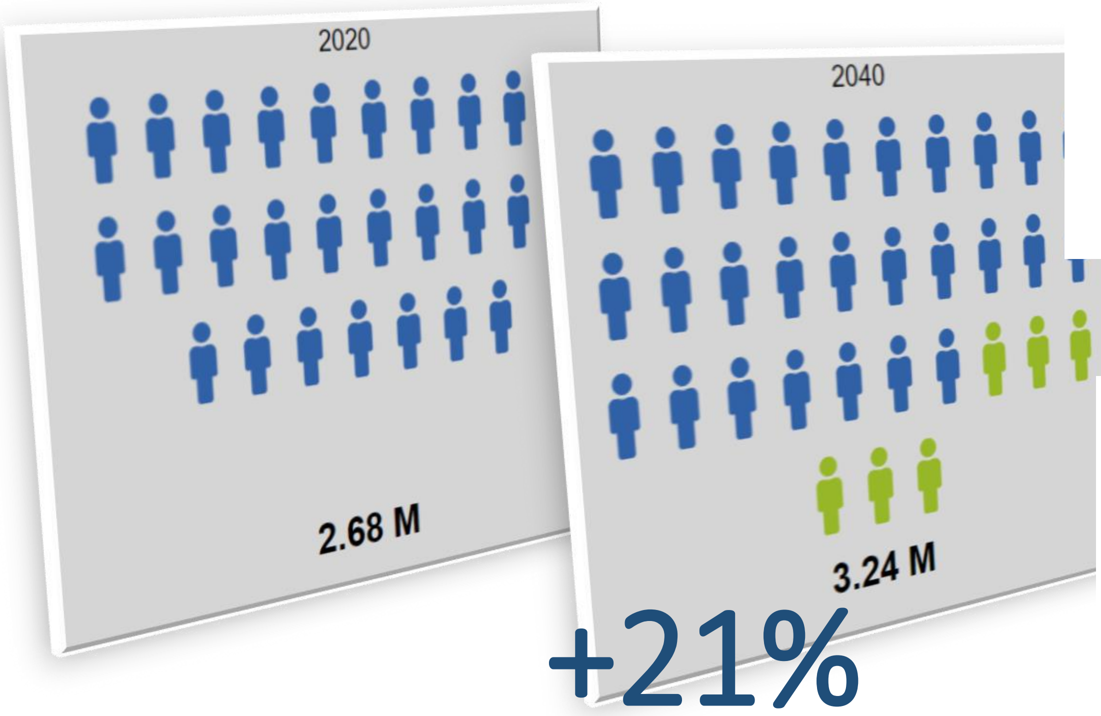
CNAO

The National Center for Oncological Hadrontherapy

Treating cancer with radiation therapy: from (basic) physics to clinical *live* treatment planning with particles

Alessandro Vai, *Medical Physics Unit*

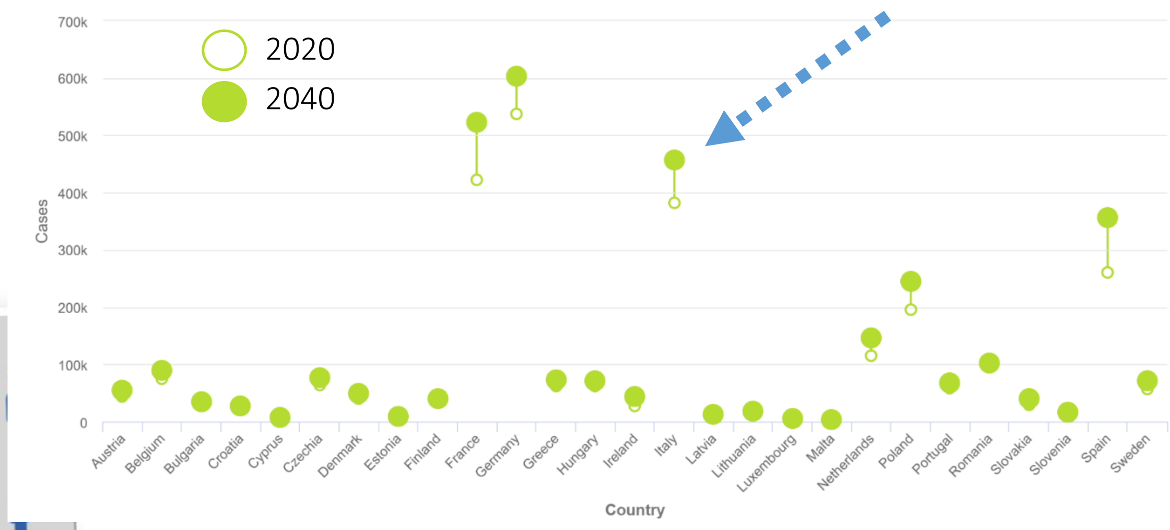
Estimated cancer incidence: both sexes, non-melanoma skin, all ages

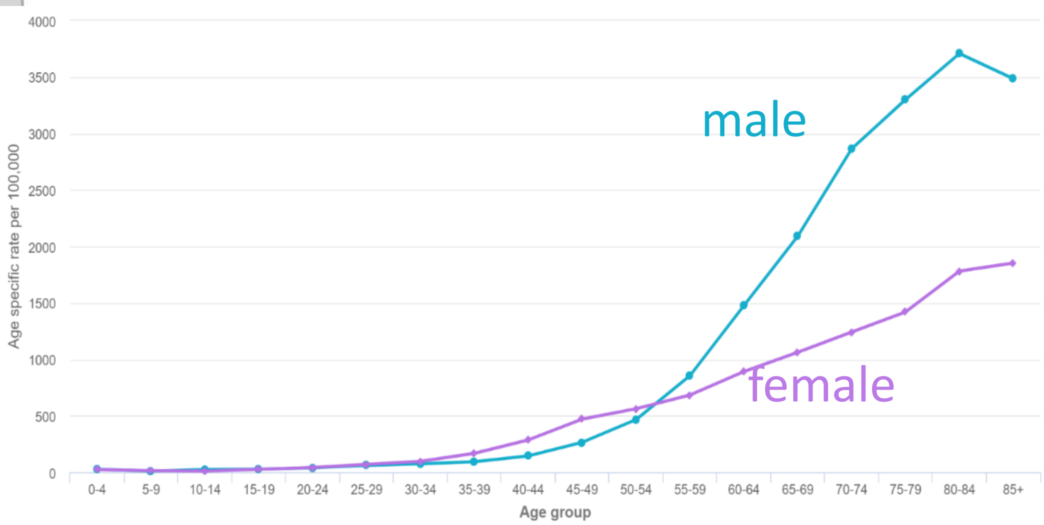


+21%

= 100 000

Increase due to demographic change





source: ECIS – European Cancer Information System

EU Policy against Cancer – 3 pipelines

1) Prevention

Tobacco consumption continues to be the **leading cause of preventable cancer**, with 27% of all cancers attributed to tobacco use[21]. By eliminating tobacco use, nine out every ten cases of lung cancer could be avoided.

- Reduce harmful alcohol consumption through support to capacity-building and best practice; reduce young people's exposure to online marketing and advertising of alcohol products; implement evidence-based brief interventions – 2021-2025.
- Address unhealthy diets, obesity and physical inactivity by reducing carcinogenic contaminants in food; addressing childhood obesity and reviewing the EU school fruit, vegetables and milk scheme; supporting Member States and stakeholders on reformulation of and on effective policies to reduce marketing of unhealthy food products; propose harmonised, mandatory front-of-pack nutrition labelling; launch the 'HealthyLifestyle4All' political commitment –
- Align the EU's air quality standards more closely with the WHO guidelines and promote sustainable and smart mobility – 2022-2023.
- Reduce exposure to carcinogenic substances through the amendment to the Carcinogens and Mutagens Directive – 2021-2025.
- Adopt a new Occupational Safety and Health Strategic Framework to further reduce workers' exposure to chemicals – 2021-2027.
- Launch of the Horizon Europe Partnership on Assessment of Risks from Chemicals – 2021.

Flagship initiatives on prevention

- Eliminate cancers caused by human papillomaviruses through EU support for Member States on vaccination with the aim to vaccinate at least 90% of the EU target population of girls and to significantly increase the vaccination of boys by 2030 – 2021-2030

Other actions

Feb-2022

- Improve health literacy on cancer risk by updating the European Code against Cancer – 2021-2025.
- Create a 'Tobacco-Free Generation', including reviewing the Tobacco Products and the Tobacco Taxation Directives and the legal framework on cross-border purchases of tobacco; update the Council Recommendation on Smoke-Free Environments, and support implementing the Framework Convention on Tobacco Control – 2021-2025.
- Review EU legislation on alcohol taxation and cross-border purchases of alcohol products, and propose mandatory labelling of ingredients and nutrient content, along with health warnings on alcoholic beverages – 2021-2023.

2) Early detection - screening

Flagship initiatives on early detection

- Develop a new EU Cancer Screening Scheme to ensure that by 2025, 90% of the target population is offered breast, cervical and colorectal cancer screening – 2021-2025.

Other actions

- Update and explore expansion of the Council Recommendation on cancer screening – 2022.
- Develop new guidelines and quality assurance schemes for screening, diagnosis, treatment, rehabilitation, follow-up and palliative care for colorectal and cervical cancer, including accreditation and certification programmes, while continuously updating the existing guidelines on breast cancer – 2021-2025.
- Update the European Cancer Information System to monitor and assess cancer screening programmes – 2021-2022.

3) Delivering high quality standard of care

The treatment of cancer continues to rest largely on three major modalities: surgery, radiotherapy and systemic therapies, including chemotherapy. To these we can add a number of other approaches: immunotherapy, targeted therapy and gene therapy.

Radiotherapy is currently an essential component in the management of cancer patients, either alone or in combination with surgery or chemotherapy, both for cure and for palliation. Of those cancer patients who are cured, it is estimated that 49% are cured by surgery, about 40% by radiotherapy alone or combined with other modalities, and 11% by chemotherapy alone or combined [I.3].

About 100,000 pts treated in Italy with radiotherapy (AIRO)

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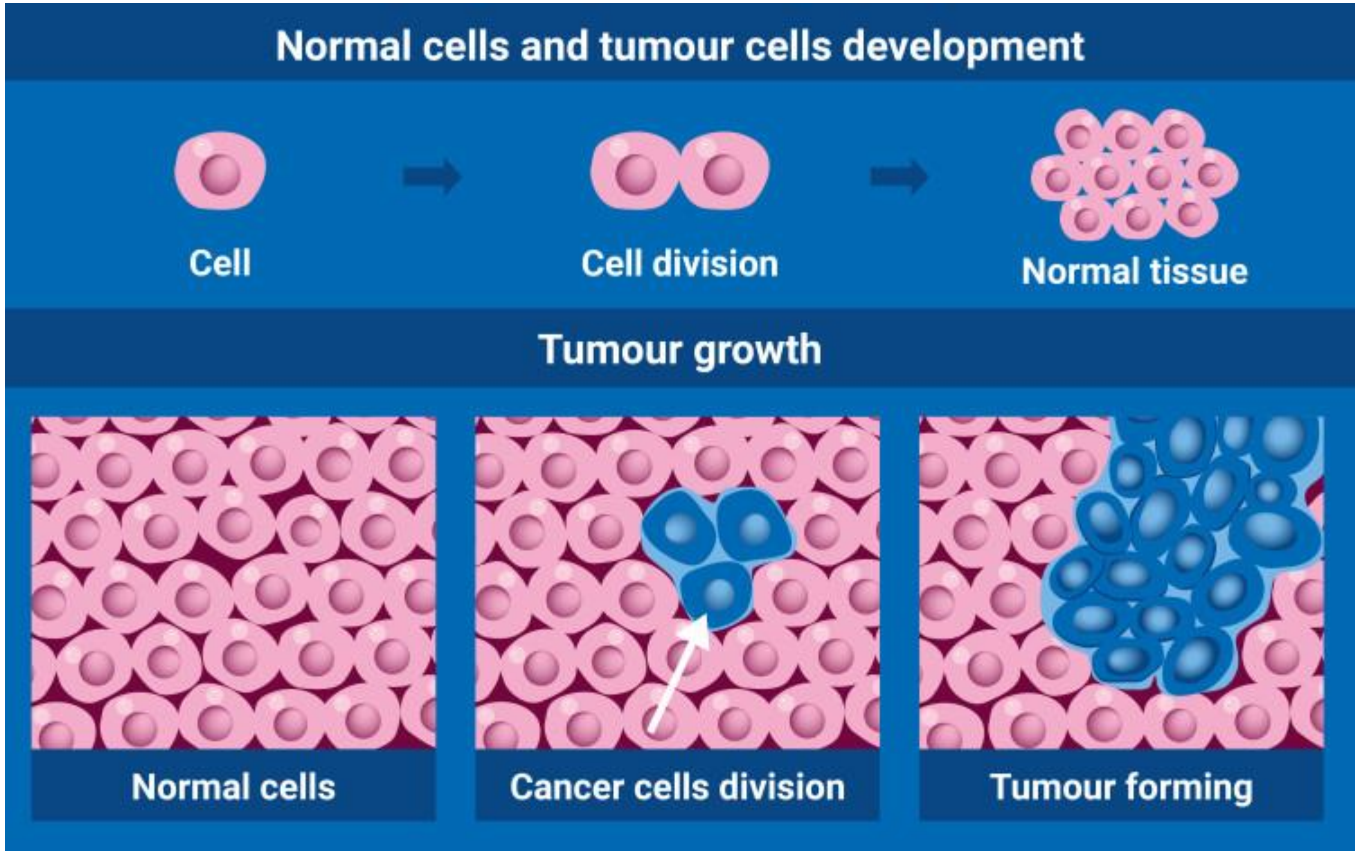
How does radiation therapy work against cancer?

Cancer is a condition in which cells of a specific part of the body begin to grow and reproduce uncontrollably, forming tumors which affect surrounding tissues and organs and sometimes spread to other parts of the body through the bloodstream or lymphatic system.



Radiotherapy involves using carefully selected doses of ionizing radiation to damage the DNA of cancer cells. The DNA controls how they divide. Radiation causes the tumour to shrink and, in some cases, die.

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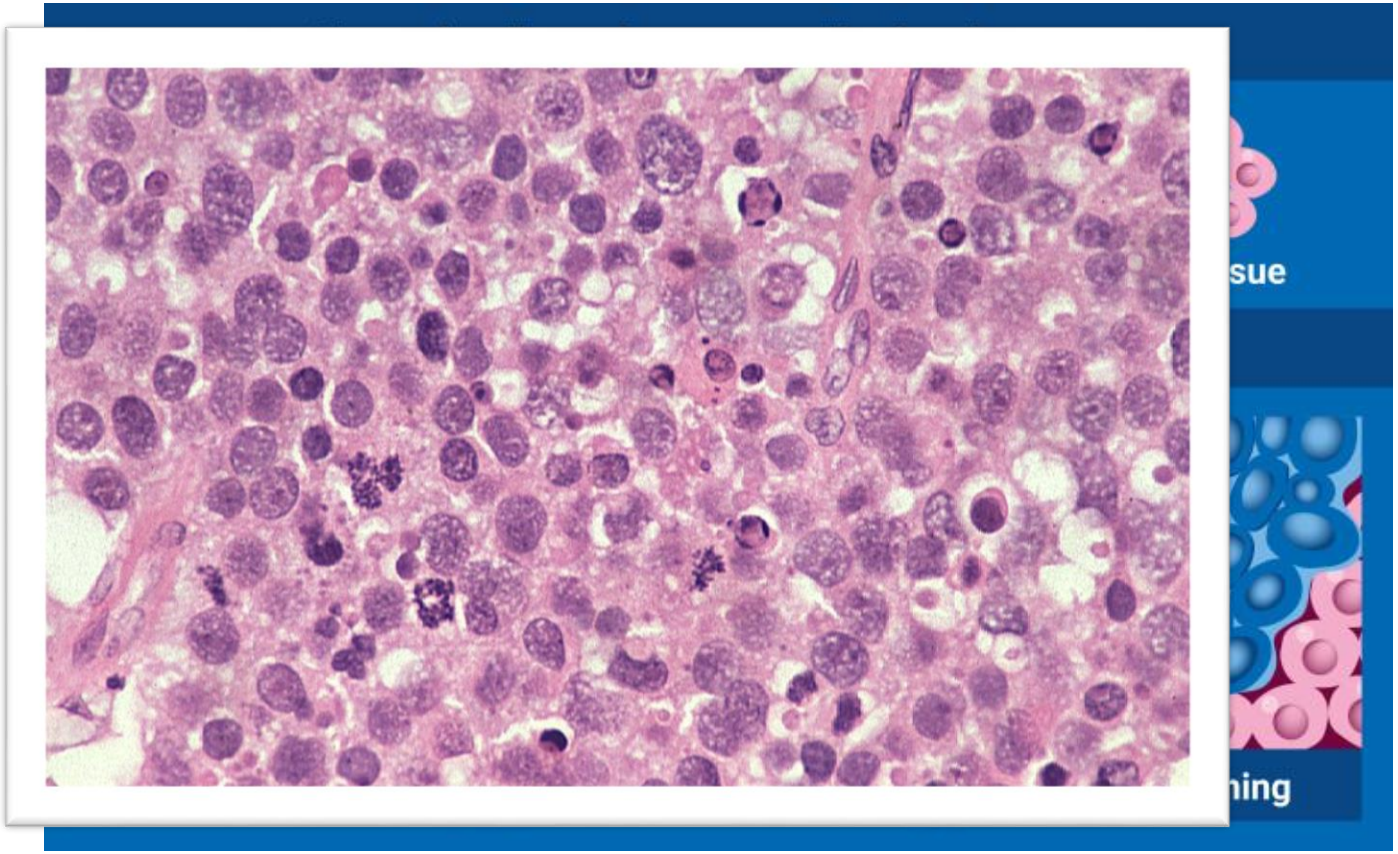


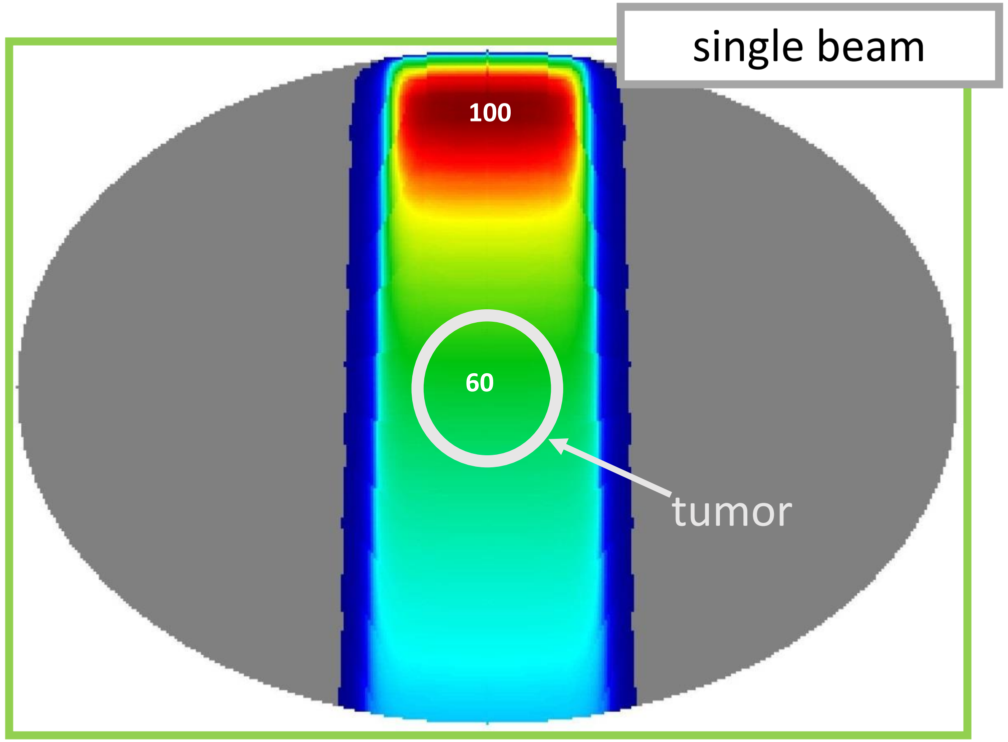
Conventional radiotherapy: photon RT

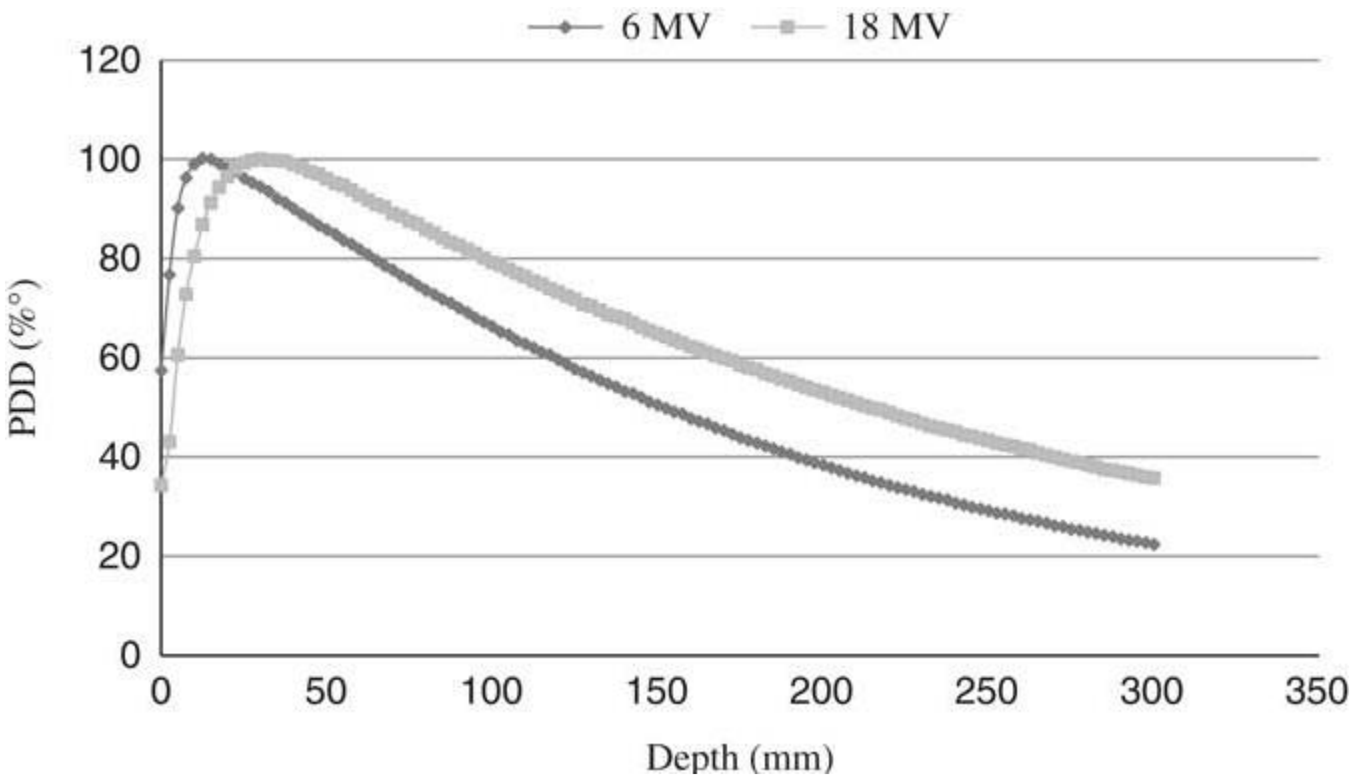
Outpatient procedure - > 1 to several wks duration

IMRT or VMAT (LINAC)
30fx : 6 weeks

Radiosurgery (CK, TomoTherapy):
3/5/7 fx: avg. 1 week

Photon percentage Depth dose curve

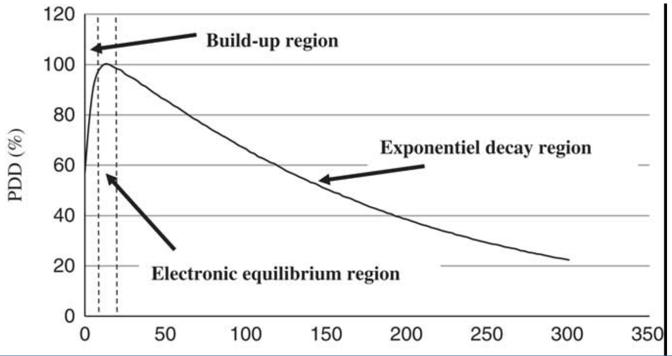




Dose to water under Reference conditions

$$D_{w,Q} = M_Q N_{D,w,Q_0} k_{Q,Q_0}$$

IAEA TRS 398 (2000)



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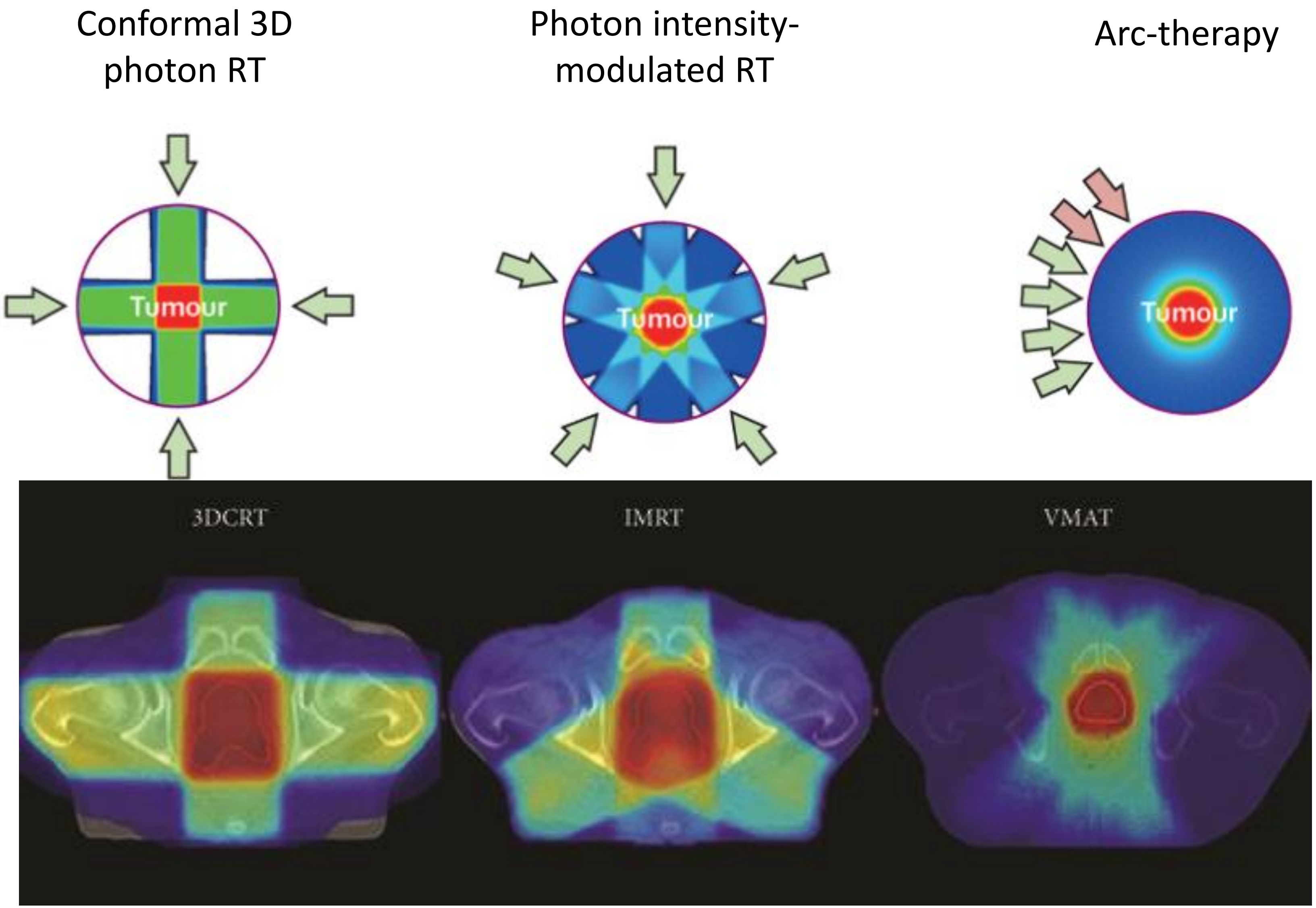
…increasing complexity



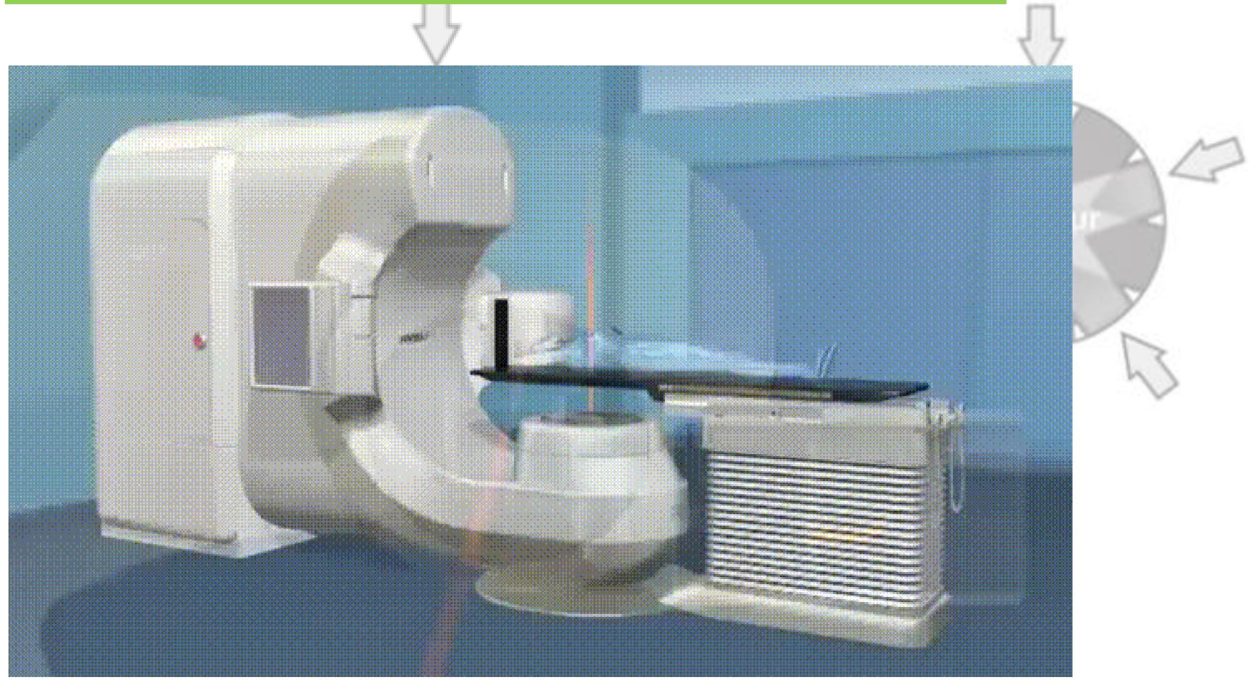
...current state-of-the-art photon RT

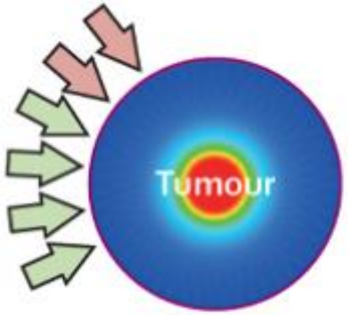
Conformal 3D photon RT

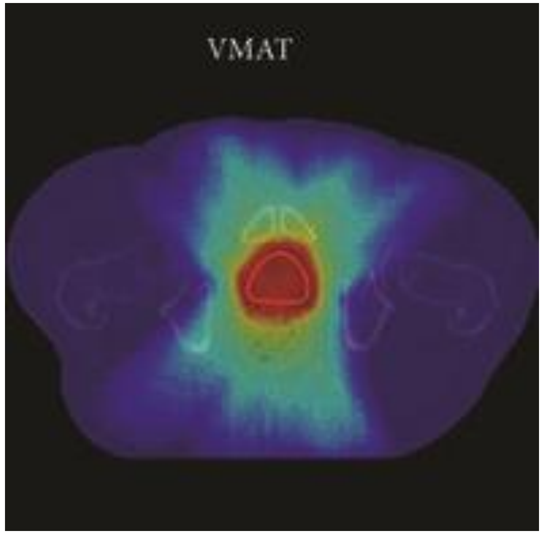
Photon intensity-modulated RT

Arc-therapy

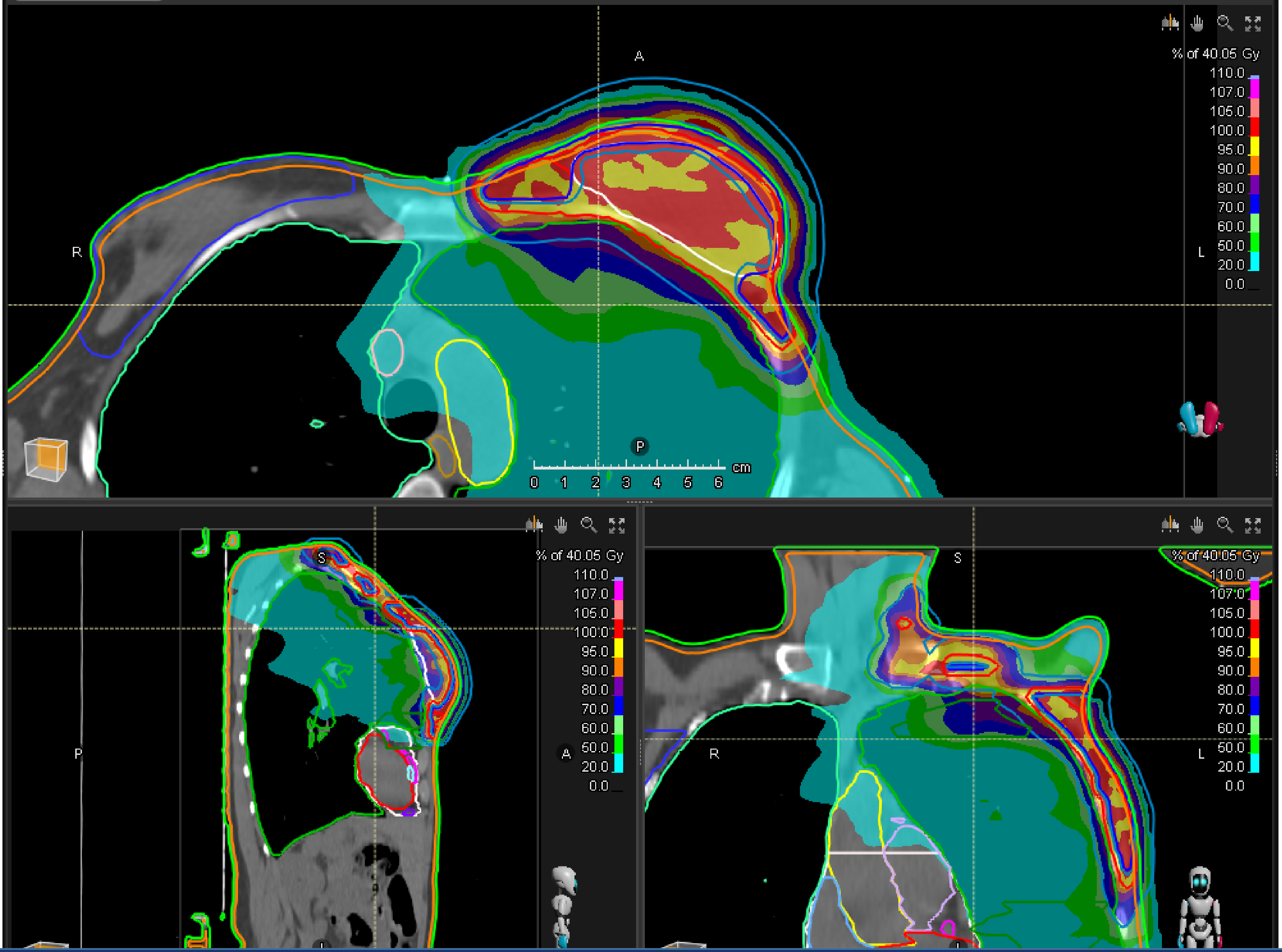
multiple beams, e.g. 175 fields (every 2°)







Breast case: 40.5Gy, arc photon therapy



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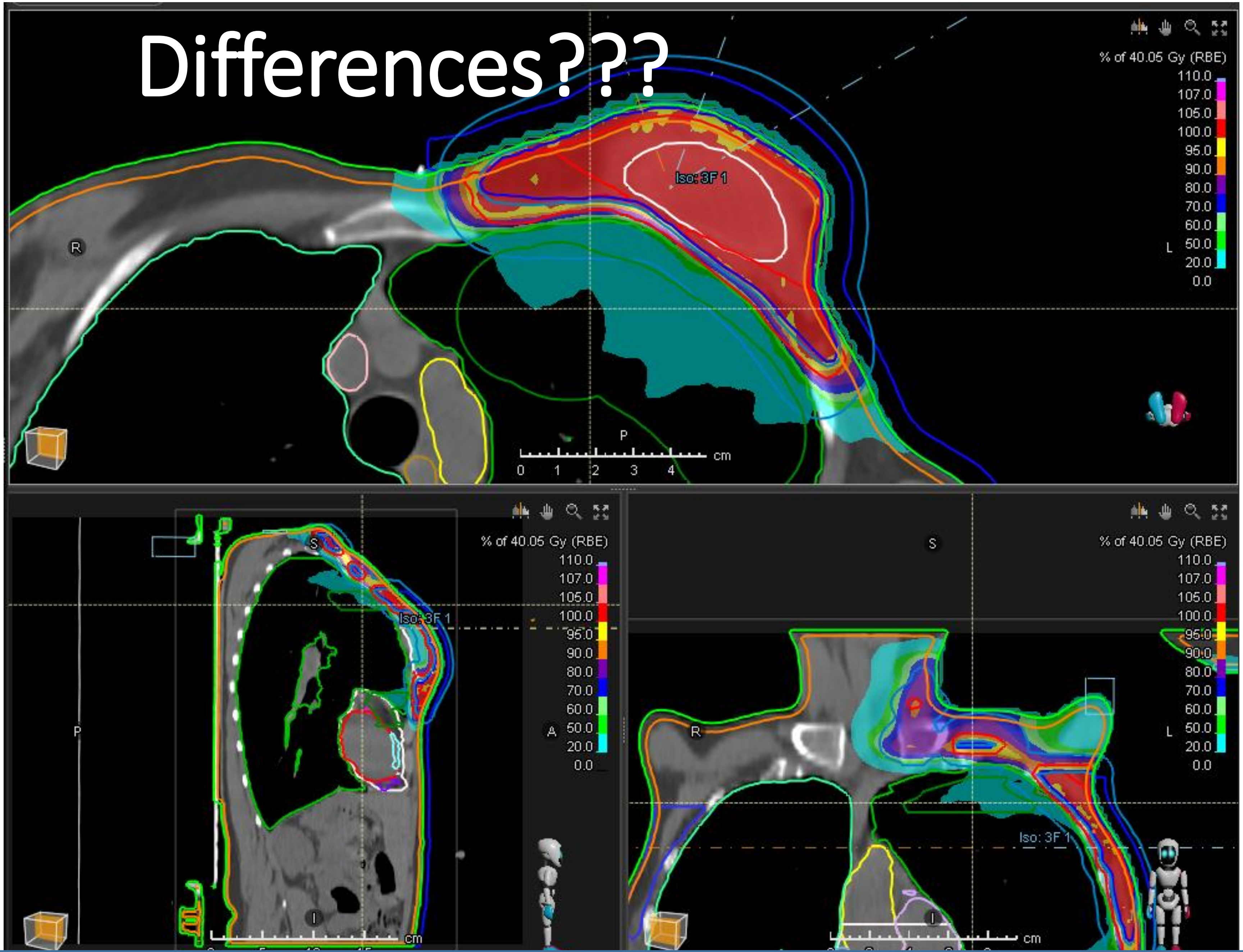
Differences???

Breast case: 40.5Gy, protons



Particle Therapy - Rationale

with respect to photons:	**p^+, C $^{6+}$ have**

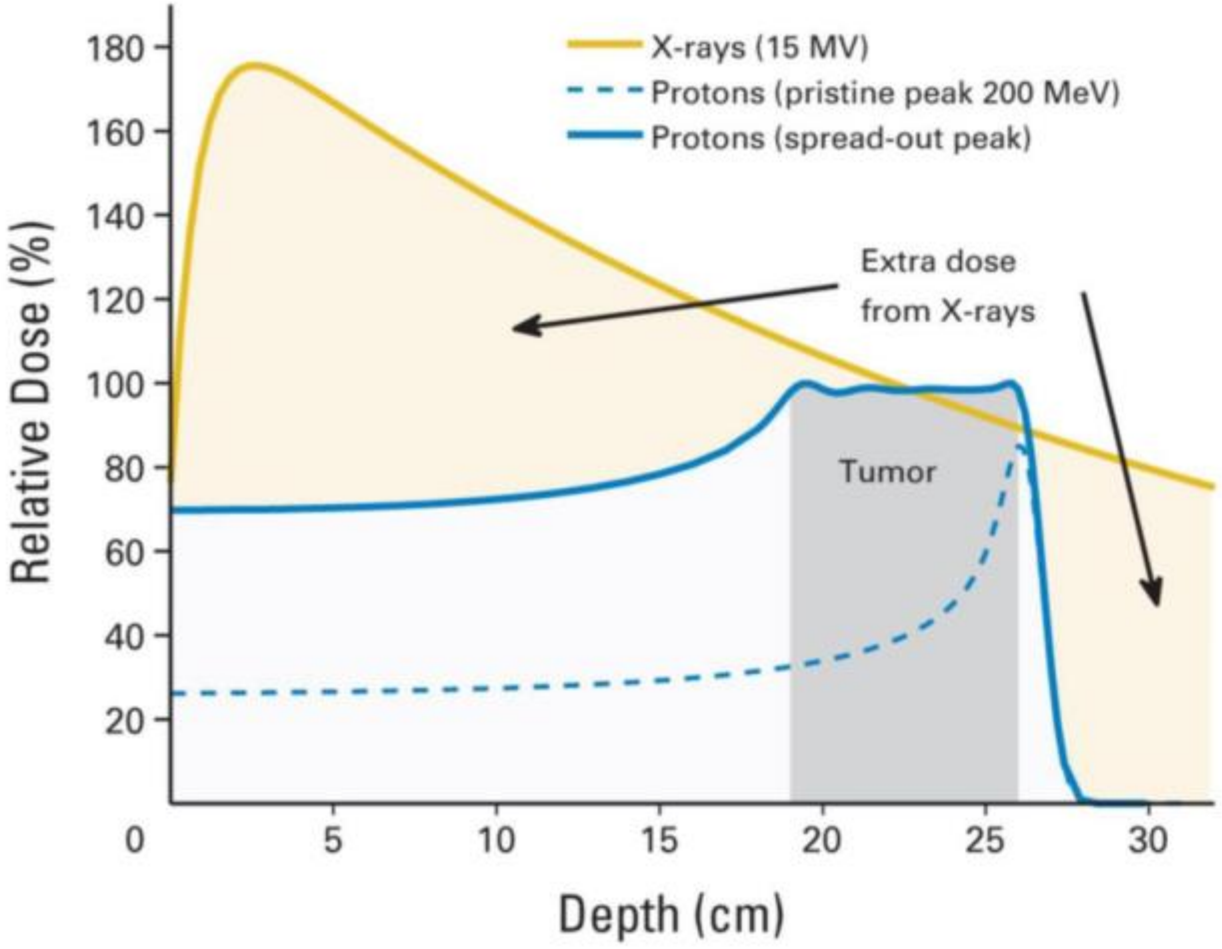
1) Superior physical dose deposition properties

Exponential dose fall off after build up + Sharper lateral penumbra	Inverse dose profile with a maximum energy deposition in the Bragg Peak → Dose at depth (target) is greater than dose at surface → Steep distal dose fall off

2) Higher relative biological effectiveness (RBE)

Reference radiation RBE	RBE > 1

Particle Therapy – *Inverse* dose profile



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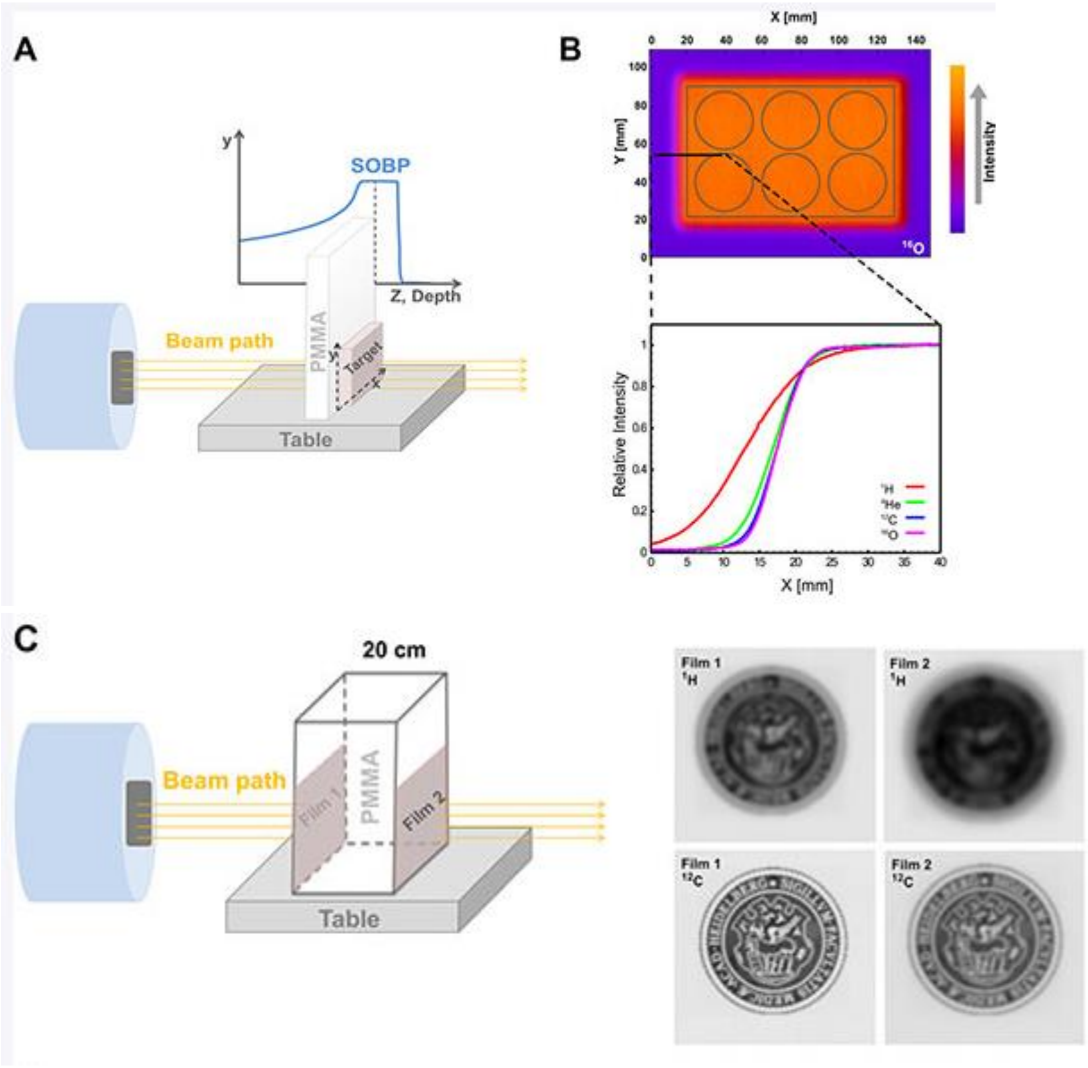
Particle Therapy – sharper lateral penumbra

www.impactjournals.com/oncotarget/ Oncotarget, Vol. 7, No. 35
Research Paper

Next generation multi-scale biophysical characterization of high precision cancer particle radiotherapy using clinical proton, helium-, carbon- and oxygen ion beams

Ivana Dokic[1,2,3,4,*], Andrea Mairani[3,5,*], Martin Niklas[1,2,3,4], Ferdinand Zimmermann[1,2,3,4], Naved Chaudhri[3], Damir Krunic[6], Thomas Tessonnier[4,7], Alfredo Ferrari[8], Katia Parodi[3,7], Oliver Jäkel[3,9], Jürgen Debus[1,2,3,4], Thomas Haberer[3], Amir Abdollahi[1,2,3,4]



(A) Schematic presentation of irradiation setup. To mimic the clinical situation of tumor treatment at a certain tissue depth, PMMA was employed as water/tissue density equivalent and placed in front of the target (cell culture plate).

