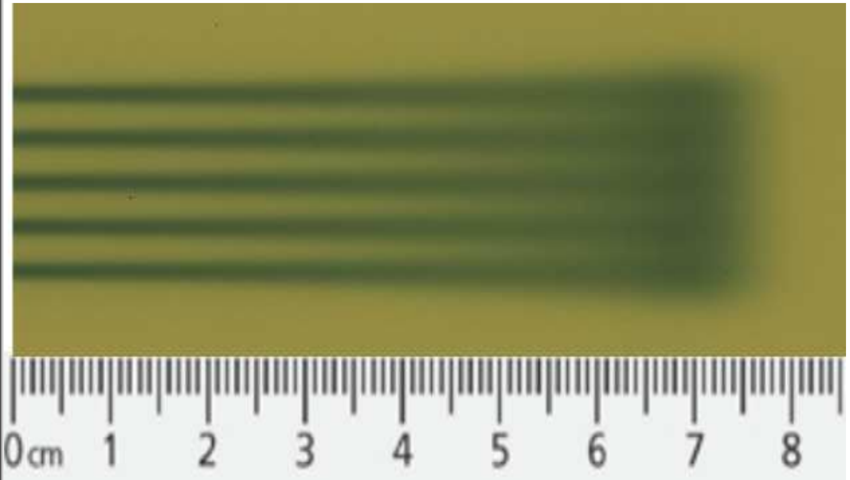
Proton MiniBeam Radiation Therapy (pMBRT)

Theoretical concept :
Y. Prezado et al., Med. Phys. 2013

Experimental beam :
CPO Mai-Juin 2014



Spatial distribution



PBS : without collimators,
High peak-valley ratio, no neutrons
Possibility to modulate intensity…

From synchrotron irradiation

(France Hadron)

Painting target volumes injected with nanoparticles ?

Phase I : NBTXR3 + 50 Gy Rx

CT scan - 24h post IT injection- Day 2

Myxoid liposarcoma
Tumor volume: 1814.4 cc
NBTXR3 volume: 45 mL (2.5%)