(**B**) The normalized lateral intensity distribution (0–40 mm along X-axis, black solid line) of all four investigated particles is shown (bottom). As the beam mass increases, the steepness of the lateral distribution increases, due to the reduced scattering for heavier ions.

(**C**) Schematic presentation of lateral scattering in proton and carbon ion beams. Left panel presents the irradiation setup used to demonstrate lateral scattering for proton and carbon beams. Right panel are the scanned images of irradiated dosimetric films.

Particle Therapy – Higher RBE

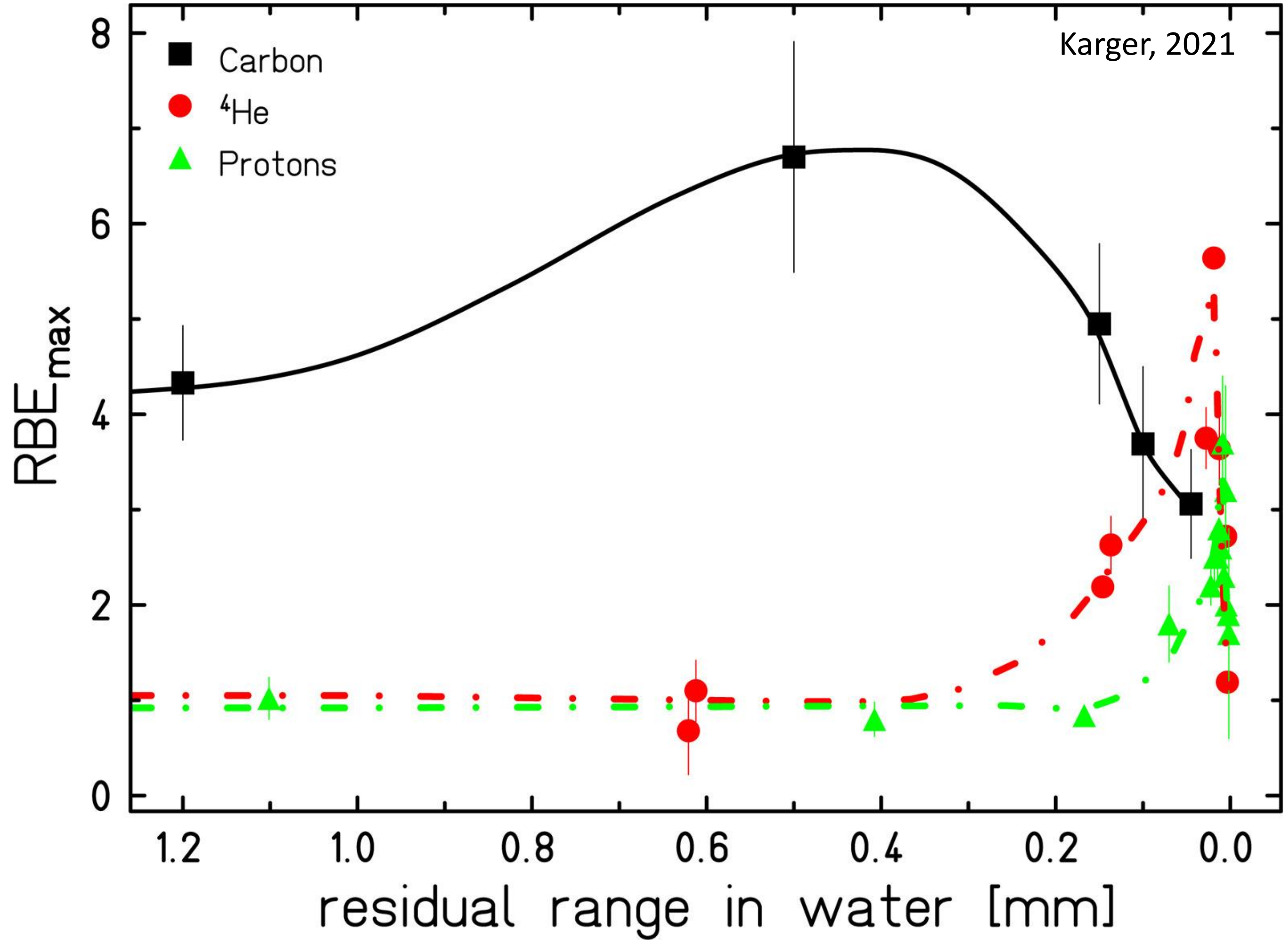
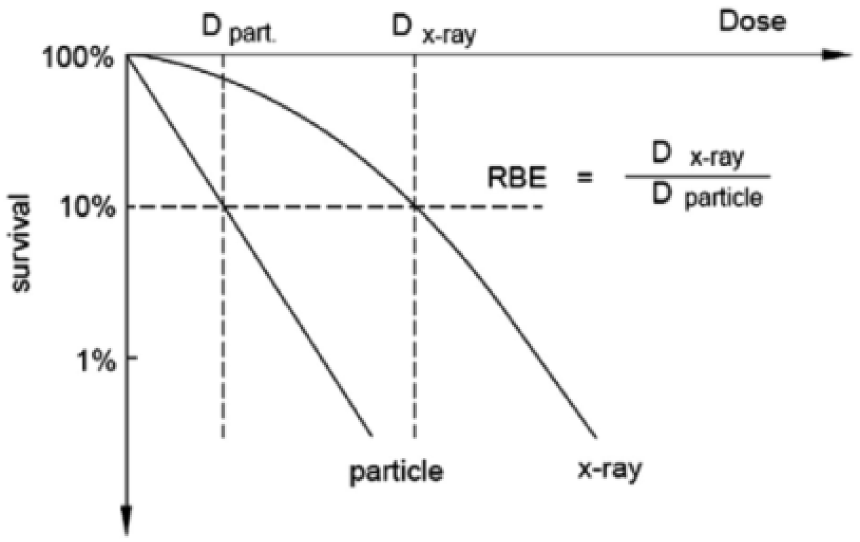
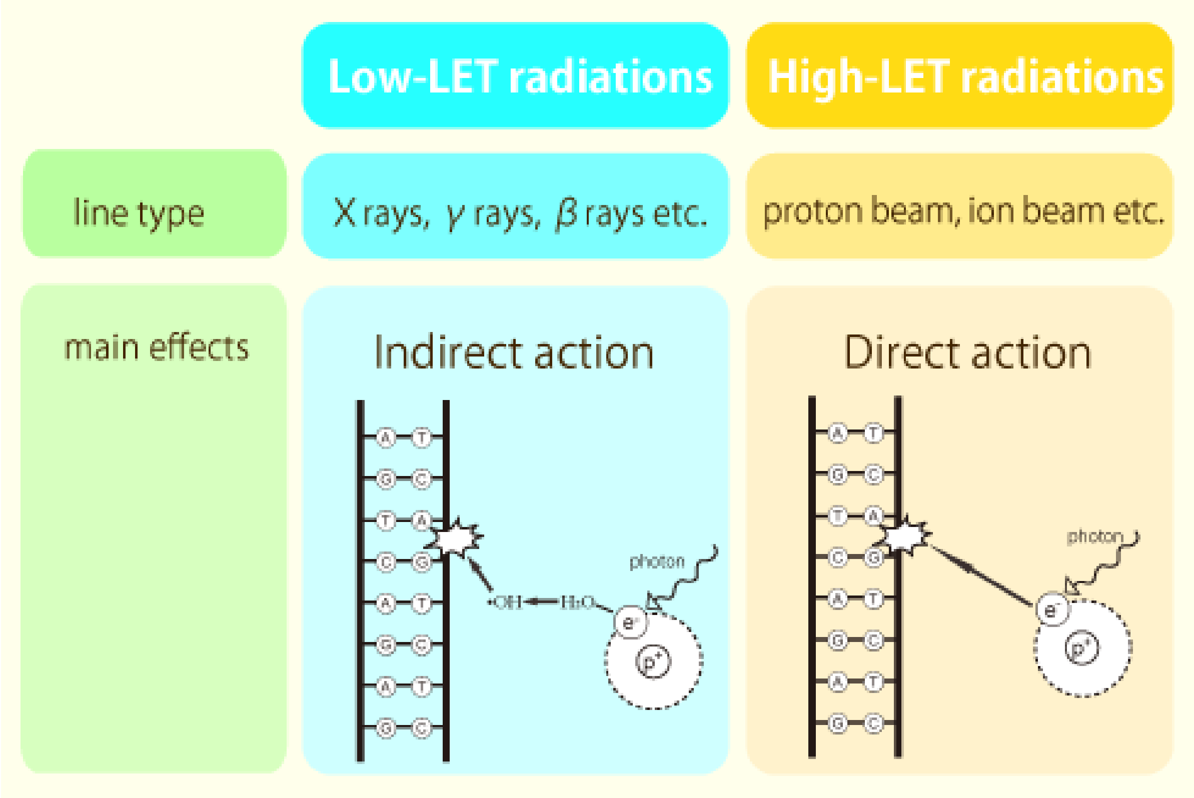


Figure 2. RBE as a function of the residual range for protons, helium (^4He) and carbon ions. Measurements (symbols) were interpolated by analytic fit curves (lines). For carbon ions, the RBE is higher and distributed over a broad residual range. In contrast, the increase of the RBE for protons and helium ions is restricted to the distal 0.1 mm of the Bragg-peak.

Translation to radio-biological studies



Particle Therapy – phys factors affecting RBE - LET



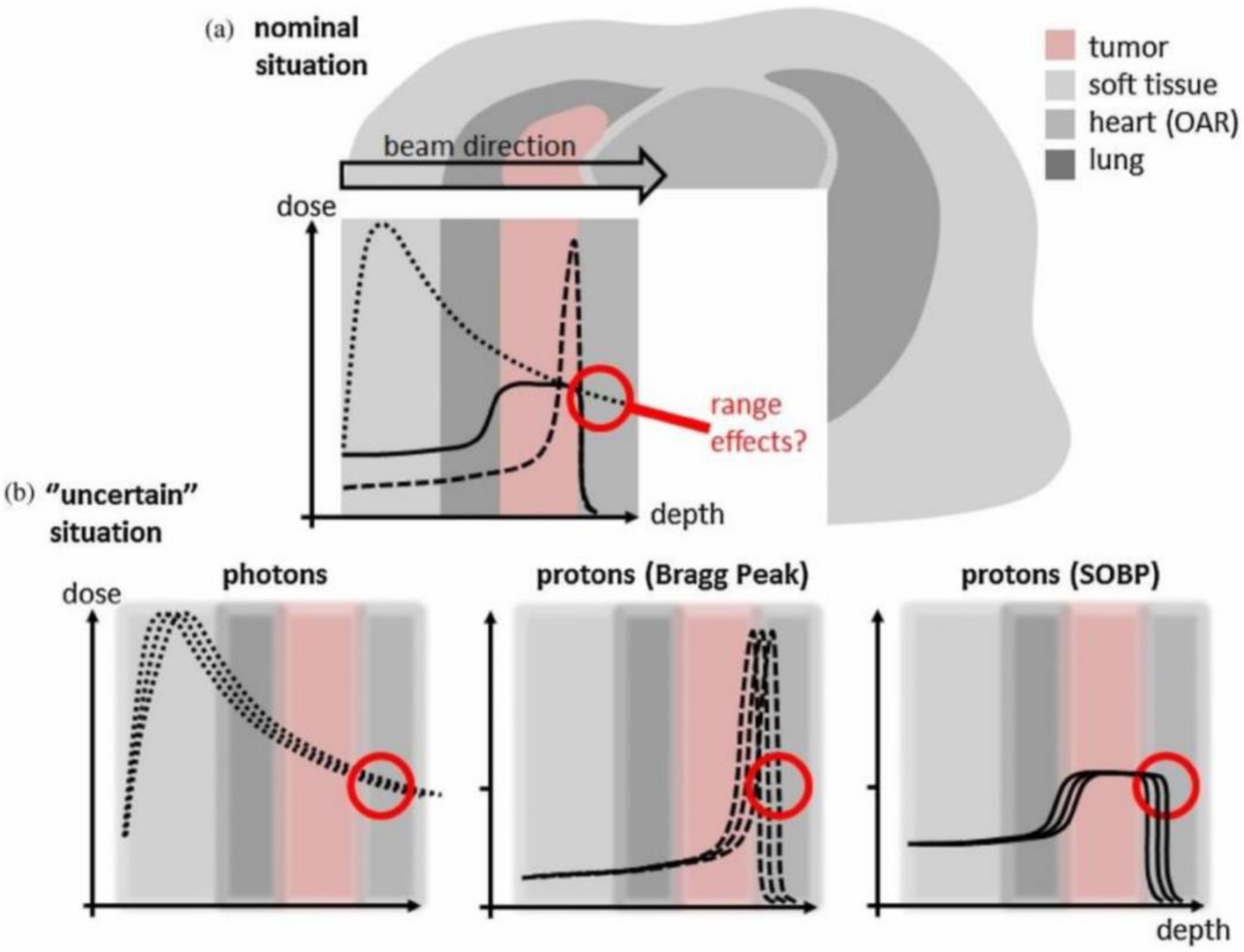
Direct action: dominant for high-LET (linear energy transfer) radiation

Irradiation has **direct effects** on deoxyribonucleic acid (DNA). For example, a secondary electron resulting from absorption of an X-ray photon interacts with the DNA to produce an effect, and this is the dominant process associated with **high-LET radiation such as carbon ion beams**.

Indirect action: dominant for X-rays and electrons from LINAC

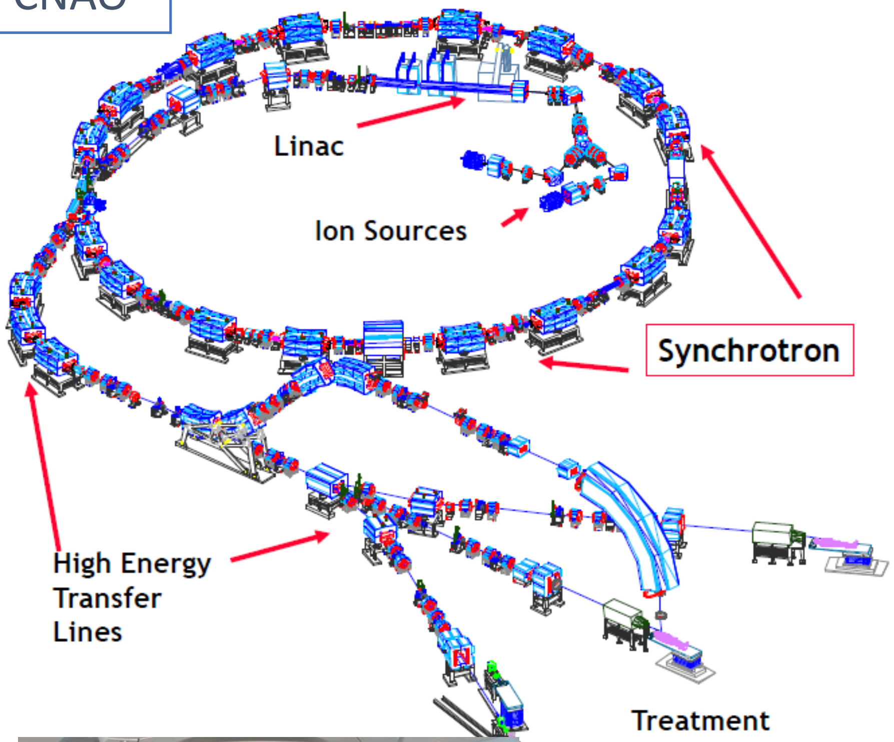
Secondary electrons can interact with a water molecule, for example, to produce a hydroxyl radical, which in turn damages the DNA molecule. The DNA helix has a diameter of about 2 nm. It is estimated that free radicals produced in a cylinder with a diameter double that of the DNA helix can affect the DNA.

PT *limits*(?) -> more prone to range uncertaintes than photons



PT limits (?) -> limited availability & more expensive (2-3x)

@ CNAO



4700 pts treated since 2011 (400 ocular melanoma pts)

@ worldwide

https://www.ptcog.site/index.php/facilities-in-operation-public

PT limits (?) -> limited availability & more expensive (2-3x)

Cyclotron, 2 fixed-beam lines, 2 rooms with gantry, 1 experimental room

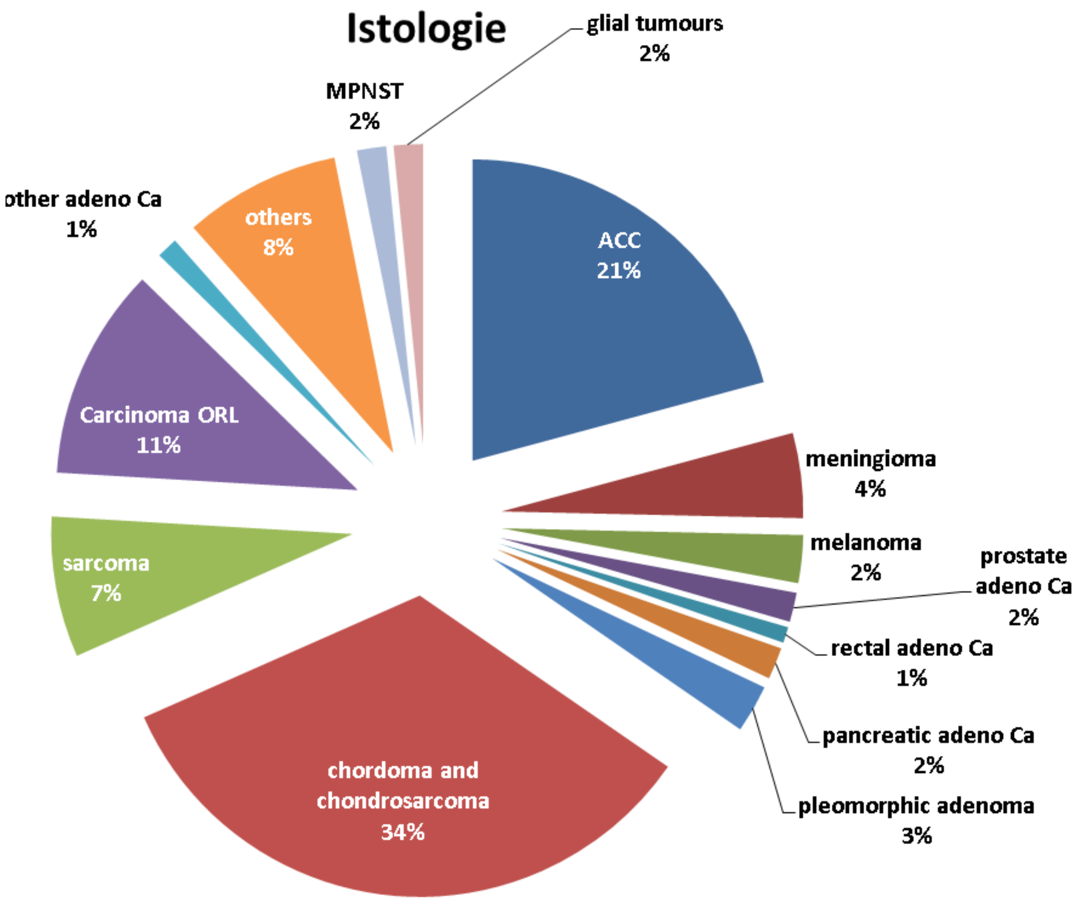
Mevion "compact" cyclotron solution

Minimal layout is always quite large

CNAO Clinical Activity: Sites and Histology

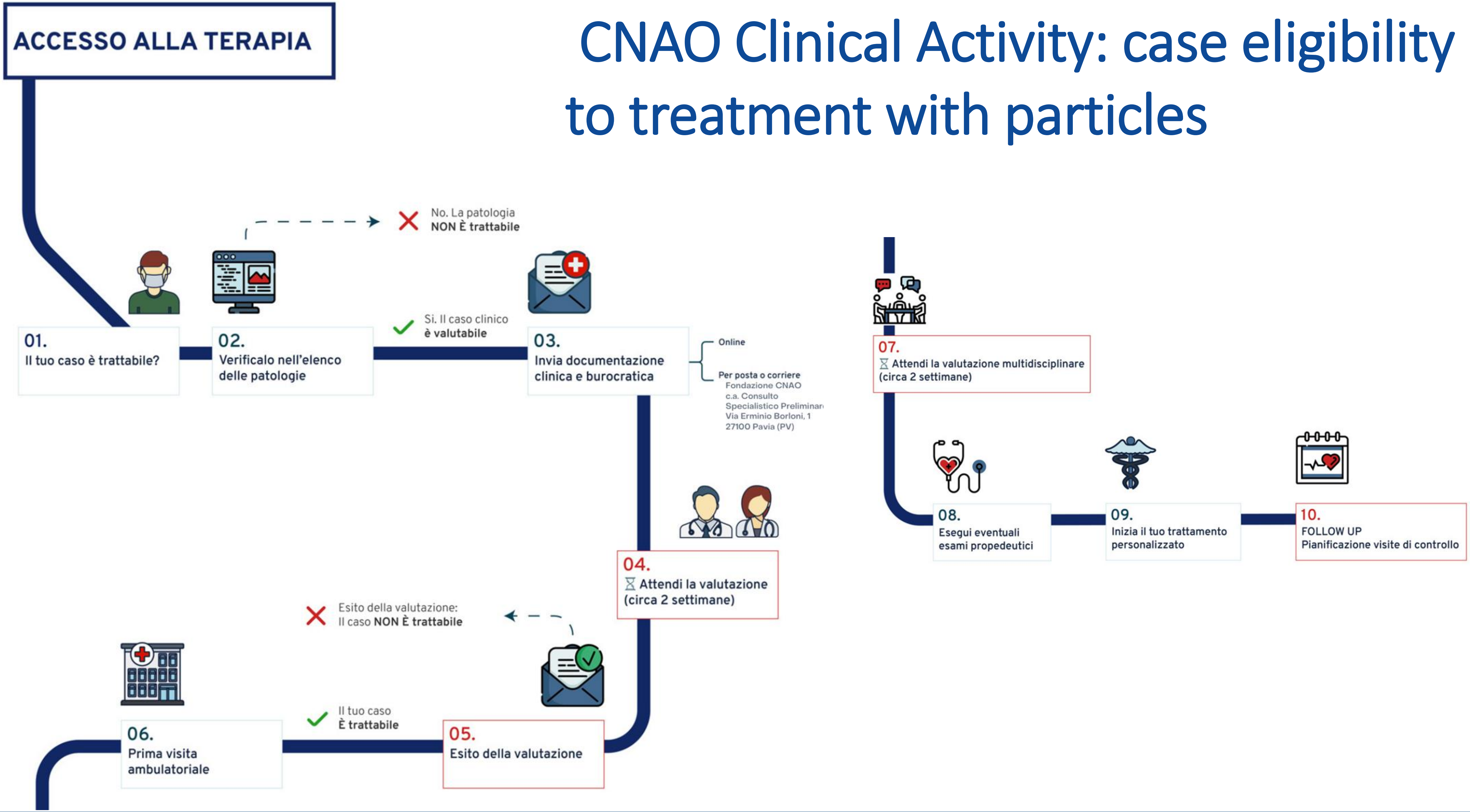
23 Phase II Trials

- Chordomas- chondrosarcoma
- Salivary gland tumors
- Soft tissue Sarcoma
- Mucosal Melanoma
- Adenoidocistic carcinoma
- Recurrent pleomorfic adenoma
- Meningioma
- Orbital tumors
- Locally advanced head and neck tumors
- High risk prostate cancer
- Inoperable pancreatic cancer
- HCC
- Re-irradiation of recurrent rectal cancer
- Re-irradiation of Head and neck carcinoma



26% protons + 74% C-ions
79% definitive RT + 21% re-irradiation

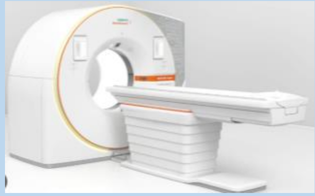
CNAO Clinical Activity: case eligibility to treatment with particles

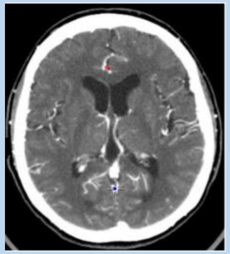


Radiation therapy clinical workflow

Diagnostic imaging

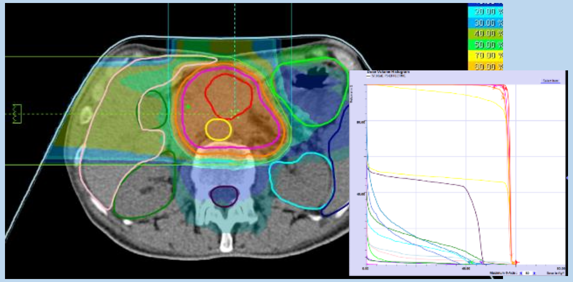
- Mask -> abdominal & thoracic compression
- Computed tomography (CT) imaging
- Additional imaging (PET, MRI, etc)





Treatment Planning

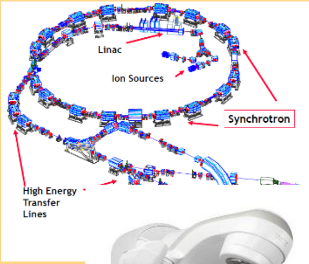
- Define tumor and therapeutic
- Prepare treatment plan
- Treatment plan QA

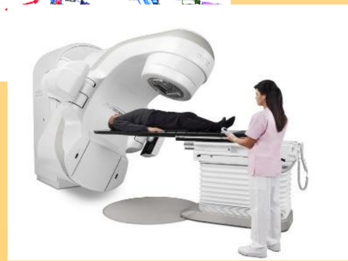


Preparation

Treat. Delivery

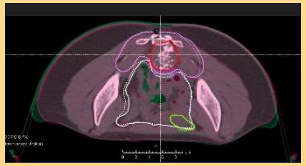
- Patient positioning
- Pre-treatment imaging
- Beam delivery





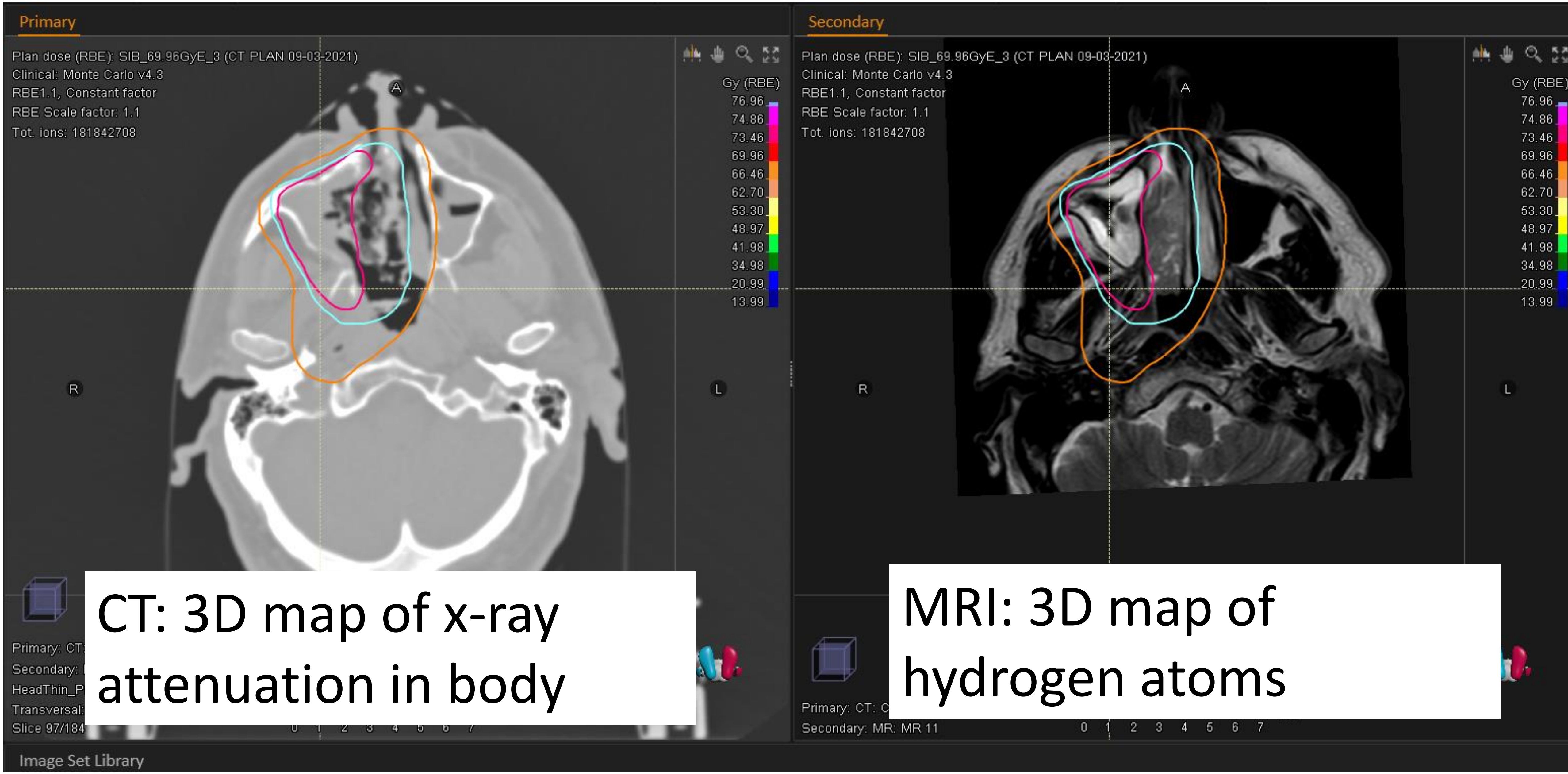
Treat. monitoring

- Re-evaluative imaging



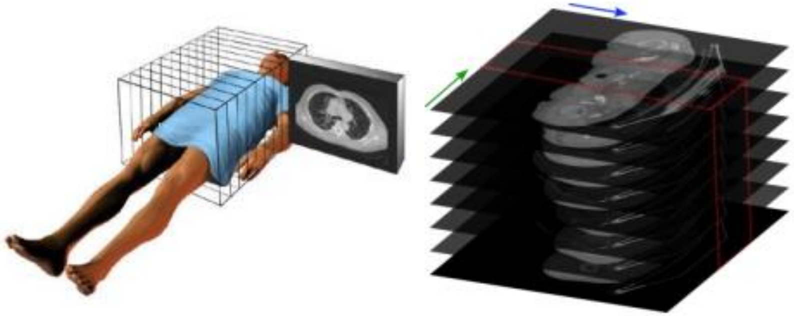
Delivery

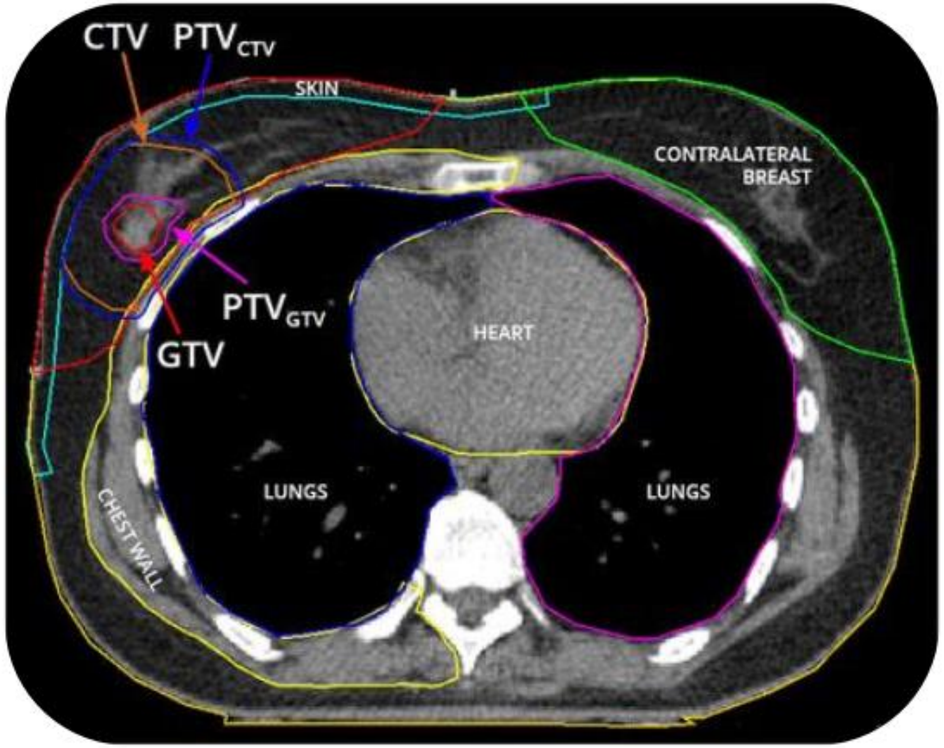
Diagnostic **imaging**



CT: 3D map of x-ray attenuation in body

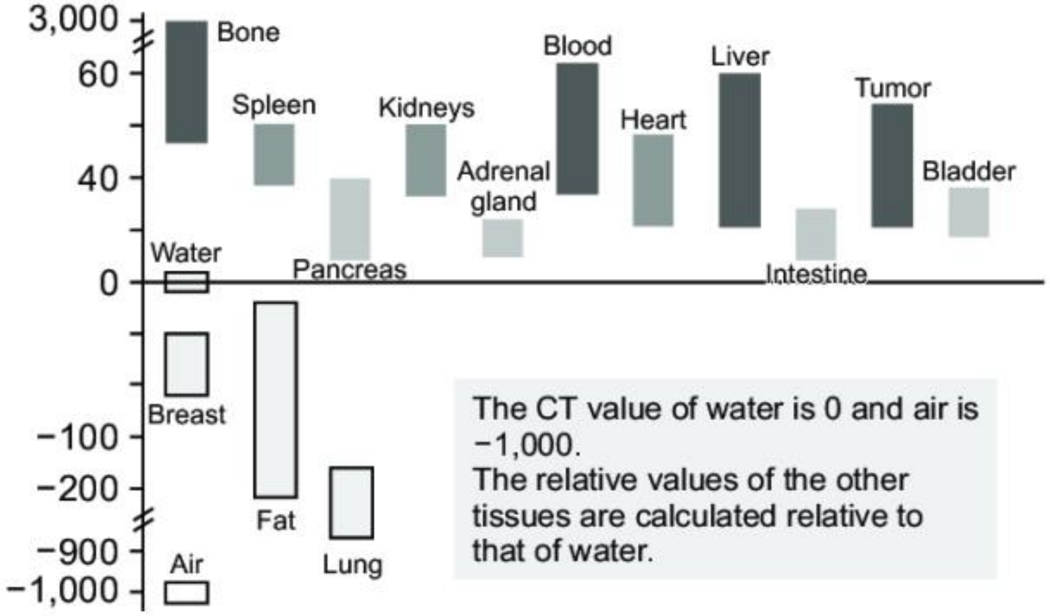
MRI: 3D map of hydrogen atoms



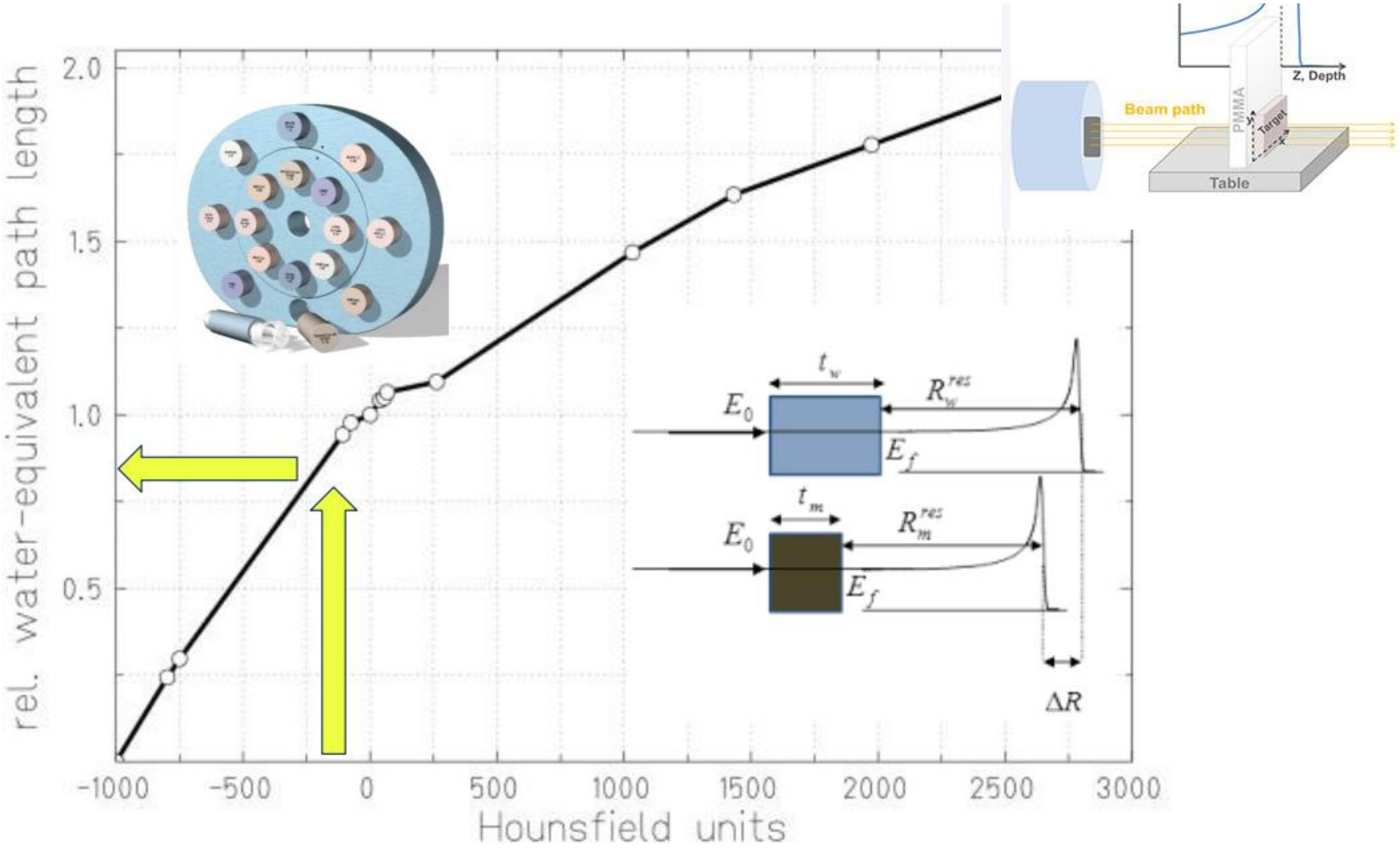


$$\mu = \text{CT linear attenuation coefficient}$$

$$HU = \left(\frac{\mu_{material} - \mu_{water}}{\mu_{water}} \right) \times 1000$$



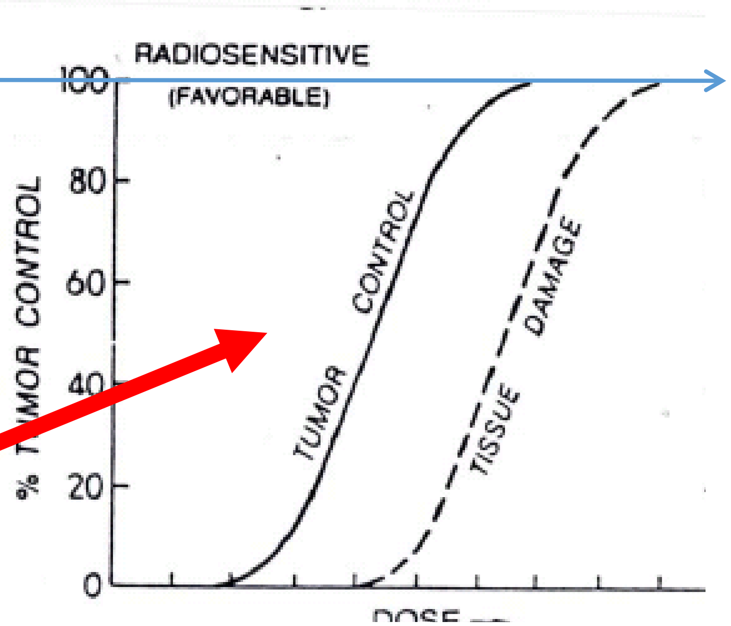
rWEPL


rel. water-equivalent path length
2.0
1.5
1.0
0.5
-1000
-500
0
500
1000
1500
2000
2500
3000
Hounsfield units
Z, Depth
Beam path
PMMA
Target
Table
t_w
R_w^{res}
E_0
E_f
t_m
R_m^{res}
E_0
E_f
ΔR

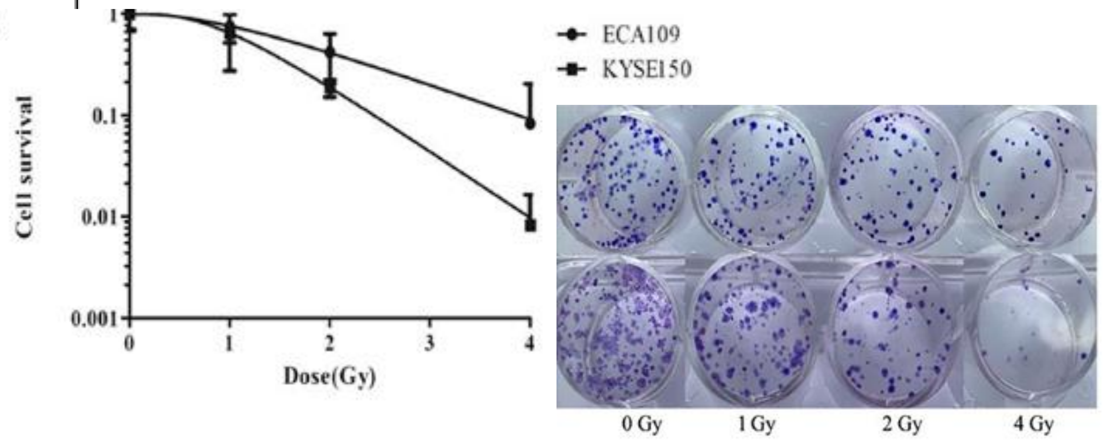
Prescribed radiation dose to target is based on accepted clinical protocols, whose rationale is based on radiobiological studies and clinical trials.

Diagnosi e sede : melanoma mucoso della fossa nasale operato R1 pT3 cN0 M0

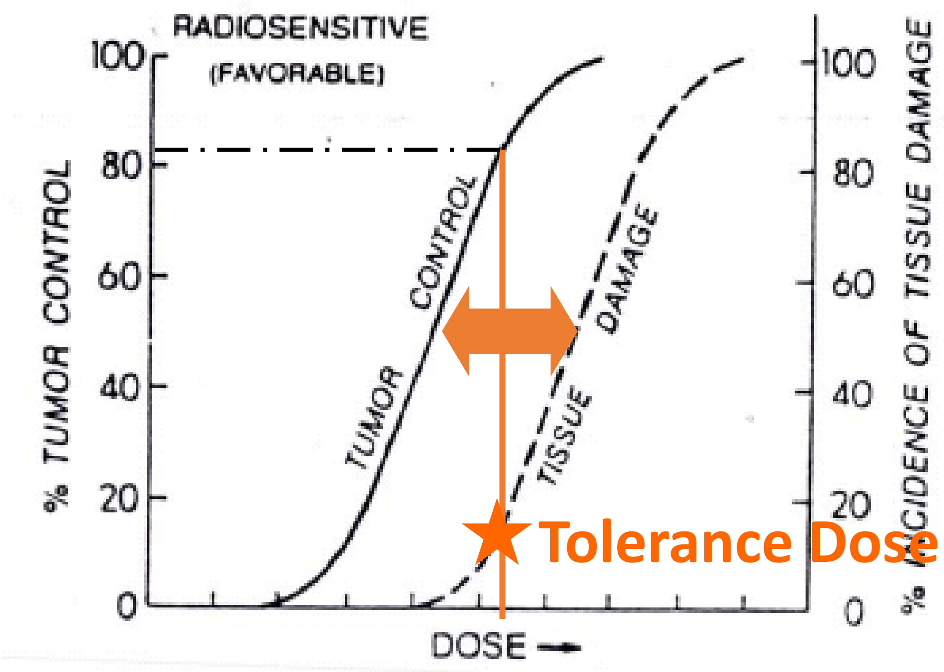
Volume bersaglio	PTV 1	PTV 2		
Sede	CTV LD*	CTV HD*		
Particella (p- C)	C	C		
Dose/frazione Gy[RBE]	4.1	4.1		
n. frazioni/die	1	1		
n. frazioni/settimana	4	4		
n. frazioni totali	10	6 (--> 16 totali)		
Dose totale Gy[RBE]	41	24.6 (--> 65.6 totali)		
Boost (sequenziale – SIB)	sequenziale			
Data	19/4/2023	19/4/2023		

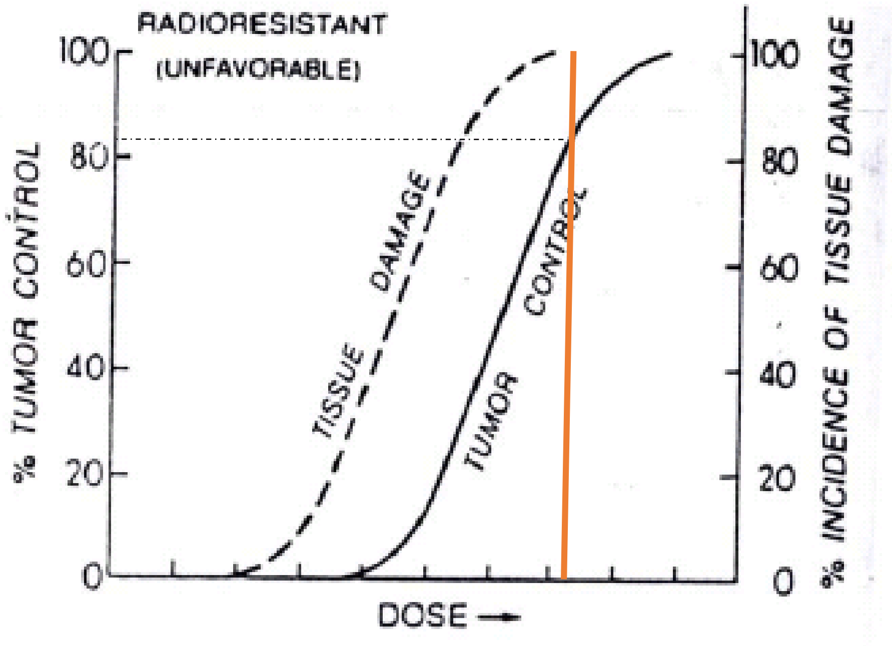


LOCAL CONTROL of the DISEASE in 80% (90%) of the patients



NORMAL TISSUES



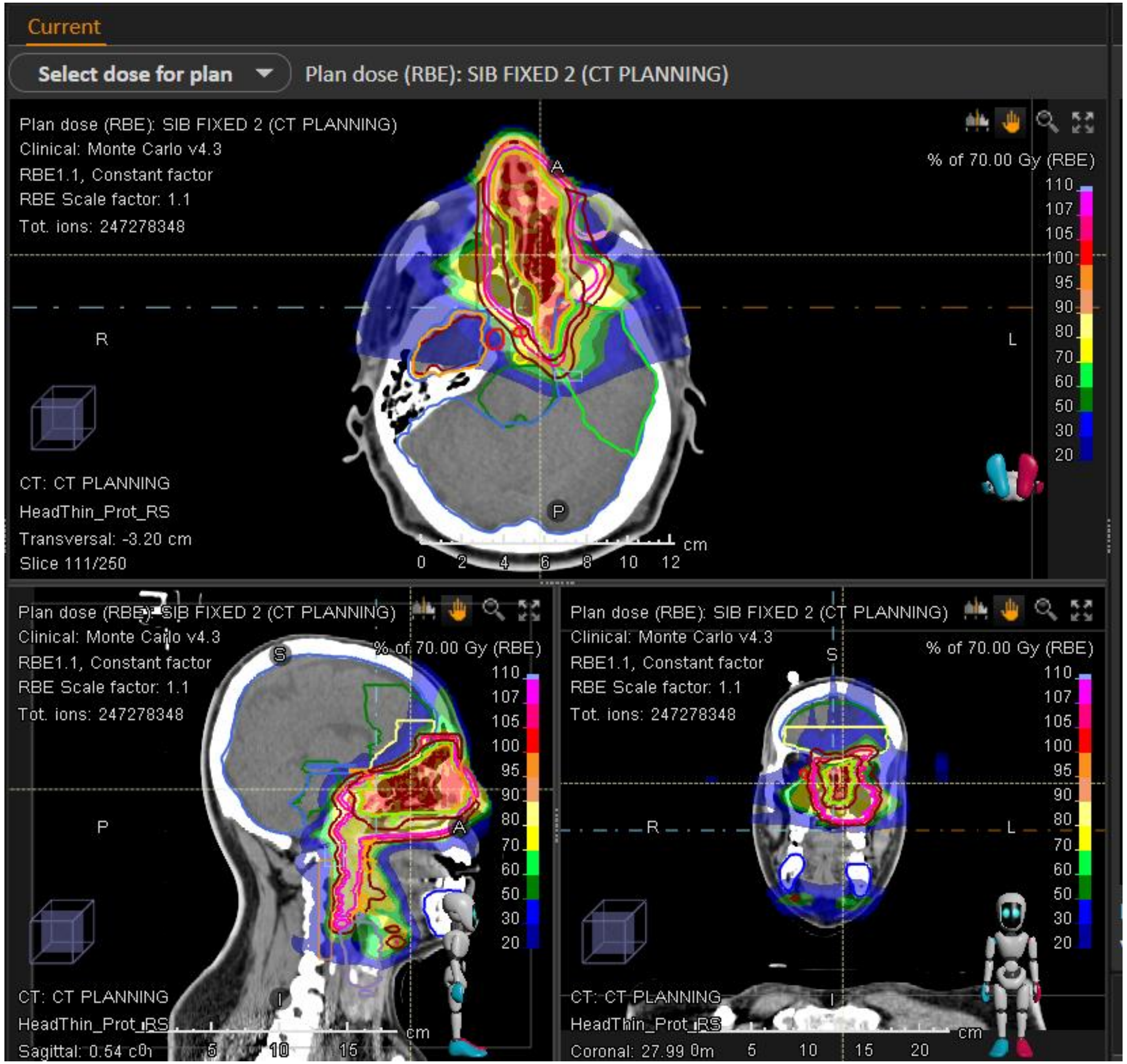


TOLLERANCE DOSE for a specific complication for 5% (50%) of the patients

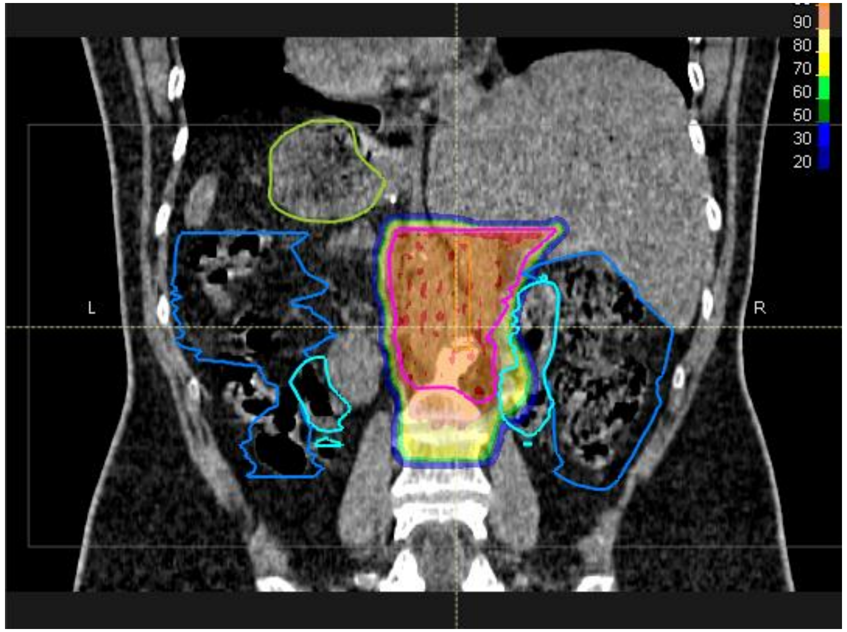
OPTIMIZATION → MAX TD →

dose that produces an acceptable probability of treatment complication

Nervi ottici, chiasma Dmax 40, D20% 28; rispettivi PRV: Dmax 60
Lobi temporali, cervelletto D2cc: 54 (contenere il più possibile isodose dei 40 Gy)
Lobo frontale: D2cc 54 (contenere il più possibile isodose dei 45 e dei 50 Gy)
Tronco Dmax 35, PRV tronco Dmax 40
Mandibola, ATM: Dmax 41; Carotidi: no hotspots; Ipofisi Dmedia 40;
Coclea sinsitra: Dmedia 40, Coclea destra Dmax 40
Occhi, Dmax 40; Dmedia 20; retine Dmax40; cristallini Dmedia 8 se possibile
Camere anteriore Dmax 40 , Dmedia 15
Midollo Dmax 5; parotide sisnitra Dmedia 26;
Laringe Dmax 40; faringe no hotspots, Dmedia 50; cavo orale Dmedia 30
No sovradosi > 102% all'interno del target

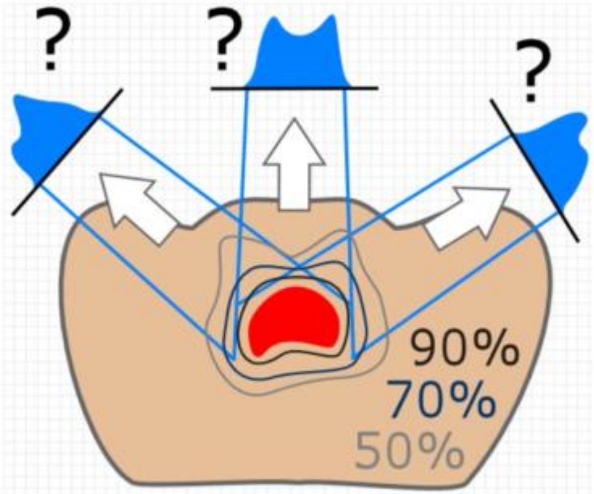


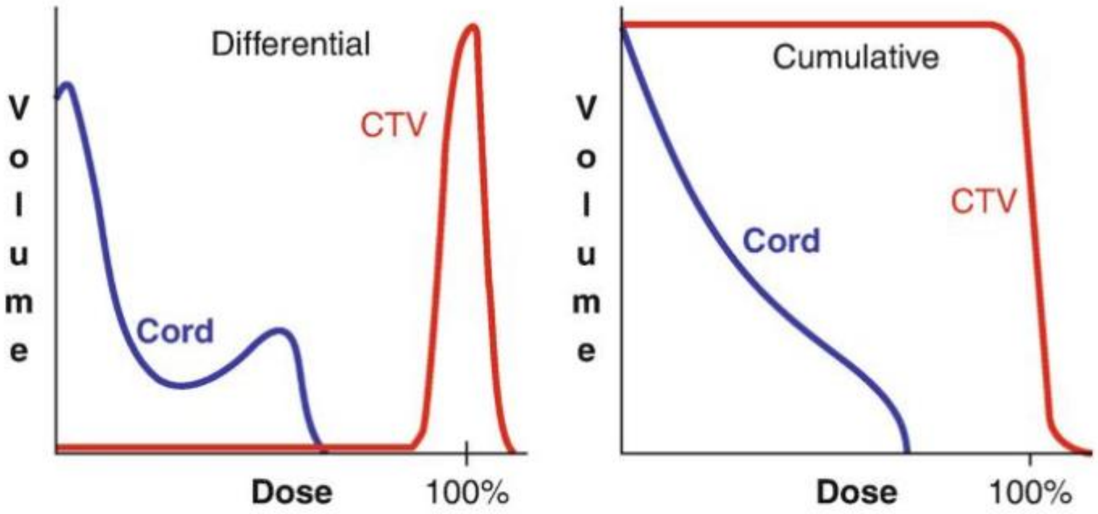
...using a treatment planning system (TPS) commissioned on each specific machine.



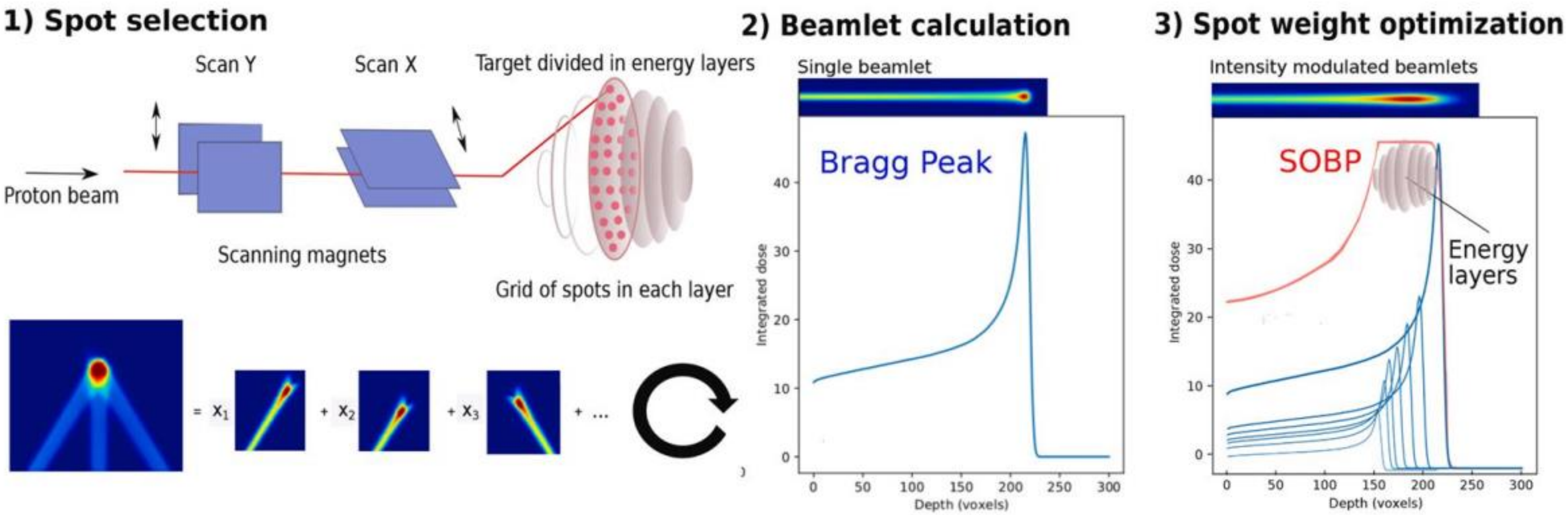
Inverse planning

Define beams arrangement and optimization goals

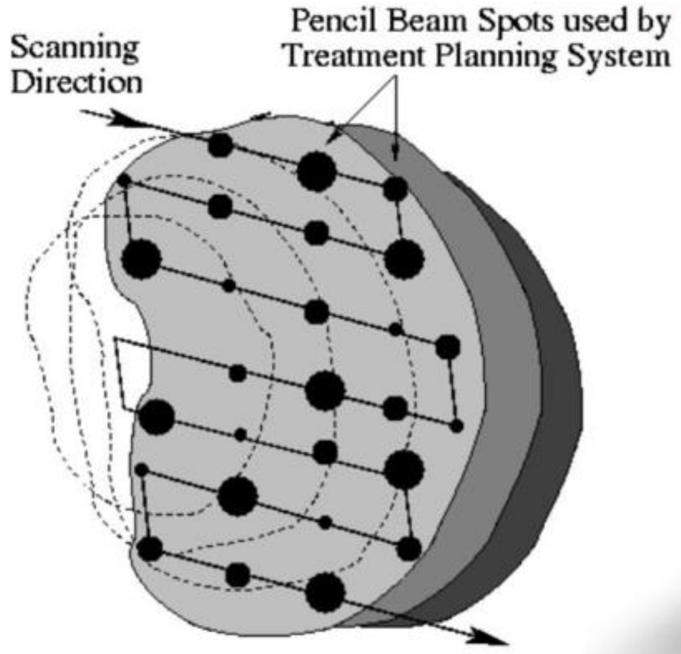


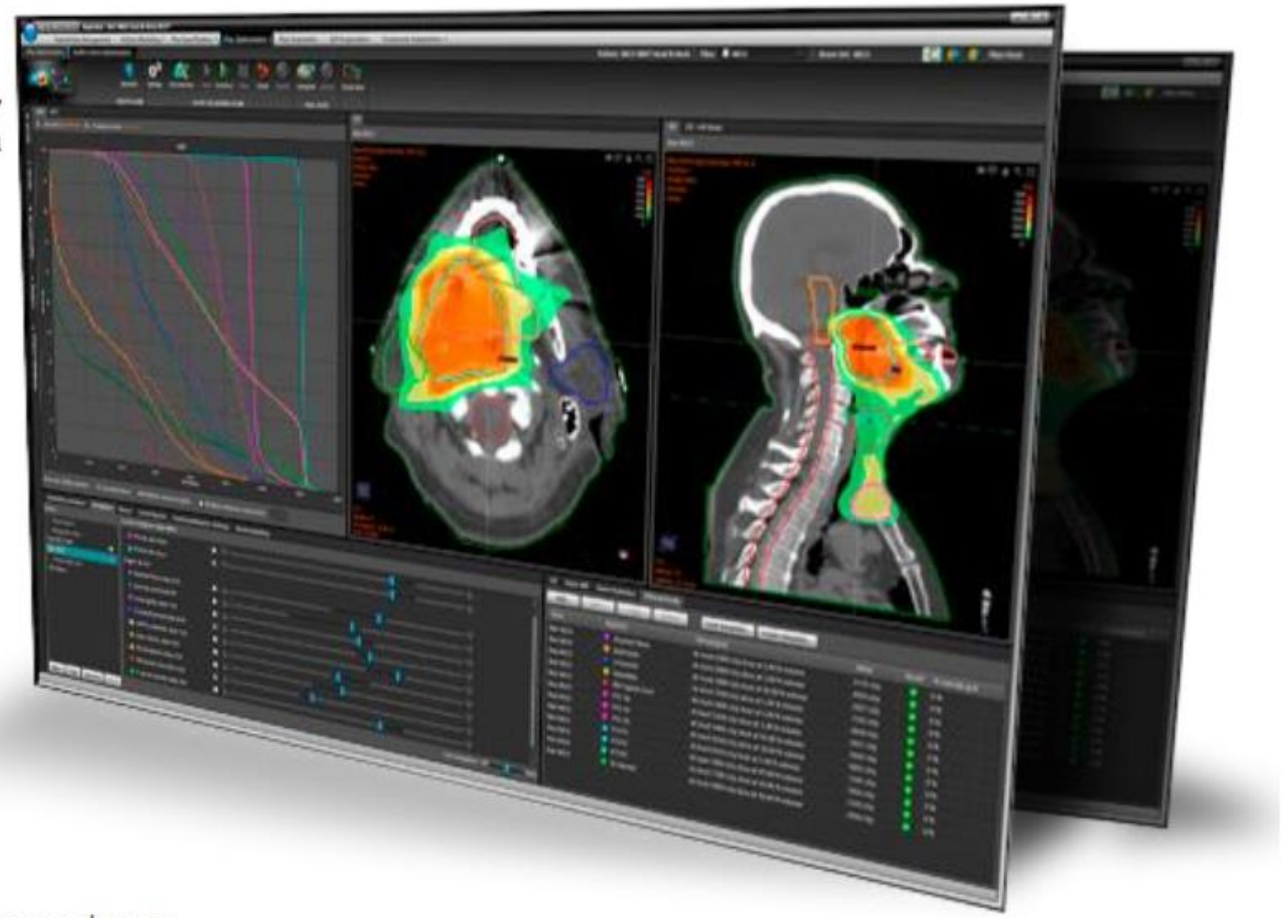


Spots assignment



Cost function



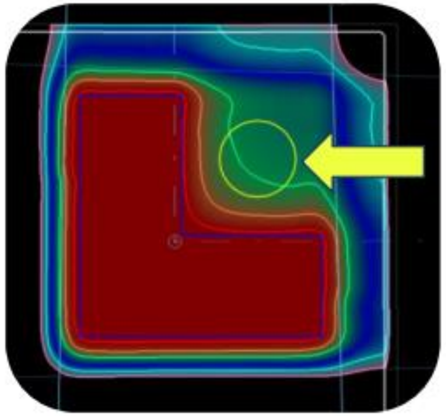


$$\text{Minimize C:}\ \ C = \sum_{\text{Structures}} \left[\left(\frac{\text{Structure importance}}{\#\ \text{structure voxels}}\right) \sum_{\text{Structure Voxels}} \left((\text{Applicable penalties})(\text{Rx Dose} - \text{Actual Dose})^2\right)\right]$$

Optimization tecniques

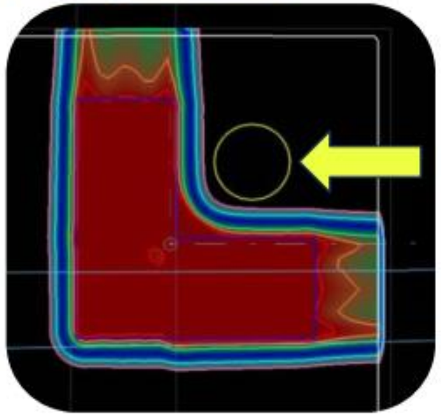
- Single Field Optimization - **SFO**

  Uniform dose is delivered to the entire target by each field individually.



- Multi Field Optimization - **MFO**

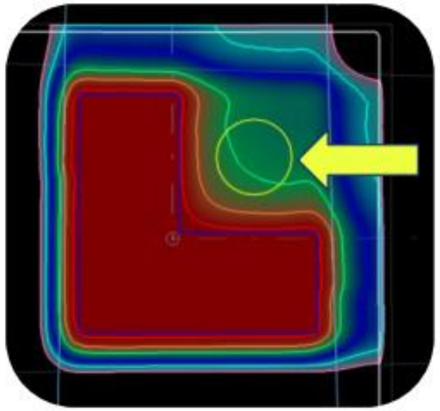
  Spot weights of all fields are optimized together. The spot weight of one field may rely on another field's dose to create an integrated uniform target dose.



Optimization tecniques

- Single Field Optimization - **SFO**

  Uniform dose is delivered to the entire target by each field individually.



Less sensitive to setup/range errors

Less sparing of critical structures

Single Field Uniform Dose - SFUD

Optimization tecniques

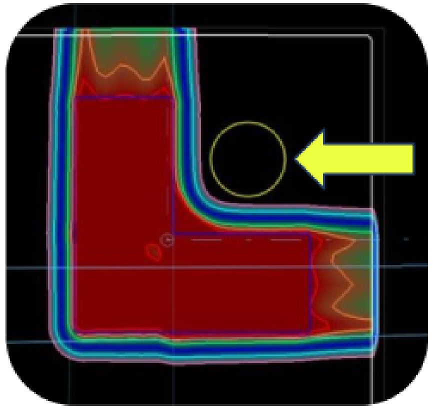
More sensitive to setup/range errors

Better for sparing critical structures

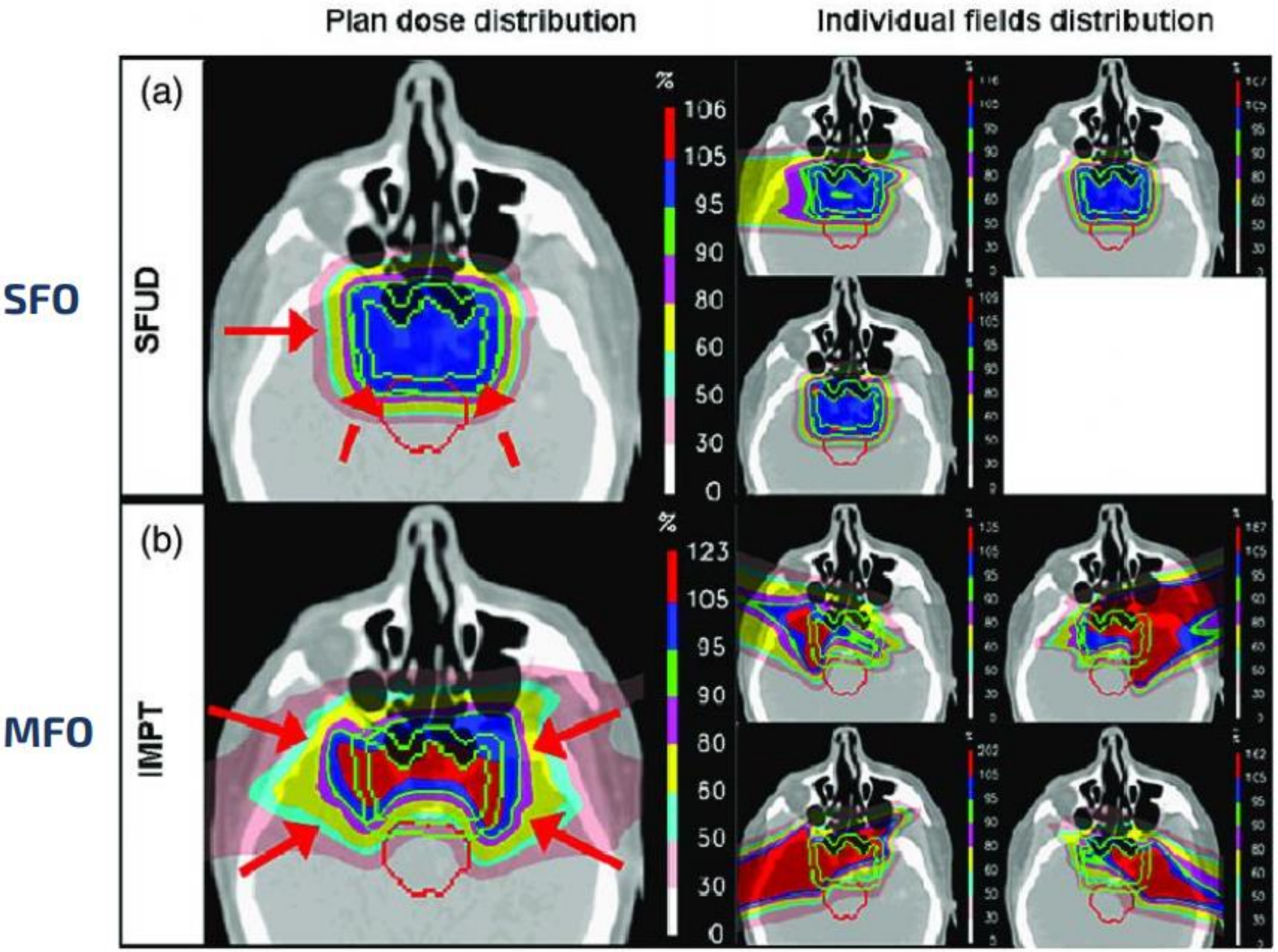
Intensity Modulated Particle Therapy - IMPT

- Multi Field Optimization - **MFO**

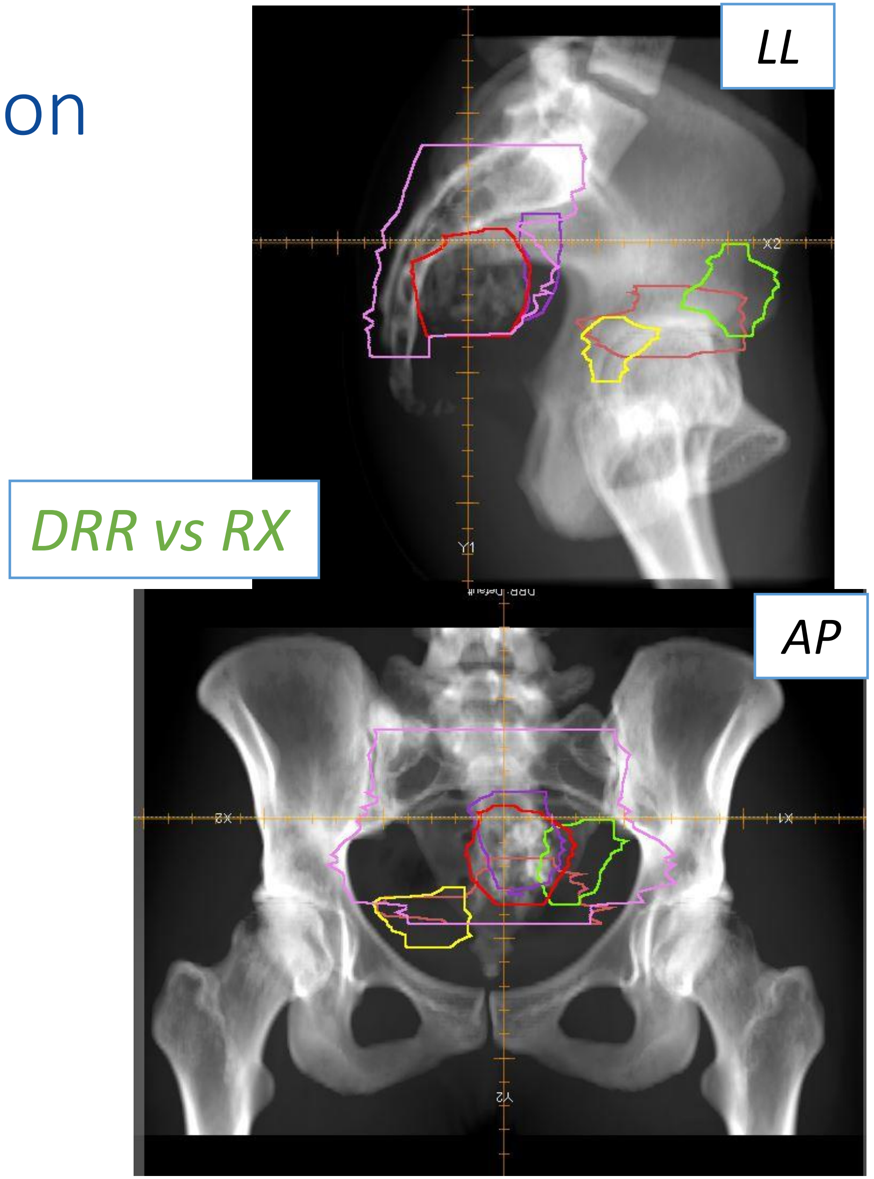
  Spot weights of all fields are optimized together. The spot weight of one field may rely on another field's dose to create an integrated uniform target dose.

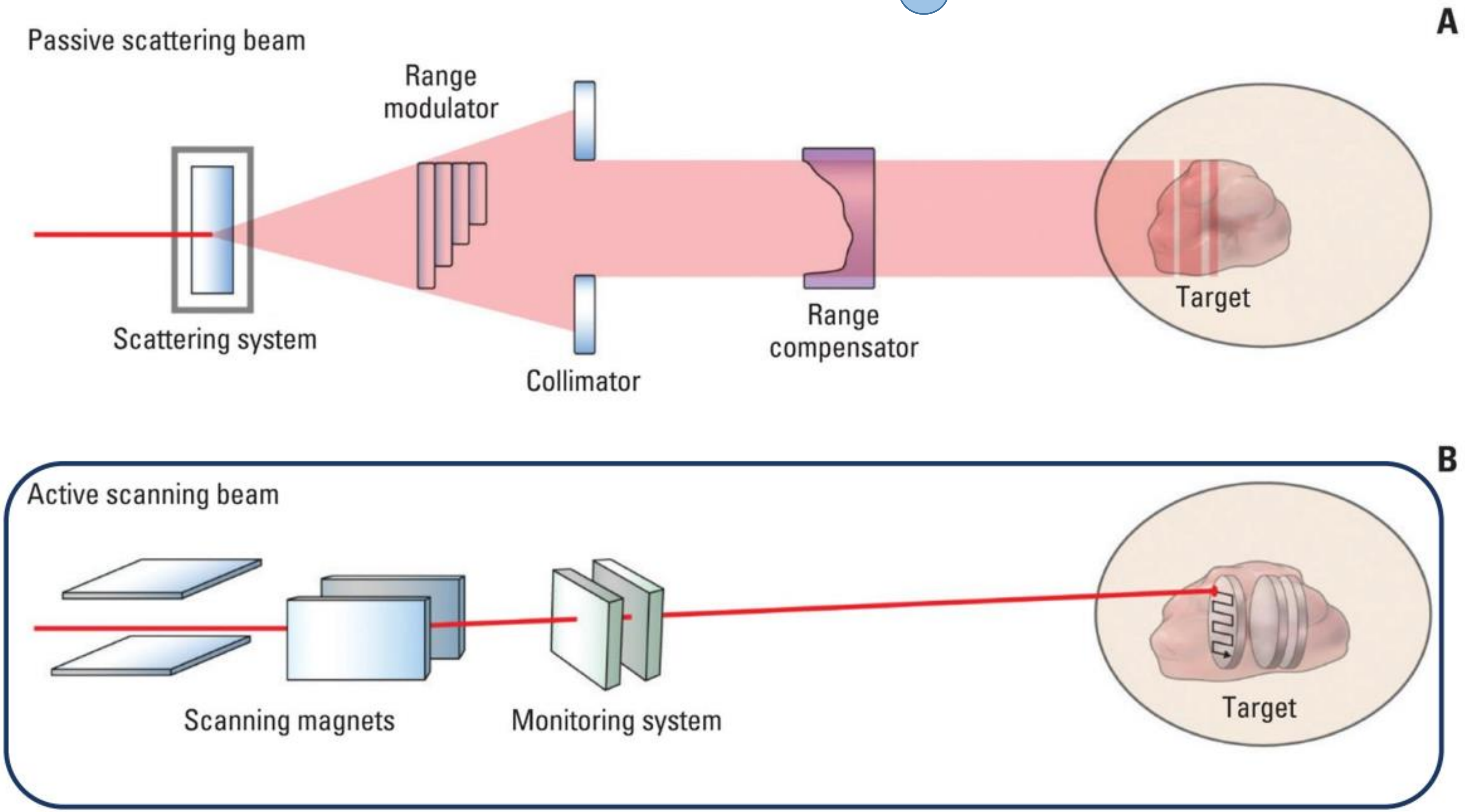


Treatment planning

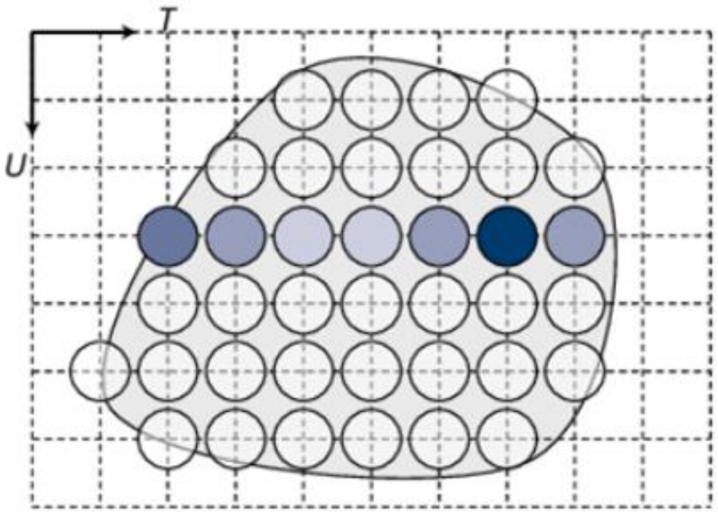


Patient positioning + Daily imaging verification

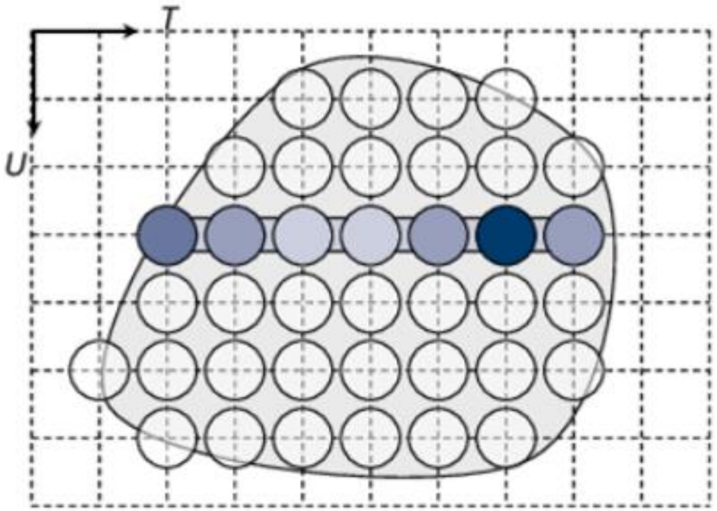


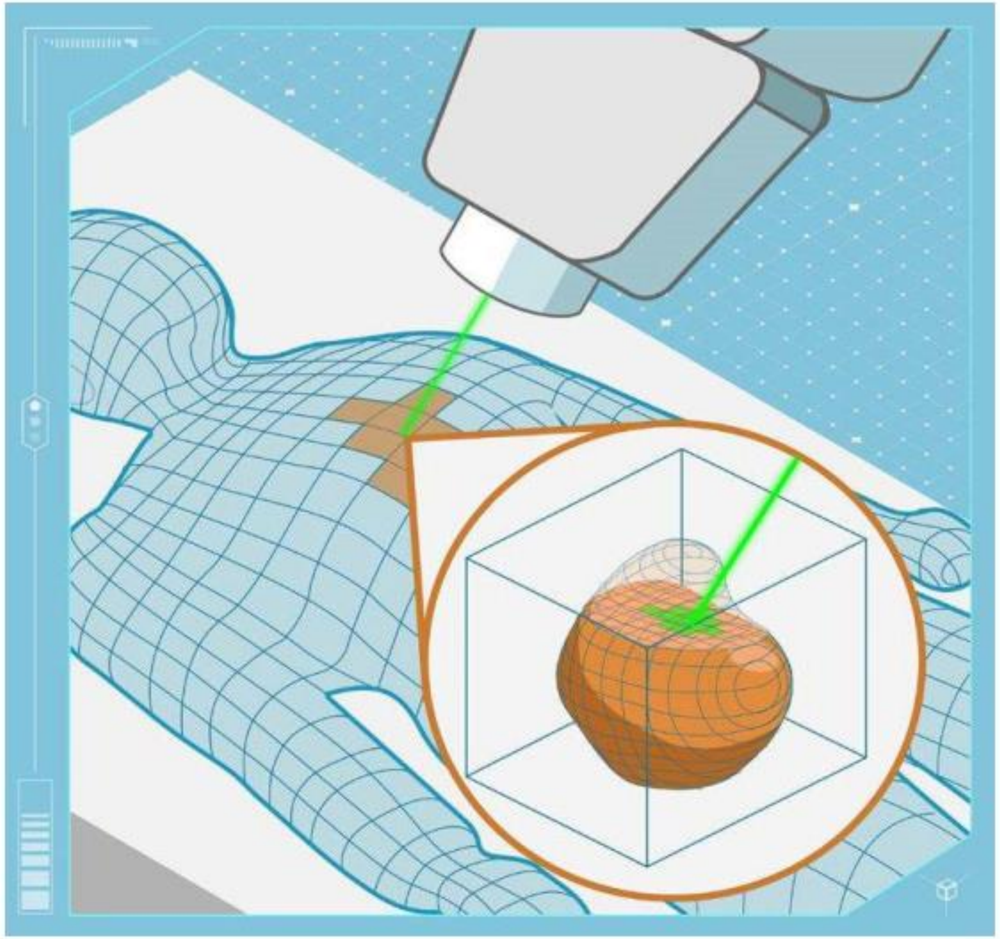

A
Passive scattering beam
Range modulator
Scattering system
Collimator
Range compensator
Target
B
Active scanning beam
Scanning magnets
Monitoring system
Target

spot scanning

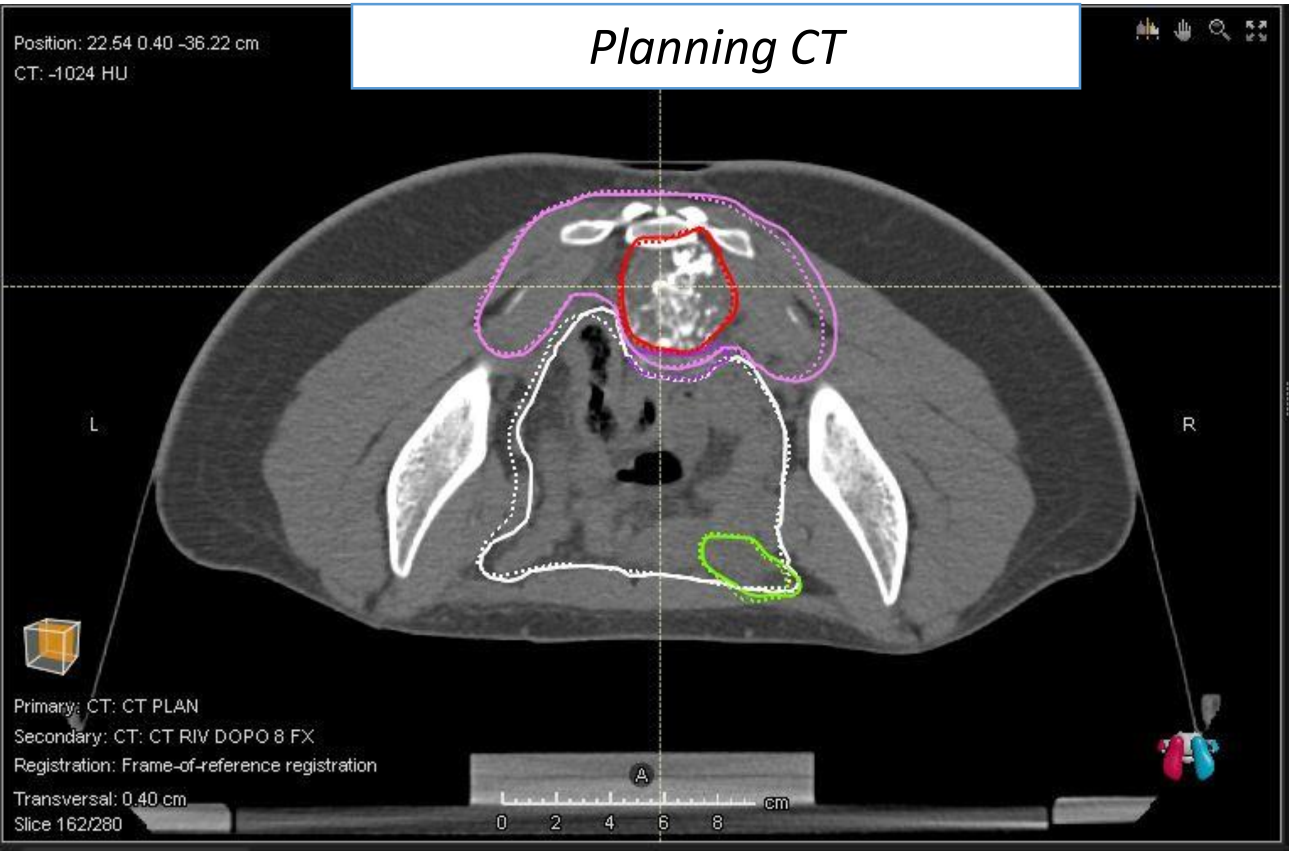


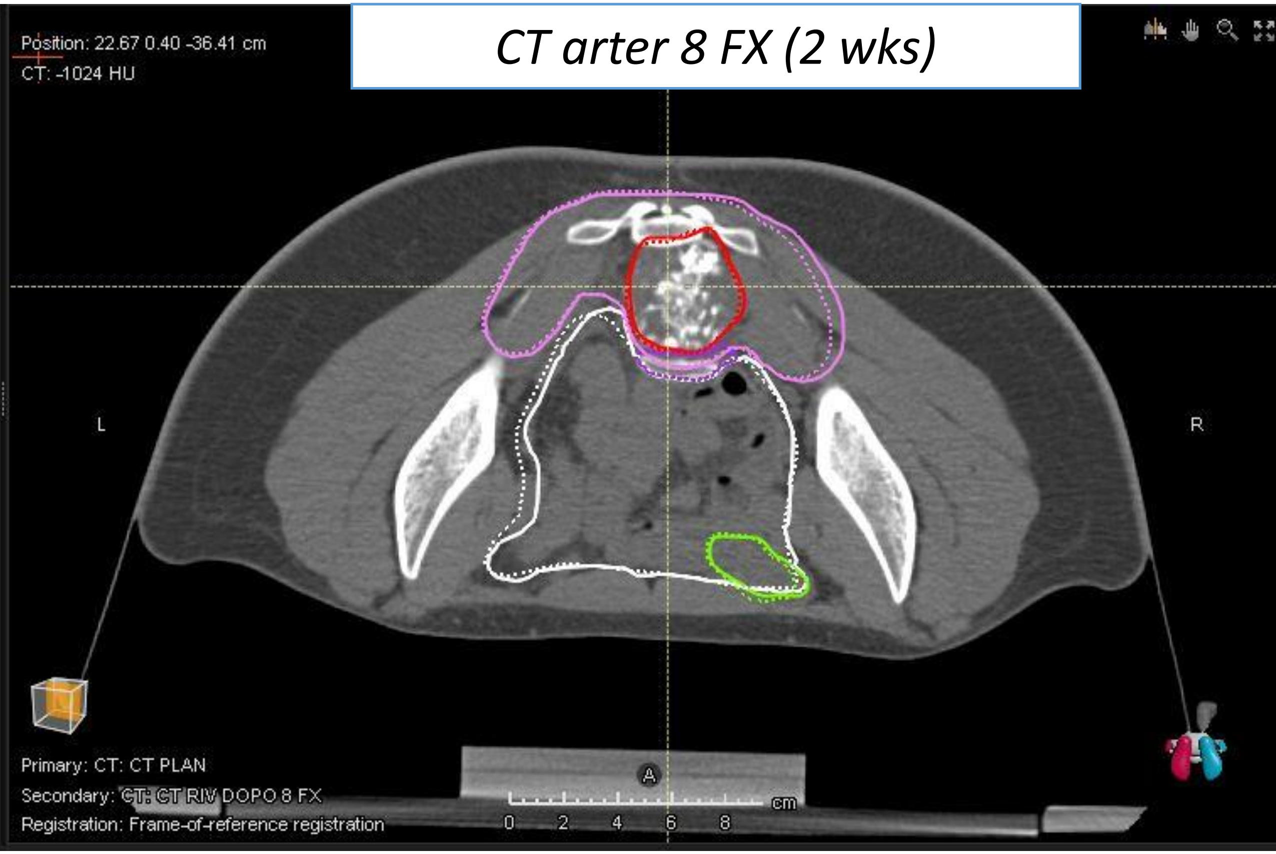
raster scanning





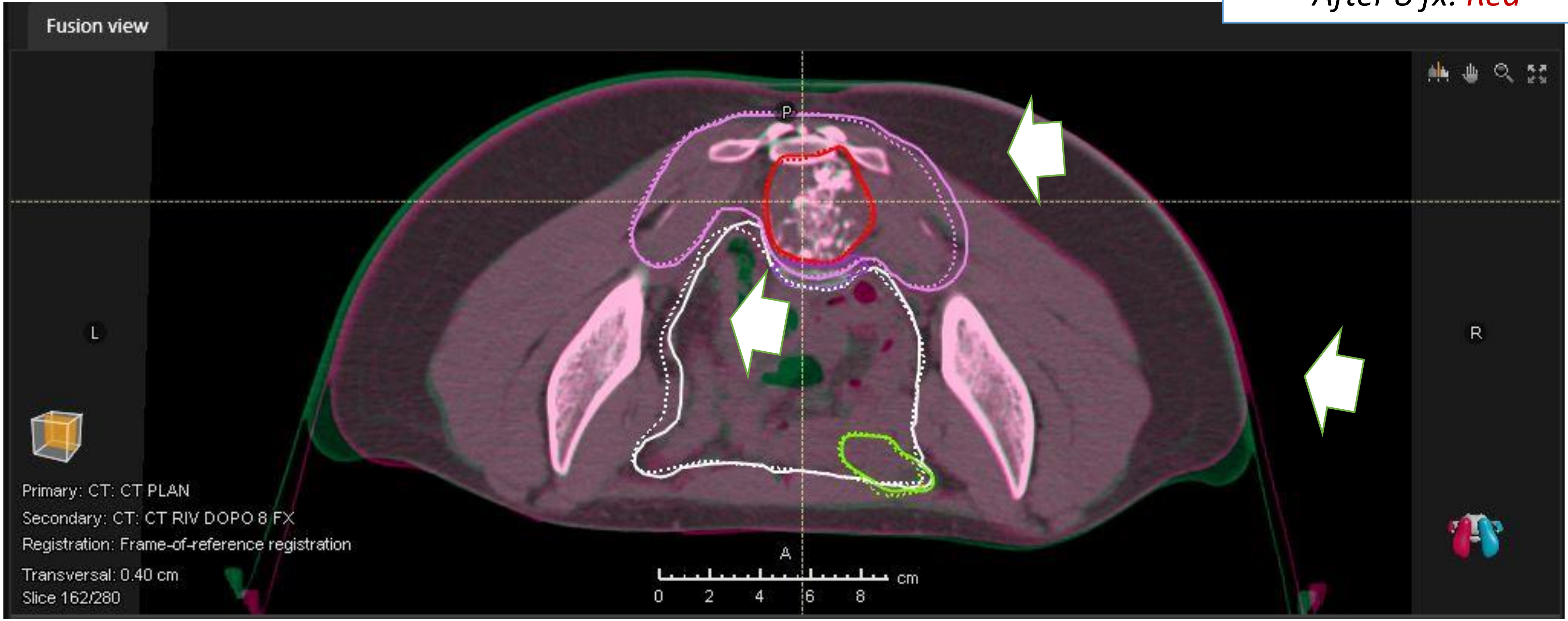
re-evaluative CT



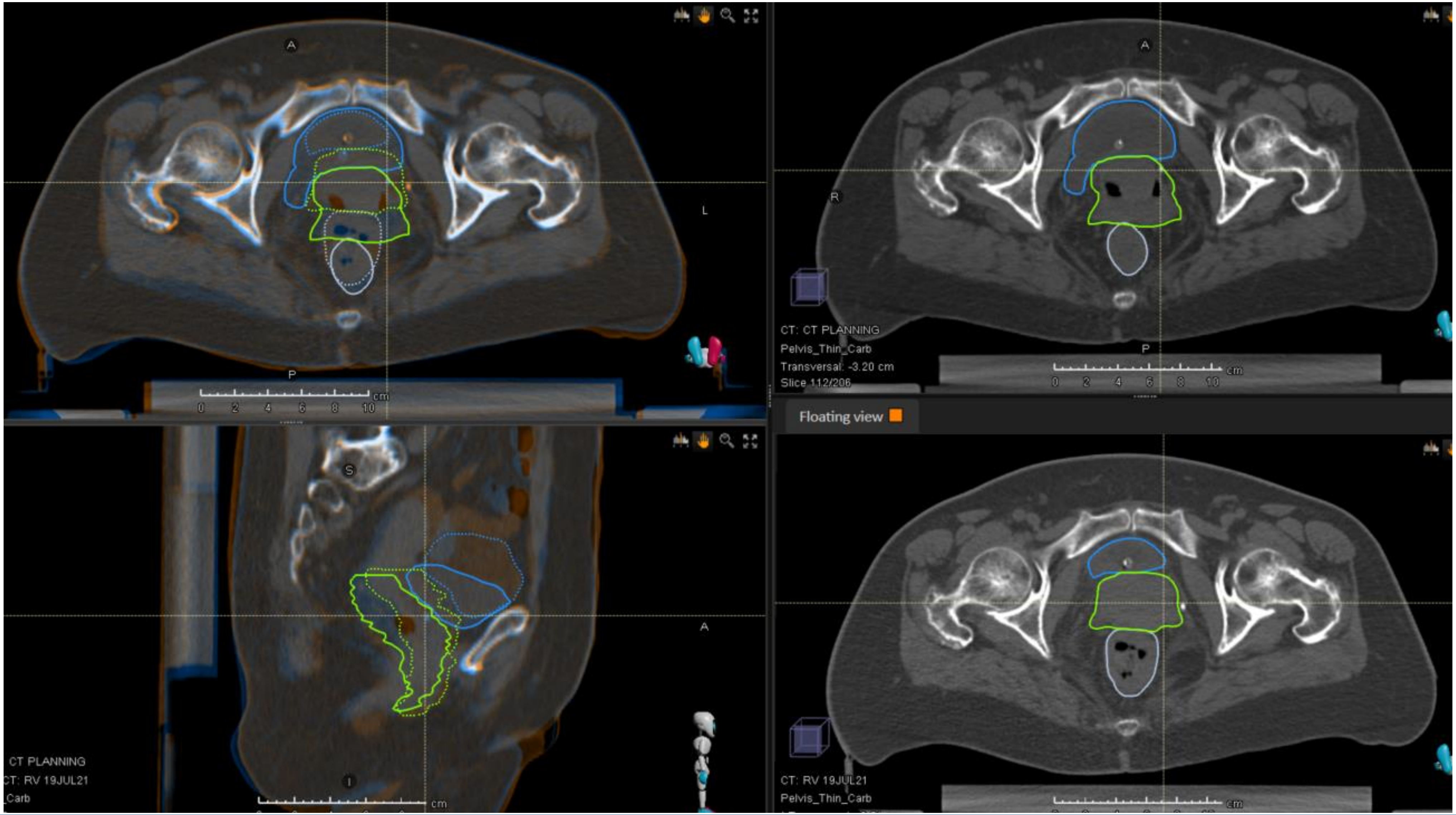


REPRODUCIBLE!