ASCO, 2014
http://www.nanobiotix.com/news/release/

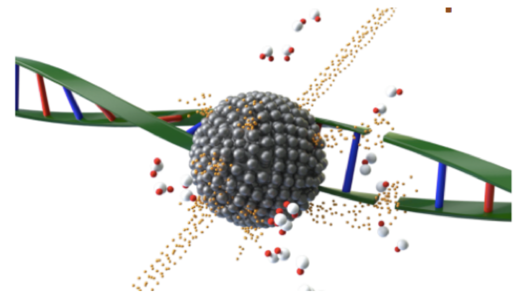
From irradiations with photons

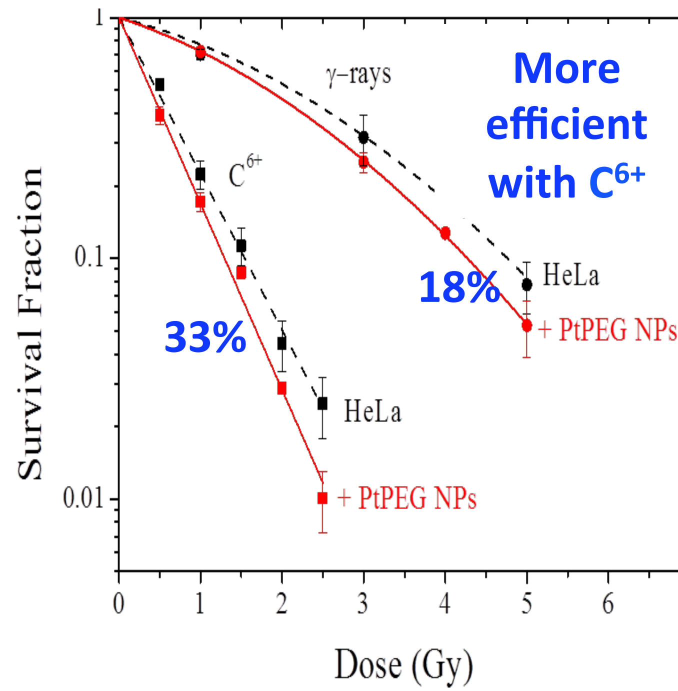
ISMO

Sandrine
LACOMBE