Planning: Green
After 8 fx: Red



NOT REPRODUCIBLE!



Sources of uncertaintes in range determination

- Measurement uncertainty in water for commissioning
- Stopping power / mean excitation energy of water in beam modeling
- Beam reproducibility
  - energy constancy
  - momentum spread
- Patient setup
  - Organ motion
  - Anatomical changes
- CT imaging and calibration
- CT conversion to tissue
  - rWEPL-to-energy dependence
  - Metal implants
- Biology

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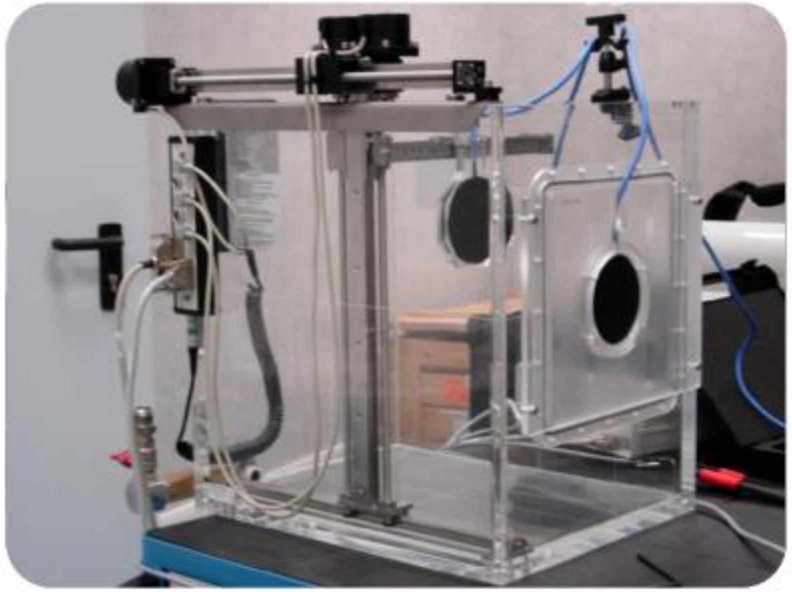

- Measurement uncertainty in water for commissioning
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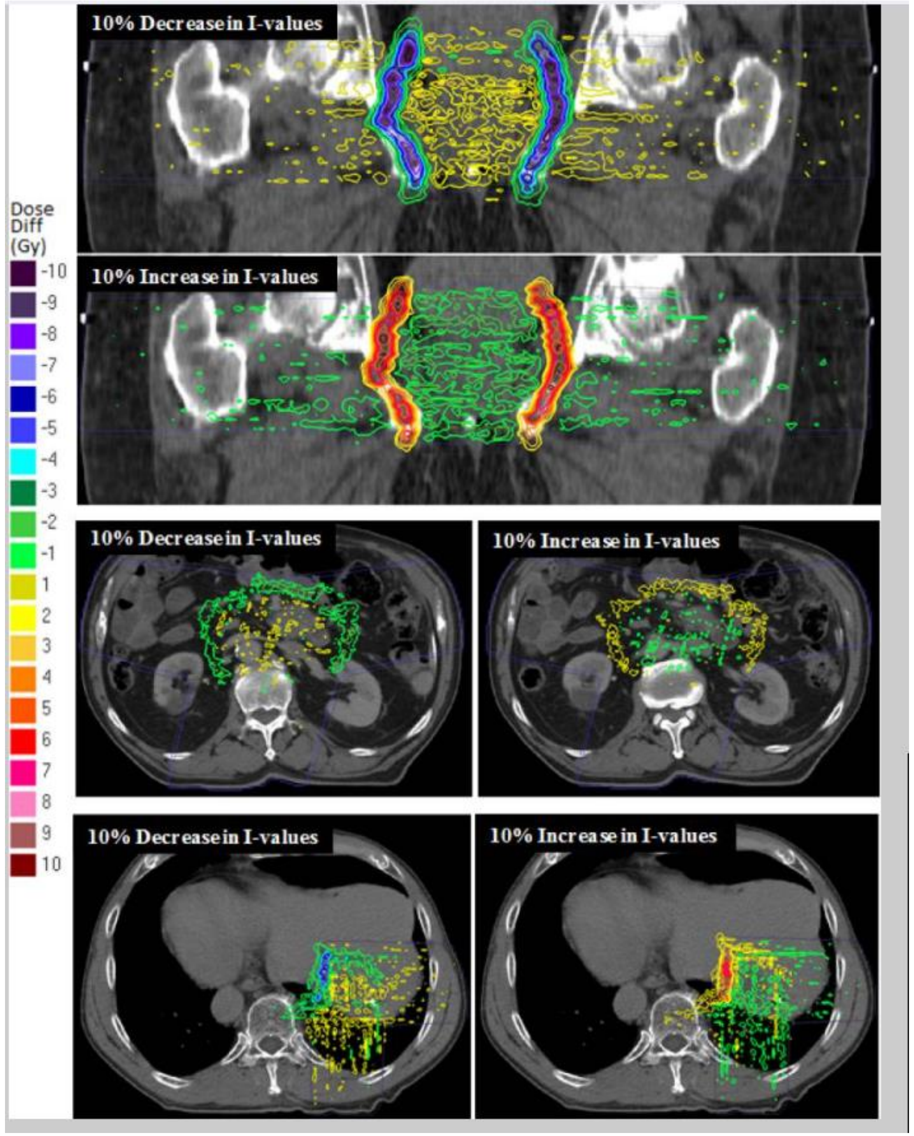
Clinical impact of uncertainties in the mean excitation energy of human tissues during proton therapy

Abigail Besemer,[1] Harald Paganetti,[2] and Bryan Bednarz[1]

Phys Med Biol. 2013 Feb 21; 58(4): 887–902.

Modification of tissue I-values impacted both the proton range and SOBP width. R_{90} range shifts up to 7.7 mm (4.4.%) and R_{80} range shifts up to 4.8 mm (1.9%) from the nominal range were recorded. Modulating the tissue I-values by 10% the nominal value resulted in up to a 3.5% difference mean dose in the target volumes and organs at risk (OARs) compared to the nominal case. The range and dose differences were the largest for the deeper-seated prostate and pancreas cases. The treatments that were simulated with randomly sampled I-values resulted in range and dose differences that were generally within the upper and lower bounds set by the 10% uniform variations. This study demonstrated the impact of I-value uncertainties on patient dose distributions. Clearly, sub-millimeter precision in proton therapy would necessitate a reduction in I-value uncertainties to ensure an efficacious clinical outcome.



CNAO

- Measurement uncertainty in water for commissioning
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    - Energy constancy
    - **Momentum spread**
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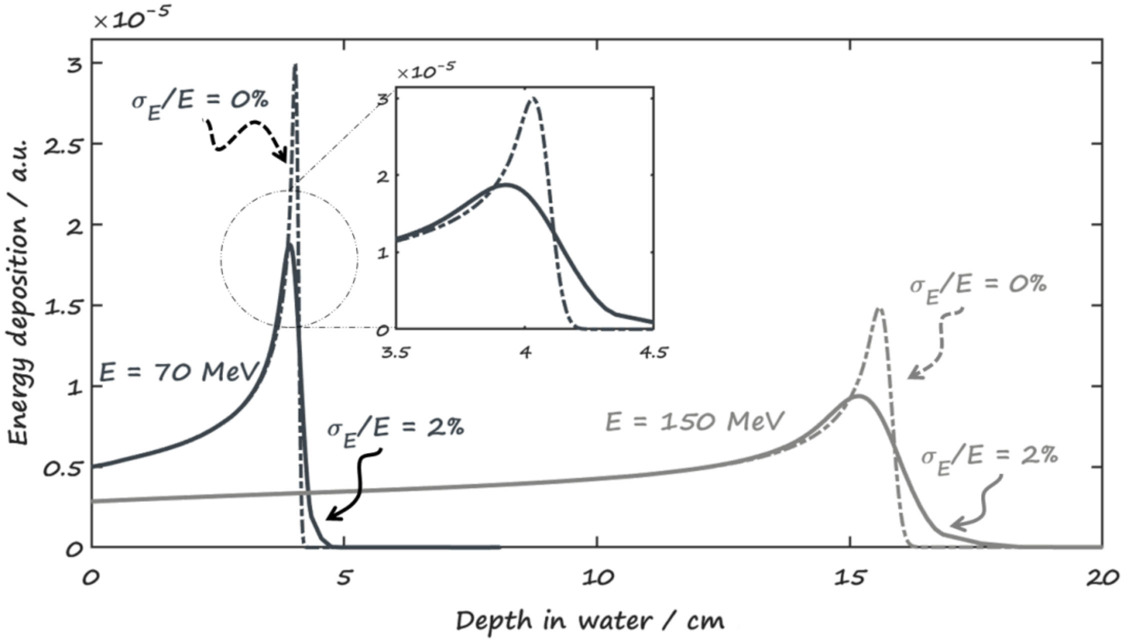

- Measurement uncertainty in water for commissioning
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- Patient setup
  - **Organ motion (intra-fraction)**
  - Anatomical changes (inter-fraction)
- CT imaging and calibration
- CT conversion to tissue
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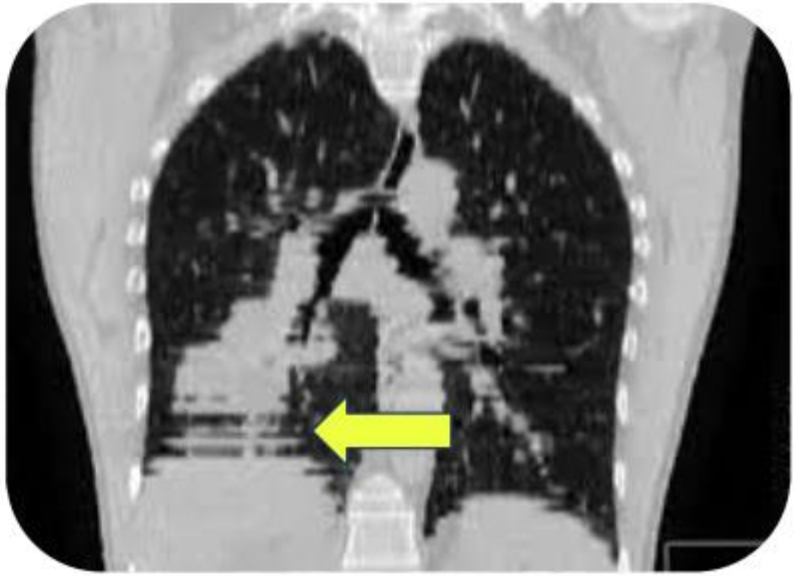
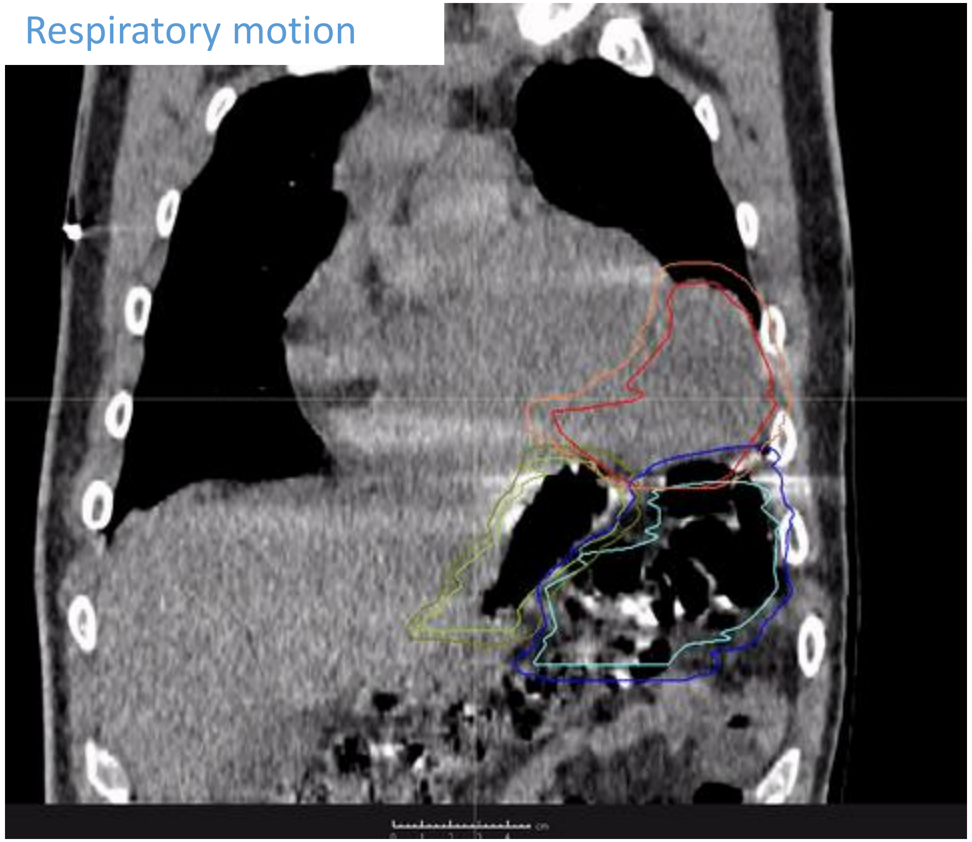
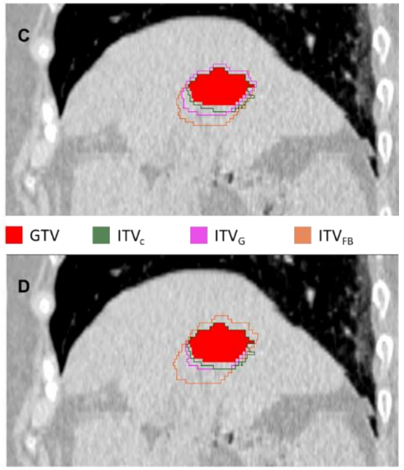
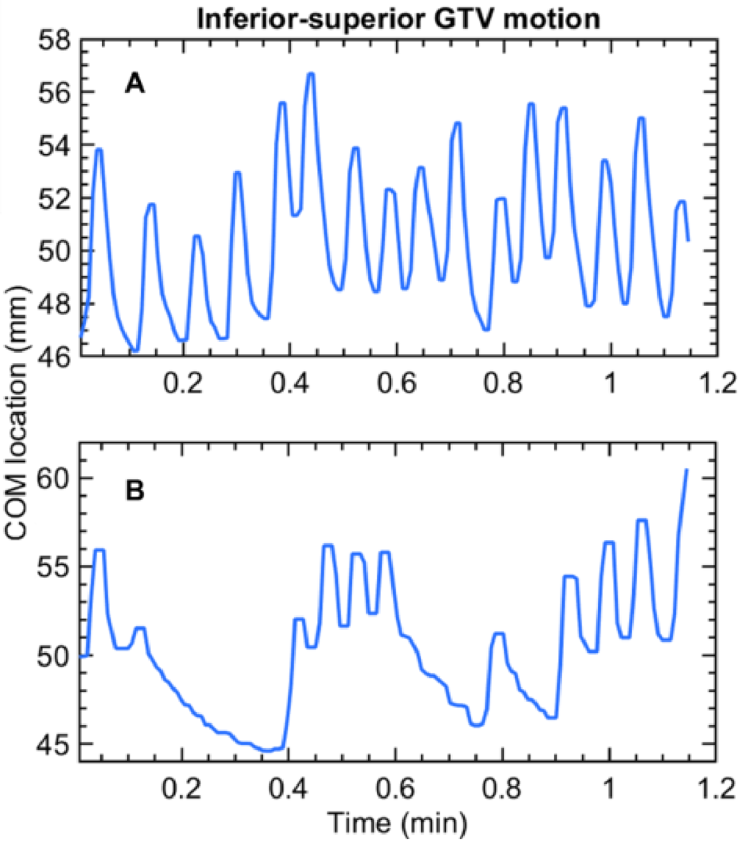
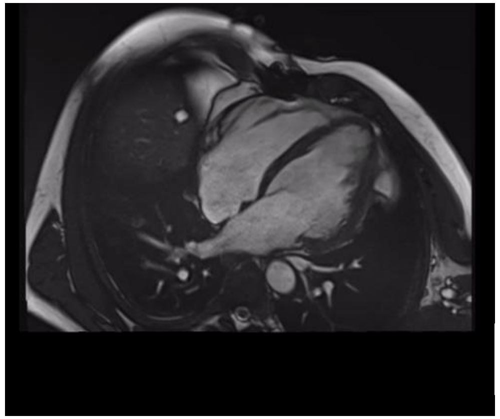


Respiratory motion

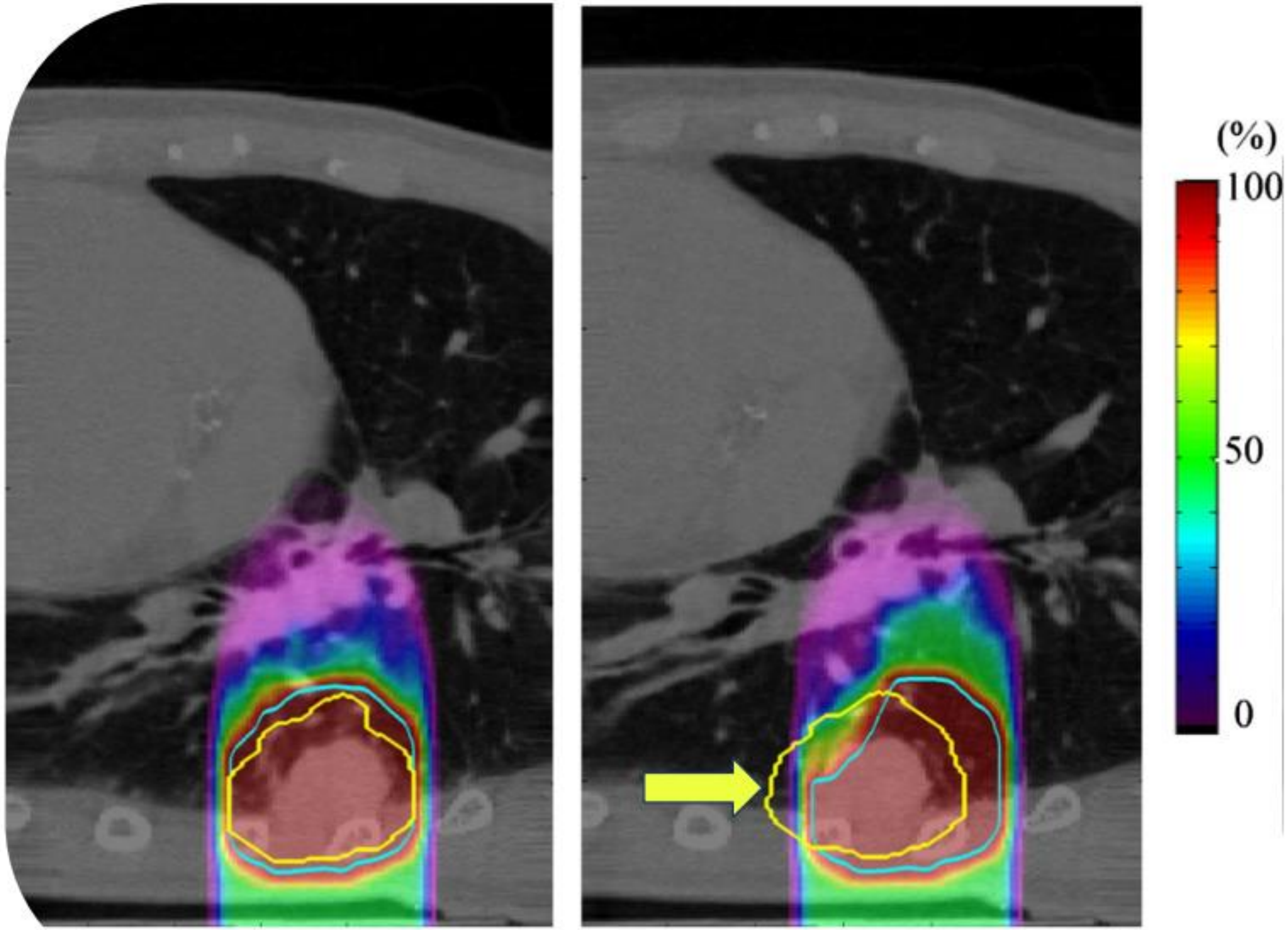








Cardiac motion



(a) Exhale (b) Inhale

- Measurement uncertainty in water for commissioning
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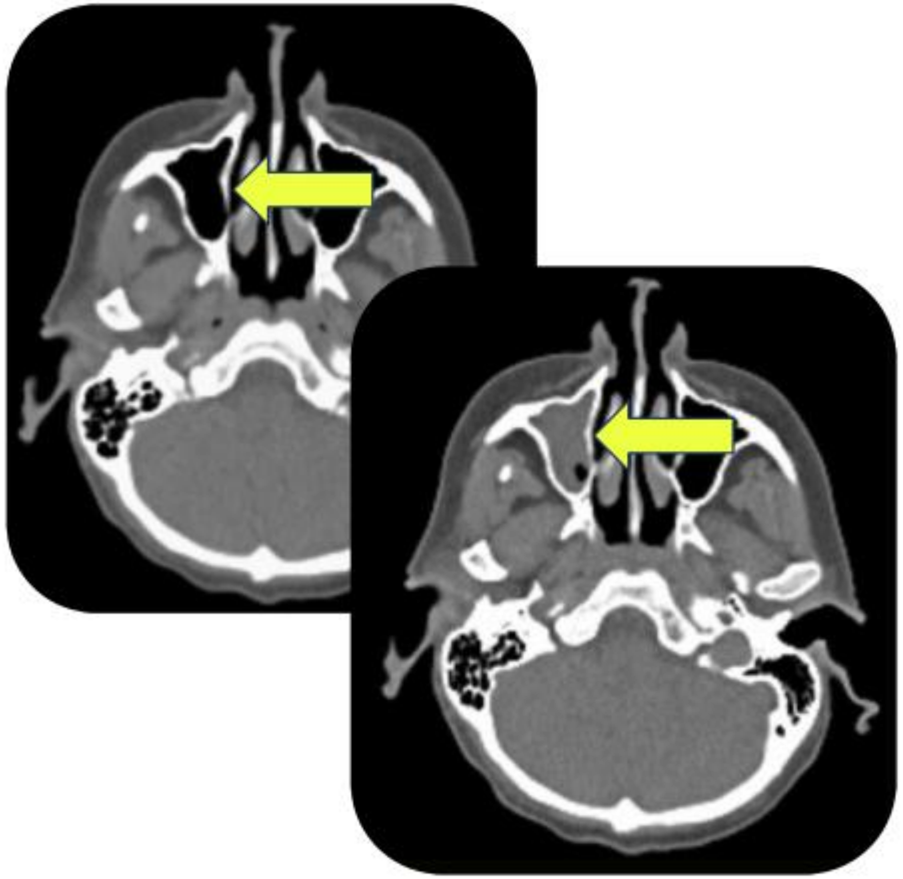
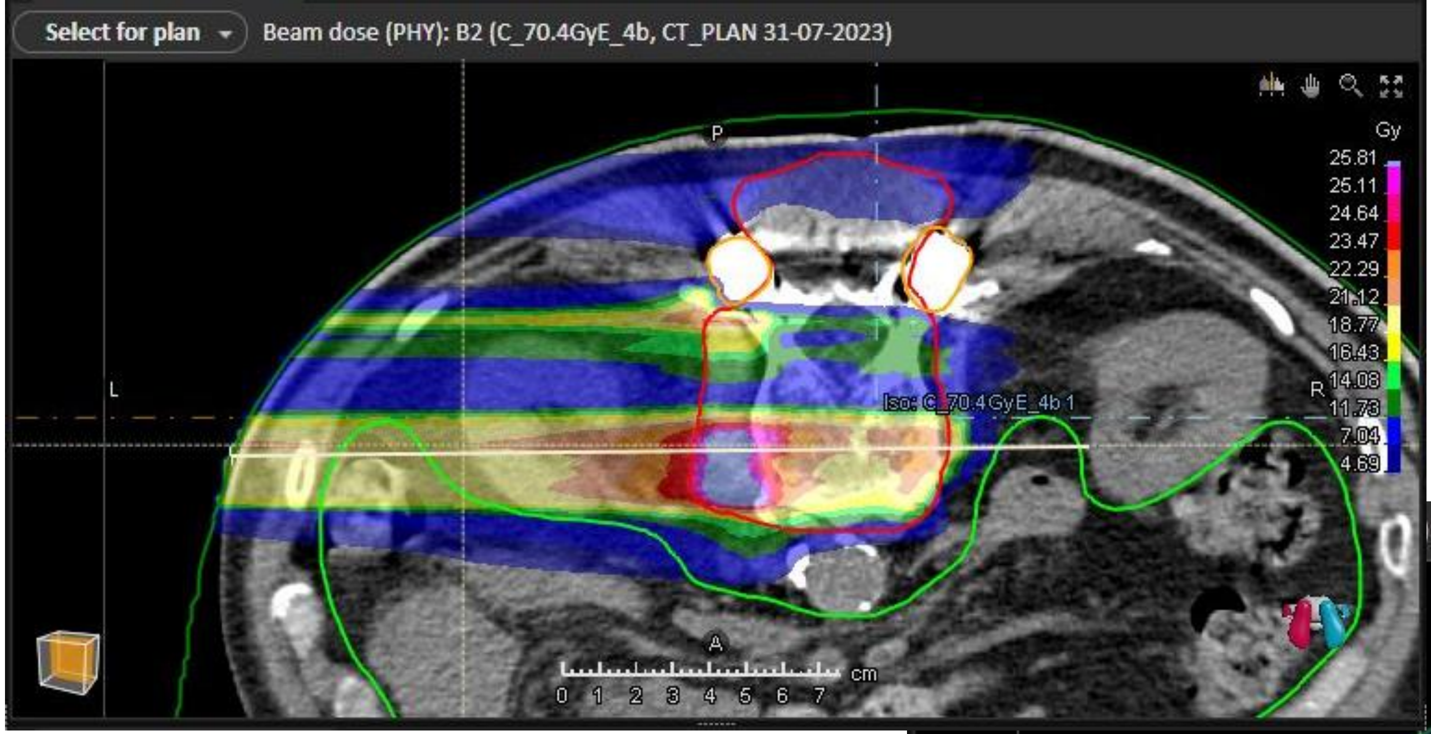
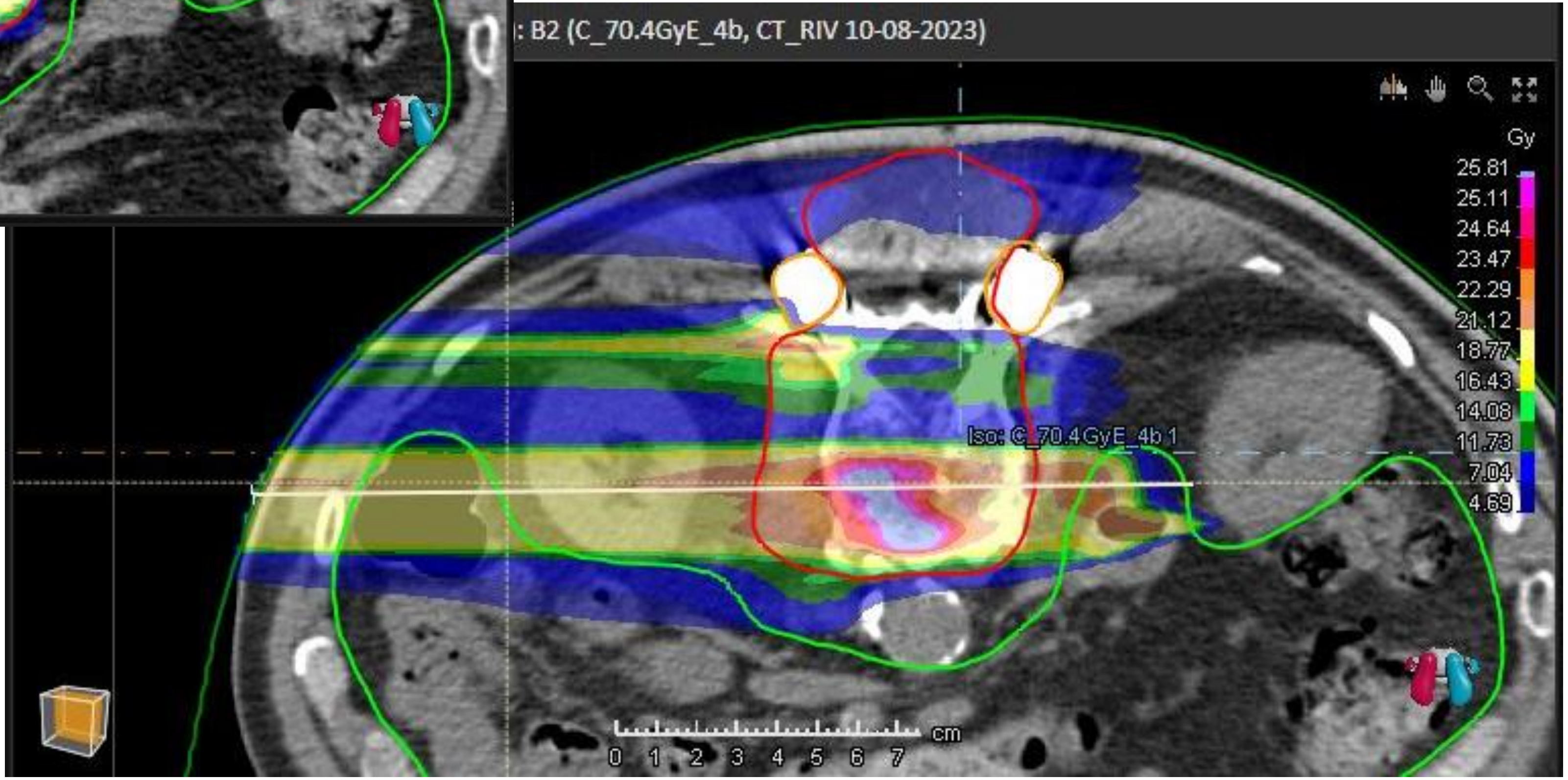



Select for plan
Beam dose (PHY): B2 (C_70.4GyE_4b, CT_PLAN 31-07-2023)
Gy
25.81
25.11
24.64
23.47
22.29
21.12
18.77
16.43
14.08
11.73
7.04
4.69
P
L
R
A
Iso: C_70.4GyE_4b 1
0 1 2 3 4 5 6 7 cm


: B2 (C_70.4GyE_4b, CT_RIV 10-08-2023)
Gy
25.81
25.11
24.64
23.47
22.29
21.12
18.77
16.43
14.08
11.73
7.04
4.69
Iso: C_70.4GyE_4b 1
0 1 2 3 4 5 6 7 cm

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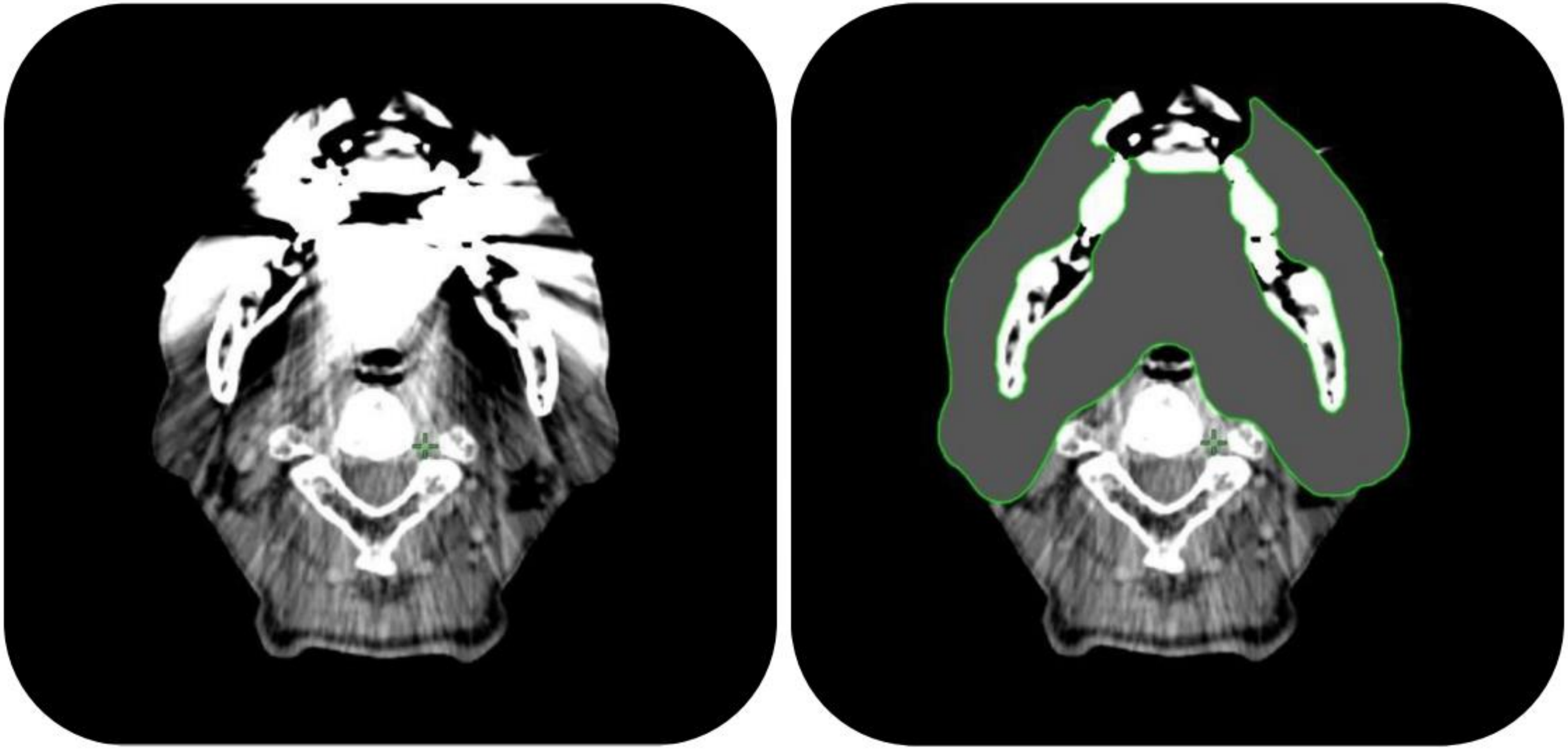

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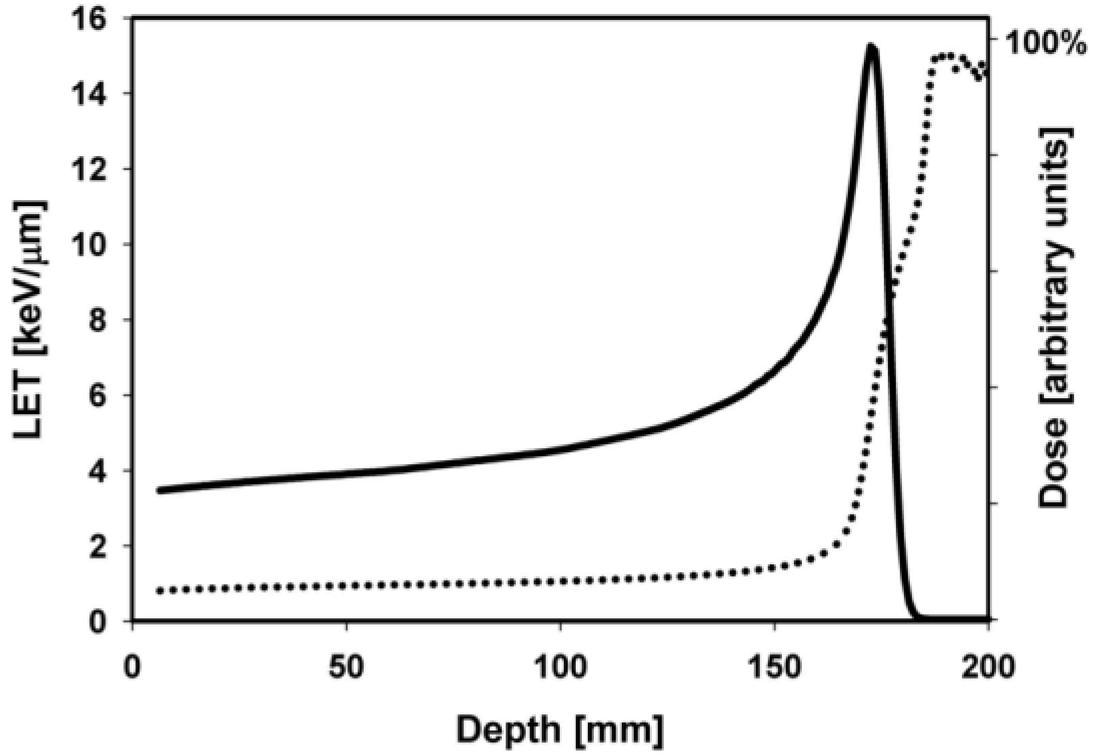
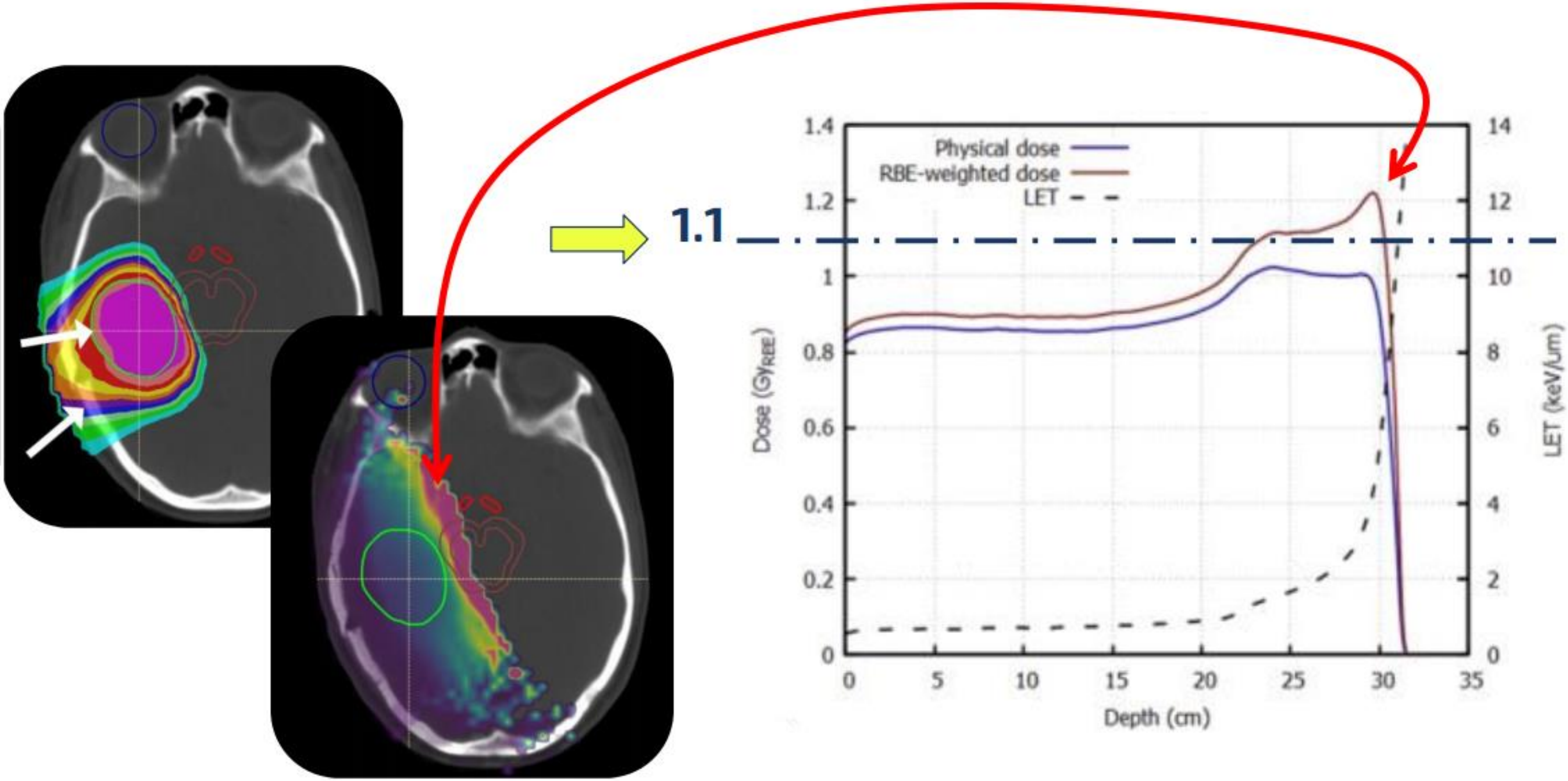


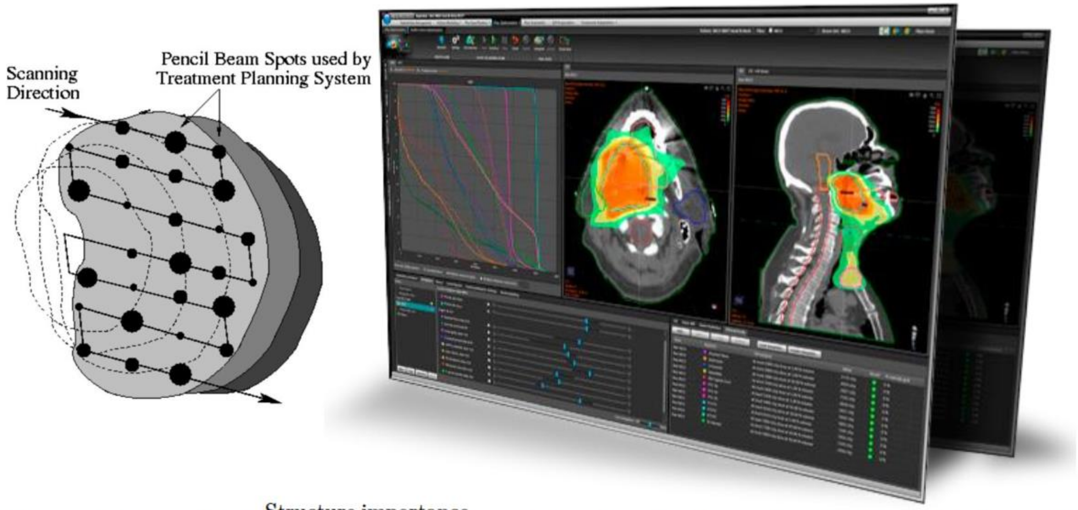

1.1
Physical dose
RBE-weighted dose
LET
Dose (Gy$_{RBE}$)
LET (keV/μm)
Depth (cm)
1.4
1.2
1
0.8
0.6
0.4
0.2
0
14
12
10
8
6
4
2
0
0
5
10
15
20
25
30
35