Erika
PORCEL

UNIVERSITÉ PARIS SUD



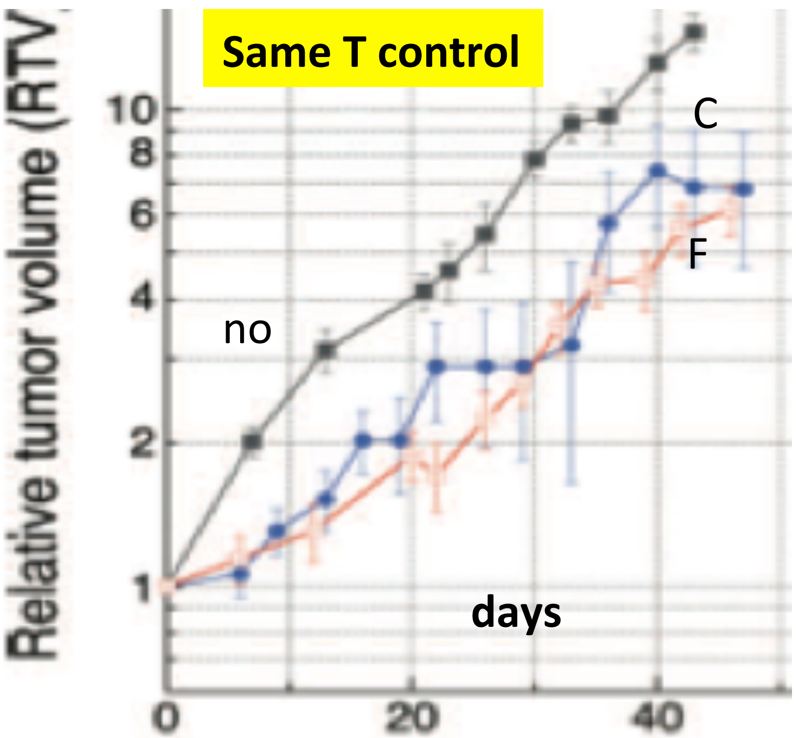


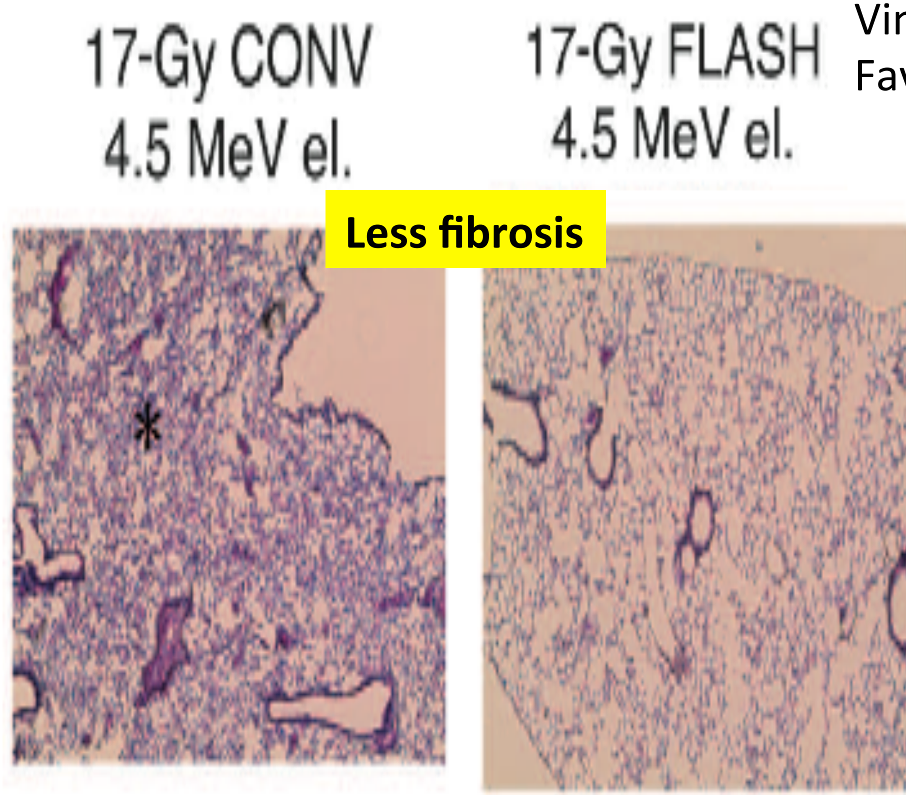
Porcel et al, 2010, 2014
Jong-Ki Kim et al // for protons 2012

"FLASH –Effect" Ultrahigh dose-rate FLASH irradiation

Sci Transl Med 16 July 2014

Vincent Favaudon



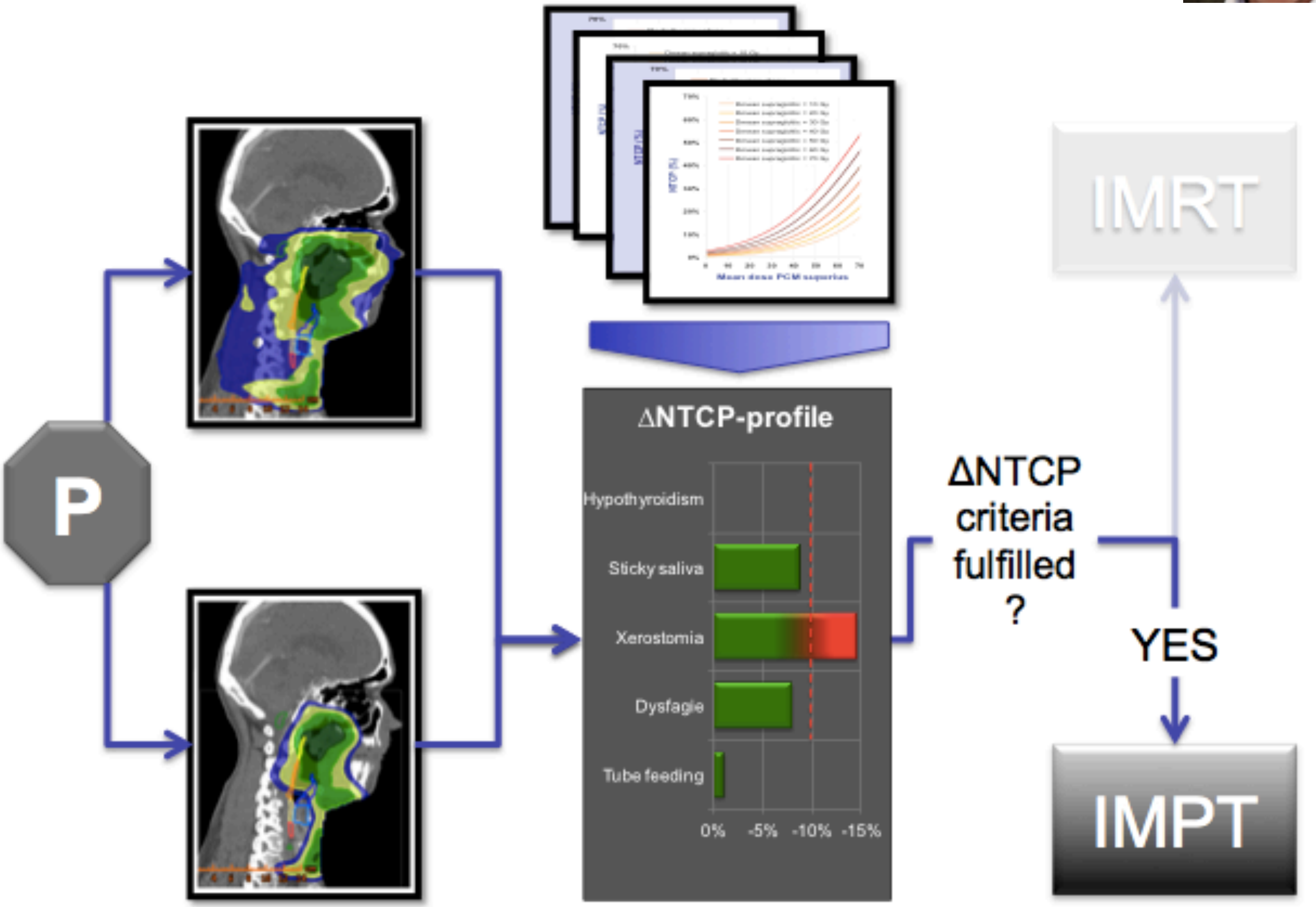


From electrons irradiations

Johannes (Hans) A. Langendijk

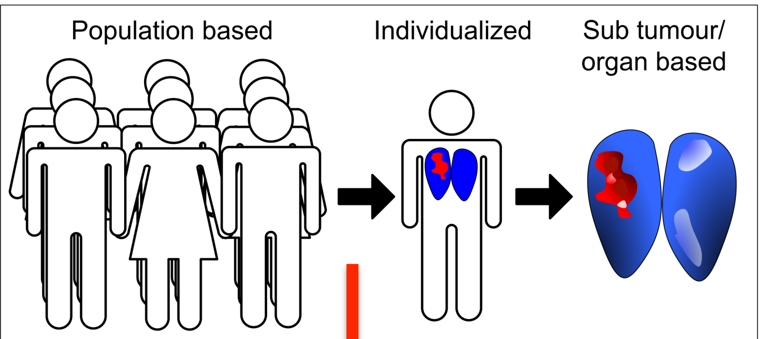
Model-based selection

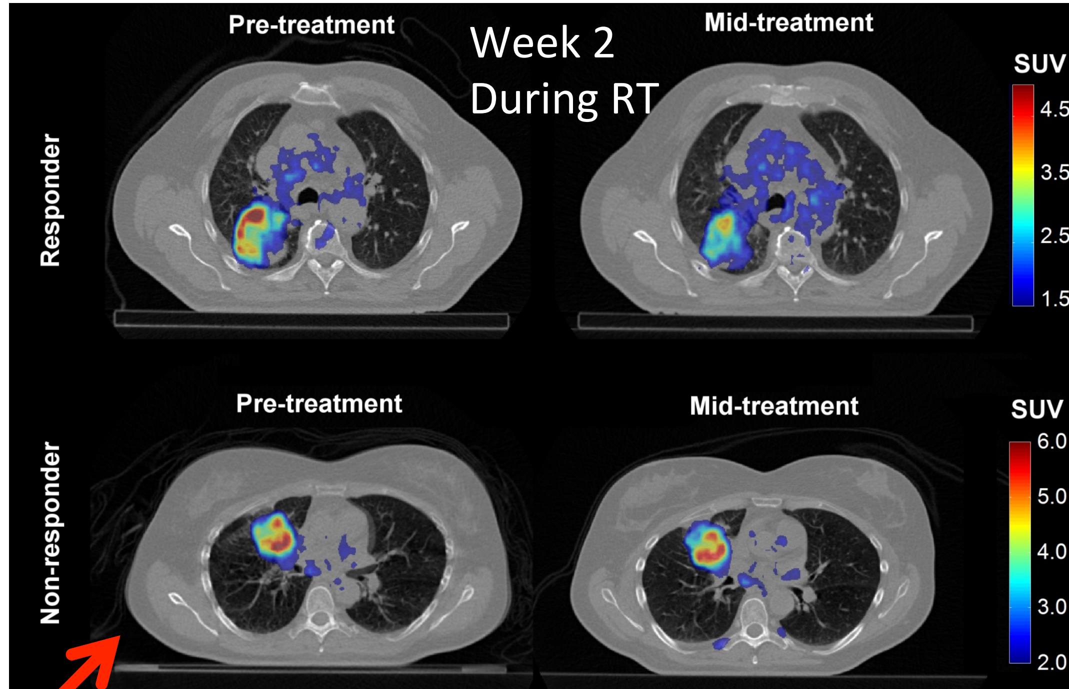
Decision support system



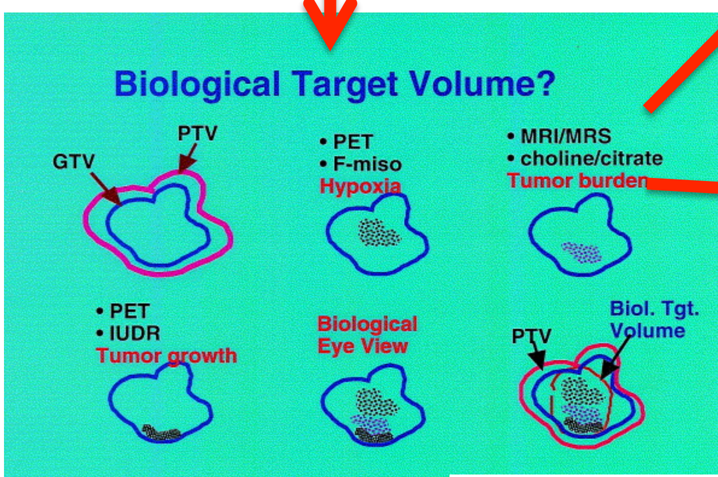
PET Guided Radiotherapy

Philippe Lambin,
Maastro, Belgium





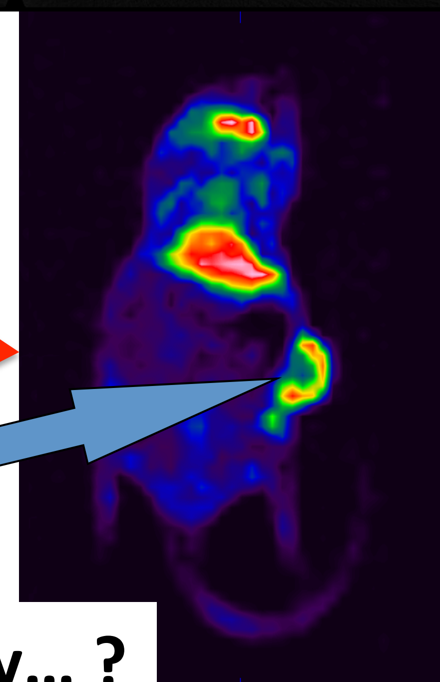
Van Elmpt et al



Ling et al

Drug Uptake
89Zirconium – Cetuximab

« Cold spot »:
Less Drug Uptake
(GTV_{LDU})



From Dosimetry to Biometry… ?

Aerts et al

Conclusions

1. Treatment planning is a process, not just isodoses
2. We evolve from passive techniques to PBS and, into PBS, from SFUD to IMPT
3. In all approaches, need to take into account several limits and uncertainties (mainly range)
4. Robust solutions, multiple criteria optimisation, fast planning including MonteCarlo, range verification, scanning patterns, repainting and retracking, adaptive delivery… are promising solutions in the road map of proton therapy
5. Biological models are needed for protons (mainly for new special techniques) and required for ions (not discussed here)

Treatment Planning in protontherapy

Thank you !

Questions ?