To mitigate the impact of uncertaintes on plan quality ->**Robust** optimization

Add penalties into the cost function for robustness

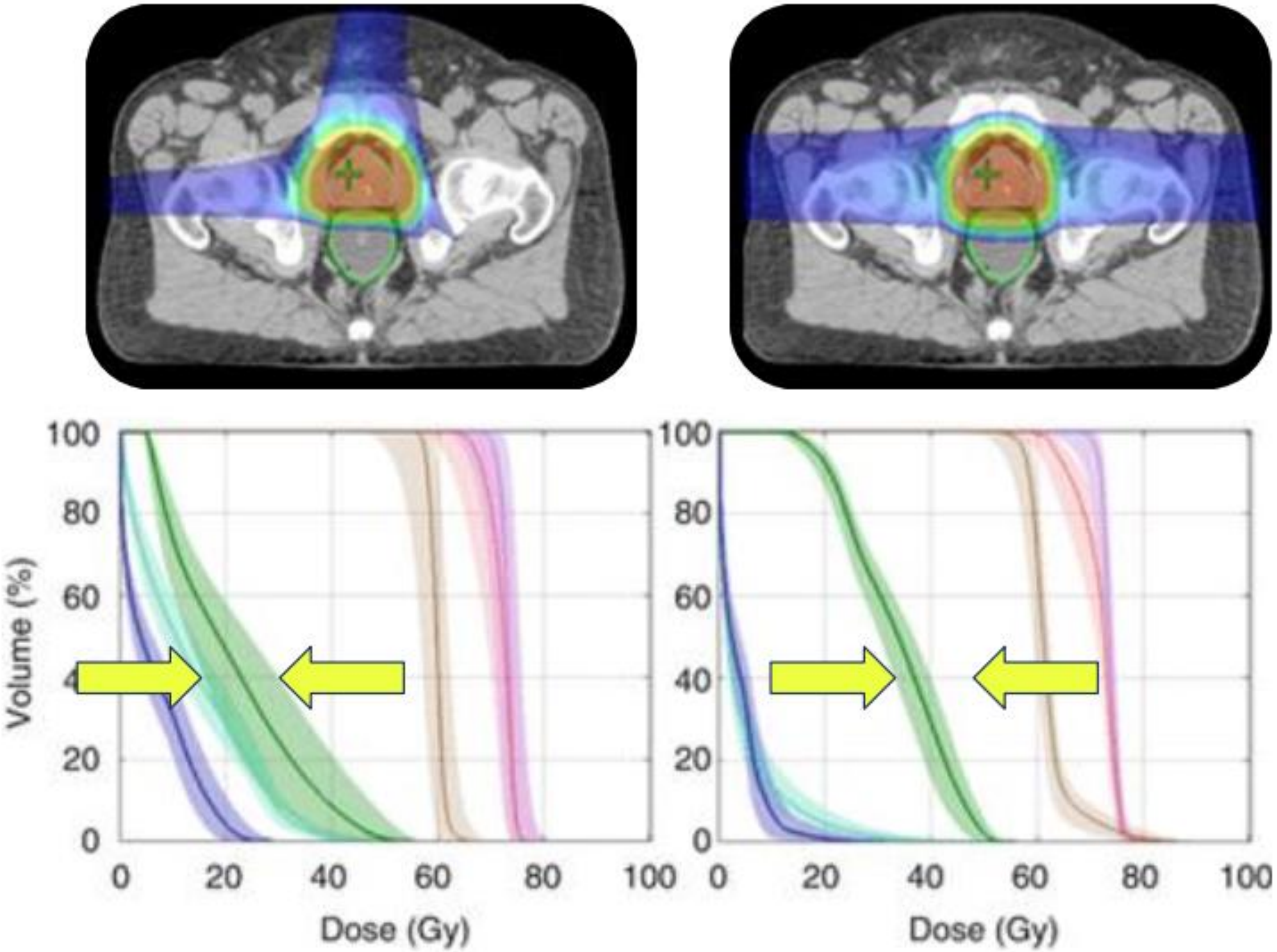
● Allow the planning system to score robustness on a spot-by-spot basis and **how one spot will affect the overall sensitivity to potential plan degradation**

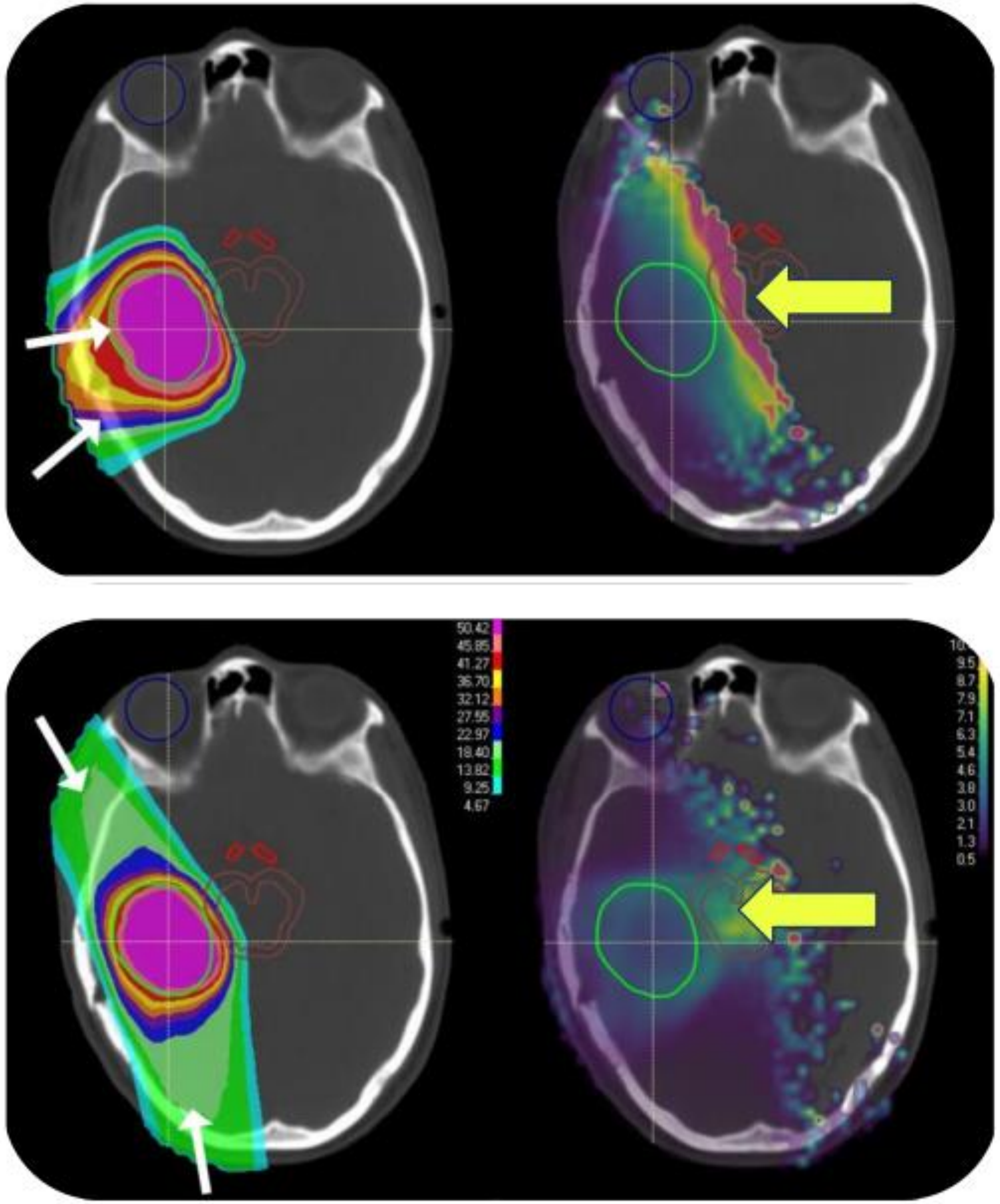
● **Spots with *poor* robustness** (high sensitivity to plan degradation) **will be penalized** by iteratively decreasing and, potentially, eliminating their intensity

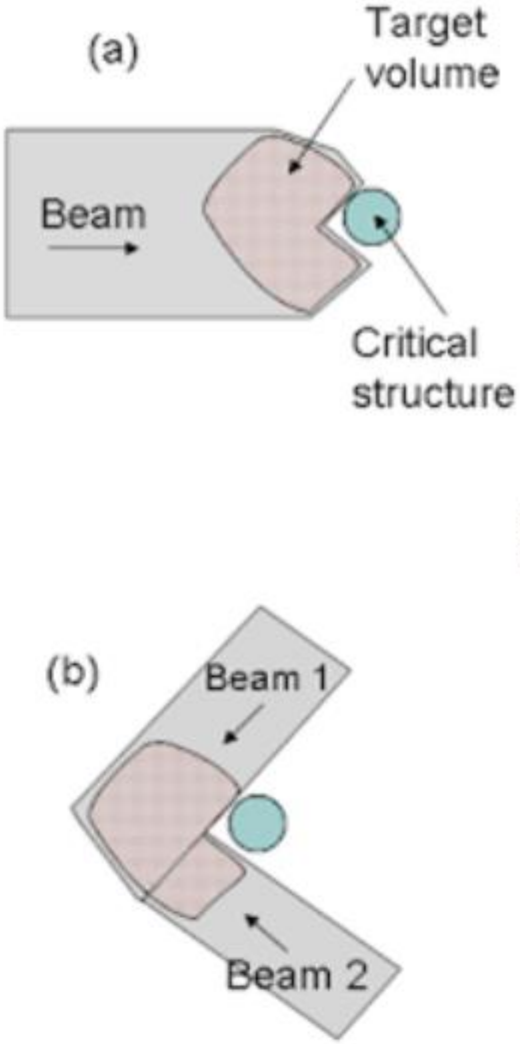


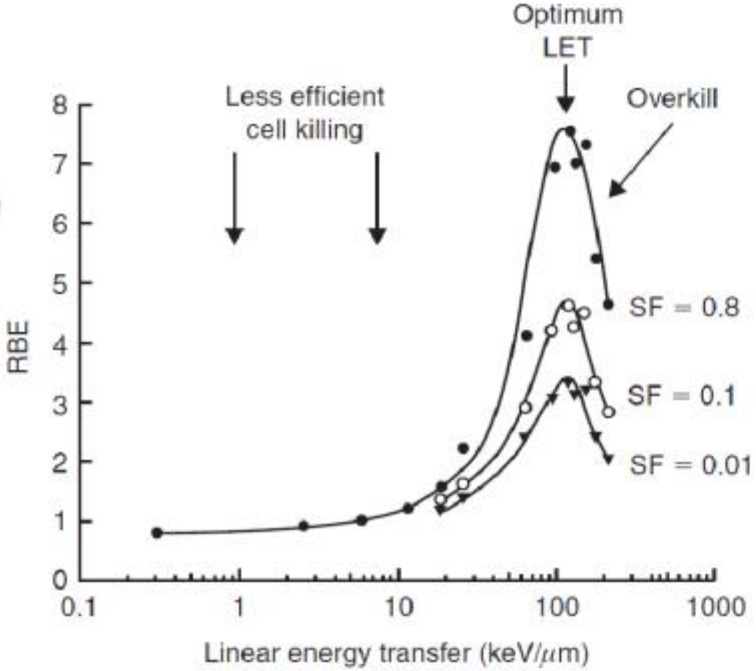
$$\text{Minimize C:}\quad C = \sum_{\text{Structures}} \left[\left(\frac{\text{Structure importance}}{\#\text{ structure voxels}}\right) \sum_{\text{Structure Voxels}} \left((\text{Applicable penalties})(\text{Rx Dose} - \text{Actual Dose})^2\right)\right]$$

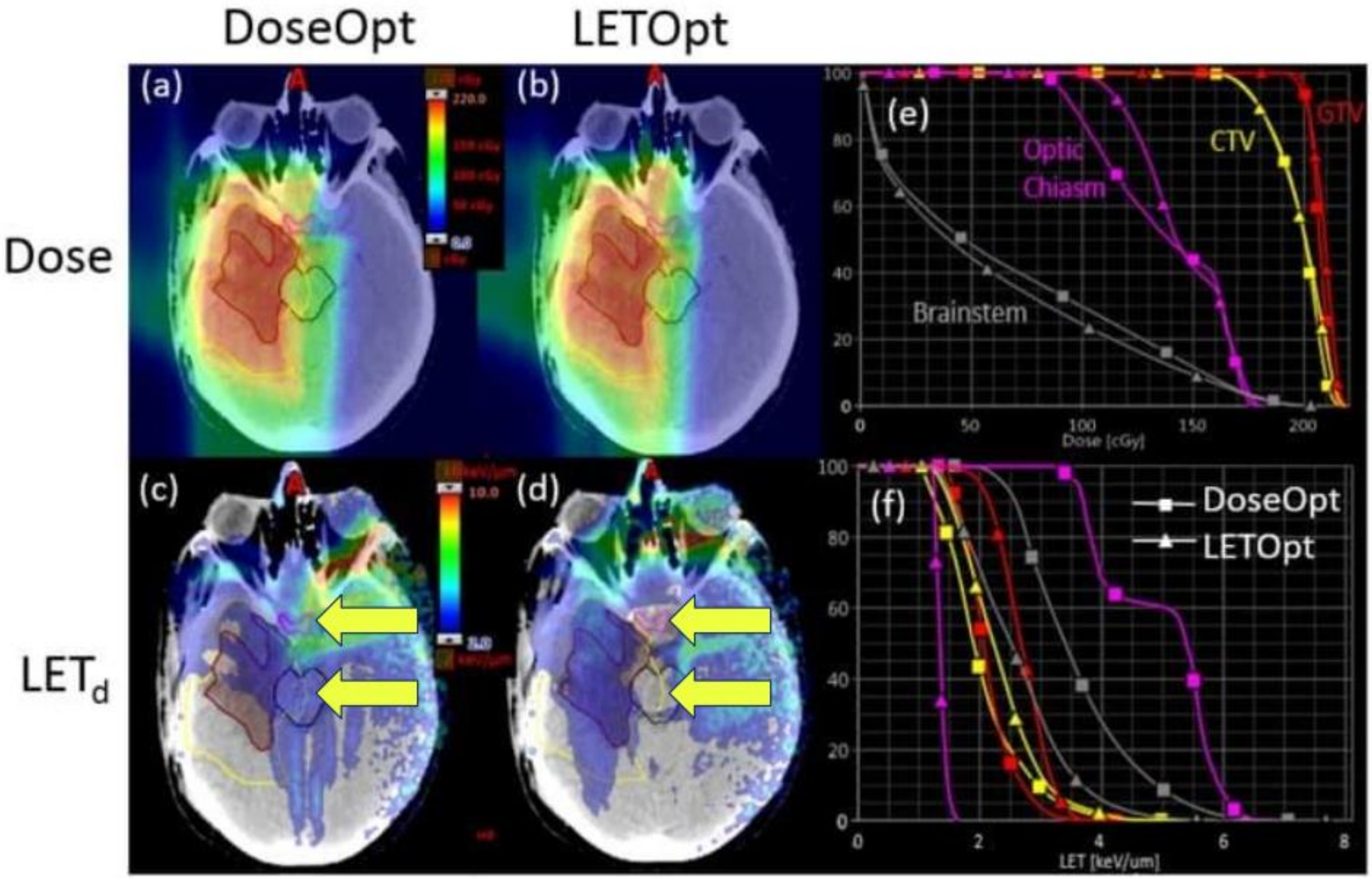
Beam arrangements




50.42
45.85
41.27
36.70
32.12
27.55
22.97
18.40
13.82
9.25
4.67
9.5
8.7
7.9
7.1
6.3
5.4
4.6
3.8
3.0
2.1
1.3
0.5

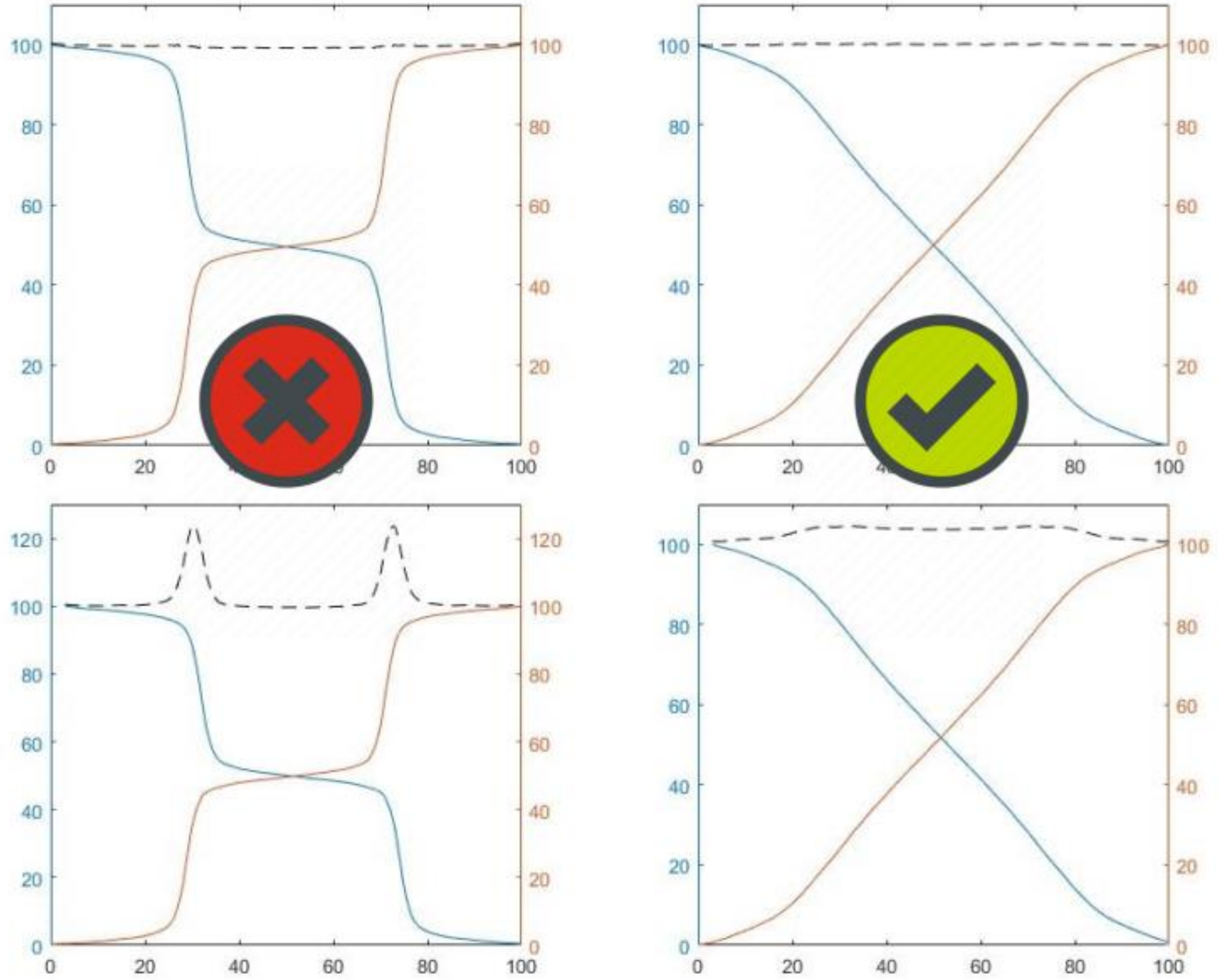

(a)
Target volume
Beam
Critical structure
(b)
Beam 1
Beam 2


Optimum LET
Less efficient cell killing
Overkill
RBE
SF = 0.8
SF = 0.1
SF = 0.01
Linear energy transfer (keV/μm)



DoseOpt
LETOpt
Dose
LET$_d$
(a)
(b)
(c)
(d)
(e)
(f)
GTV
CTV
Optic
Chiasm
Brainstem
Dose [cGy]
LET [keV/um]
DoseOpt
LETOpt

CNAO



CNAO

4-D optimization to mitigate **intra-fraction** motion

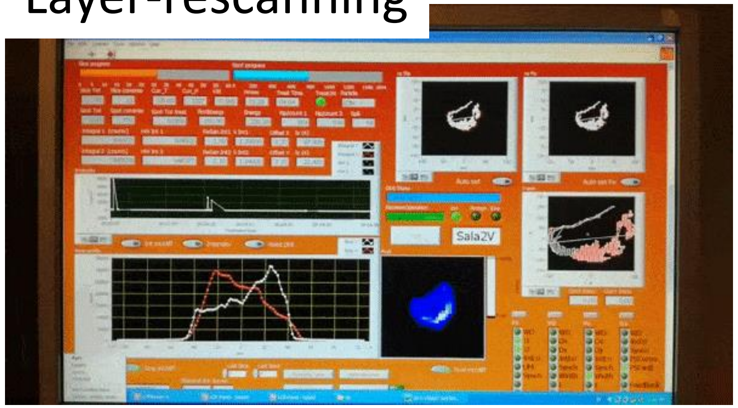
Compression

Motion reduction due to shallow compression

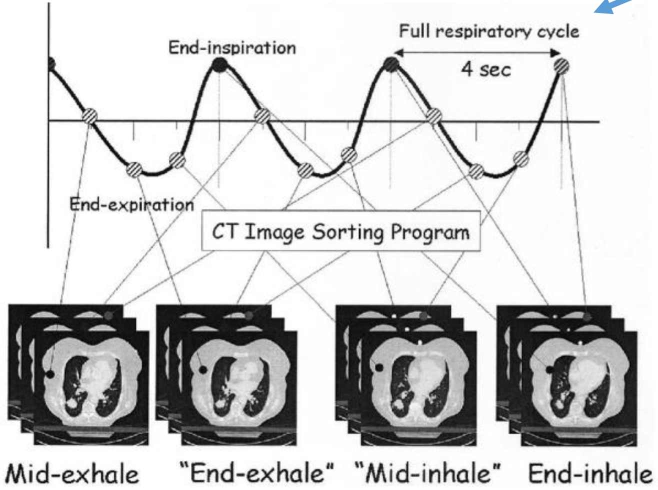
Gating

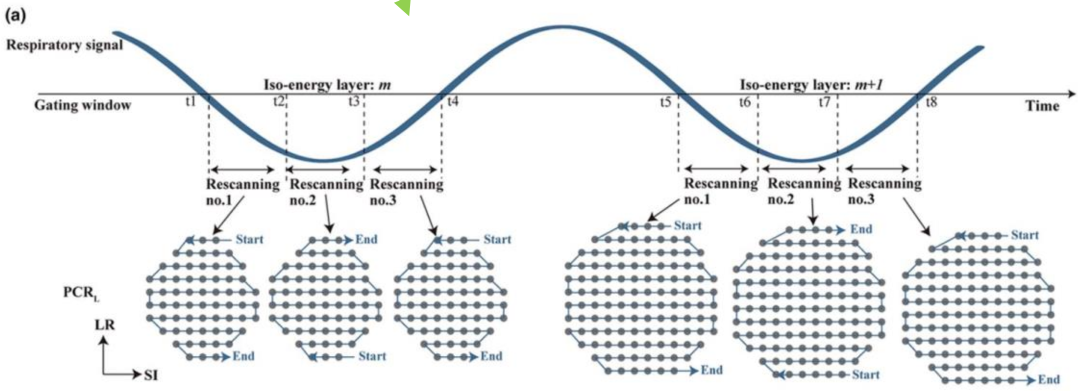
Image and treat tumor at specific respiratory phase

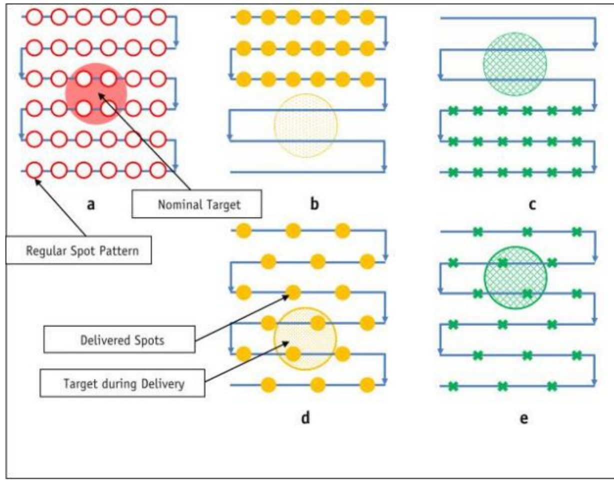
Layer-rescanning



For each tumor section deliver 1/5 of the dose for 5 times (to reduce local over/under dosage points)



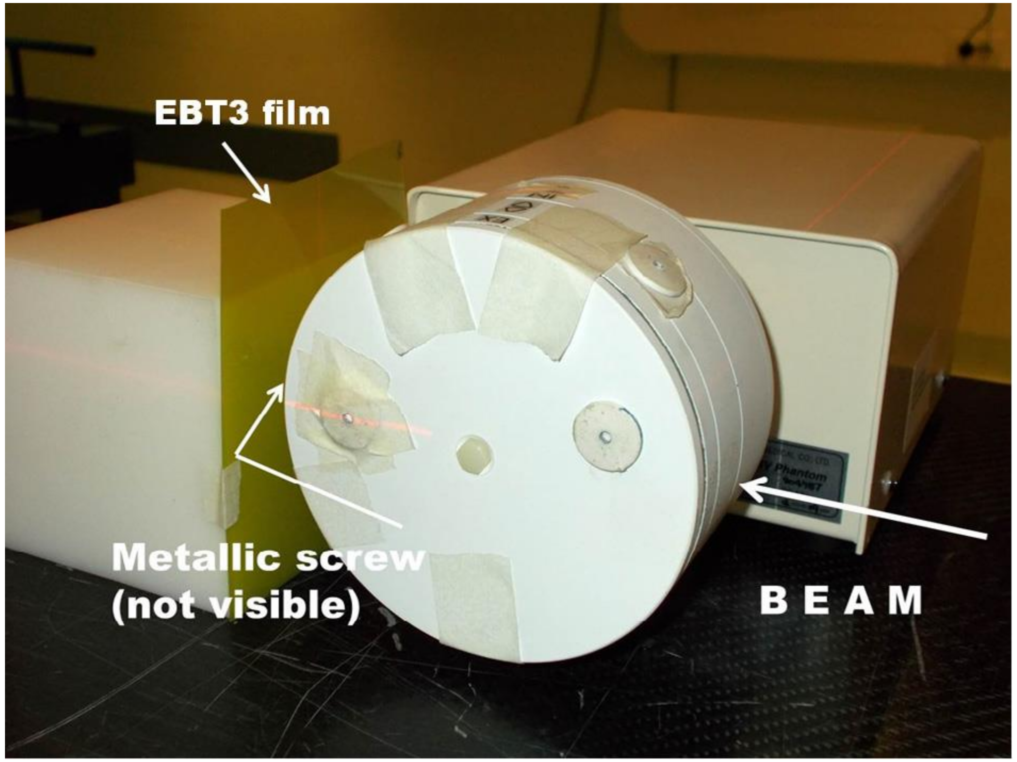


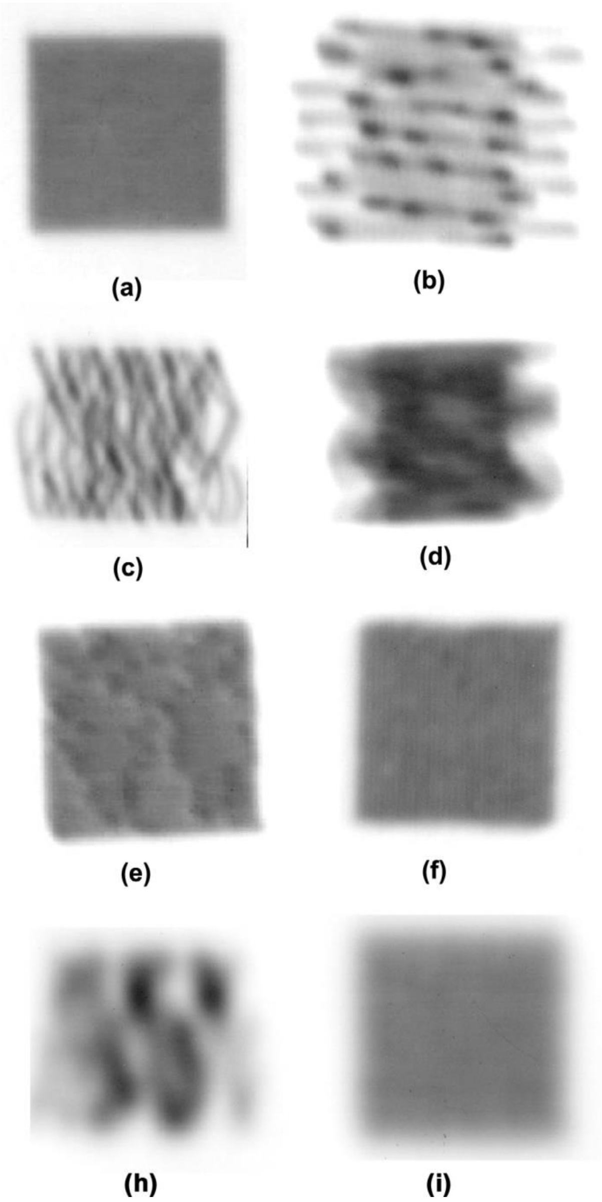


Commissioning of the 4-D treatment delivery system for organ motion management in synchrotron-based scanning ion beams

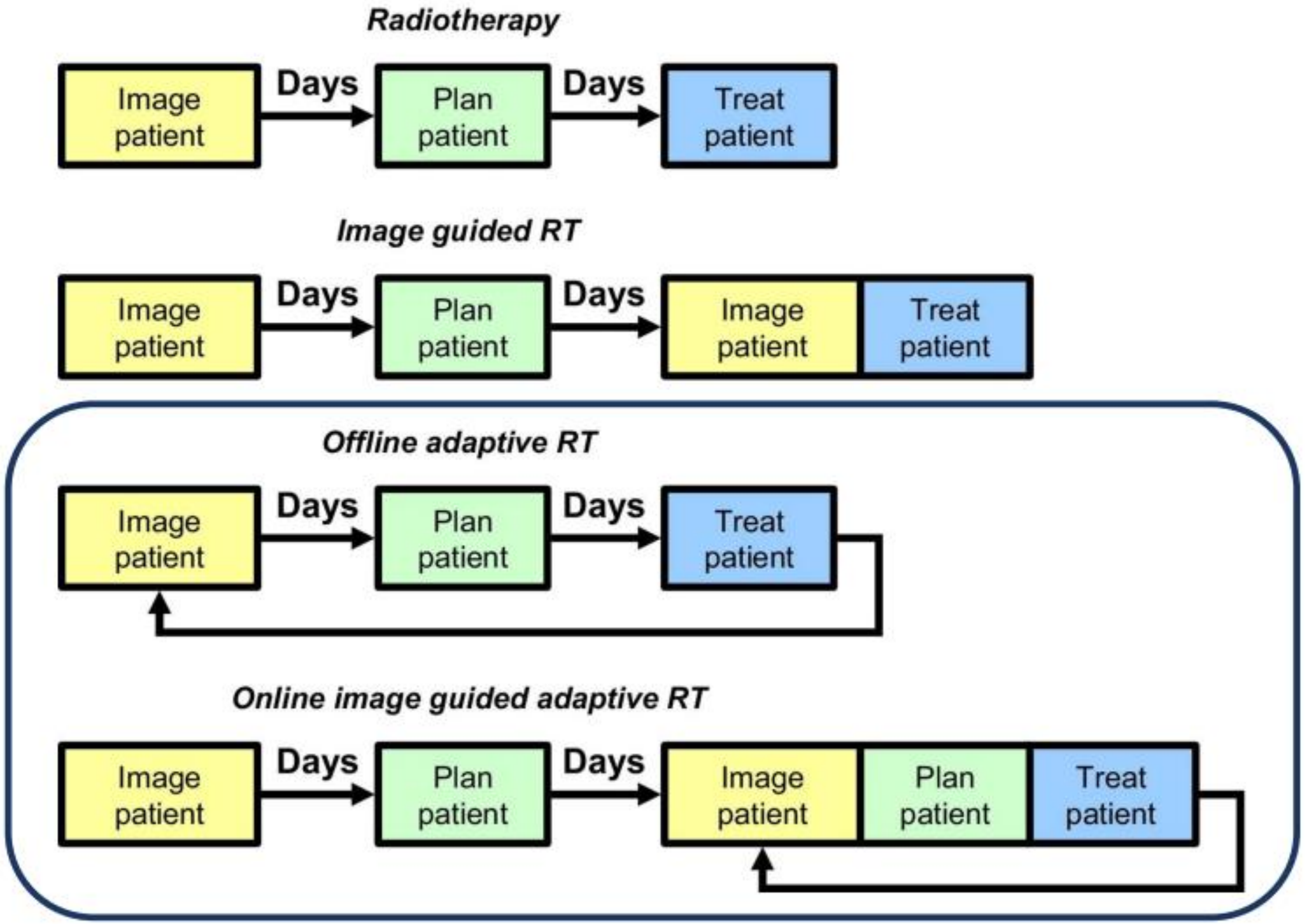
CrossMark

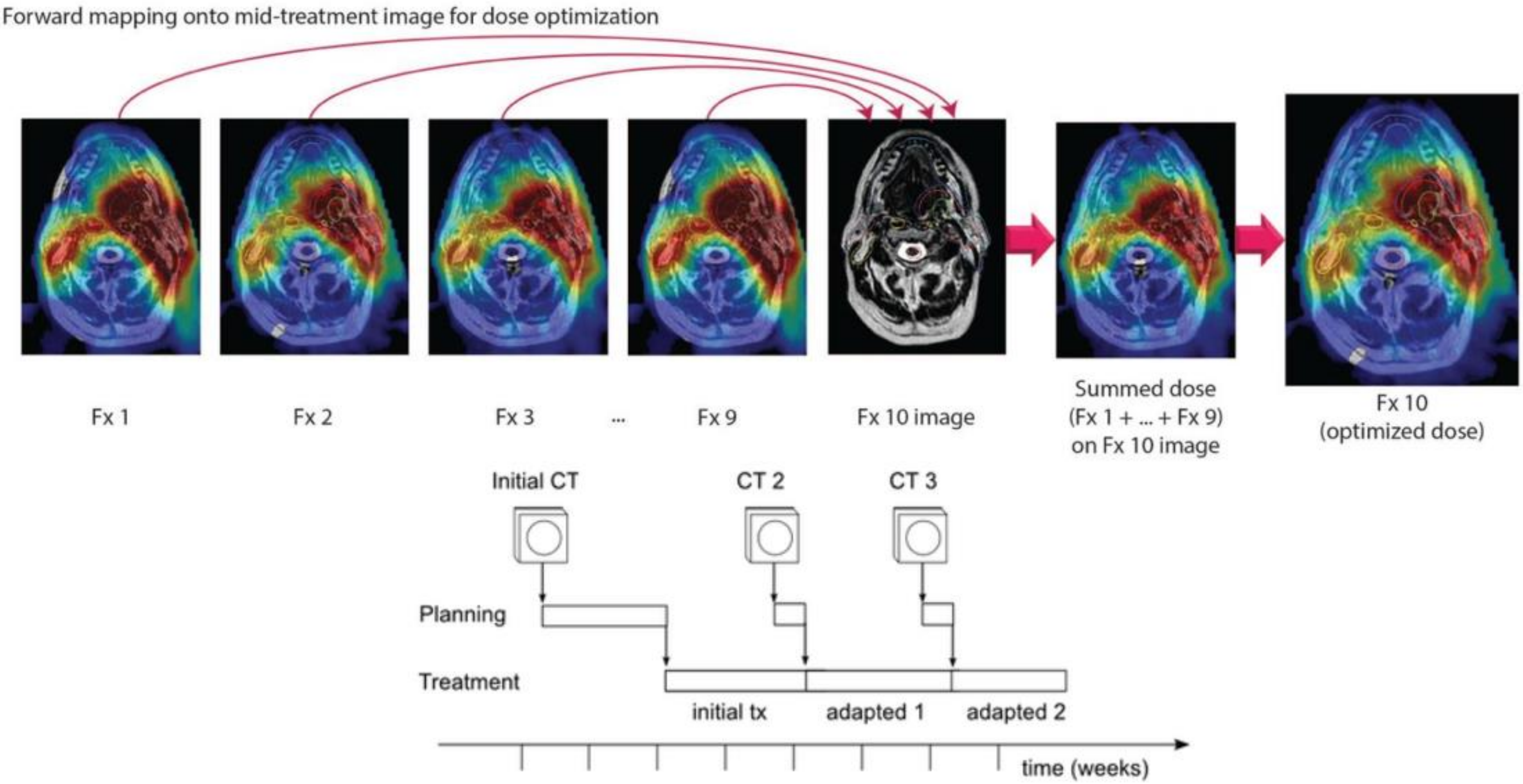
Mario Ciocca [a,*], Alfredo Mirandola [a], Silvia Molinelli [a], Stefania Russo [a], Edoardo Mastella [a], Alessandro Vai [a], Andrea Mairani [a], Giuseppe Magro [a], Andrea Pella [a], Marco Donetti [a], Francesca Valvo [a], Piero Fossati [a,b], Guido Baroni [a,c]





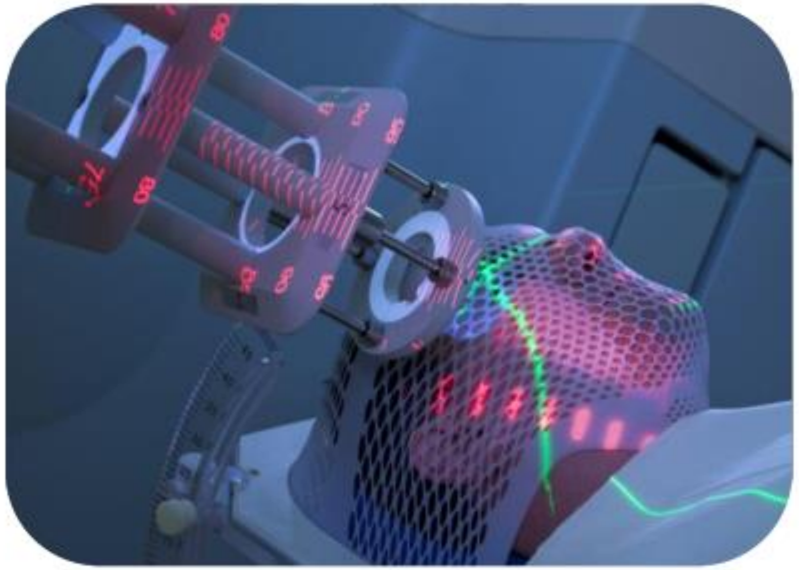
Adaptive replanning

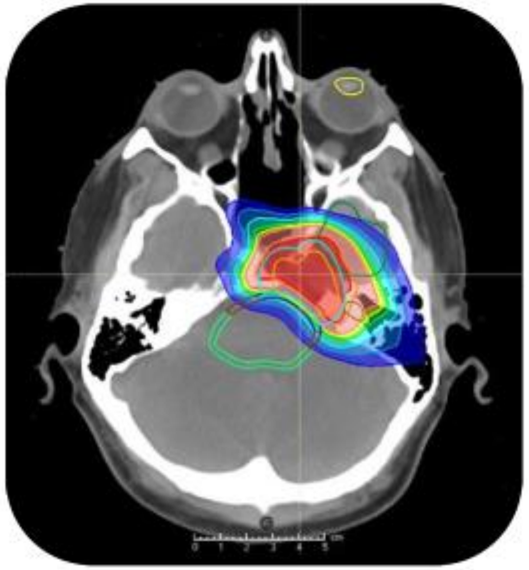



Forward mapping onto mid-treatment image for dose optimization
Fx 1
Fx 2
Fx 3
...
Fx 9
Fx 10 image
Summed dose
(Fx 1 + ... + Fx 9)
on Fx 10 image
Fx 10
(optimized dose)
Initial CT
CT 2
CT 3
Planning
Treatment
initial tx
adapted 1
adapted 2
time (weeks)

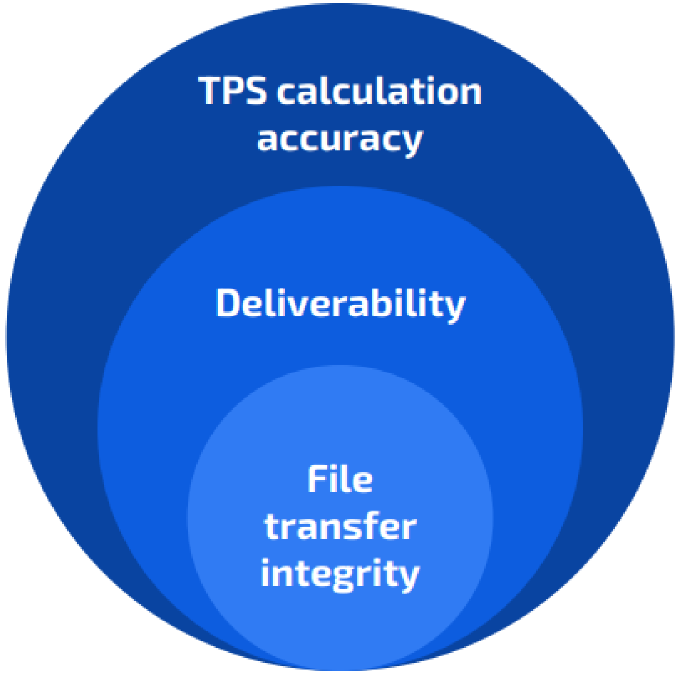
Plan verification strategies

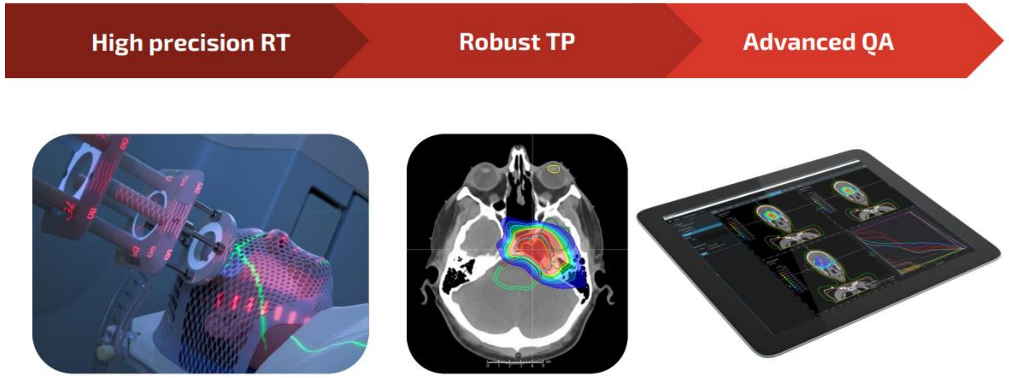
High precision RT | Robust TP | Advanced QA

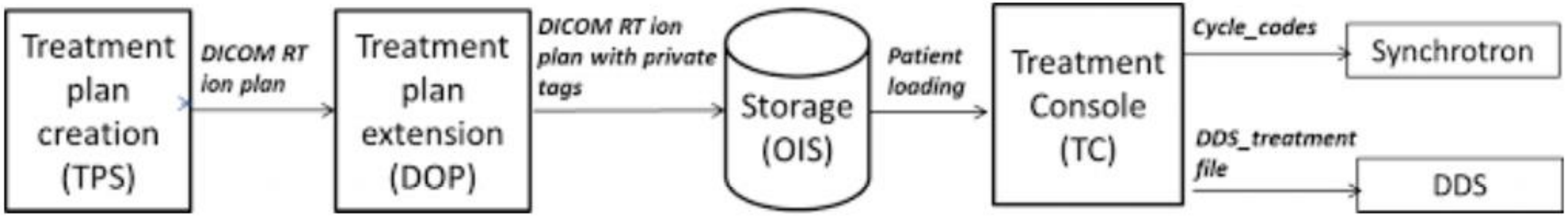




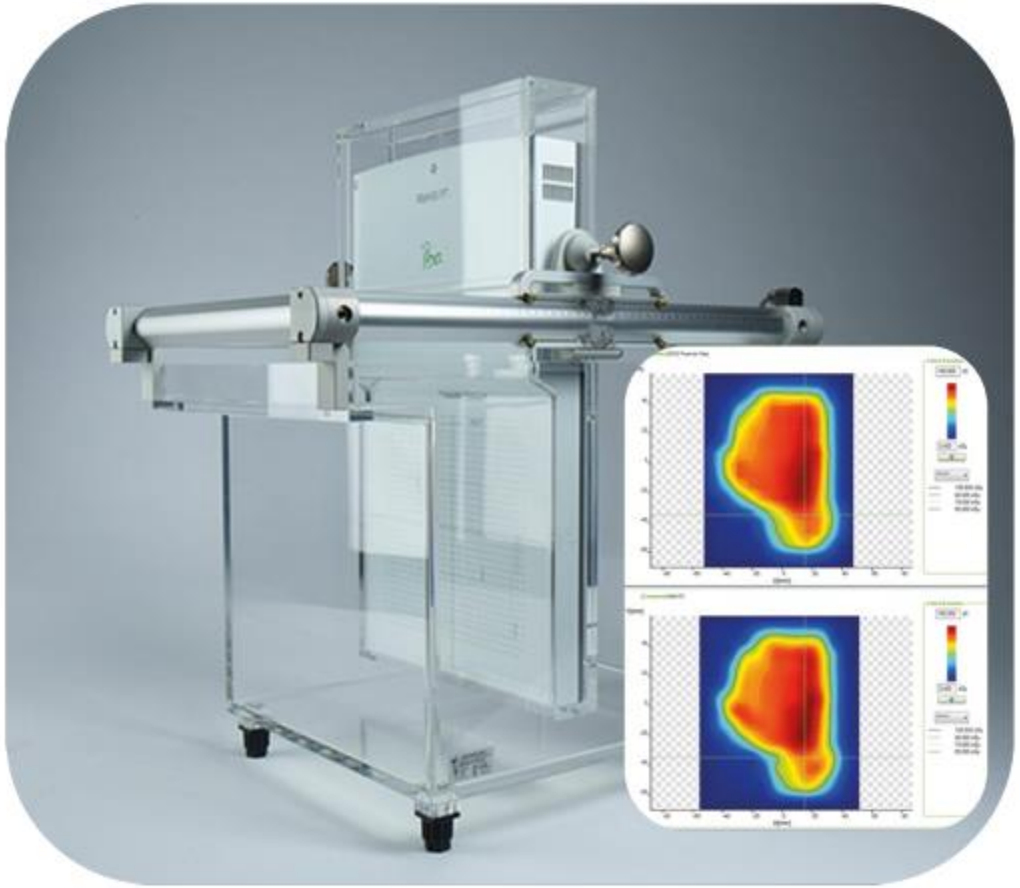
Plan verification strategies

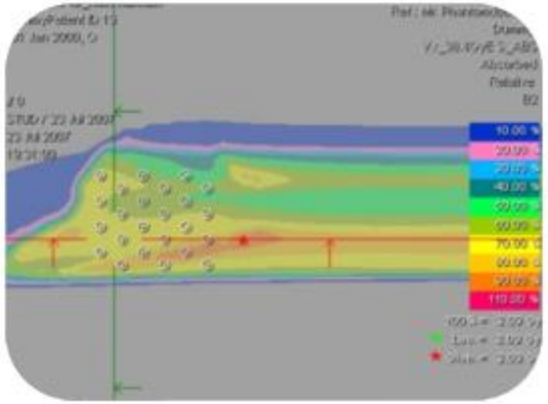






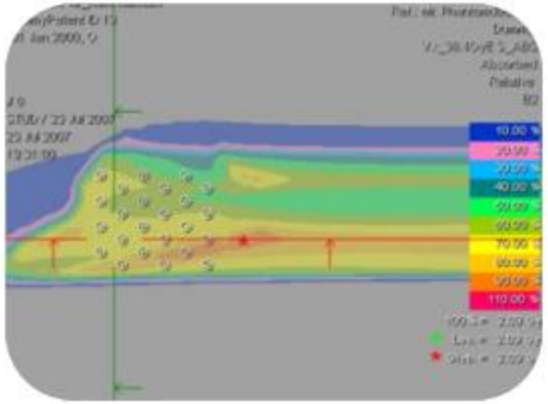
Experimental verification



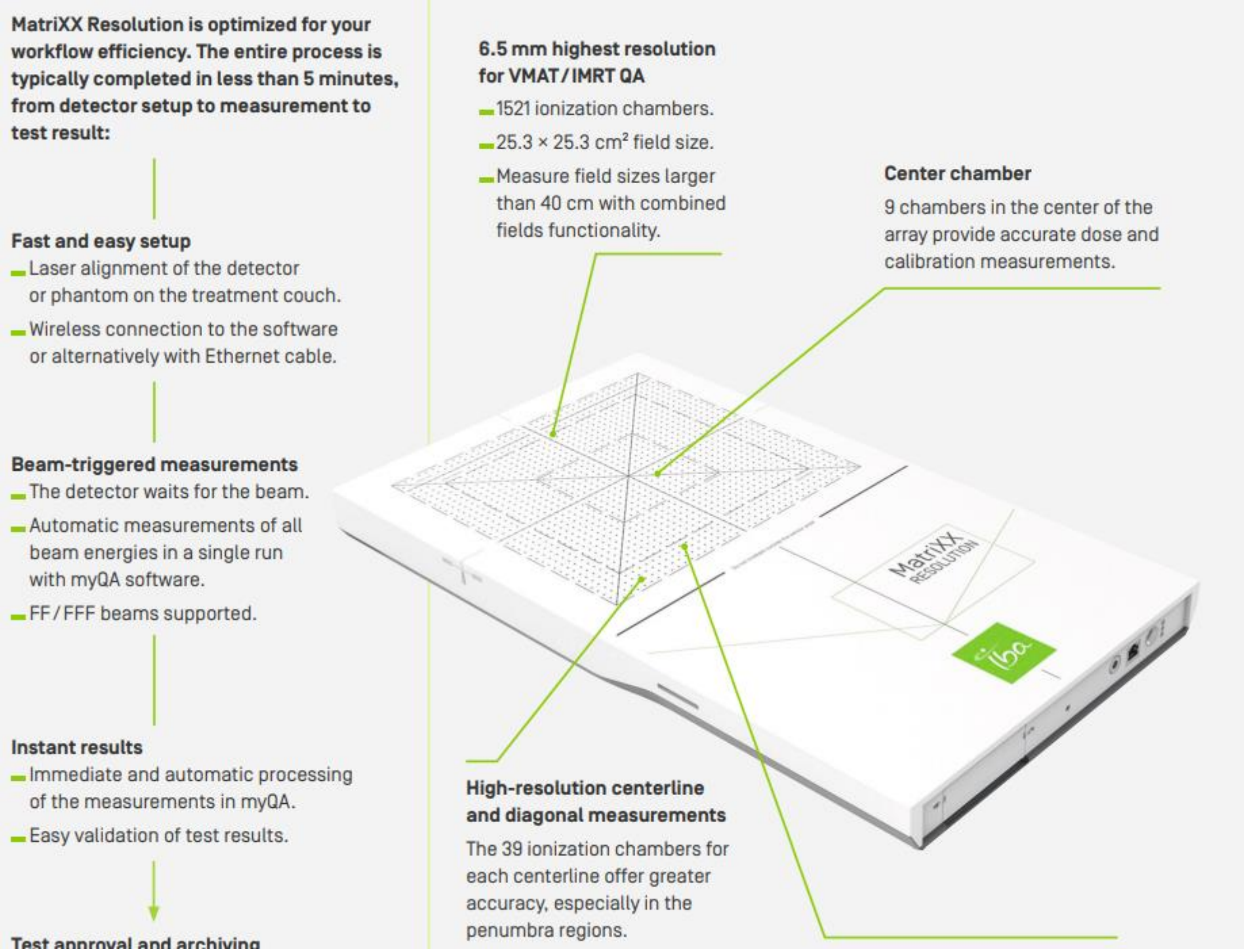


Experimental verification

- 3D evaluation
- Point-by-point deviation
- Few dose points available
- Not suitable for highly inhomogeneous regions
- Poor sensitivity to range variation
- Not sensitive to delivery failures far from the measured points
- Time consuming



Experimental verification



- 2D (or quasi-3D) evaluation
- Hundreds of points available
- Limited spatial resolution
- Tools for handling steep dose gradients within the plane
- Not sensitive to range variations
- Not sensitive to delivery failures far from the measured points
- Time consuming

In-silico verification

- **Independent dose calculation engine using the patient CT**
- 3D evaluation
- Millions of points available
- Same resolution of the planned dose matrix
- Tools for handling steep dose gradients in 3D
- Highly sensitive to range variations
- Highly sensitive to delivery failures
- Fast and unique solution in sight of daily plan adaptatio

RESEARCH ARTICLE

MEDICAL PHYSICS

Dosimetric validation of a GPU-based dose engine for a fast in silico patient-specific quality assurance program in light ion beam therapy

Giuseppe Magro[1] | Martina Fassi[2] | Alfredo Mirandola[1] | Eleonora Ross
Silvia Molinelli[1] | Stefania Russo[1] | Alessia Bazani[1] | Alessandro Vai[1]
Mario Ciocca[1] | Marco Donetti[1] | Andrea Mairani[1,3]

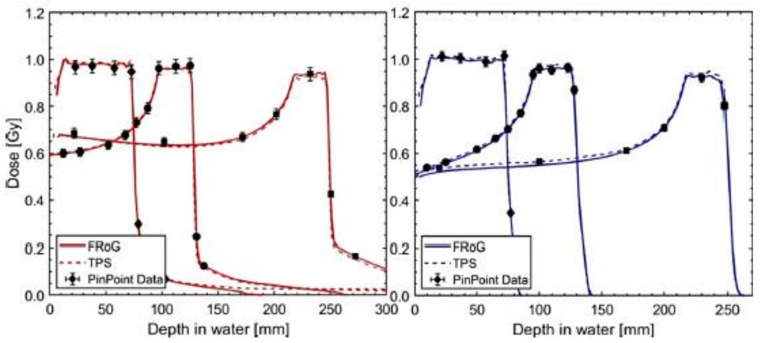


FIGURE 4 Pinpoint chamber measurements (points) against FRoG (solid line) and TPS (dashed lines) for three refere namely S6C4, S3C11, and S3C23 (S = size in cm, C = center in cm), with the former requiring a 3-cm thick range shifter. TF based on an analytical PB algorithm for carbon ions (red lines) and on a Monte Carlo algorithm for protons (blue lines)

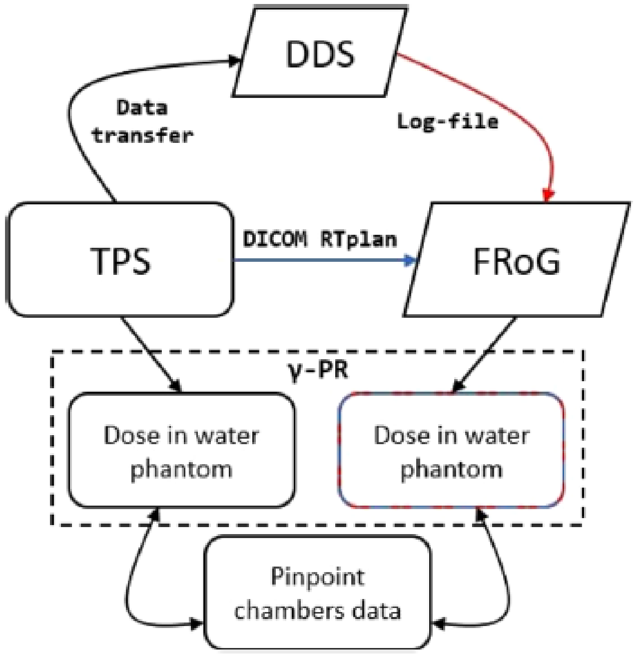
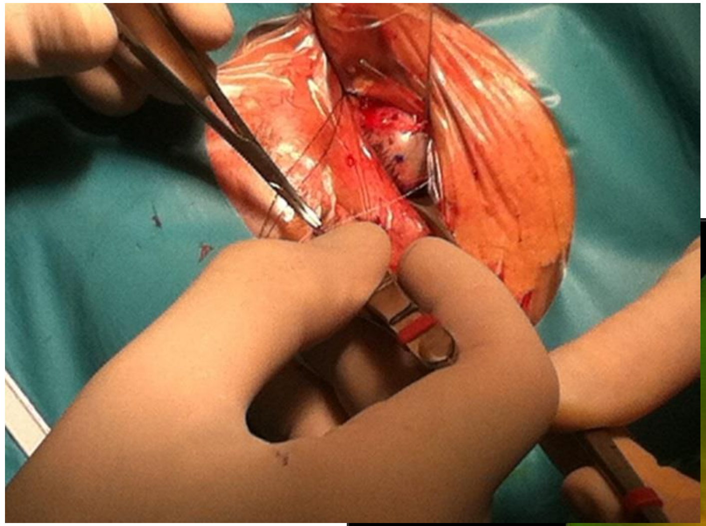
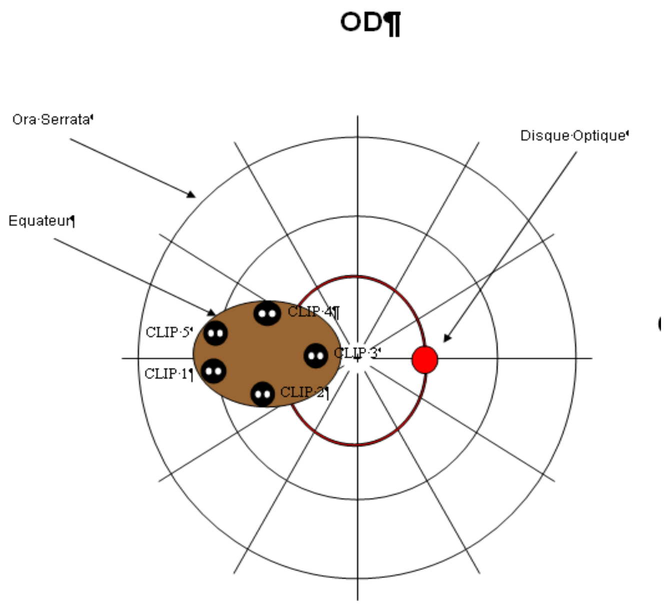


FIGURE 1 Schematic representation of the FRoG validation workflow based on machine *log-files*, DICOM RTplans, and pinpoint chambers measurements. Both the *log-file* (red lines) and the DICOM RTplan (blue lines) file are inputs into the FRoG's "water phantom" box in the diagram

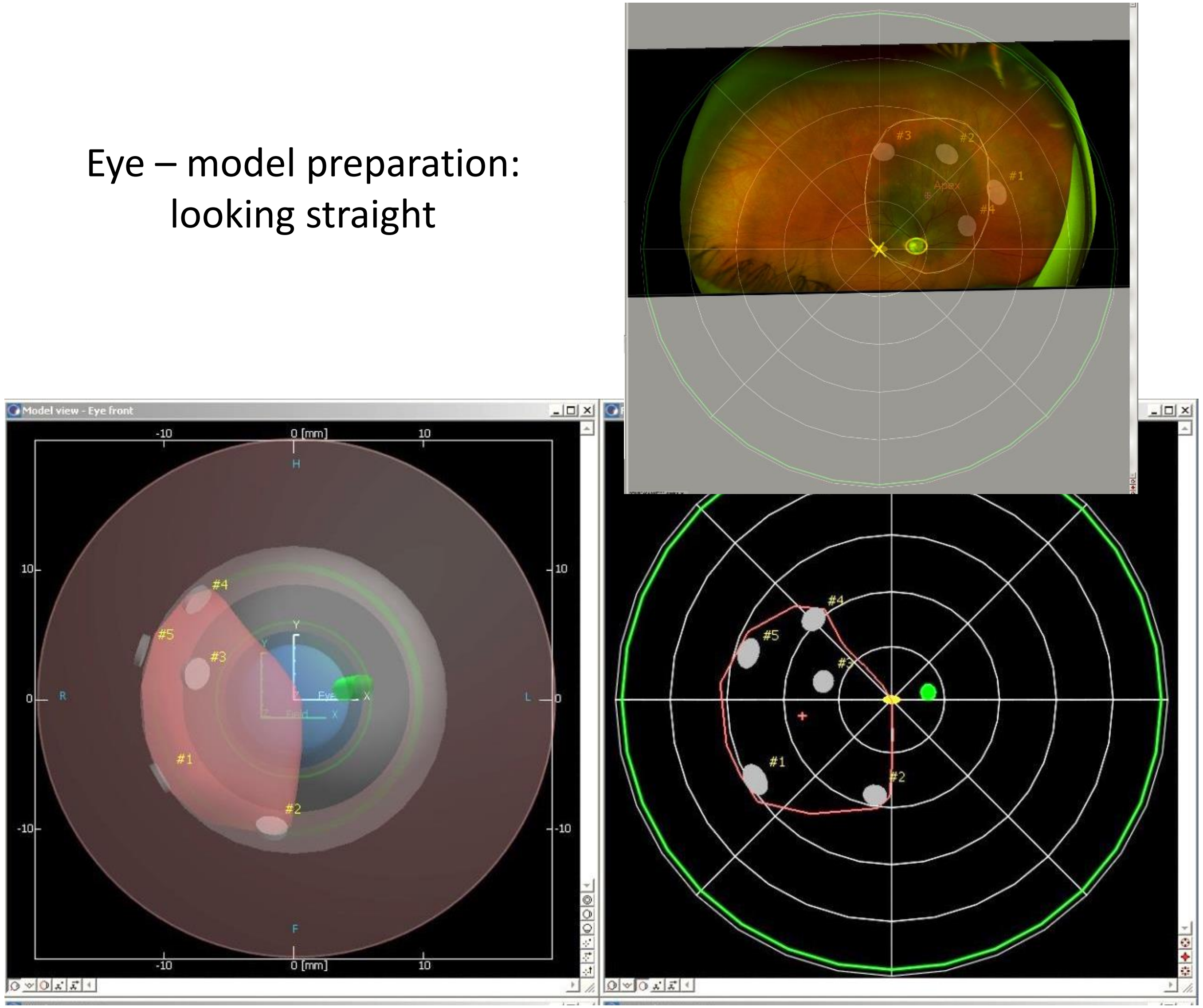
Model-based (no CT) PT treatment: eye-melanoma



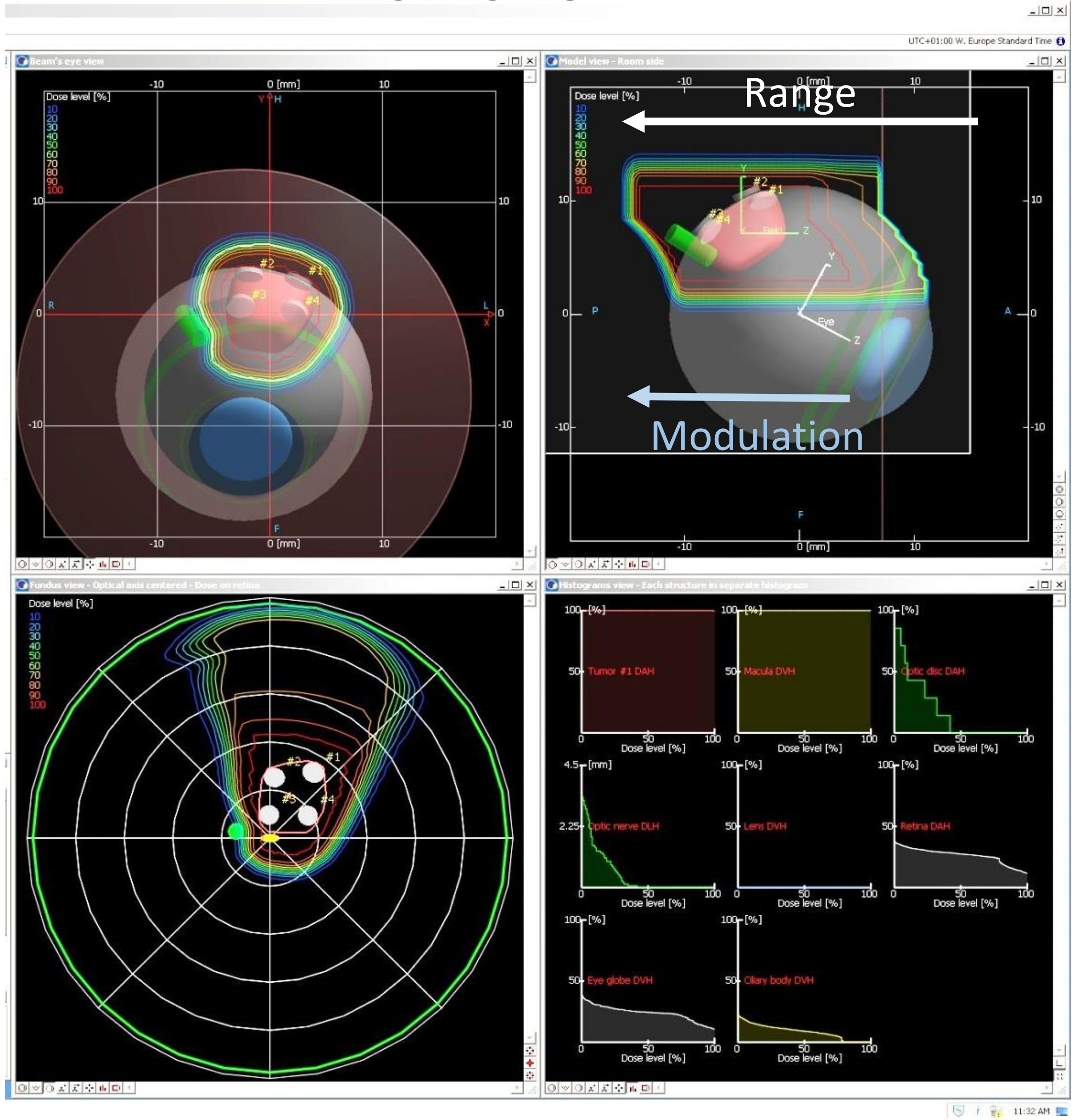


Eye-melanoma treatment

Eye – model preparation: looking straight



Plan preparation: eye staring at gazing angle direction



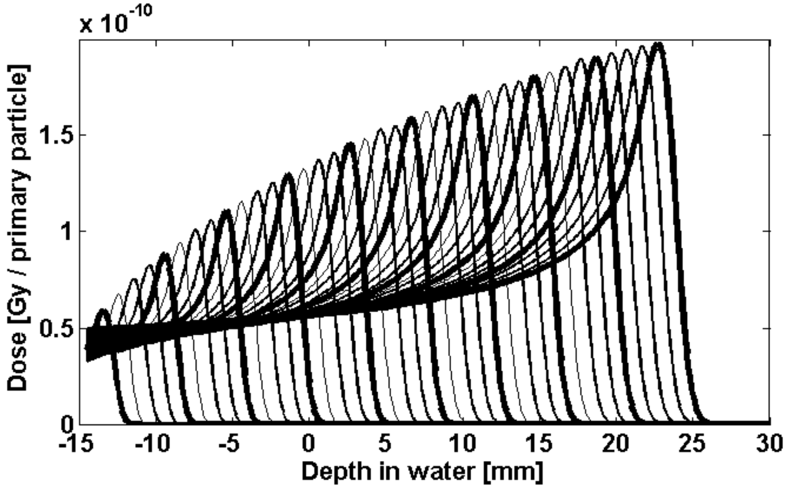
Eye-melanoma treatment

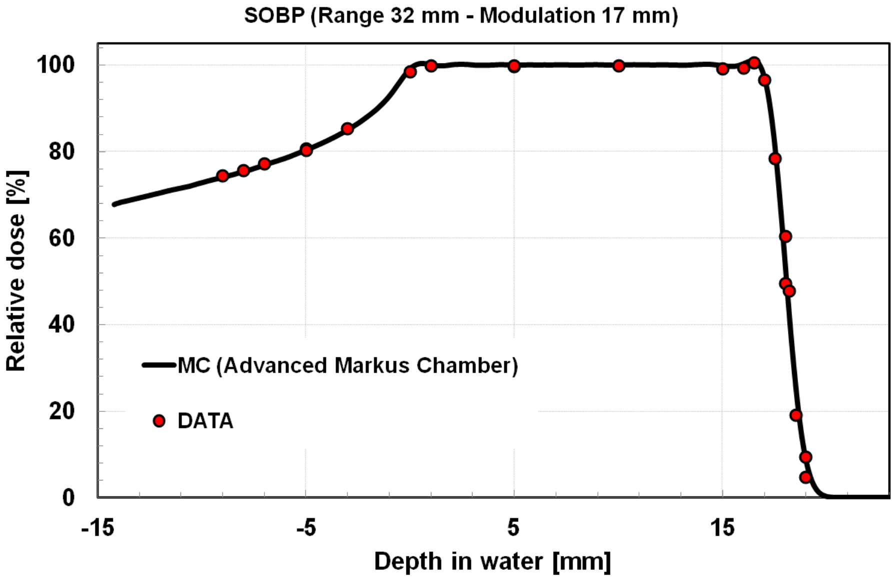
Design and commissioning of the non-dedicated scanning proton beamline for ocular treatment at the synchrotron-based CNAO facility

Med. Phys. 46 (4), April 2019

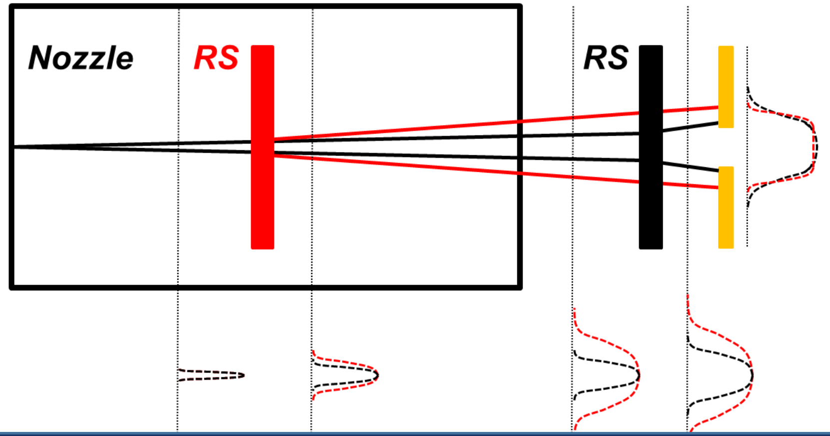
Mario Ciocca, Giuseppe Magro, Edoardo Mastella,[a] Andrea Mairani, Alfredo Mirandola, Silvia Molinelli, Stefania Russo, Alessandro Vai, and Maria Rosaria Fiore
Fondazione CNAO, strada Campeggi 53, 27100 Pavia, Italy

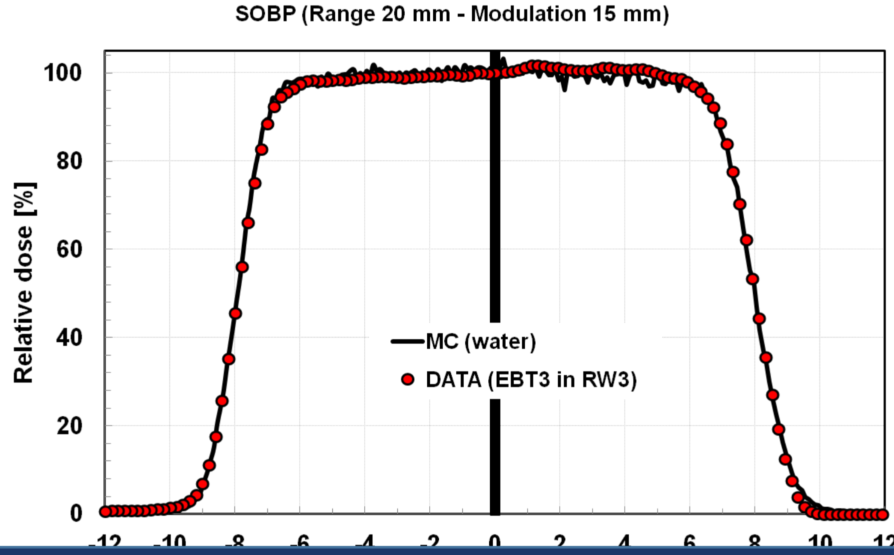
MC optimized PB weights



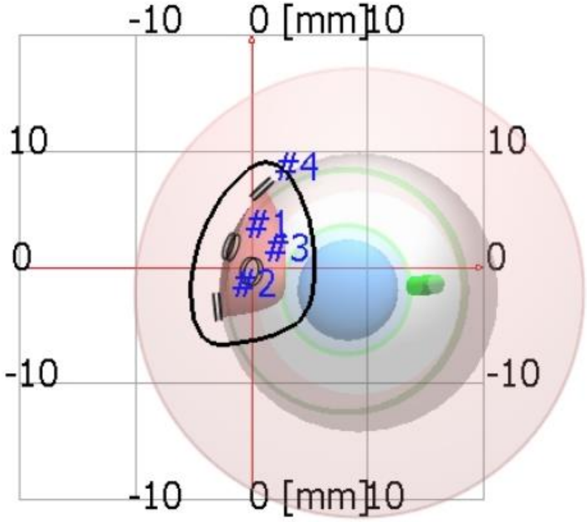


Beamline optimization





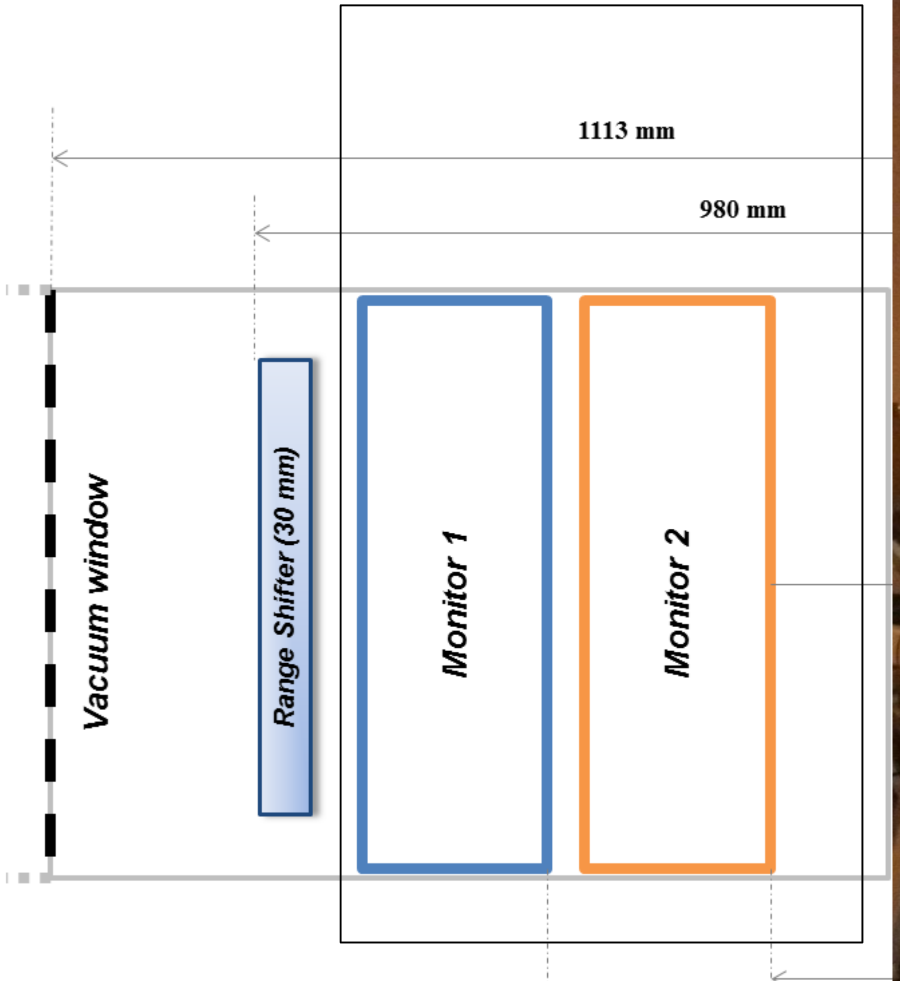
CNAO

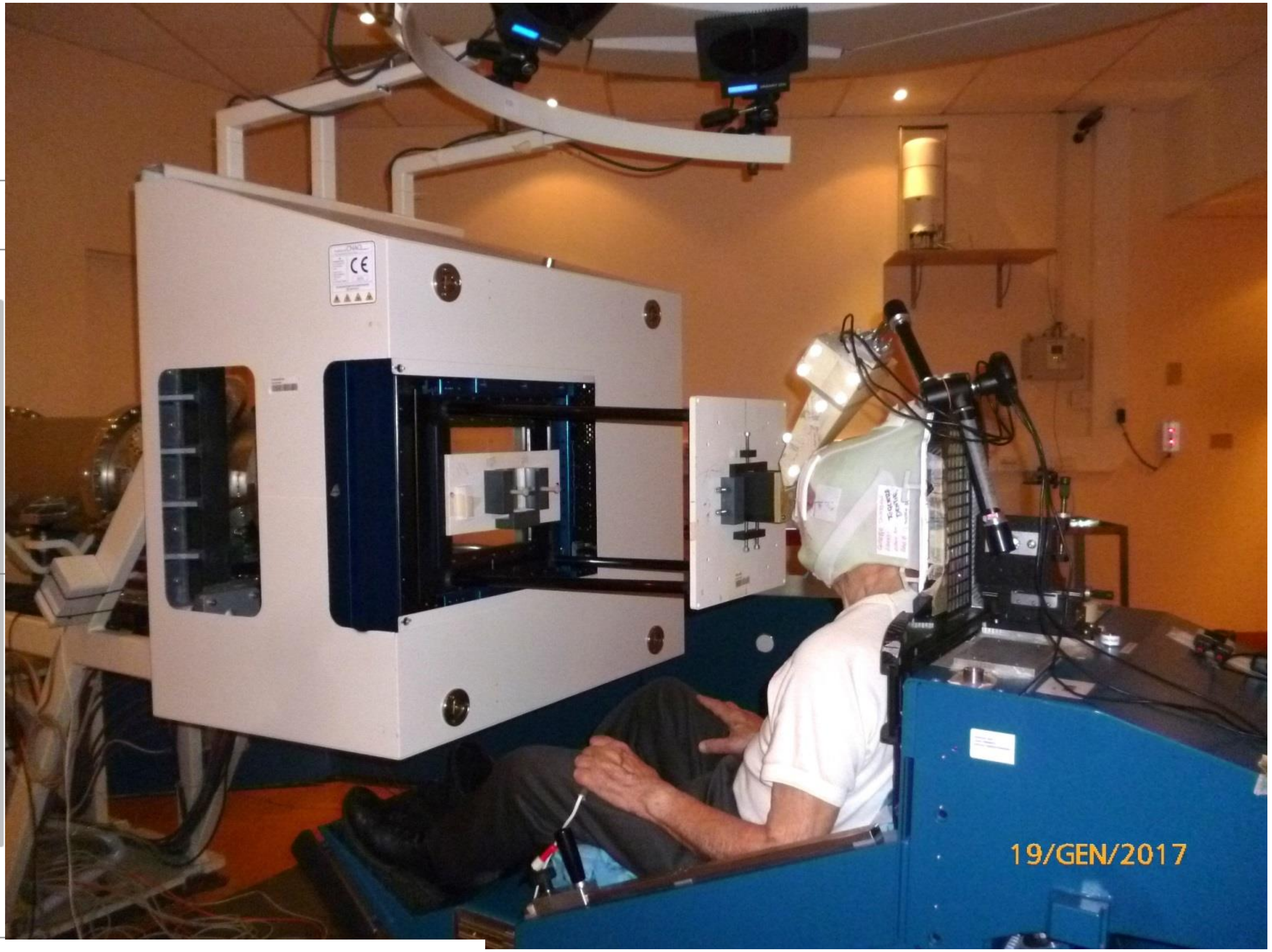


INFN-Pavia

Individualized bras collimator (aperture)

Treatment delivery





- ✓ ≈ 400 pts treated so far (since Aug 2016)
- ✓ about 3’ delivery time
- ✓ 60 Gy (RBE) prescribed in 4 daily fractions

On-going studies for medical physicist @ CNAO… improving plan quality outcome

Radiotherapy and Oncology 107 (2013) 267–273

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Proton radiotherapy

Selection of patients for radiotherapy with protons aiming at reduction of side effects: The model-based approach

Johannes A. Langendijk[a,*], Philippe Lambin[b], Dirk De Ruysscher[c], Joachim Widder[a], Mike Bos[d], Marcel Verheij[e]

[a]Department of Radiation Oncology, University Medical Center Groningen, University of Groningen, The Netherlands; [b]Department of Radiation Oncology (MAASTRO Clinic) & Research Institute GROW, University Hospital Maastricht, The Netherlands; [c]Department of Radiation Oncology, University Hospitals Leuven/KU Leuven, Belgium; [d]Health Council of the Netherlands; [e]Department of Radiotherapy, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, The Netherlands

Radiotherapy and Oncology 121 (2016) 381–386

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Model based patient selection

Toward a model-based patient selection strategy for proton therapy: External validation of photon-derived normal tissue complication probability models in a head and neck proton therapy cohort

Pierre Blanchard[a,c], Andrew J. Wong[a], G. Brandon Gunn[a], Adam S. Garden[a], Abdallah S.R. Mohamed[a], David I. Rosenthal[a], Joseph Crutison[a], Richard Wu[b], Xiaodong Zhang[b], X. Ronald Zhu[b], Radhe Mohan[b], Mayankkumar V. Amin[b], C. David Fuller[a], Steven J. Frank[a,*]

[a]Department of Radiation Oncology; [b]Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, Houston, USA; [c]Department of Radiation Oncology, Gustave Roussy Cancer Campus, Villejuif, France

cancers

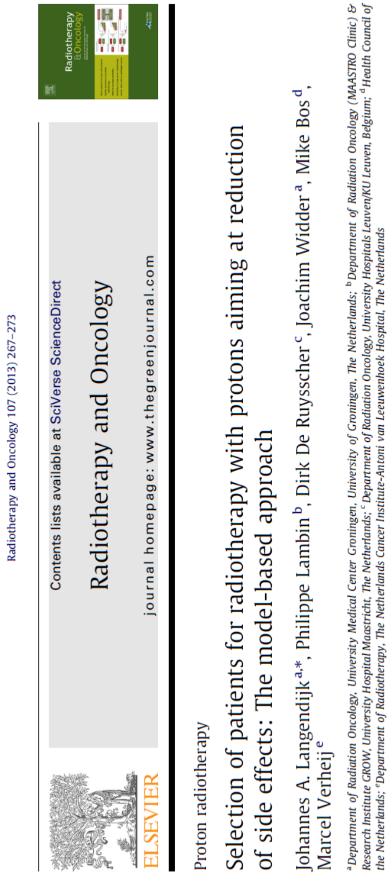
MDPI

Article

Proton Radiation Therapy for Nasopharyngeal Cancer Patients: Dosimetric and NTCP Evaluation Supporting Clinical Decision

Alessandro Vai[1,*], Silvia Molinelli[1,†], Eleonora Rossi[1,†], Nicola Alessandro Iacovelli[2,*], Giuseppe Magro[1], Anna Cavallo[2], Emanuele Pignoli[2], Tiziana Rancati[2], Alfredo Mirandola[2], Stefania Russo[1], Rossana Ingargiola[1], Barbara Vischioni[1], Maria Bonora[1], Sara Ronchi[1], Mario Ciocca[1] and Ester Orlandi[1]

Traslate better dose distribution to an expected reduced risk of toxicity….


Radiotherapy and Oncology 107 (2013) 267–273
Contents lists available at SciVerse ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com
ELSEVIER
Proton radiotherapy
Selection of patients for radiotherapy with protons aiming at reduction of side effects: The model-based approach
Johannes A. Langendijk [a,*], Philippe Lambin [b], Dirk De Ruysscher [c], Joachim Widder [a], Mike Bos [d], Marcel Verheij [e]
[a] Department of Radiation Oncology, University Medical Center Groningen, University of Groningen, The Netherlands; [b] Department of Radiation Oncology (MAASTRO Clinic) & Research Institute GROW, University Hospital Maastricht, The Netherlands; [c] Department of Radiation Oncology, University Hospitals Leuven/KU Leuven, Belgium; [d] Health Council of the Netherlands; [e] Department of Radiotherapy, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, The Netherlands

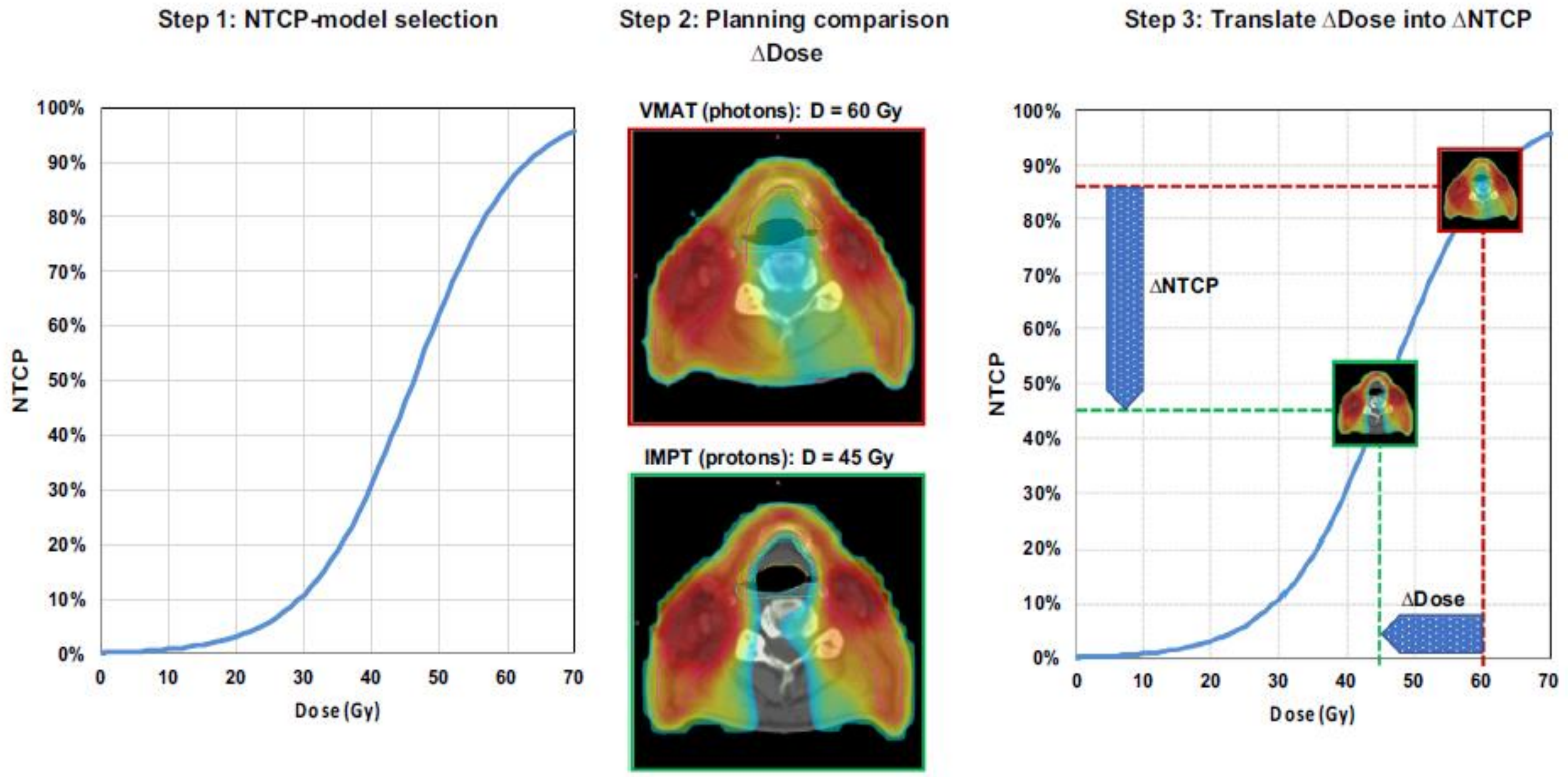
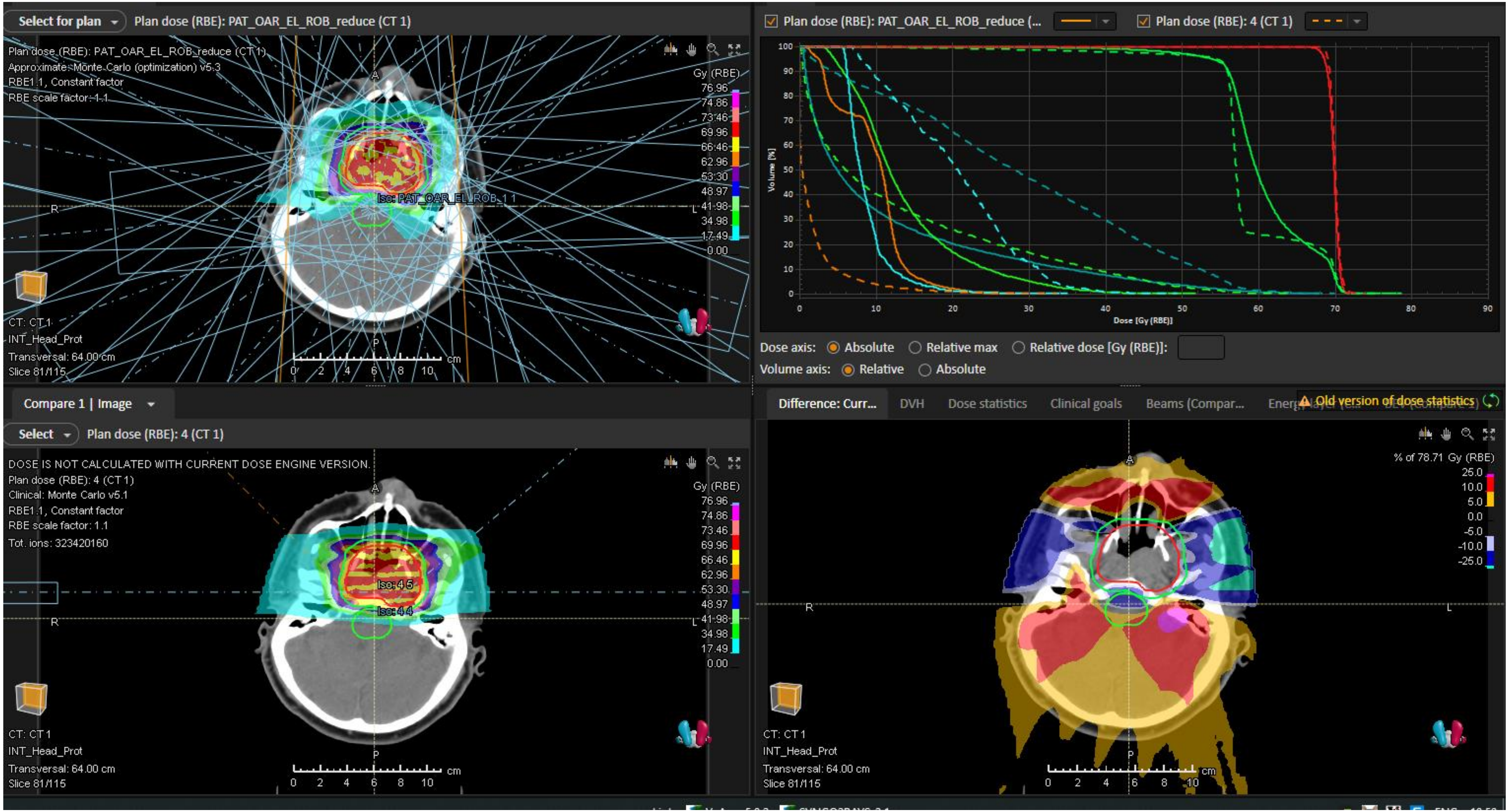


Figure 1 Graphical display of the model-based selection procedure. The first step includes selection of an NTCP-model. Based on the dose-volume parameters included in the selected NTCP-model, the dose distribution is optimized for both techniques (model-based plan optimization) and Δdose is assessed (step 2). Finally, the outcome of step 2 is integrated in the NTCP-model to translate Δdose into ΔNTCP (step 3). (Color version of figure is available online.)



Select for plan
Plan dose (RBE): PAT_OAR_EL_ROB_reduce (CT 1)
Plan dose (RBE): PAT_OAR_EL_ROB_reduce (CT 1)
Approximate: Monte Carlo (optimization) v5.3
RBE1.1, Constant factor
RBE scale factor: 1.1
Iso: PAT_OAR_EL_ROB 1 1
Gy (RBE)
76.96
74.86
73.46
69.96
66.46
62.96
53.30
48.97
41.98
34.98
17.49
0.00
CT: CT 1
INT_Head_Prot
Transversal: 64.00 cm
Slice 81/115
Plan dose (RBE): PAT_OAR_EL_ROB_reduce (...
Plan dose (RBE): 4 (CT 1)
Volume [%]
Dose [Gy (RBE)]
Dose axis: Absolute Relative max Relative dose [Gy (RBE)]:
Volume axis: Relative Absolute
Compare 1 | Image
Select
Plan dose (RBE): 4 (CT 1)
DOSE IS NOT CALCULATED WITH CURRENT DOSE ENGINE VERSION.
Plan dose (RBE): 4 (CT 1)
Clinical: Monte Carlo v5.1
RBE1.1, Constant factor
RBE scale factor: 1.1
Tot. ions: 323420160
Iso: 4 5
Iso: 4 4
Difference: Curr...
DVH
Dose statistics
Clinical goals
Beams (Compar...
Old version of dose statistics
% of 78.71 Gy (RBE)
25.0
10.0
5.0
0.0
-5.0
-10.0
-25.0

On-going studies at CNAO… CARA VT

CARA-VT: on-going plan comparison study (protons vs photons)

in collaboration with San Matteo Hospital (Pavia)

for cardiac radioablation of ventricular tachycardia

- ✓ 15 VT pts, undergoing invasive trans-catheter ablation, so far enrolled (30 pts foreseen)
- ✓ ECG-gated CT scan
- ✓ Photon plan (VMAT) vs proton plans (PBS, different strategies): comparison of DVHs for target volumes (CTV, ITV, PTV) and OARs (sub-cardiac structures, lung, breast, etc.)

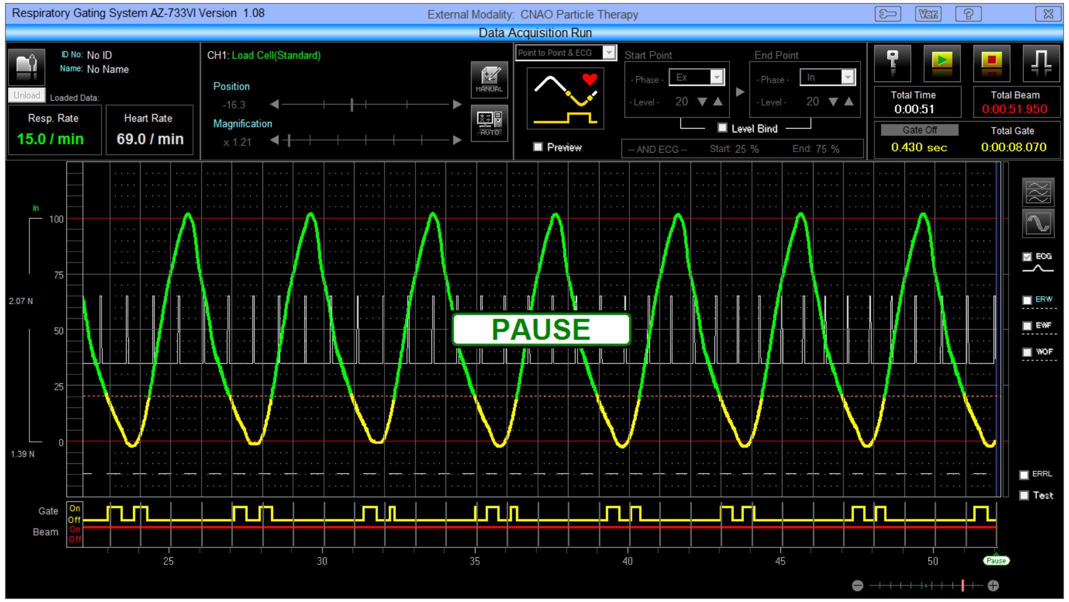
On-going studies at CNAO… CARA VT

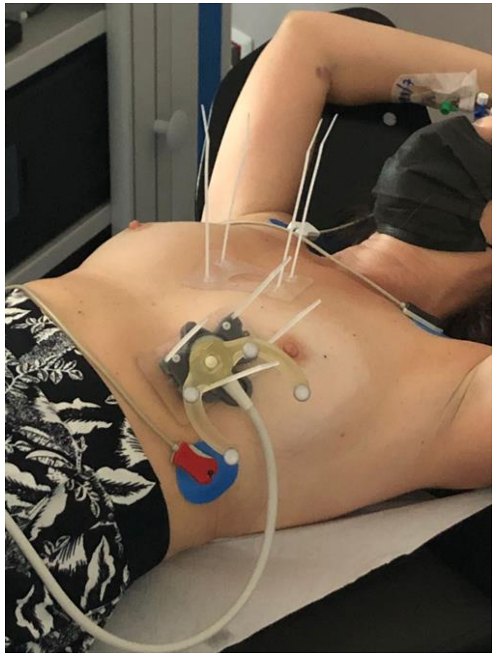
Case Report: Treatment Planning Study to Demonstrate Feasibility of Transthoracic Ultrasound Guidance to Facilitate Ventricular Tachycardia Ablation With Protons

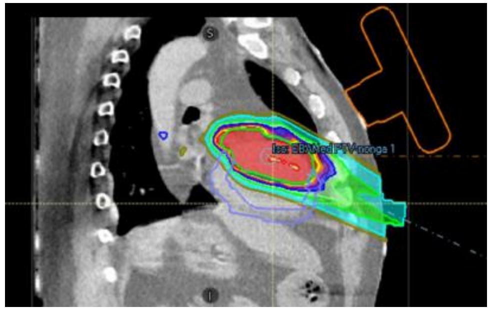
Rosalind Perrin[1], Patrick Maguire[2], Adriano Garonna[1], Georg Weidlich[3], Shelley Bulling[4], Marie Fargier-Voiron[4], Cedric De Marco[4], Eleonora Rossi[5], Mario Ciocca[5], Viviana Vitolo[5] and Alfredo Mirandola[5]*

[1] EBAMed SA, Geneva, Switzerland, [2] MedDevicePharma LLC, Foster City, CA, United States, [3] Radiation Oncology, National Medical Physics and Dosimetry Company, Palo Alto, CA, United States, [4] Clinique de Genolier, Genolier, Switzerland, [5] Centro Nazionale di Adroterapia Oncologica (CNAO), Pavia, Italy

Frontiers in Cardiovascular Medicine

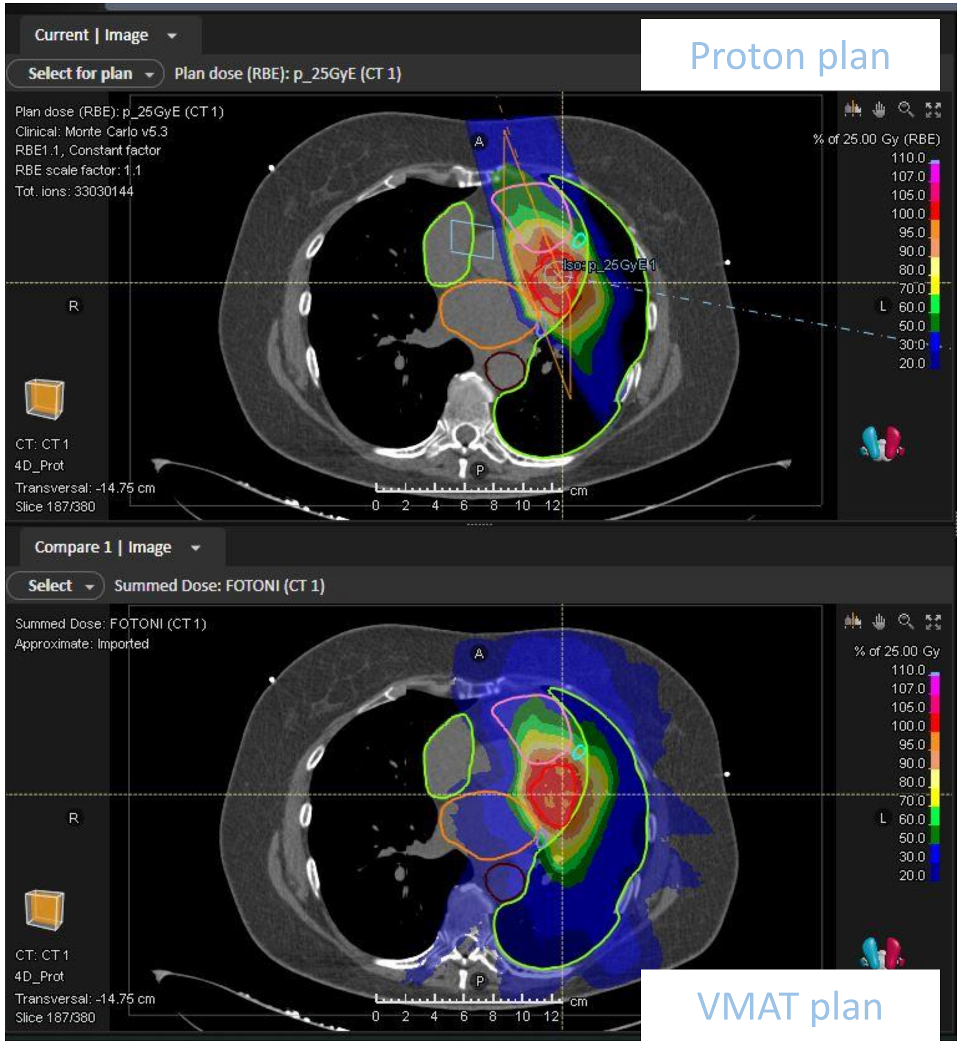


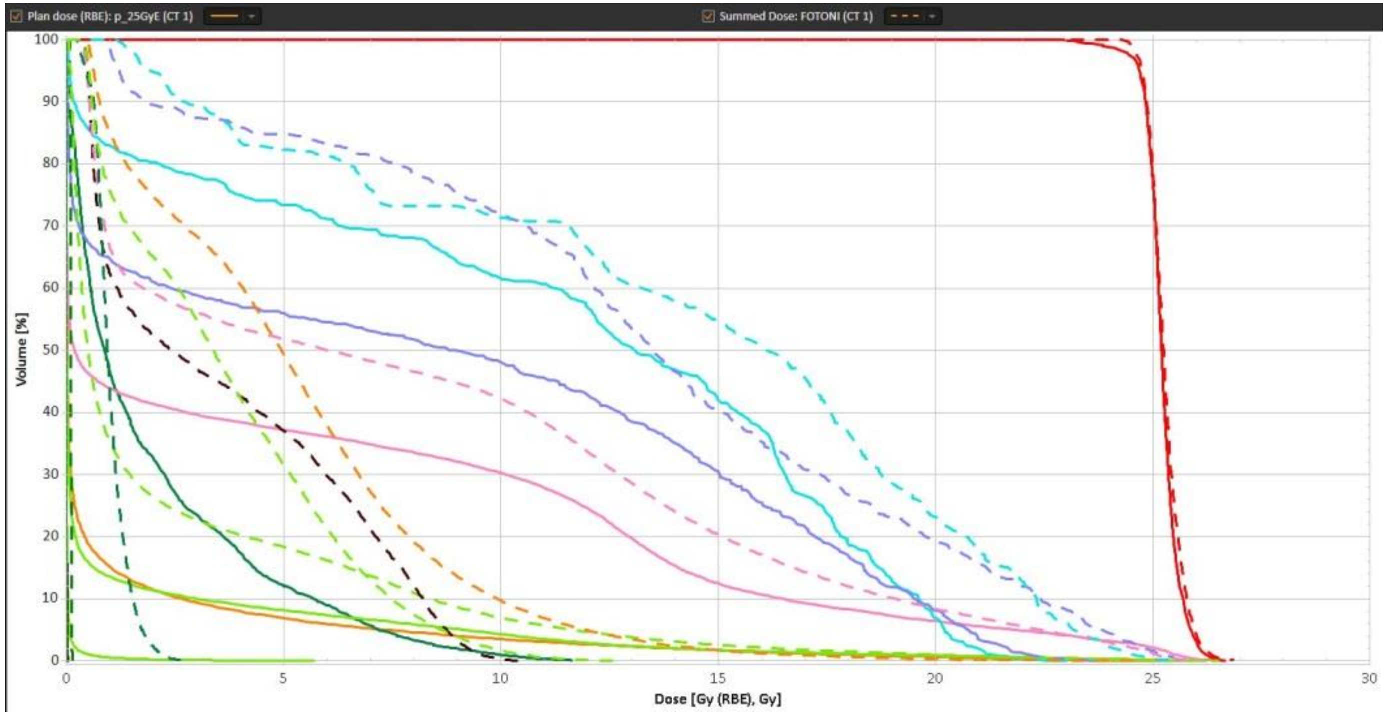




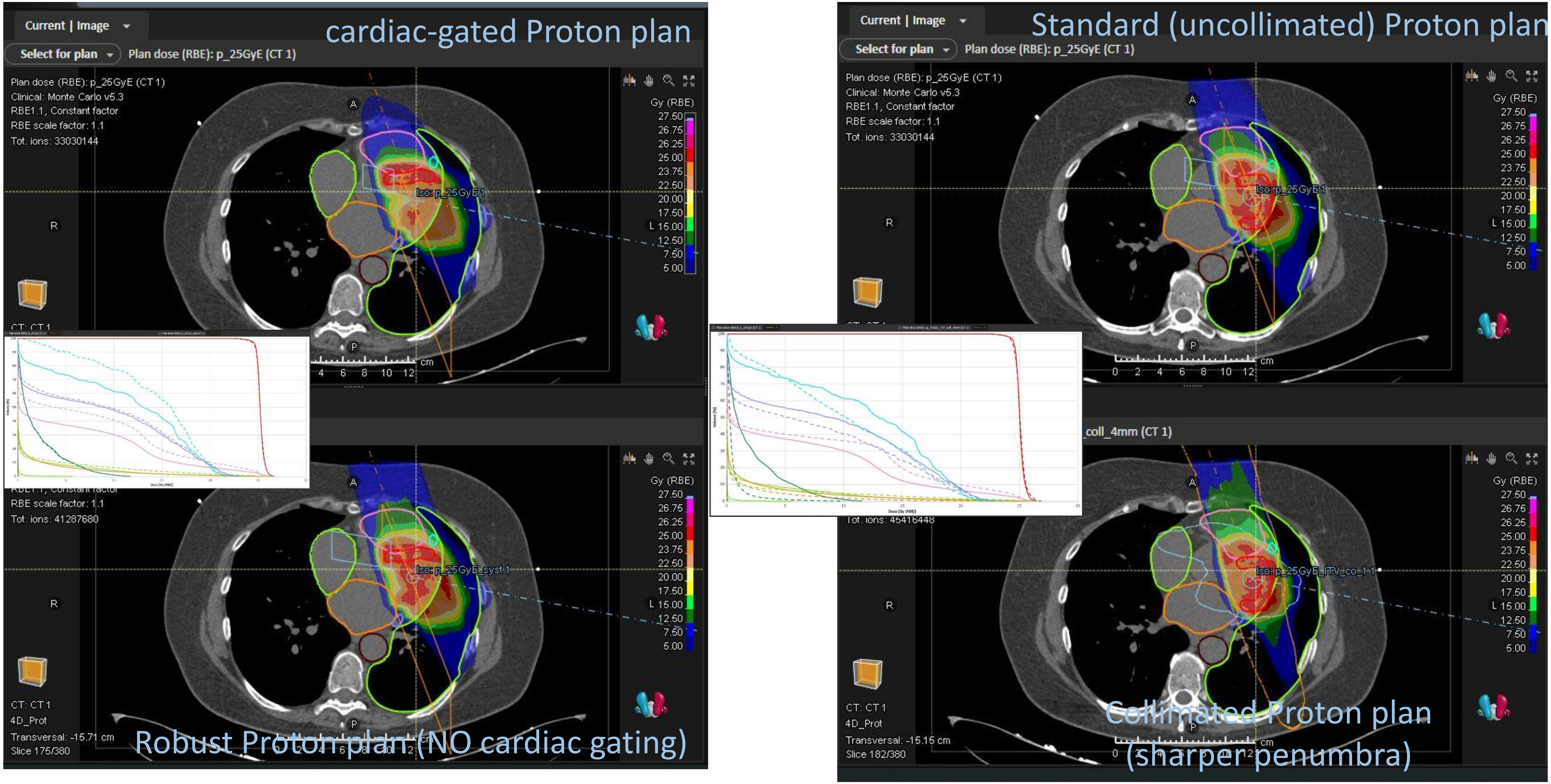
Combined respiratory and cardiac gating (ANZAI system)

On-going studies at CNAO… CARA VT





On-going studies at CNAO… CARA VT



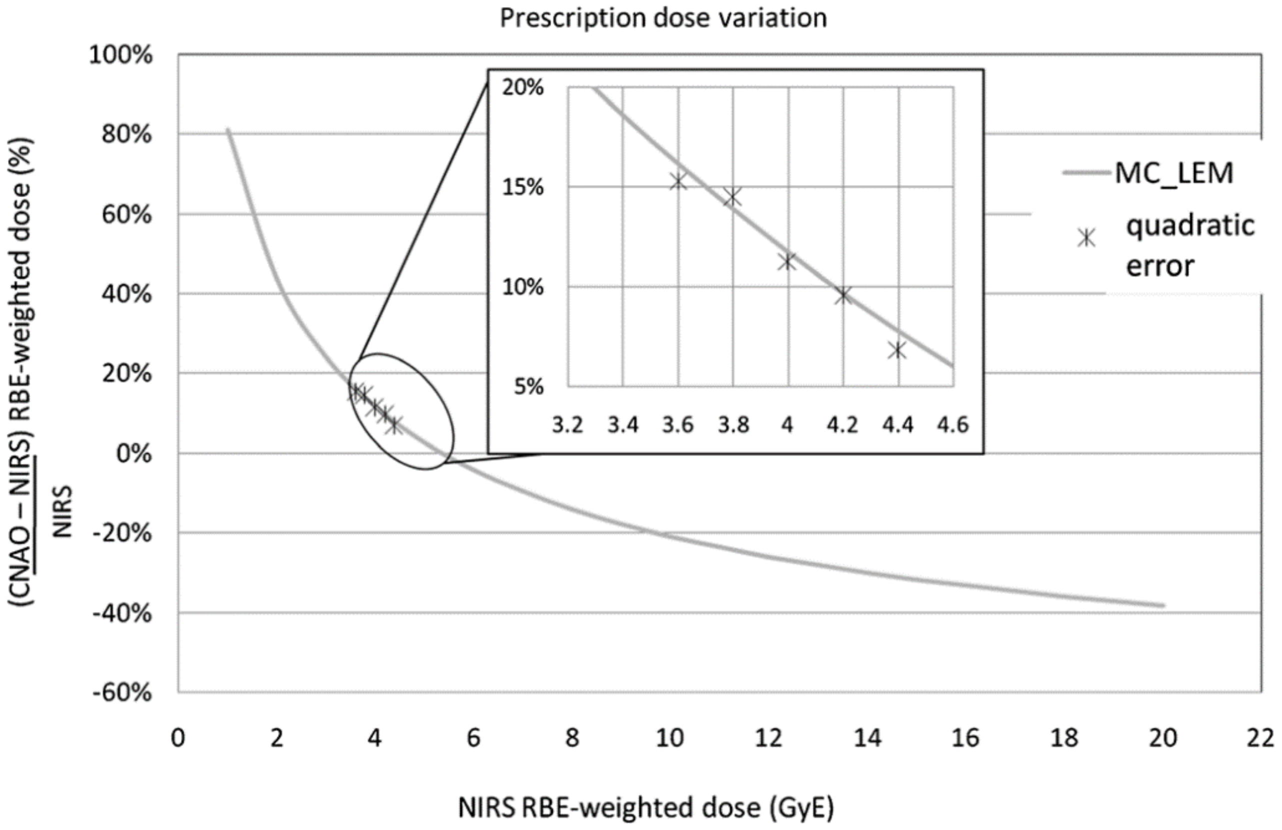
On-going studies at CNAO… toxicity studies

IOP PUBLISHING — PHYSICS IN MEDICINE AND BIOLO
Phys. Med. Biol. 57 (2012) 7543–7554 — doi:10.1088/0031-9155/57/22/75

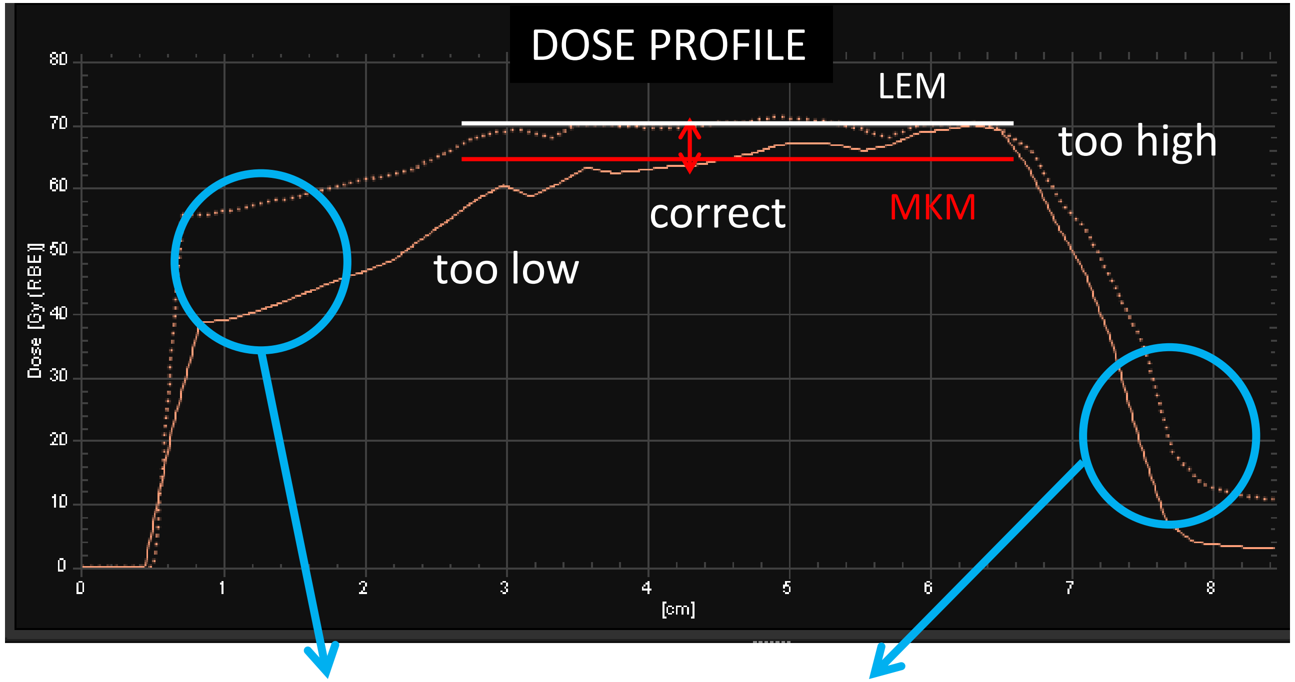
Dose prescription in carbon ion radiotherapy: a planning study to compare NIRS and LEM approaches with a clinically-oriented strategy

Piero Fossati[1,2,4,5], Silvia Molinelli[1], Naruhiru Matsufuji[3], Mario Ciocca[1], Alfredo Mirandola[1], Andrea Mairani[1], Junetsu Mizoe[1,3], Azusa Hasegawa[3], Reiko Imai[3], Tadashi Kamada[3], Roberto Orecchia[1,2,4] and Hirohiko Tsujii[3]

[1] Centro Nazionale di Adroterapia Oncologica (CNAO), Pavia, Italy
[2] Dipartimento di Scienze e Tecnologie Biomediche, Università di Milano, Milano, Italy
[3] Research Center for Charged Particle Therapy, National Institute of Radiological Sciences, Chiba, Japan
[4] Istituto Europeo di Oncologia, Milano, Italy



On-going studies at CNAO… toxicity studies



And OARs dose constraints? – NO correction applied

On-going studies at CNAO… toxicity studies

Contents lists available at ScienceDirect

Radiotherapy and Oncology

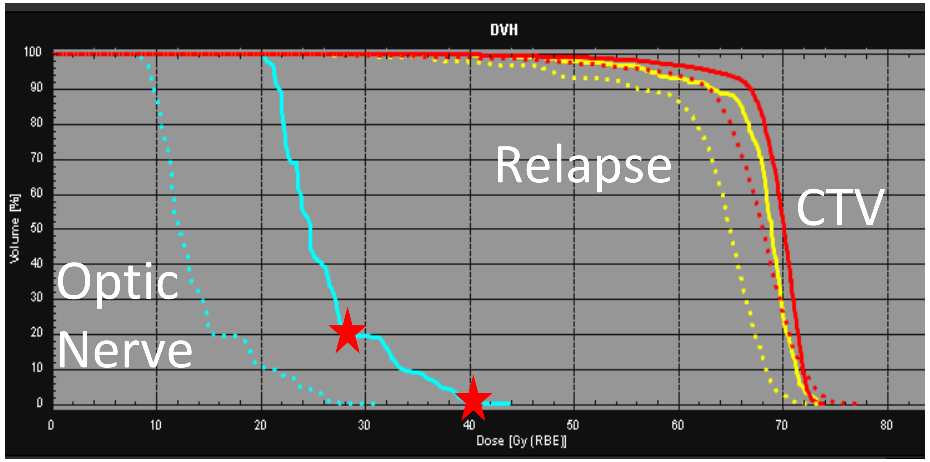
journal homepage: www.thegreenjournal.com

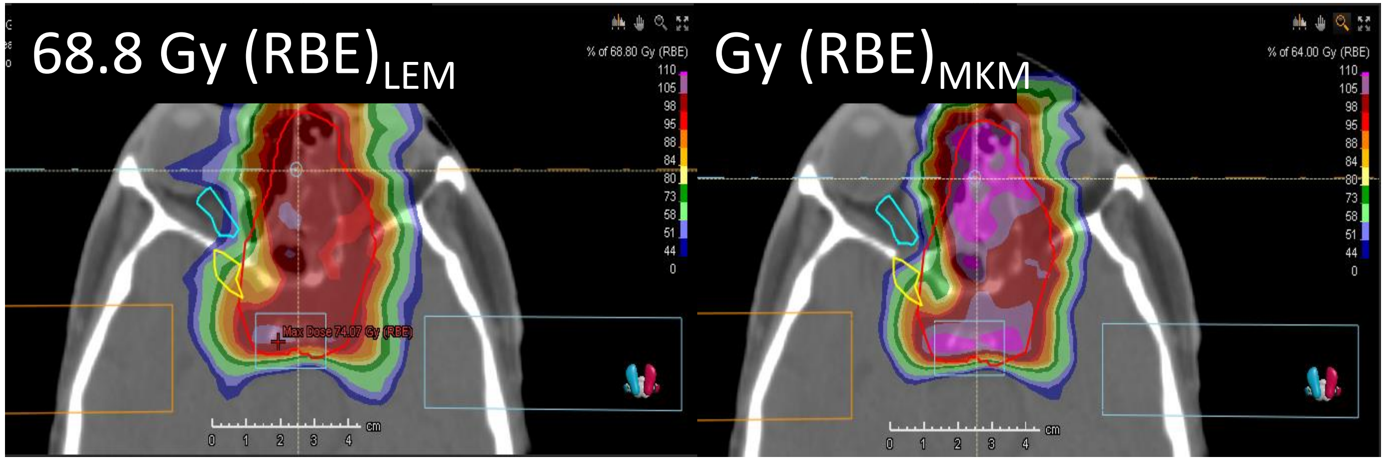
Original Article

RBE-weighted dose in carbon ion therapy for ACC patients: Impact of the RBE model translation on treatment outcomes

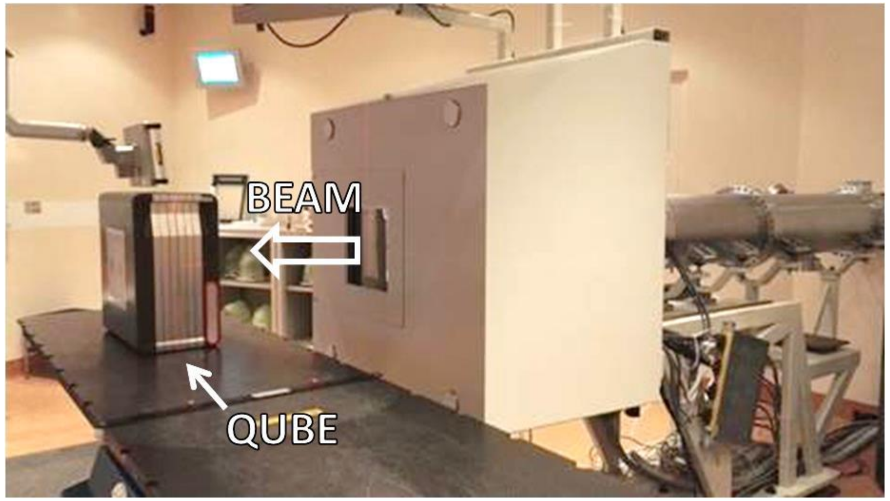
Silvia Molinelli [a,*], Maria Bonora [a], Giuseppe Magro [a], Silvia Casale [b], Jon Espen Dale [c], Piero Fossati [d], Azusa Hasegawa [e], Alfredo Mirandola [a], Sara Ronchi [a], Stefania Russo [a], Lorenzo Preda [a,f], Francesca Valvo [a], Roberto Orecchia [a,g], Mario Ciocca [a], Barbara Vischioni [a]

[a] Clinical Department, National Center for Oncological Hadrontherapy (CNAO); [b] Department of Diagnostic Medicine, Institute of Radiology, IRCCS San Matteo University Hospital Foundation, Pavia, Italy; [c] Department of Oncology and Medical Physics, Haukeland University Hospital, Bergen, Norway; [d] MedAustron Ion Therapy Center, Wiener Neustadt, Austria; [e] Osaka Heavy Ion Therapy Center, Osaka, Japan; [f] Department of Clinical-Surgical, Diagnostic and Paediatric Sciences, University of Pavia; and [g] European Institute of Oncology, Milan, Italy





On-going studies for medical physicist @ CNAO…
detectors characterizations



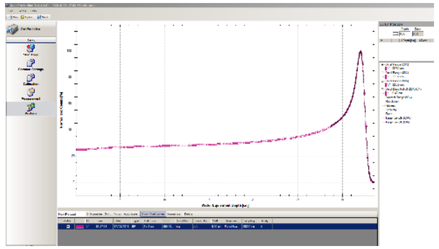
Medical Physics
The International Journal of Medical Physics Research and Practice

Research Article

Characterization of a multilayer ionization chamber prototype for fast verification of relative depth ionization curves and spread-out-Bragg-peaks in light ion beam therapy

Alfredo Mirandola, Giuseppe Magro, Marco Lavagno, Andrea Mairani, Silvia Molinelli, Stefania Russo, Edoardo Mastella, Alessandro Vai, Davide Maestri, Vanessa La Rosa, Mario Ciocca

First published: 6 April 2018 | https://doi.org/10.1002/mp.12866



Characterization of a MLIC Detector for QA in Scanned Proton and Carbon Ion Beams

Alessandro Vai, MS[1]; Alfredo Mirandola, MS[1]; Giuseppe Magro, PhD[1]; Davide Maestri, MS[1]; Edoardo Mastella, MS[1]; Andrea Mairani, PhD[1,2]; Silvia Molinelli, MS[1]; Stefania Russo, MS[1]; Michele Togno, PhD[3*]; Sara La Civita, MS[3†]; Mario Ciocca, MS[1]

Physica Medica 34 (2017) 48–54

Contents lists available at ScienceDirect

Physica Medica

journal homepage: http://www.physicamedica.com

Original paper

Characterization of a commercial scintillation detector for 2-D dosimetry in scanned proton and carbon ion beams

S. Russo[a,*], A. Mirandola[a], S. Molinelli[a], E. Mastella[a], A. Vai[a], G. Magro[a], A. Mairani[a,b], D. Boi[c], M. Donetti[a,d], M. Ciocca[a]

[a] Fondazione CNAO, Pavia, Italy
[b] HIT – Heidelberg Ion Beam Therapy Center, Heidelberg, Germany
[c] Department of Physics, Università degli Studi di Cagliari, Cagliari, Italy
[d] Istituto Nazionale di Fisica Nucleare, Section of Torino, Torino, Italy

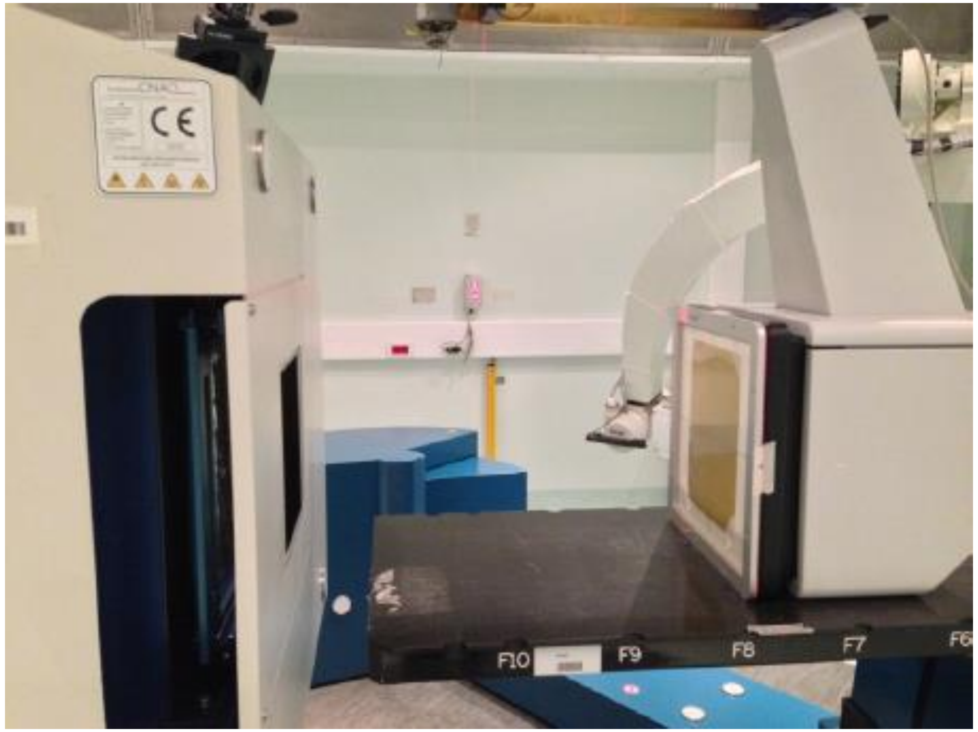
Phys Med. 2023 Mar:107:102561. doi: 10.1016/j.ejmp.2023.102561. Epub 2023 Mar 8.

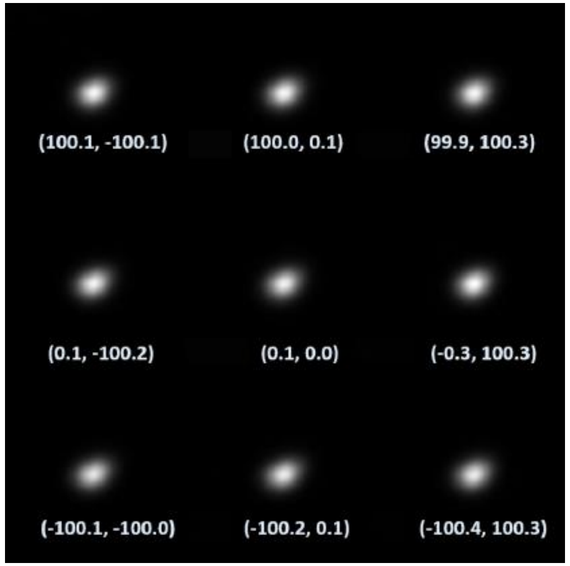
Characterization of a flat-panel detector for 2D dosimetry in scanned proton and carbon ion beams

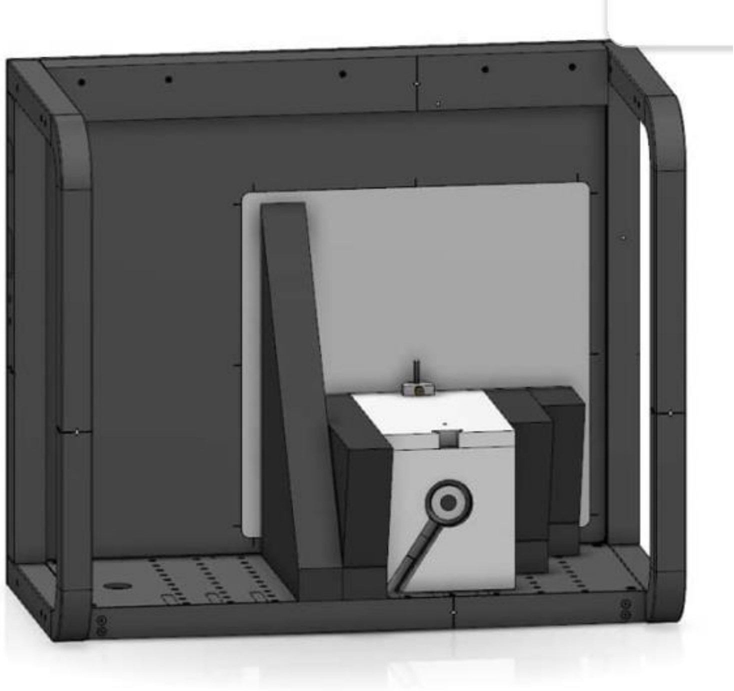
Eleonora Rossi [1], Stefania Russo [2], Davide Maestri [3], Giuseppe Magro [2], Alfredo Mirandola [2], Silvia Molinelli [2], Alessandro Vai [2], Loïc Grevillot [4], Marta Bolsa-Ferruz [4], Séverine Rossomme [5], Mario Ciocca [2]

Affiliations + expand

PMID: 36898300 DOI: 10.1016/j.ejmp.



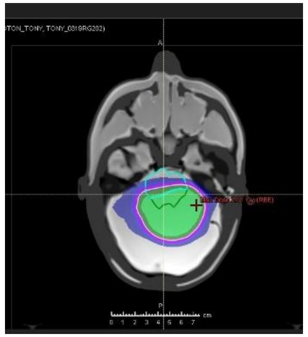


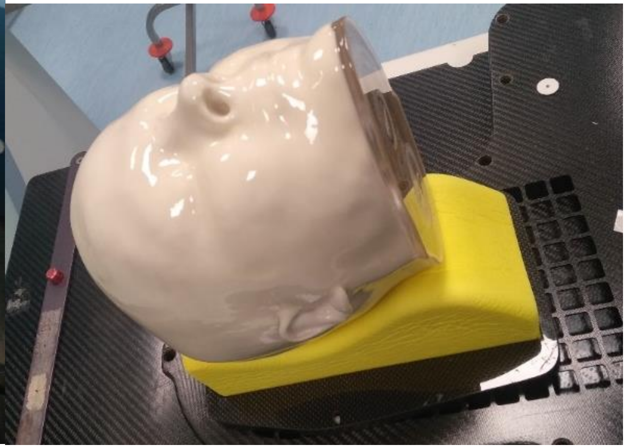


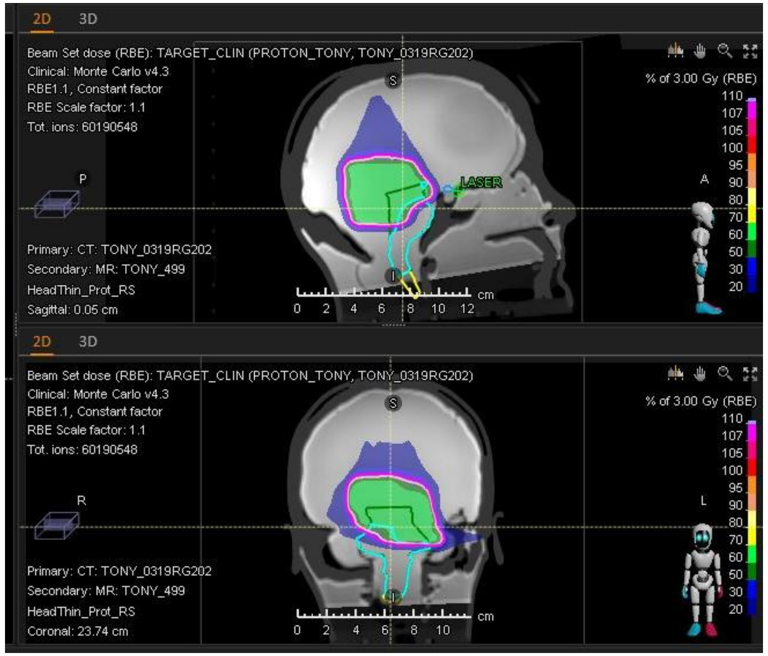
Gel dosimetry with protons and carbon ions

- Testing the use of commercial anthrophormic 3D printed phantoms filled with (VIP polymer) gel sensitive to radiation
- Validation with p and C-ions
- End-to-End test on both protons and C-ion clinical plans

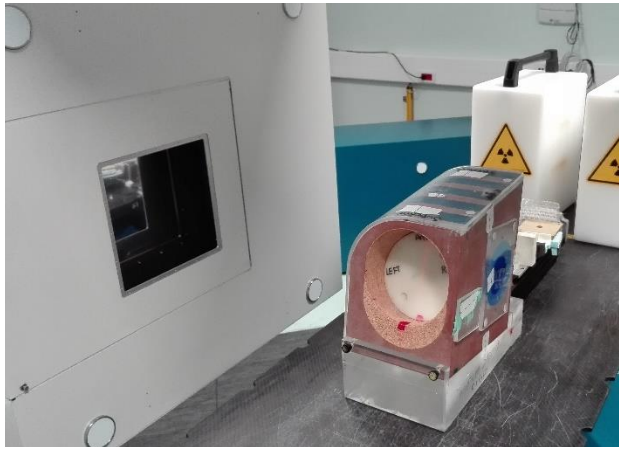
RTsafe







Ongoing scientific collaboration with IROC Houston QA Center for protons and carbon ions approval (credentialing)



4-D phantom

H&N phantom

End-to-end tests

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

MD Anderson Dosimetry Lab
1515 Holcombe Blvd.
Houston, TX 77030
(713) 745-8989

Report of
Proton H&N Phantom Irradiation

Date of Report:	June 13, 2022
Institution:	Fondazione CNAO - Protons
Physicist:	Alessandro Vai
Radiation Machine:	Hitachi, Synchrotron
Irradiation Technique:	Proton
Treatment Planning System:	RaySearch Laboratories RayStation (Monte Carlo)
Date of Irradiation:	April 22, 2022

Description of procedure

An anthropomorphic H&N phantom incorporating a cylindrical insert was imaged and irradiated to approximately 6.6 Gy (RBE) using a proton technique. The dosimetry insert consisted of one primary PTV containing two TLD capsules, and three organs at risk (OARs), each containing one TLD capsules. The TLD capsules provided point dose information. Two sheets of GAFChromic™ Dosimetry Media provided dose profiles through the center of primary PTV.

The dosimetric precision of the TLD is 3%, and the spatial precision of the film and densitometer system is 1mm.

Summary of TLD and film results:

Location	IROC-H v. Inst.	Criteria	Acceptable
PTV Superior	0.98	0.93 – 1.07	Yes
PTV Inferior	0.98	0.93 – 1.07	Yes

Film Plane	Gamma Index*	Criteria	Acceptable
Axial	99%	≥ 85%	Yes
Sagittal	98%	≥ 85%	Yes

*Percentage of points meeting gamma-index criteria of 7% and 4 mm.

The phantom irradiation results listed in the table above **do meet** the criteria established by IROC in collaboration with the cooperative study groups. Therefore, your institution **would have satisfied** the phantom irradiation component of the credentialing process to enter patients in certain clinical trials that allow the use of proton therapy.

TLD and Film Analysis by: Jessica Lowenstein and Nadia Hernandez

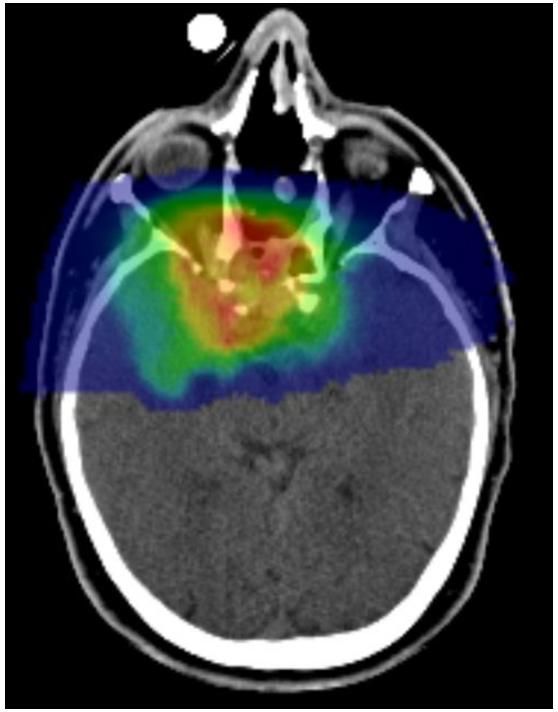
Report Checked by:

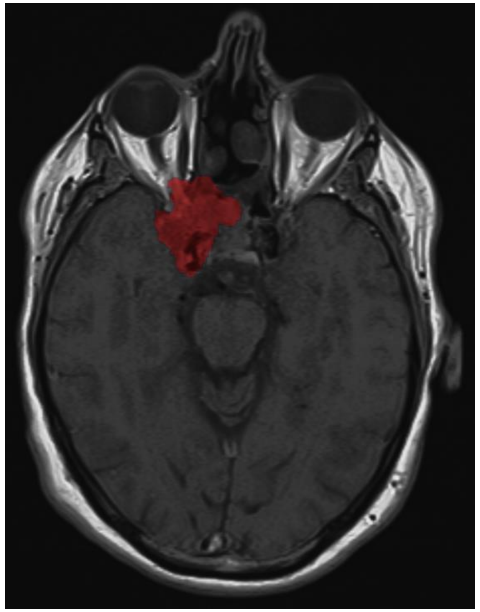
Stephen Kry, Ph.D.
Director, IROC Houston QA Center

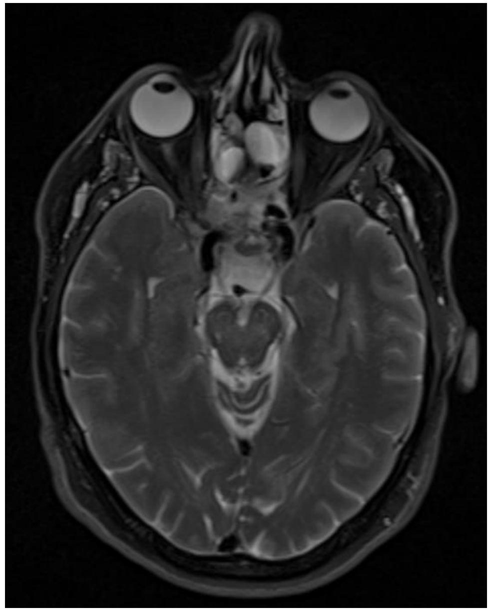
Multi-parametric Imaging for PT: integrating macro & microstructural models

Courtesy of Chiara Paganelli (POLIMI)

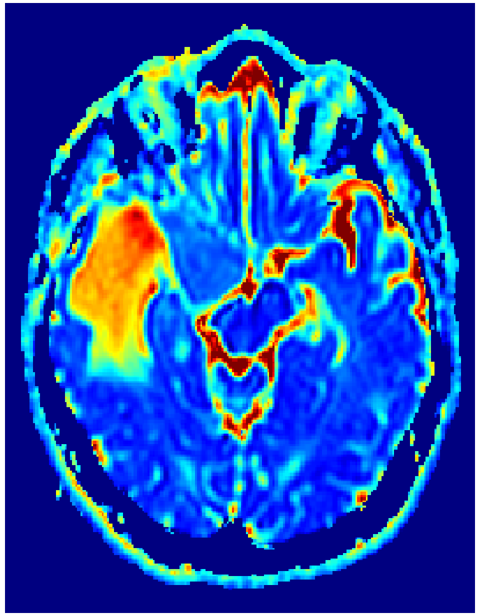
MACRO:
CT + dose maps

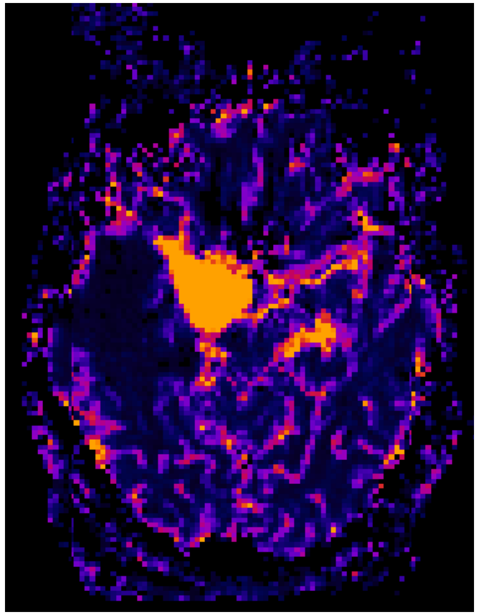






MACRO:
Anatomical MRI (T1-w, T2-w)

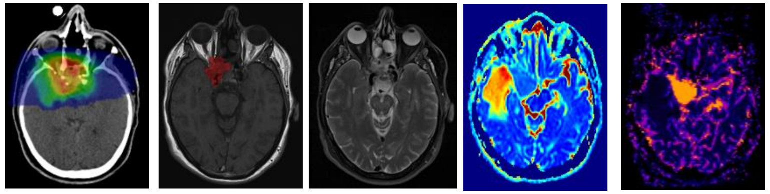




MICRO:
Quantitative MRI (DWI, PWI)

Multi-parametric Imaging for PT: integrating macro & microstructural models

GOAL: patient stratification and PT treatment personalization at different scales



CT + dose maps
Anatomical MRI (T1-w, T2-w)
Quantitative MRI (DWI, PWI)

MULTI-PARAMETRIC IMAGING

↓

PRE-PROCESSING
image segmentation, intensity normalization, ...

↓

FEATURE EXTRACTION
Radiomics, candidate features, biomarkers, …

→ **MACRO**
modelling of properties at the MACRO level
(e.g. DWI, PWI,…)

↔ **MICRO**
modelling of properties at the MICRO level
(e.g. cellularity, angiogenesis)

MACHINE LEARNING-BASED MODELS

KNOWLEDGE-BASED RADIOBIOLOGICAL / STRUCTURAL MODELS
Tumour control probability, microstructural model, …

VALIDATION

TECHNICAL		**BIOLOGICAL – CLINICAL**			
REPRODUCIBILITY **REPEATABILITY**	**EXTERNAL COHORT / CROSS-VALIDATION**	**CLINICAL OUTCOME** **(e.g. follow-up)**	**CORRELATION TO VALIDATED SURROGATE**	**SIMULATIONS (e.g. Monte Carlo)**	**PHANTOM STUDIES**

AIRC

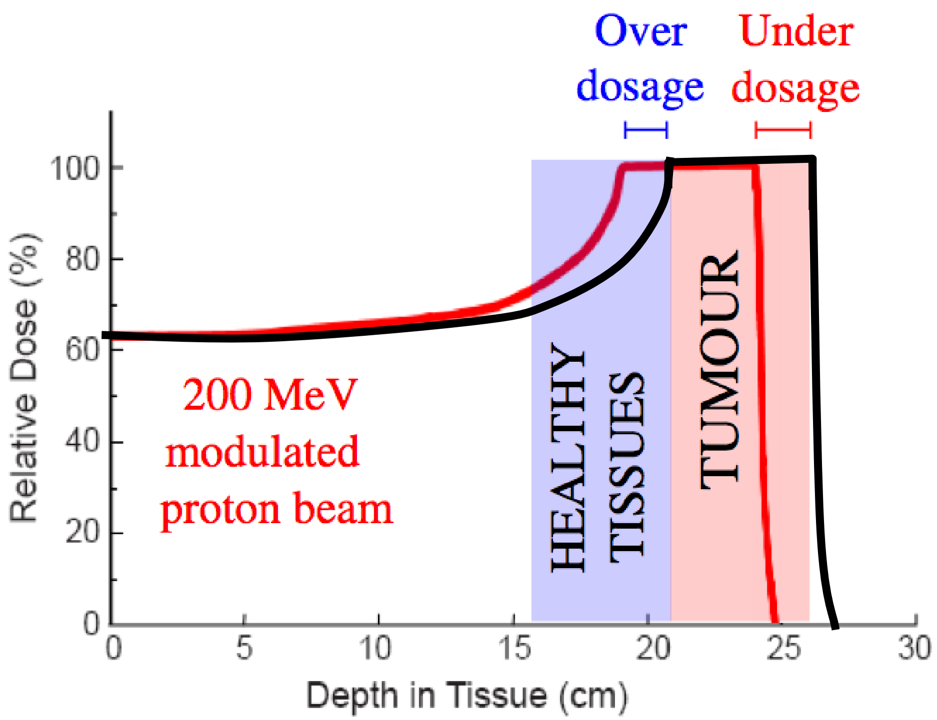
TAILOR

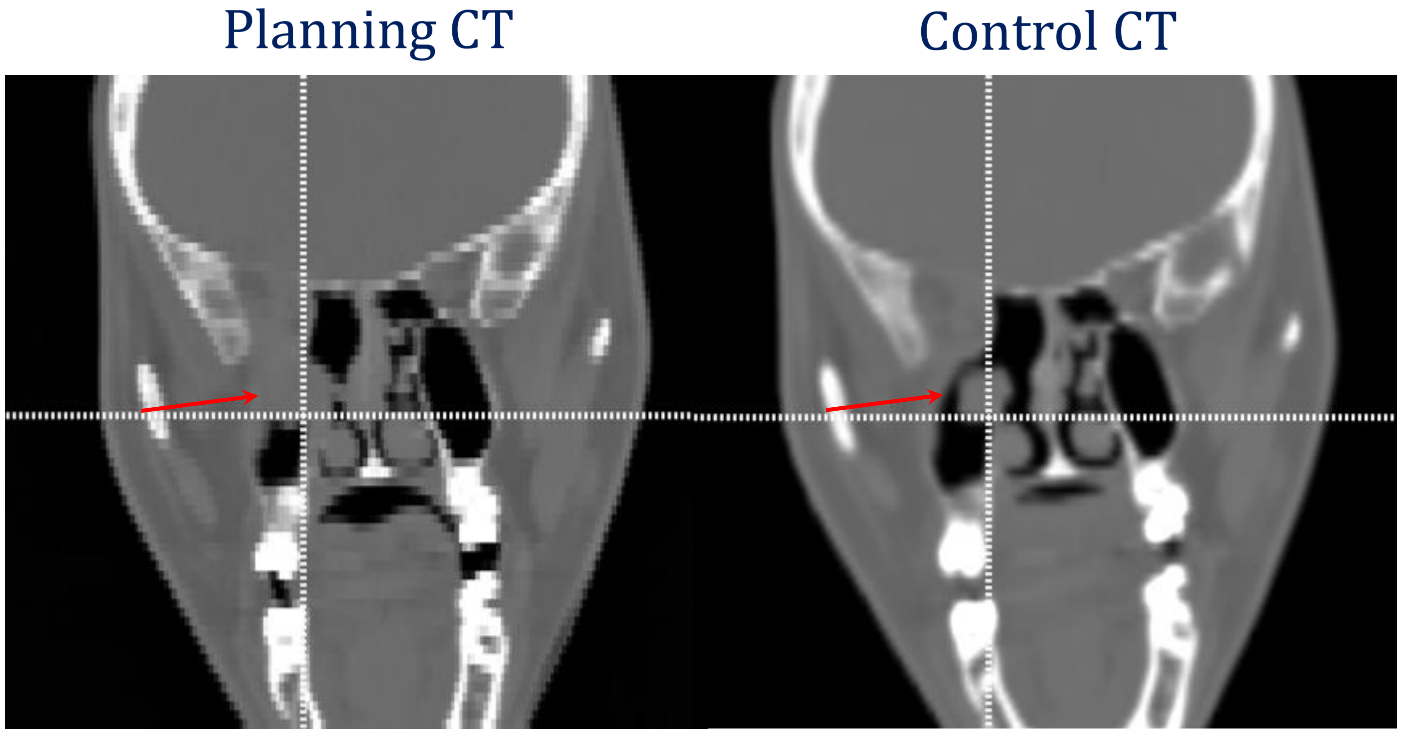
AIRC IG-2020 n. 24946
PI: Prof. Baroni G.

In-vivo range verification in particle therapy

Courtesy of Elisa Fiorina (INFN)

Main clinical motivation: inter-fractional morphological changes





Zhu X, Fakhri GE. *Theranostics. 2013;3(10):731-740*.

In-vivo range verification in particle therapy

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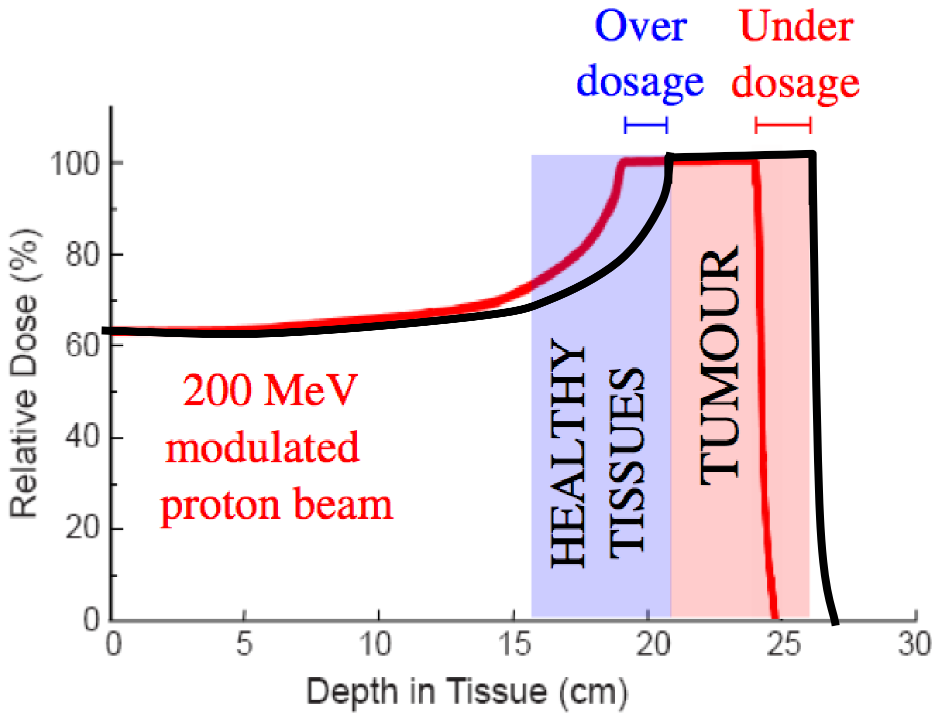
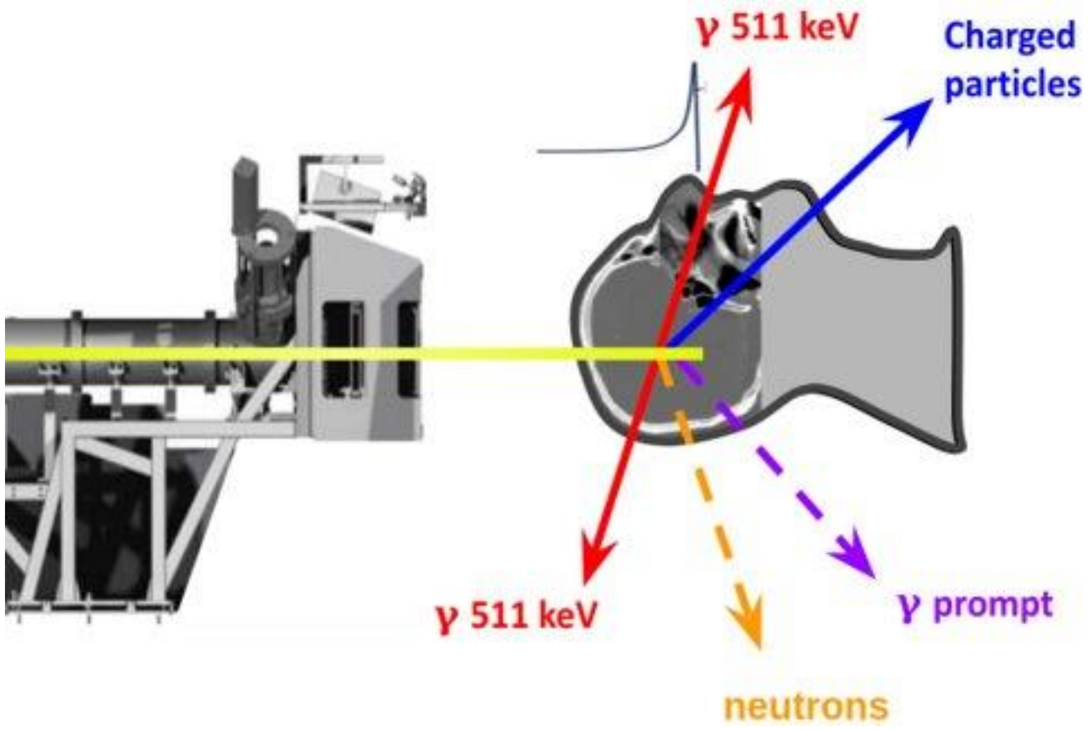
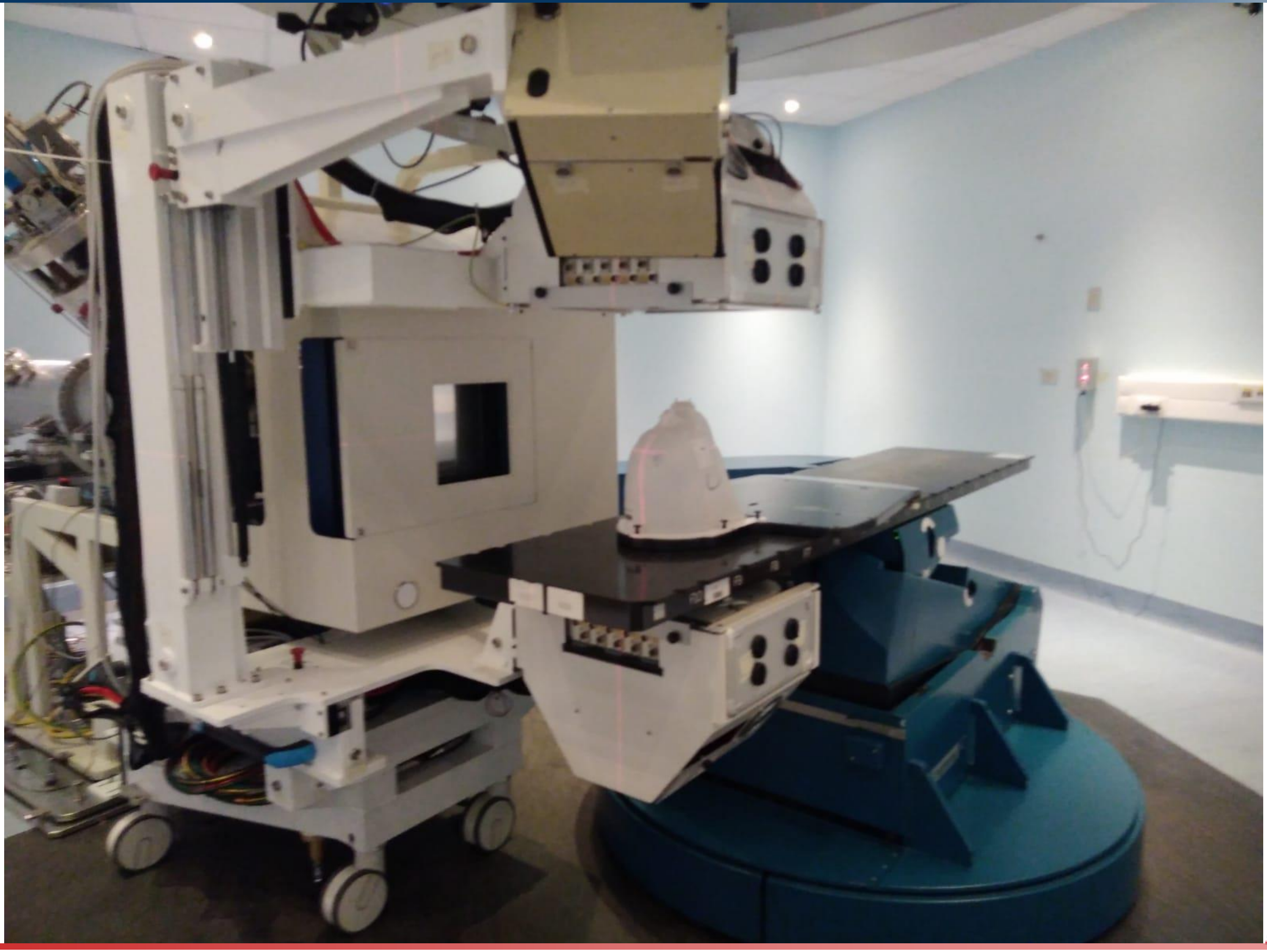


Zhu X, Fakhri GE. *Theranostics. 2013;3(10):731-740*.



Range monitoring by means of passive signals from beam/tissue nuclear interactions

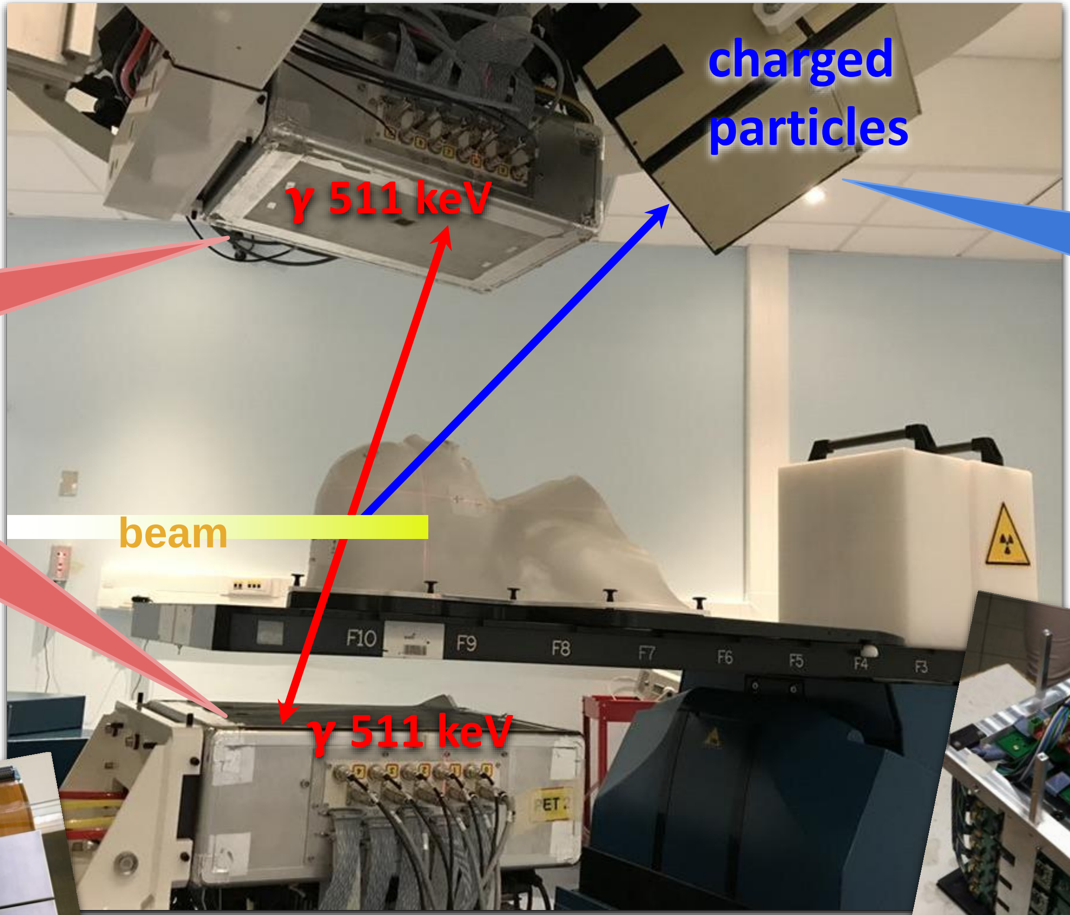
The INSIDE bimodal system



The INSIDE bimodal system

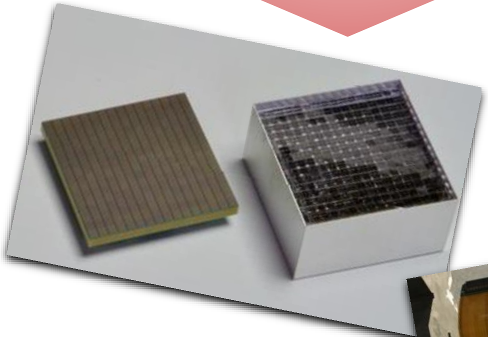
In-beam PET

- positron emitters
- proton and carbon ion in-vivo verification

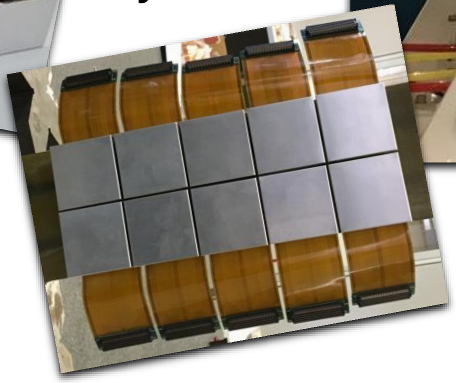


Dose Profiler

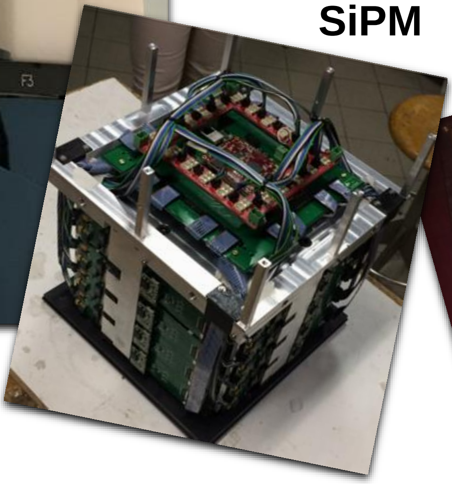
- secondary protons
- carbon ion in-vivo verification



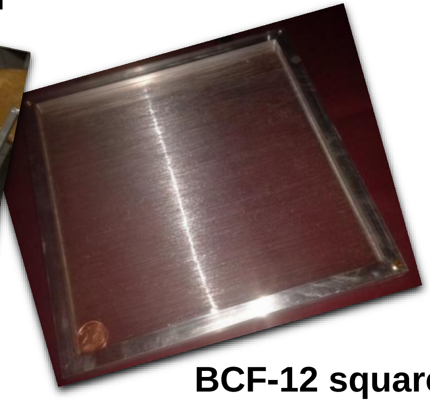
SiPM



LFS pixelated crystals



SiPM



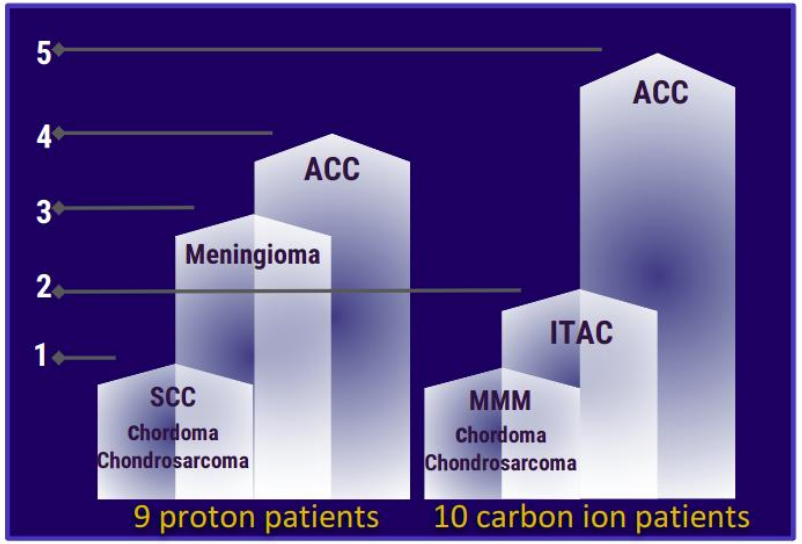
BCF-12 square scintillating fibres

M.G. Bisogni at al, JMI 2017; Ferrero et al., Sci.Rep 2018; Traini et al., Phys. Med., 2017

The INSIDE clinical trial

From July 2019 to February 2020

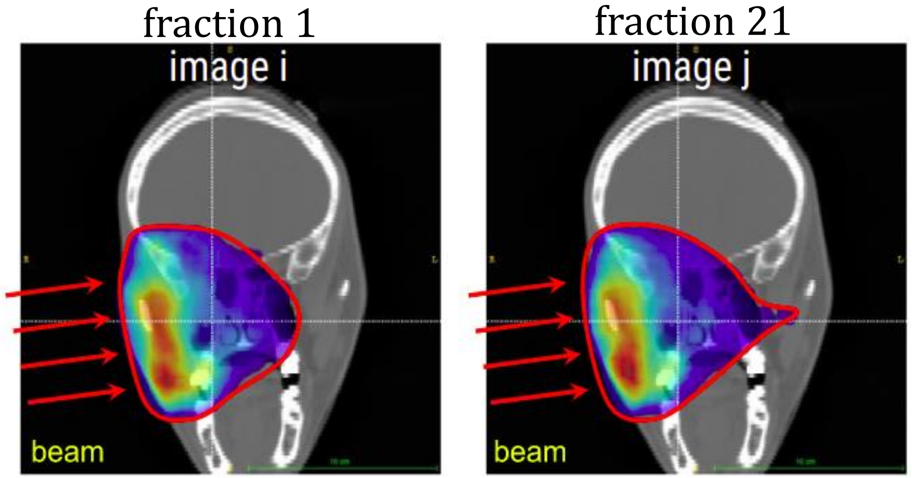
CNAO

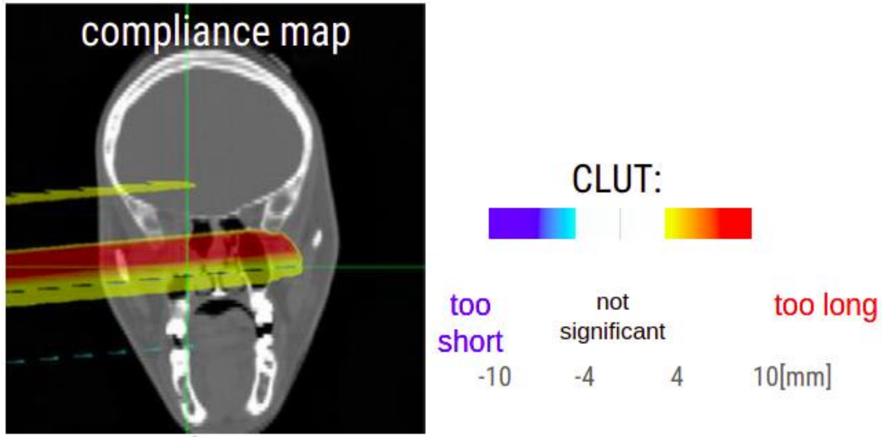


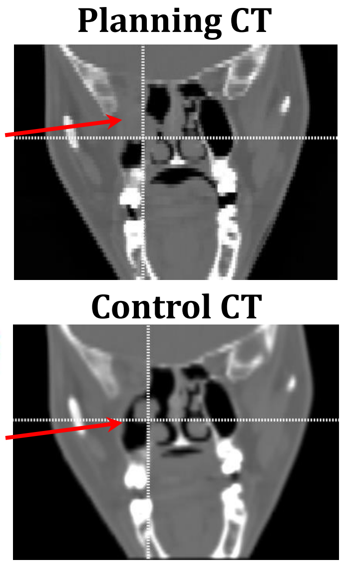
- head-and-neck and brain pathologies
- average percentage of monitored fraction = 38%

11 patients underwent control CTs during treatment:
Among them, 3 patients (ACC) had morphological changes without replanning

- clinical workflow not slowing down by INSIDE acquisition procedure
- recruitment and emergency procedures successfully tested







Morphological changes detected!

ClinicalTrials.gov NCT03662373

E. Fiorina et al, Frontiers 2021

InSide

Future steps at CNAO… Beyond protons and carbon ions

Helium ions for radiotherapy? Physical and biological verifications of a novel treatment modality

Michael Krämer,[a] Emanuele Scifoni, Christoph Schuy, and Marta Rovituso
Biophysics, GSI Helmholtzzentrum für Schwerionenforschung GmbH, Planckstr. 1, 64291 Darmstadt, Germany

Walter Tinganelli
Biophysics, GSI Helmholtzzentrum für Schwerionenforschung GmbH, Planckstr. 1, 64291 Darmstadt, Germany and Trento Institute for Fundamental Physics and Application (TIFPA-INFN), 38123, via Sommarive 14, Trento, Italy

Andreas Maier, Robert Kaderka, and Wilma Kraft-Weyrather
Biophysics, GSI Helmholtzzentrum für Schwerionenforschung GmbH, Planckstr. 1, 64291 Darmstadt, Germany

Stephan Brons and Thomas Tessonnier
Heidelberger Ionenstrahl-Therapiezentrum (HIT), Im Neuenheimer Feld 450, 69120 Heidelberg, Germany and Radioonkologie und Strahlentherapie, Universitätsklinikums Heidelberg, Im Neuenheimer Feld 400, 69120 Heidelberg, Germany

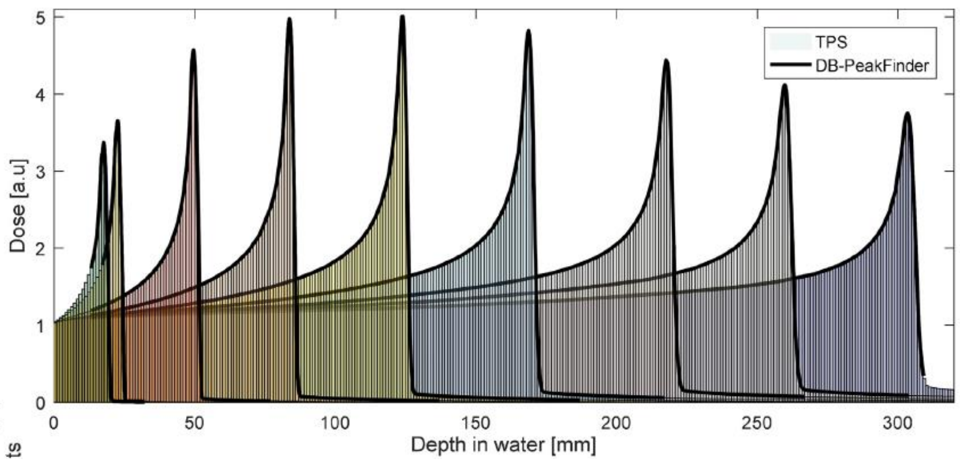
Katia Parodi
Heidelberger Ionenstrahl-Therapiezentrum (HIT), Im Neuenheimer Feld 450, 69120 Heidelberg, Germany; Radioonkologie und Strahlentherapie, Universitätsklinikums Heidelberg, Im Neuenheimer Feld 400, 69120 Heidelberg, Germany; and Ludwig-Maximilians-Universitaet Muenchen (LMU Munich), Department of Medical Physics, Am Coulombwall 1, 85748 Munich, Germany

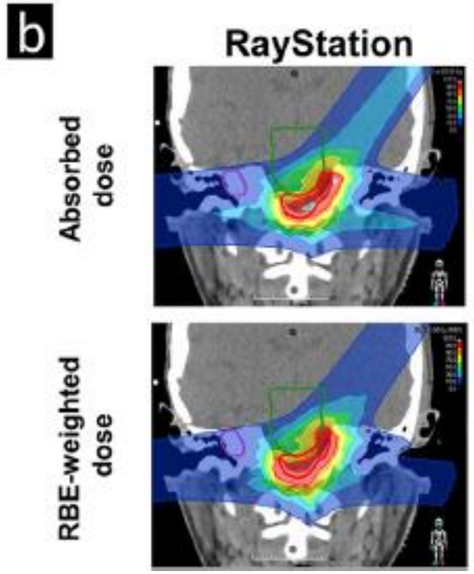
Marco Durante
Biophysics, GSI Helmholtzzentrum für Schwerionenforschung GmbH, Planckstr. 1, 64291 Darmstadt, Germany and Trento Institute for Fundamental Physics and Application (TIFPA-INFN), 38123, via Sommarive 14, Trento, Italy

Radiotherapy with heavy charged particles is an established option for the treatment of certain kinds of tumors. Most heavy charged particle treatments are nowadays performed with protons and carbon ions (Table I). There is, however, some room for unconventional beams other than these two ions. Whereas the usage of pions certainly is history, there is growing interest, for example, in fast helium ion beams. To some extent, they fill the gap between protons and carbon ions. From the physical point of view, they might be advantageous since they cause less projectile fragmentation than carbon ions and less lateral beam spread than protons (see Fig. 1). From the radiobiological point of view, their Relative Biological Effectiveness (RBE) is closer to protons, though not negligible, but certainly lower than that of carbon ions. This might be beneficial in certain treatment situations, for example, for pediatric patients.

Commissioning of Helium Ion Therapy and the First Patient Treatment With Active Beam Delivery

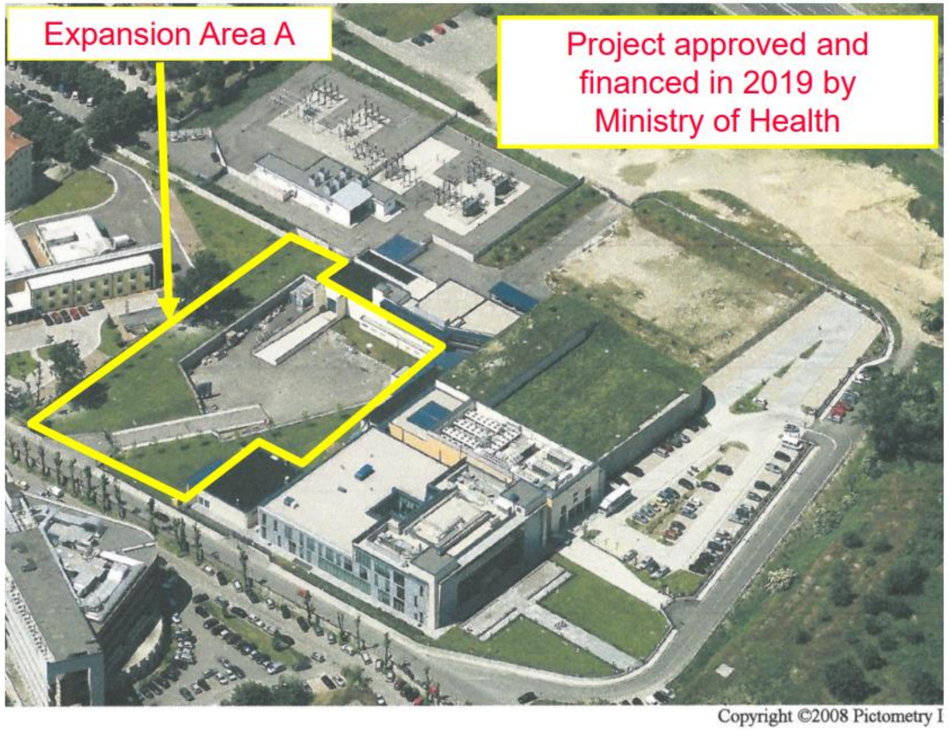
Thomas Tessonnier, PhD,[*,†,‡] Swantje Ecker, MSc,[*] Judith Besuglow, MSc,[†,‡,§,‖] Jakob Naumann, PhD,[*] Stewart Mein, PhD,[†,‡,§,¶] Friderike K. Longarino, MSc,[†,‡,§,‖] Malte Ellerbrock, PhD,[*] Benjamin Ackermann, MSc,[*] Marcus Winter, PhD,[*] Stephan Brons, PhD,[*] Abdallah Qubala, MSc,[*,‡,#] Thomas Haberer, PhD,[*] Jürgen Debus, MD, PhD,[*,†,‡,§,¶] Oliver Jäkel, PhD,[*,‡,**] and Andrea Mairani,[*,†,‡,††]

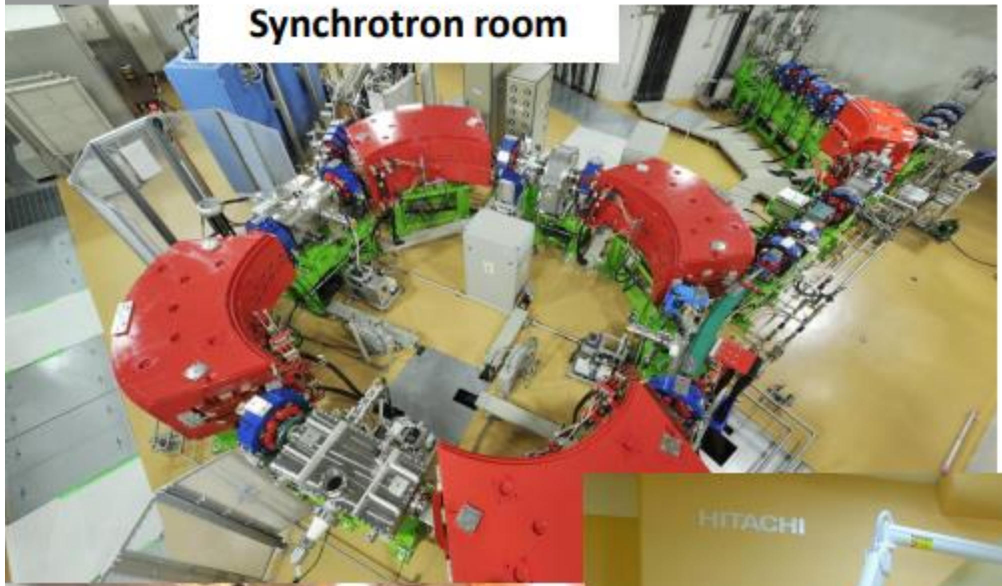




CNAO

Future steps at CNAO… commercial proton gantry





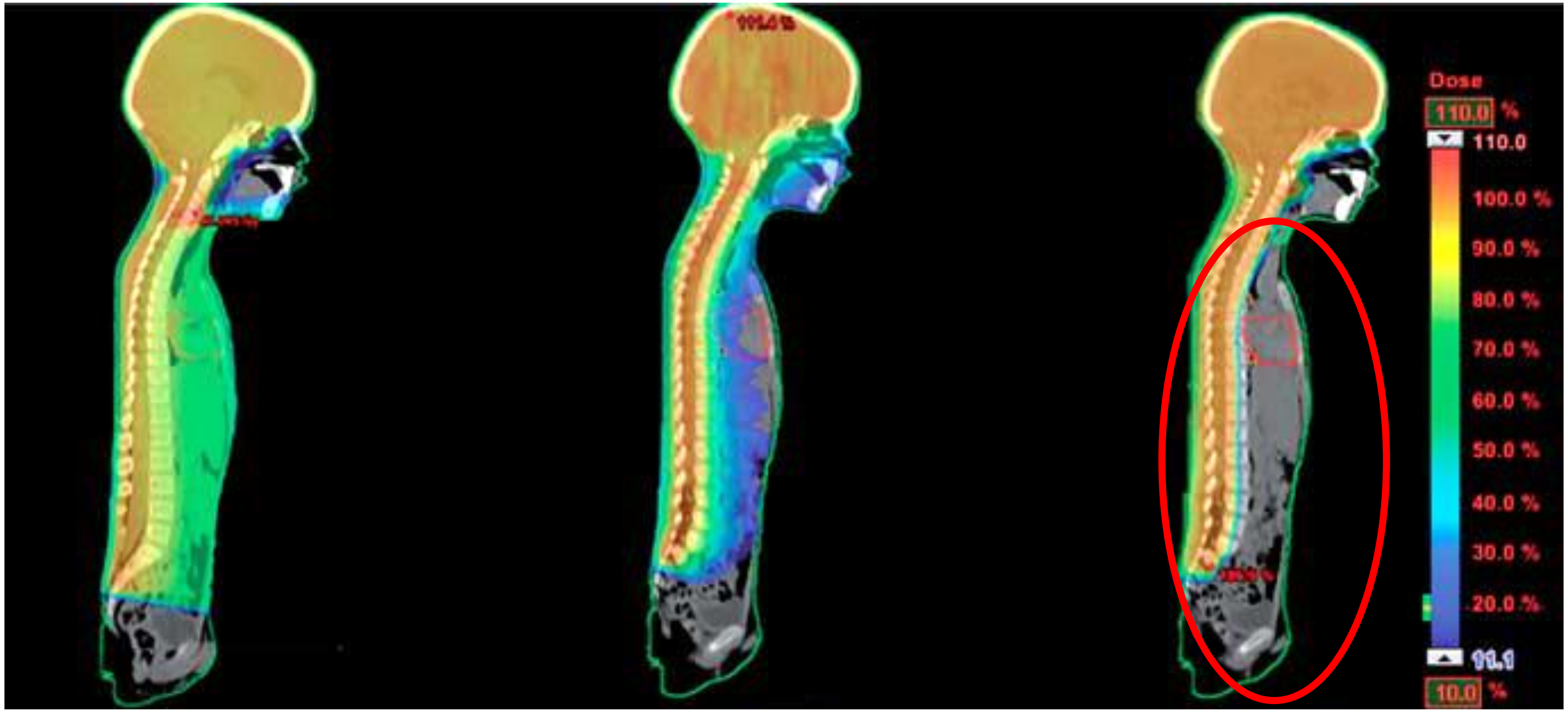
Contract signed with Hitachi:
December 5th, 2019

Future steps at CNAO…

Review

Dosimetric Comparison and Potential for Improved Clinical Outcomes of Paediatric CNS Patients Treated with Protons or IMRT

Kris S. Armoogum [1,†,*] and Nicola Thorp [2,†]



Protons: similar target coverage, while significant reduction in integral dose to normal tissues (lower dose bath)

Future steps at CNAO…

✓ Proton arc therapy (combined or not with upright positioning): increased degree of freedom in plan optimization

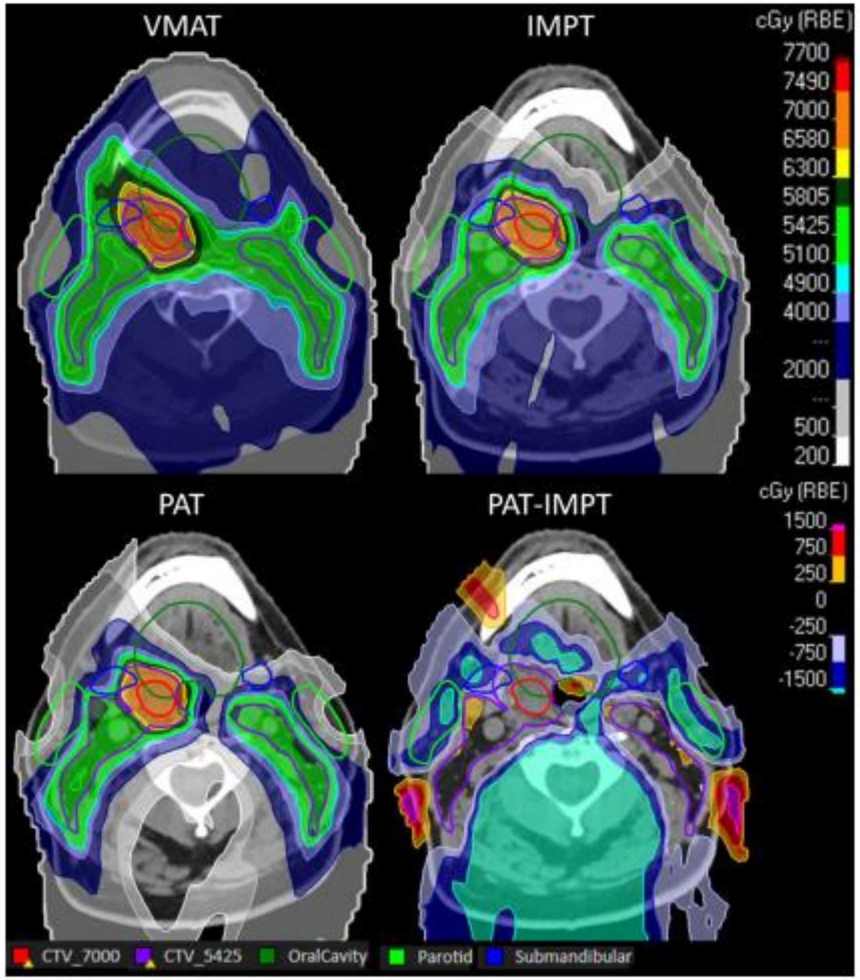
Radiotherapy and Oncology 184 (2023) 109670

Original Article

Proton arc therapy increases the benefit of proton therapy for oropharyngeal cancer patients in the model based clinic

Bas A. de Jong [a,*], Erik W. Korevaar [a], Anneke Maring [a], Chimène I. Werkman [a], Daniel Scandurra [a], Guillaume Janssens [b], Stefan Both [a], Johannes A. Langendijk [a]

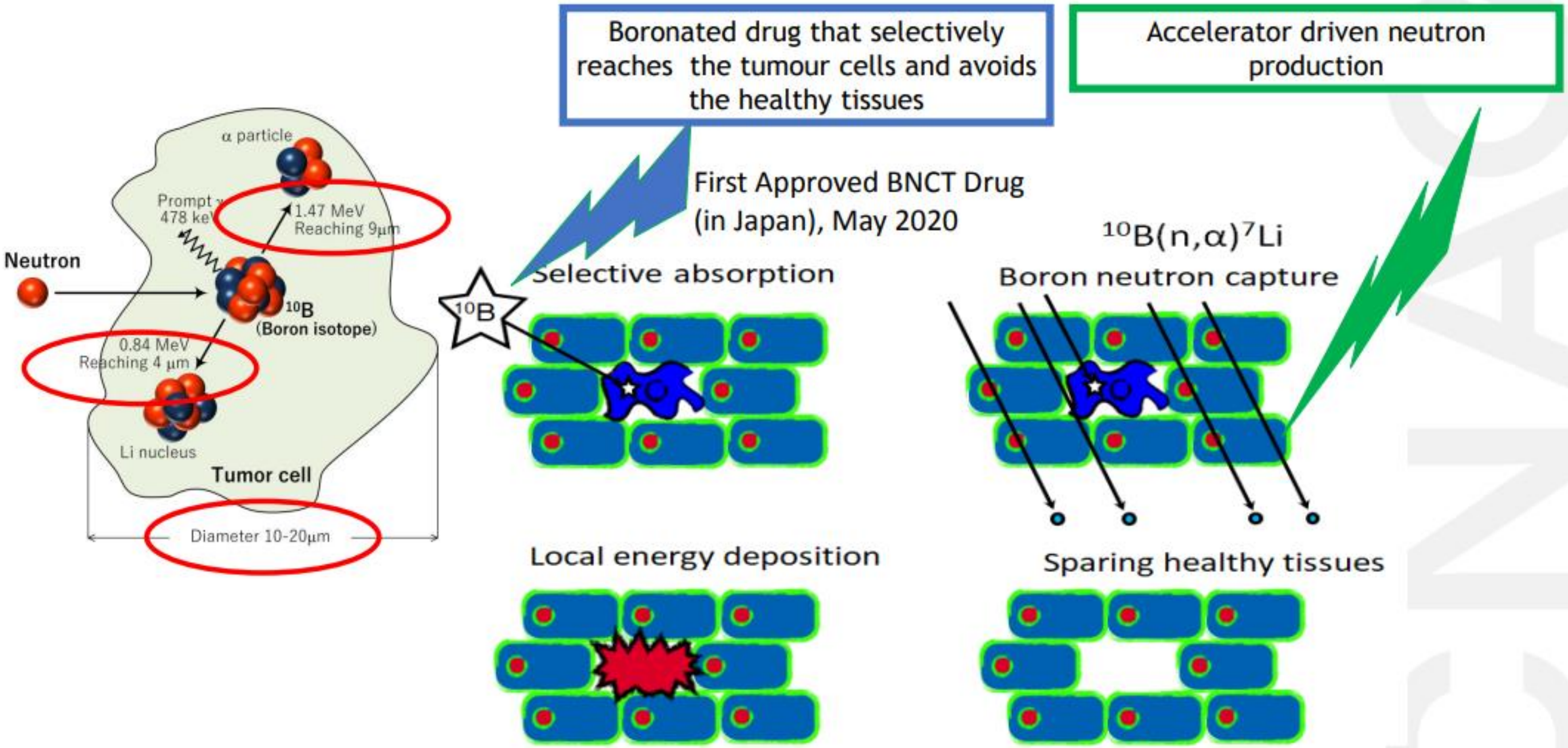
[a] *Department of Radiation Oncology, University Medical Center Groningen, University of Groningen, The Netherlands;* [b] *Ion Beam Applications SA, Louvain-la-Neuve, Belgium*



Future steps at CNAO… BNCT

(Sergey Taskaev, Frascati 2019)

Future steps at CNAO… BNCT



Thanks!
Grazie!

alessandro.vai@cnao.it